Genetics of human populations: evolutionary and epidemiological applications

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Contents

Introduction

1.1 Genetic variation

This thesis is focused on the genetic variation in human populations and in its applications to epidemiological and demographic questions. Although the general framework of this research is in Genetics, this introduction does not expect to be a general compendium but to simply provide a general insight to contextualize the genetic concepts and questions included in this work.

The identification of the *deoxyribonucleic acid* (*DNA*) molecule and its structure was one of the most important discoveries of the twentieth century and it is fitting to start this thesis paying homage to it. Also known as the molecule of heredity, it encodes the genetic instructions used in the development and functioning of all known living organisms. The pathway that led to its discovery started in 1866, when Gregor Mendel published his results on the inheritance of "factors" in pea plants. Some years later (1869) the Swiss chemist Friedrich Miescher discovered "nuclein" (now nucleic acid) from the nuclei of white blood cells. Then, in the following decades, several scientists such as Phoebus Levene, that identified the base, sugar and phosphate nucleotide unit or Rosalind Franklin, that produced the first single X-ray diffraction image of DNA, carried out a series of research efforts that revealed additional details about the DNA molecule. Without the scientific foundation provided by these pioneers, Watson and Crick may have never reached their conclusion in 1953 that the DNA molecule exists in the form of a three-dimensional double helix [1].

Currently, it is well known that the human genome has approximately 3 billion base pairs of nucleotides, organized into linear chromosomes within the nucleus of the cell and in mitochondria. Chromosomes in humans can be divided into two types: autosomes and sex chromosomes. Human cells have 23 pairs of chromosomes, 22 pairs of autosomes and one pair of sex chromosomes, giving a total of 46 per cell including both protein-coding DNA genes and non-coding DNA. In addition human cells have many hundreds of copies of mitochondrial DNA (mtDNA) inherited from the mother.

The sequence of nuclear DNA between any two humans is nearly 99.9% identical (http://www.genome.gov/). Around 0.01% of DNA differences is the cause of the whole genetically determined variability among humans and, consequently, of diseases. These

differences are represented approximately by 300,000 bases located mostly in non-coding regions of the genome. Indeed, most of the protein-coding genes present in the genome are highly conserved [2]. The whole genetic information that an organism inherits constitute its genotype while the observed properties, such as morphology, development, or behavior, constitute its phenotype. Phenotypic variations are mainly due to interactions between genotype and environmental factors. The proportion of phenotypic variance attributable to the genetic variance constitutes the heritability, while the environment and gene-environment interactions explain the rest of the variance. In general, the heritability of most human physical traits is in the range of 30% to 60% and the remaining proportion is attributed to the environment.

Genetic variants usually have specific allele frequencies within populations, and present patterns of variations that many times are geograpgically structured in a similar manner to some physical features such as eye color, height, skin pigmentation, or the distribution of some diseases. Population genetic differences can provide insights into the change of the genetic structure over time, demonstrating whether particular genetic sequences have been preserved in the genome or not. The origin and evolution of this variability is the central key to improve our knowledge of human population genetics and epidemiology.

1.1.1. Origins of genetic diversity

The complex patterns of genetic diversity in modern populations are the product of many demographic and evolutionary events acting at different timescales. *Mutation* and *genetic recombination*, generating new alleles and new combination of pre-existing alleles at different loci respectively, are the main sources of genetic variability in humans. A briefly description of both processes is presented below.

- **Mutation**

A mutation is a random change in the nucleotide sequence of the individual genome. It may depend on external influences such as electromagnetic radiation or chemical mutagens, which affect the mechanism of DNA replication and repair. Random events,

such as errors in the replication process, the substitution of a single base, or an insertion/deletion by mobile genetic elements, are thought to be the main sources of punctual mutations in our genome. Mutations can be somatic or can affect the germ cells. Somatic mutations affect any cell in the body ("soma"), are limited to the descendants of the original cell that developed the mutation and play a key role in transforming normal cells into cancerous cells. In contrast, germline mutations act on the lineage of germ cells. Mutations in these cells are transmitted to offspring and consequently contribute to evolutionary changes in future generations.

- **Genetic recombination**

Recombination is a crucial mechanism which occurs mainly during meiosis. In this process, exchange of genetic material between two homologous chromatids generates novel allele combinations in the offspring. In the crossing-over, which occurs during prophase I of meiosis, the swapping of genetic material of the germ line in points known as chiasmata, allows recombination of genes between homologous chromatids altering the linkage between loci on the same chromosome. Currently it is well known that recombination does not occur uniformly across the genome and that females have higher recombination rates than males [3]. Comparisons of radiation-hybrid and cytogenetic maps have shown that there is substantial variation in recombination rates across different regions of the genome, with significant, although weak, relationship between promoter regions and a lack of recombination in centromeric regions [4]. In general, gene functions associated with cell surfaces and external functions tend to show higher recombination rates (immunity, cell adhesion, extracellular matrix, ion channels, signaling) whereas those with lower recombination rates are typically internal to cells (chaperones, ligase, isomerase, synthase) [5]. Genetic recombination allows organisms to evolve in response to changing environments through the combination of advantageous alleles at different loci.

1.1.2. Linkage disequilibrium and haplotype blocks

Recombination between alleles on the same chromosome is extremely rare when they are very close to each other. The combination of specific alleles in a cluster of tightly-linked loci generates a structure known as a haplotype. In general, these alleles are likely to be inherited together. However, sometimes recombination may act on the haplotypes generating new linkage groups and increasing the total amount of haplotypes in the genome. The extent to which loci are linked can be calculated measuring the *linkage disequilibrium* (*LD*). It is a measure of the non-random association of alleles at two or more loci. The rate of LD decay is dependent mainly on the number of generations for which the population has existed. As such, different human populations have different degrees and patterns of LD. So, it is well-known that populations of African-descent are the most ancestral and have smaller regions of LD due to the accumulation of more recombination events [6]. Many different measures have been proposed for assessing the strength of LD, most of which capture the strength of association between pairs of biallelic sites. Two important pairwise measures of LD are r^2 and D'. Both are based on D, the coefficient of disequilibrium. The value of D is the difference between the frequency of gametes carrying the pair of alleles A and B at two loci (p_{AB}) and the product of the frequencies of those alleles (p_A and p_B) [7]:

$$D_{AB} = p_{AB} - p_A p_B$$

D can be negative or positive, whereas both D' and r2 range between zero (no linkage) and one ("complete" linkage), but their interpretation is slightly different. D' is equal to 1 if just two or three of the possible haplotypes are present, and it is <1 if all four possible haplotypes are present, making intermediate values of D' difficult to interpret. On the other hand, r^2 measures the statistical correlation between two sites, and takes the value of 1 if only two haplotypes are present [8]. It is a correlation coefficient between the two alleles and it will only be large if both are similar in frequency. Summarizing, a value of one for D' is related to the absence of at least one of the expected haplotypes which would be possible given the alleles at the two loci, and it is highly dependent on allele frequencies. By contrast, r^2 takes the value of one if the alleles at the two loci are perfectly correlated. Thus, it is possible to have $r^2 < 1$ given D' = 1, but not the other way around [9].

The non-overlapping sets of loci in strong LD with each other are called 'haplotype blocks'. A *haplotype block* is a sequence of DNA that has persisted in a population through successive generations. Usually, boundaries of these blocks are associated to recombination hotspots [7]. Haplotype blocks in humans vary in size from a few kb to more than 100 kb [8]. In addition, they vary somewhat among human populations, tending to be shorter in Africans with respect to the rest of populations [84 5].

Currently, there are several different programs to plot and quantify differences in haplotypes blocks between populations. Three of them were used in this thesis, two for graphical comparison of haplotype blocks between populations through D', Haploview [10] and HAPLOT [11], and one to assess and quantify LD variations among populations, varLD [12]. Haploview calculates several pairwise measures of LD, which are then used to create graphical representations (Figure 1A). The user has the option to choose among several commonly used definitions of haplotype block [13 14] to partition the region into segments of strong LD or, he/she may manually select groups of markers for subsequent haplotype analysis.

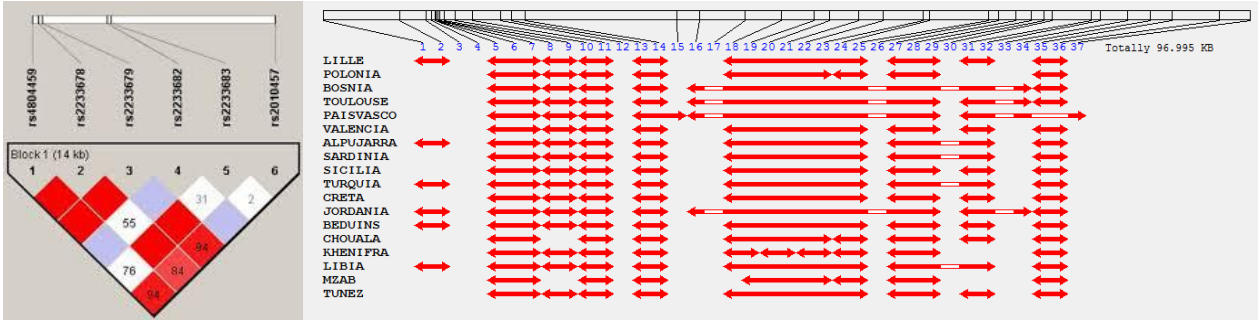


Figure 1. Haplotype block structure representation using Haploview (A) and HAPLOT (B). The upper bar of both plots shows a representation of SNPs in a regional context (i.e. physical distance) and the lower panel displays LD measurements on a color and numeric scale (HaploView) and haplotype block structure in different populations (HAPLOT).

In HAPLOT different block partition algorithms can be selected to generate block structures. Block definitions based on D′ confidence interval [15], four-gamete test [16], and solid spine of LD [10] are embedded in Haploview and are called by HAPLOT directly for block pattern plotting (Figure 1B).

VarLD quantifies LD variation patterns between pairs of populations adopting a two-step approach. First, sliding windows of a predetermined number of SNPs common in both populations are considered and r^2 between every pair of SNPs in each window are calculated. Second, the extent of inter population LD differences between the SNPs in each window is quantified by the varLD score, which sums the absolute differences between the ranked eigenvalues of the matrices [17].

1.1.3. Evolutionary processes and genetic variation

As genetic variations are inherited, they are passed down through generations, generating a complex history that can be traced backwards in time. The main evolutionary forces that shape genetic variations are three: *genetic drift*, *natural selection*, and *migration*.

- **Genetic drift**

Genetic drift is a process in which allele frequencies within a population change as a result of random sampling from generation to generation. Known also as random drift, its magnitude depends mainly on the population effective size. Severe reductions in population size, known as bottlenecks or founder events, may lead to large frequency changes in populations over a short period of time. A population *bottleneck* is a sharp reduction in the size of population due to environmental events like earthquakes or floods, or human activities such as genocide, wars, etc. Instead, the *founder effect* occurs when a small group in a population splinters off from the original population and forms a new one. Genetic drift leads to a reduction of the intra-population genetic variation and an increase of the inter-population variation. Due to the smaller population size, inbreeding and genetic homogeneity increase and unfavorable alleles can be accumulated making the new population more vulnerable to extinction or diseases. Genetic drift is measurably effective only in small populations, and likely it played a major role in the early stages of human evolution. However, even nowadays, there are small and culturally isolated communities like the Amish or the Dunkers in large societies such as the United States. The first immigrated to Pennsylvania from Switzerland in the early 18th century, whereas the

Dunkers fled from Germany in 1719-1729 to avoid religious intolerance, crossed the Atlantic, and settled in the farmlands of eastern Pennsylvania. Both are mostly closed breeding groups. In such sub-populations, genetic drift is still an important evolutionary mechanism.

- **Natural Selection**

Natural selection is the process whereby some of the inherited genetic variation will result in differences between individuals in their capacity to survive and produce healthy offspring. There are mainly three types of selection that shape genetic variation and strongly affect the distribution of allele frequencies in the populations. Sometimes mutations that occur in a functionally important sequence decrease the fitness of the individuals that carry them. These harmful mutations are selected against and removed from the populations by means of the *purifying selection*, also known as *negative selection*. This type of selection may result in a particular effect called *stabilizing selection* due to the fact that the population stabilizes on a particular trait value decreasing the genetic diversity. Other times a new mutation may confer a selective advantage and increase the fitness of individuals that carry it. This is the case of the *positive selection*, also called *advantageous selection*, in which a novel selective genetic variant rises in frequency and spreads through the population until it reaches fixation. The propagation of advantageous mutations through this process may generate a phenotypic change that is described as *adaptive evolution*. The diversity around the positively selected allele will decrease substantially and sometimes positive selection is accompanied by genetic hitchhiking. *Genetic hitchhiking* occurs when a neutral or even a slightly deleterious allele increases in frequency, because it is linked to the beneficial mutation selected. The third mechanism of selection is the *balancing selection*. This selective regime, known as *heterozygote advantage*, increases genetic variation due to the fact that heterozygous individuals present a higher fitness compared to homozygotes. Mutations that do no confer any advantage or harm to their carriers are described as *neutral mutation*.

Natural selection can vary in the space, and also over the time. Geographic distribution of human skin color, for example, shows a clear geographic pattern: populations inhabiting

areas close to the equator in general have dark skin, whereas populations in higher latitudes have lighter skin. This gradual change in skin pigmentation has been related to photo protection and vitamin D synthesis. UV radiations are necessary for the skin to synthesize vitamin D. In regions with lower incidence of sunlight, lighter skins allow a deeper penetration of UV and vitamin D synthesis. Particular selective regimes can also change at different time intervals, such as in the case of genes which predispose to obesity, called *thrifty genes*. These genes enable individuals to efficiently collect and process food to deposit fats, in order to have a provision for periods of dearth. They were probably positively selected during periods of food shortage, in accordance to the thrifty gene theory [18], but in the modern world, with recent dietary changes, they became detrimental increasing the risk for diabetes [19].

Literature is filled of statistic tests used to detect selection each of which has its own strengths and weaknesses, but currently no universal statistic exists that will reliably identify selection signals. The potential confounding effects of demography play an important role in this issue because demographic effects could create variation patterns in DNA sequences similar to the ones of selection. A new approach to detect selection came with the advent of whole-genome sequencing and the availability of a dense map of markers in which signatures of selection were analyzed in the context of genome-wide empirical distribution. These new approaches try to avoid the influence of population demographics, which affect the genome as a whole. Indeed, it's worth noting that demographic phenomena, such as population expansions, subdivision and bottleneck events, affect variation at all genes, while natural selection is expected to have a locus-specific effect. Currently there are several genes and genomic regions identified as potential candidates for natural selection [20], but the most validated and studied are presumed to confer resistance to malaria [21] (β-globin, G6PD, or Duffy blood group) and lactase persistence [22].

- **Migration**

In a genetic context, migration implies the movement of people from one population to another and their incorporation to the reproductive population. Although mutation is the

main source for new alleles, a new mutant allele can be introduced within a population through this process. Migration has several important effects on evolution. It can increase the intra-population diversity introducing new alleles in a population and, by moving genes around; it can make different populations genetically similar reducing the inter-population diversity. In the current world, the existence of single and isolated population is very rare and humans live in thousands of populations around the word, all interconnected by varying levels of gene flow. Despite this, sometimes the level of population interconnections may be influenced by social structures and culture. Studies carried out with mtDNA and Y-chromosome for example; point out a clear relationship between patrilocal/matrilocal cultures and different genetic patterns of mtDNA and Y-chromosome variation within and between groups. In patrilocal cultures, in which men stay in their birthplace and women move, the patterns show high mtDNA and low Y-chromosome diversity within groups, and large Y-chromosome and small mtDNA differences between groups [23] [24]. On the contrary, matrilocality, in which women stay in their birthplace and men move, may explain the opposite patterns: high Y-chromosome and low mtDNA diversity within groups, and large mtDNA versus small Y-chromosome differences between groups [25].

1.1.4. Types of genetic variants

Human genetic variants can be usefully classified as large-scale or small-scale on the basis of whether or not they can be detected by sequencing few hundred base pairs or not. They are typically classified in terms of their nucleotide composition. In this way, variants in the genome can range from the single nucleotide changes, and small insertion and deletions of few bases, through expansions or contractions in the number of tandemly repeated DNA motifs, insertions of transposable elements, insertions, deletions, duplications and inversions of megabases segments of DNA, to translocations of chromosomal segments and even changes in chromosomal number (Figure 2).

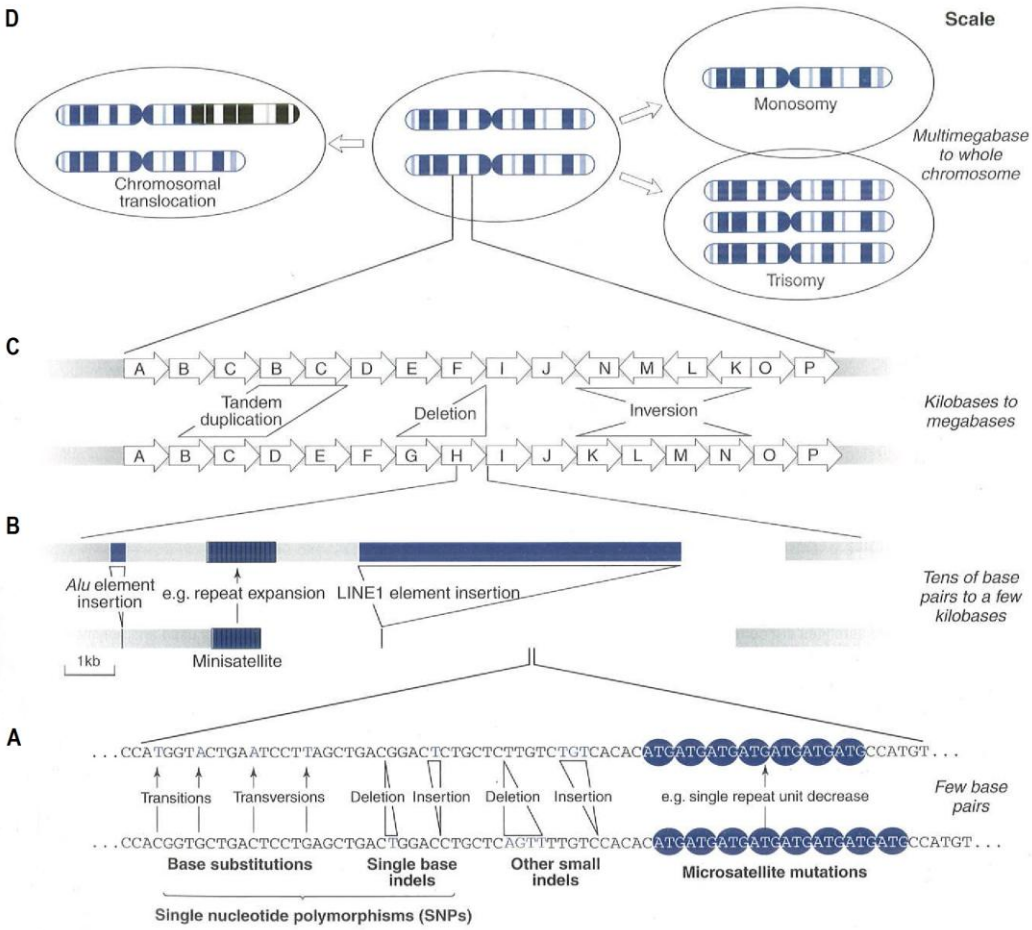


Figure 2. Overview of different classes and scales of genetic variants. A. Examples of mutations affecting a few base pairs, including examples of transition and transversion substitutions, and a change in the number of ATG repeats at a trinucleotide microsatellite. **B.** Examples of mutations affecting tens of base-pairs to a few kb, including insertions of a ~300-bp Alu element and a full length 6.1-kb LINE1element, and the expansion by several repeat units of a microsatellite. **C.** Examples of segmental mutations on the kilobase to a megabase scale. Arrows indicate the order and orientation of adjacent segments of DNA. **D.** Mutations on the multimegabase or whole chromosome scale. (Figure reproduced from M.A. Jobling et al., 2004; "Human Evolutionary Genetics origin, people & disease")

In addition, the different classes of genetic variants show different mutation rate range, as show in Figure 3.

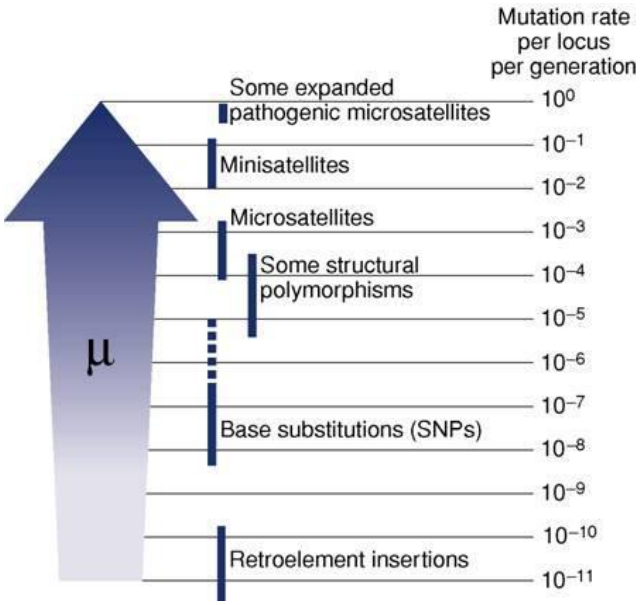


Figure 3. Overview of mutation rate (*u*) of different classes of polymorphic markers. Figure reproduced from M.A. Jobling et al., 2004; "Human Evolutionary Genetics origin, people & disease")

The following is a brief description of the two genetic variants used in the present work: single nucleotide polymorphism and Alu insertions polymorphisms.

- **Single nucleotide polymorphisms**

Single nucleotide polymorphisms (*SNPs*) are the most prevalent class of genetic variation among individuals and consist in a substitution at a single base pair. They are commonly biallelic and may be located in different genomic regions: within coding sequences, in a non-coding region, or in intergenic regions. SNPs in the coding regions are classified into synonymous and non-synonymous. Synonymous SNPs do not affect the protein sequence, while non-synonymous SNPs change the amino acid sequence of protein. In addition, non-synonymous SNPs may be missense and nonsense. Missense SNPs cause a change in amino acid of protein causing potential differential function which may lead to disease while nonsense originate a premature stop codon, or a nonsense codon in the transcribed mRNA, and consequently produces a nonfunctional protein product. Common SNPs, located in different point of the genome constitute the raw material of most part of this work. Actually, the dbSNP database of NCBI (Build 142), one of the most comprehensive SNP databases, estimates a total amount of 112,736,879 SNPs in humans. Ninety percent

of variation in the population is due to SNP sites [6]. Currently they are the most widely used markers in population and epidemiological studies mainly for their low mutation rate (approximately in the order of 10^{-7}-10^{-8} per generation), and because they are easy to genotype on large scale. Indeed, thanks to the introduction of DNA microarrays their genotyping has exponentially increased. Several SNP databases have been created in the last decades to retrieve known SNPs by position or by association with a gene such as SNPper (http://snpper.chip.org/bio/snpper-enter/) or Genome Variation Server (http://gvs.gs.washington.edu/GVS141/), or to find proxy SNPs based on LD, physical distance and/or membership in selected commercial genotyping arrays like SNAP (http://www.broadinstitute.org/mpg/snap/), which also generate regional LD or association plots. Despite this, typing large numbers of SNPs can be extremely expensive. As a consequence, selecting SNPs that have the highest information content possible may be very useful. These kinds of markers are named *tag SNPs* and are specifically selected to capture the identical variation at nearby sites in the genome (Figure 4). Alleles for these SNPs are in high LD and consequently they may predict with a small error the genetic information in other linked SNPs.

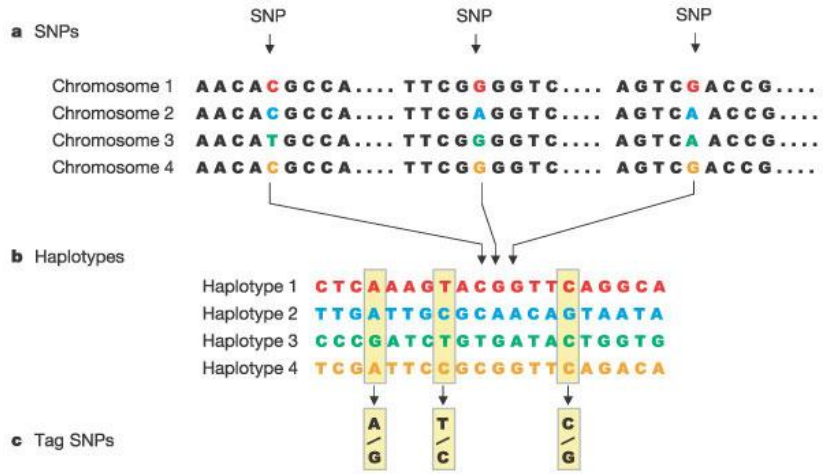


Figure 4. SNPs, haplotypes, and tag-SNPs. (a) A short segment of four individual copies of the same chromosome shows three biallelic SNPs. **(b)** Haplotypes from a larger region on these four chromosomes containing 20 SNPs, showing which allele of each SNPs the chromosome carries. **(c)** Genotyping just three of the 20 SNPs serves to identify each of these four haplotypes. Figure reproduced from the International HapMap Consortium (2003) *Nature* 426, 789-796.

As previously noted patterns of LD are population specific and, as a result, *tag SNPs* selected for one population may not work well for a different one. The fact that most SNPs included in the genotyping platforms currently available were selected on the basis of their occurrence and frequencies in European populations produces a clear ascertainment bias in the marker selection process [26]. Recently, increasing number of population and epidemiological studies in African and Asian population has been performed to try to solve this bias.

- **Alu insertion polymorphisms**

Alu insertions polymorphisms were used in this work for their usefulness as ancestry-informative markers. In general repetitive elements can be subdivided into those that are tandemly arrayed (for example, micro-satellites, mini-satellites, or alpha-satellite) or interspersed. Interspersed elements can be subdivided on the basis of their size in short interspersed nuclear elements (SINEs) under 500 bp in length, or long interspersed nuclear elements (LINEs). In this way, Alu insertions belong to the SINEs group of repetitive elements. The name was originally given to the repeated sequences located in a recognition site for the restriction enzyme AluI. Full-length Alu elements are approximately 300 bp long. They are commonly found in introns, 3' untranslated regions of genes and intergenic regions [27]. The Alu family has not coding capacity but it is one of the most successful mobile genetic elements: there are >1 million Alu copies in the human genome [28], comprising more than 10% of its total mass [29], as a result of their continued mobilization activity over the past ~65 million years [27]. Due to their recent evolutionary introduction into the human genome many of the Alu elements are polymorphic (presence or absence of insertion) between individuals and populations. In population studies they are a useful tool for several reasons: i) there is no specific mechanisms to remove newly inserted Alu repeats inserts; ii) Alu insertions have a known ancestral state, absence of insertion [30]; iii) they are identical by descent, that is, they are homoplasy-free, being the products of unique evolutionary events [31]; and iv) they are highly conservative with a very low mutation rate. Currently and in past years Alu insertion markers have been used as ancestry-informative tools to detect differences between populations and to estimate bio-geographical ancestry [32].

1.2. Population genetic studies based on neutral markers

Population genetic studies mainly regard the distribution and changes of allele frequency in a given population or in different populations. Originally these studies had the aim to reconstruct our evolutionary history and, in the last past years, clarified many demographic issues trying to reconstruct the genetic history of world wide populations. All human populations are actually interconnected by a constant flux of migration, which leads to a lower genetic diversity between populations. Nevertheless, genetic differences between populations still persist and are currently informative not only to understand past migrations but also to interpret epidemiological differences.

In the last years many researchers have collaborated to improve the knowledge in these fields. Projects such as the *Human Genome Project* (HGP) or recently the *1000 Genomes Project* were born with this aim. The first one was launched in 1990 and thanks to the rapid technological advances, was completed in 2003, two years before the originally time plan. The principal goals were : i) identify all the genes contained in human DNA, ii) determine the sequences of the 3 billion chemical bp that make up human genome and, finally iii) develop new tools to obtain and analyse the data and store this information in databases. This project started a new era of the genetic research: the systematic study of human genetic variation. Some years later, in September 1993, the *Human Genome Diversity Project* (HGDP) was launched and from this point many progresses have been made to understand the patterns and causes of human variation. The HGDP collection (1050 individuals from 52 world populations) is an important resource for both human population genetics and evolutionary studies, as well as for biomedical studies. Indeed, these data can be used to estimate the incidence of a particular risk allele or as control samples for association studies.

In 2002 another project officially started its activity: *The International HapMap Project*. With the aim of avoiding the expensive sequencing procedure, this project used a new characteristic approach based on the linkage mapping to create the first haplotype map of the Human Genome. While the HGP studied all the human genome, this Project studied only the 0.1% of human DNA genetic variants not shared between individuals, specifically SNPs. As previously said, sets of nearby SNPs on the same chromosome are inherited in blocks, constituting a haplotype block. Blocks may contain a large number of SNPs, but

only one SNP in high LD with them is enough to uniquely identify the whole haplotype of a determined block. These SNPs, known as tag SNPs, were used to create the first haplotype map of the genome. This Project was formed by researchers at academic centres, non-profit biomedical research groups and private companies in Japan, the United Kingdom, Canada, China, Nigeria and the United States. HapMap is a powerful resource not only to study genetic differences between populations, but also for association studies and to identify genetic factors related to infection, environmental factors, drugs and/or vaccines. The three different phases of the Project have a different number of samples and markers. In the *Phase I* (2005) [33] a total of 1M SNPs in 270 samples (4 populations) were analysed. In the *Phase II* (2007) [5] there was an increasing in the numbers of markers (3.1M SNPs) but the samples remained the same. Finally, in the *Phase 3* (2010) [34] 1.6M SNPs were genotyped in 1184 samples. These samples include 11 global ancestry groups: CEU (Utah residents with Northern and Western European ancestry from the CEPH collection), CHB (Han Chines in Beijing, China), JPT (Japanese from Tokyo, Japan), YRI (Yoruba in Ibadan, Nigeria), ASW (African ancestry in Southwest USA), CHD (Han Chinese in Metropolitan Denver, Colorado), GIH (Gujarati Indians in Houston, Texas), LWK (Luhya in Webuye, Kenya), MEX (Mexican ancestry in Los Angeles, California), MKK (Maasai in Kinyawa, Kenya), and TSI (Tuscans in Italy).

There are some uncertainties about the usefulness of the HapMap data mainly because populations vary in local LD and haplotype structure [35] [36], but the samples from which scientists selected tag SNPs come exclusively from people of European origin. To try to solve these problems, in 2008, another project was launched: the *1000 Genomes Project (1000 GP)*. It extended the data from the International HapMap Project, providing a resource of almost all variants, including SNPs and structural variants, and their haplotype contexts. Using next generation sequencing technologies, the 1000 GP aimed at characterizing over 95% of variants with a MAF≥1% in the whole genome (using a low coverage (4X-6X) approach) and with a MAF≥0.1% in the exome (using a high coverage (>50X) approach), in populations from Europe, East Asia, South Asia, West Africa and America. The *Pilot Project* identified approximately 14 million SNPs in 179 individuals (4 populations) [37]. Then, in 2012, the *Phase 1* of the Project continued with the identification of 38million SNPs, 1.4 million indels and 14,000 larger deletions in 1094 individuals (14 populations) [38]. Finally, in 2014, data from the *Phase 3* was released in a total of 26

populations (2504 individuals). The populations included in the 1000GP included several populations from the HapMap Project together with a collection of samples collected specifically for the project (Figure 5).

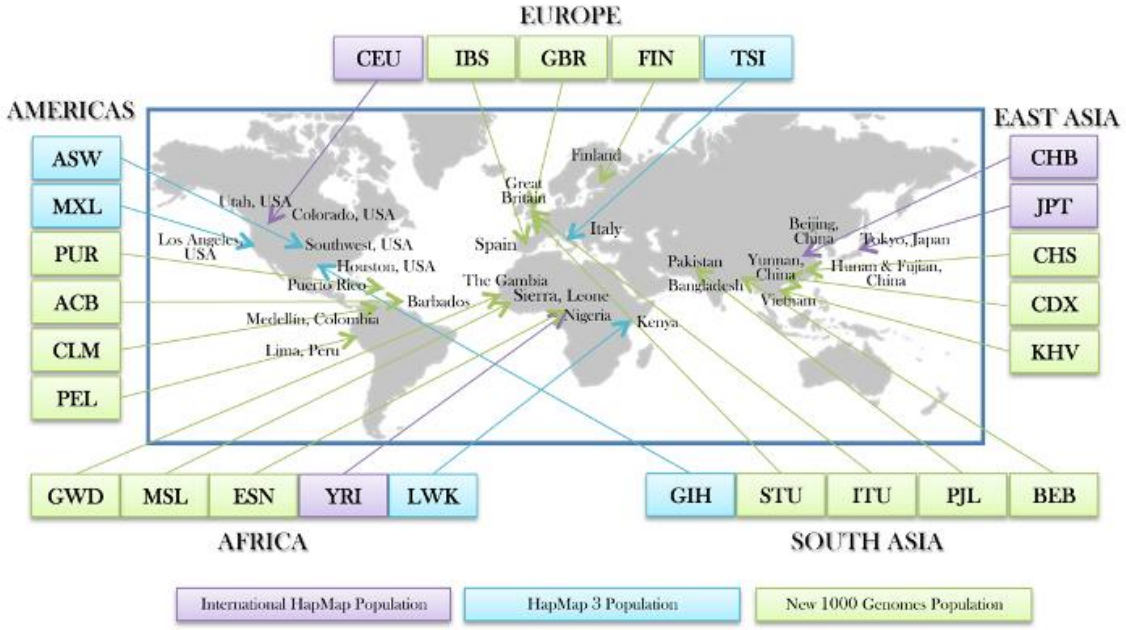


Figure 5. Populations included in the 1000 Genomes Project.

Figure reproduced from http://www.1000genomes.org/cell-lines-and-dna-coriell.

The whole dataset is publicly available from: http://browser.1000genomes.org/index.html. These data may be useful as datasets for population genetics, imputation panels, epidemiologic studies, and also to design new genotyping arrays based on new variants. Regarding the imputation procedures, for common variants, the accuracy of using the 1000 GP Phase I data to impute genotypes at sites is typically 90–95% in non-African and approximately 90% in African-ancestry genomes. For low frequency variants (1–5%), imputed genotypes have between 60% and 90% accuracy in all populations, including those with admixed ancestry [38].

Thanks to the modern technologies used in the DNA analysis, in the past 30 years, our knowledge of the history and relationships among human populations has dramatically increased. At first, preferential attention was devoted to uniparental genetic markers. Because of their lack of recombination, uniparental markers (mtDNA and the non-

recombining region of the Y chromosome) allow a detailed phylogenetic analysis and in addition, they are easier and cheaper to genotype than recombining markers. But, studying only the variation present in a single locus, they give a complete picture of the history of those loci, but cannot be as informative about population histories as many independent loci, such as autosomal markers. In the last years, analysis of autosomal markers revealed a geographical/genetic structure of human populations and an African origin of modern humans. Individual ancestry and population substructure can be actually detectable with very high resolution. In this context, a recent work published in Science [39] in 2008, performed with 51 populations from the HGDP using 650,000 common SNPs, revealed that individuals belonging to the same recognized population almost always show similar ancestry proportions. In addition, not only major splits between different continents but, also sub-lineages within continents were detected. The relationship between haplotype heterozygosity and geography supported the "out of Africa" model of human origin. This hypothesis was also supported by a letter published in the same year in Nature [40] showing an increase in the LD patterns with the geographic distance from Africa (Figure 6).

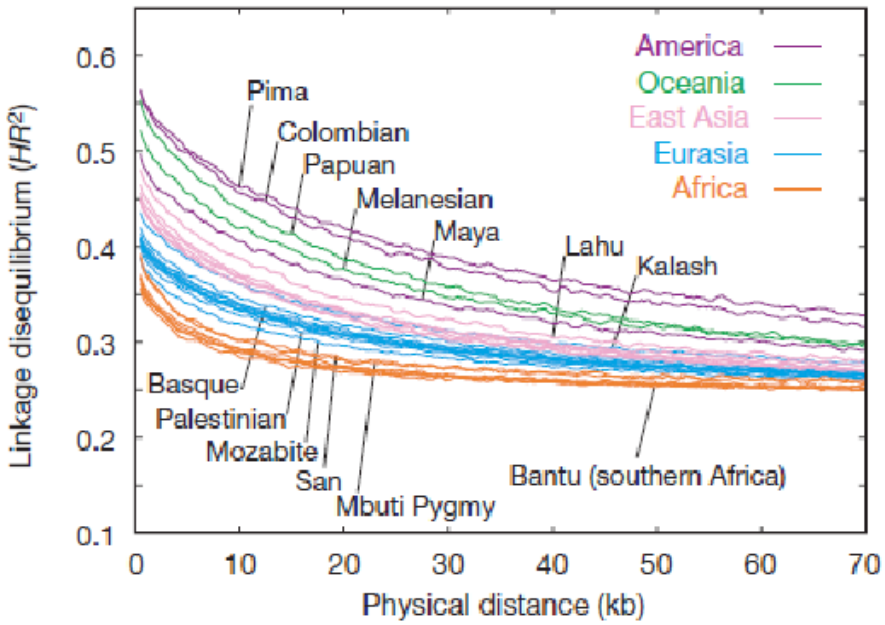


Figure 6. LD as a function of physical distance. Figure reproduced from Jakobsson et al., 2008.

The 1000 Genomes Project Phase 1 results showed that individuals from different populations carried different profiles of rare and common variants, and that low-frequency variants showed substantial geographic differentiation. Specifically, variants present at 10% and above across the entire sample were almost found in all the populations studied. By contrast, 17% of low-frequency variants in the range 0.5–5% were observed in a single ancestry group, and 53% of rare variants at 0.5% were observed in a single population. Regarding the derived allele frequency, its distribution showed substantial divergence between populations below a frequency of 40%, such that individuals from populations with substantial African ancestry (YRI, LWK and ASW) carried up to three times as many low frequency variants as those of European or East Asian origin, reflecting ancestral bottlenecks in non-African populations [38].

Regarding Europe, despite the low average levels of genetic differentiation among populations, a close correspondence between genetic and geographic distances was found in many studies [41] [42]. Furthermore, the larger mean heterozygosity and smaller mean LD in southern than in northern Europe are in agreement with the expectations based on population history of Europe: the prehistoric population expansion from southern to northern Europe and/or a larger effective population size in the south as compared to the north of Europe. These two parameters exhibit a continuous cline distribution across Europe [41] (Figure 7).

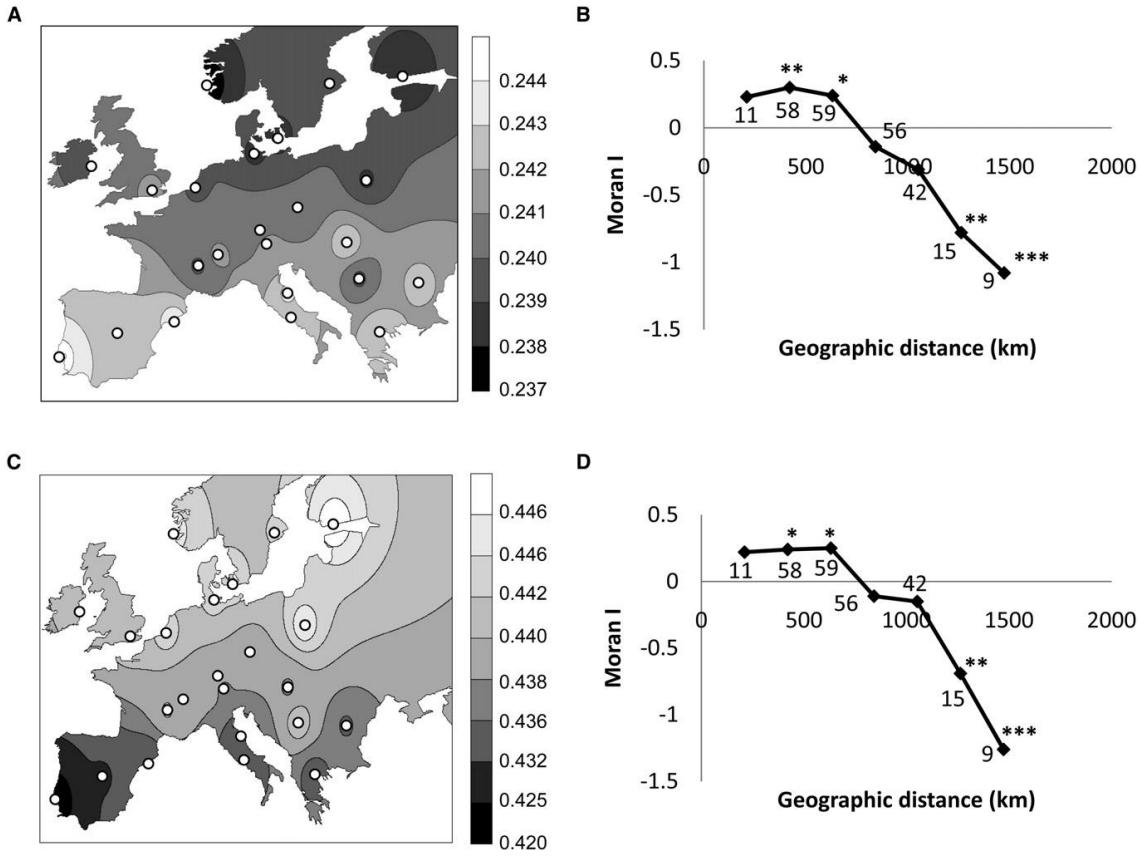


Figure 7. Geographic Distribution of Two Measures of Genetic Diversity across the European Population
(**A** and **B**) Isoline map (A) of Europe based on the mean observed heterozygosity with (**B**) corresponding spatial autocorrelogram. (**C** and **D**) Isoline map (**C**) of Europe based on the mean observed linkage disequilibrium with (**D**) corresponding spatial autocorrelogram. Figure reproduced from Lao et al., 2008.

Since the Mediterranean area is in the crossroads between three continents, several studies have been carried out on the genetic diversity currently present in North Africans, South Europeans and Middle Eastern populations. A recent work [43], based on the Population Reference Sample (POPRES) [44], detected a north–south gradient in diversity in Europe with the highest estimates of diversity in the southern part of the continent. This is consistent with the initial founding of Europe from the Middle East, the influence of Neolithic farmers within the last 10,000 years, or migrations south followed by a recolonization of Europe after the last glacial maximum. In addition they found that the South and South-Western subpopulations showed the highest proportion of haplotypes shared with Sub-Saharan Africans. This result suggests that while the initial migrations into Europe came via the Middle East, at least some degree of subsequent gene flow occurred directly from Africa.

Indeed, the higher level of genetic diversity in southern European populations compared with those in northern latitudes seems to be mostly due to gene flow from North Africa. Recent gene flow among populations, results in haplotypes shared identical by descent (IBD). Migration from one population to another generates genetic segments that share a recent common ancestor and consequently are IBD. A recent paper [45], performed with genome-wide SNP data, used these segments to estimate the gradient of haplotype sharing between Sub-Saharan Africa, North Africa, Europe and Near East. They detected a gradient of shared IBD segments from southern to northern Europe. This sharing was highest in the Iberian Peninsula for both North Africa and Sub-Saharan African IBD segments (Figure 8).

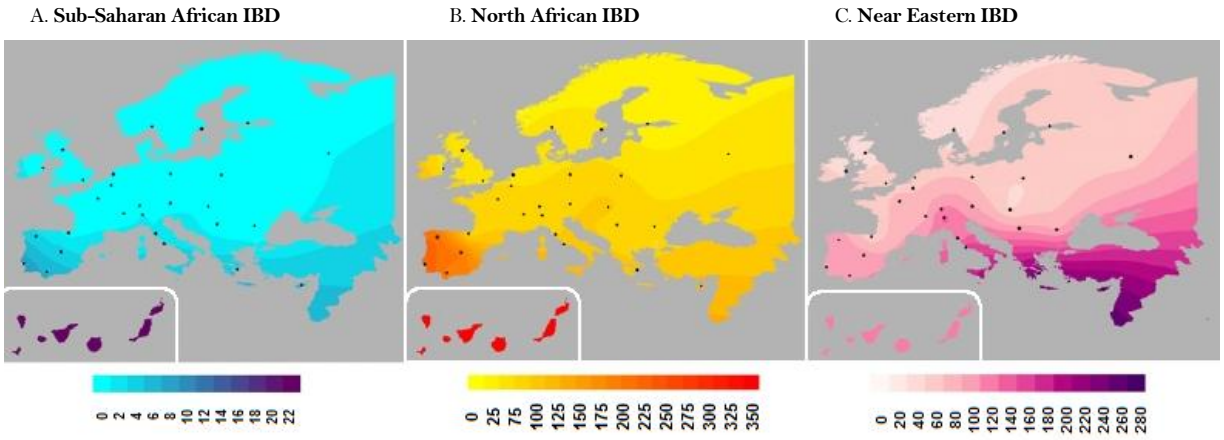


Figure 8. Genetic sharing between geographic regions represented as a density map for 30 European populations where haplotypes are IBD with (A) Sub-Saharan Africa, (B) North Africa and (C) the Near East. The Canary Islands are shown in the Lower Left. Figure reproduced from Botigué et al., 2013.

Interestingly, like previously documented [46], the Basques are an exception into this pattern because they show levels of sharing similar to other European populations. These results also showed that South Western Europe has more IBD segments shared with North Africa than Middle East, whereas eastern Mediterranean populations share more segments IBD with the Near East than with western North Africa. Northern European populations, on the contrary, show only limited IBD sharing with both North Africa and the Near East. These results support the hypothesis that recent migrations from North Africa contributed substantially to the higher genetic diversity in the current southwestern European population.

At present the overall genetic background of North African populations is an issue not fully resolved yet. A recent study [47] performed with 730.000 genome-wide SNPs, tried to characterize the patterns of genetic variation in North Africa, using a total of 152 samples of seven different populations. They observed that North Africans are not a homogenous group and most individuals display varying proportions of five distinct ancestries: Maghrebi, European, Near Eastern, and eastern/western sub-Saharan African. They identified two distinct and opposite gradients of ancestry: an east-to-west increase in likely autochthonous Maghrebi ancestry, probably derived from "back-to-Africa" gene flow more than 12,000 years ago and an east-to-west decrease in Near Eastern Arabic ancestry. The signatures of sub-Saharan African ancestry varied substantially among populations and appeared to be a recent introduction into North African populations, dating to about 1,200 years ago in southern Morocco and about 750 years ago in Egypt, possibly reflecting the patterns of the trans-Saharan slave trade that occurred during this period. In summary, they proposed that present-day North African ancestry is the result of at least three distinct episodes: i) an ancient "back-to-Africa" gene flow prior to the Holocene, ii) a more recent gene flow from the Near East resulting in a longitudinal gradient, and iii) limited but very recent migrations from sub-Saharan Africa.

Genetic and archeological studies present solid evidence placing the Middle East and the Arabian Peninsula as the first stepping-stone of modern humans outside of Africa. There is, however, little understanding of how the current Levantine peoples relate genetically to each other and to their neighbors. A recent article [48], performed with 244.919 independent SNPs, showed that recent genetic stratifications in the Levant is likely related to the population religious affiliations. Cultural changes within the last two millennia facilitated admixture between culturally similar populations from the Levant, the Arabian Peninsula, and Africa. However, the same cultural changes resulted in genetic isolation of other population groups, geographically closer but culturally very different. Consequently, Levant populations today fall into two main groups: one sharing more genetic characteristics with modern-day Europeans and Central Asians, and the other with closer genetic affinities to other Middle Easterners and Africans. Specifically, the Islamic expansion from the Arabian Peninsula beginning in the 7th century likely introduced lineages typical of this Peninsula into those who subsequently became Muslims, whereas the Crusader activity in the 11th–13th centuries introduced western European lineages

into the Levant's Christians [48]. Population structure in general and specifically in North Africa and Middle East, are particularly complex, and future disease studies should carefully take into account local demographic history. Indeed, when mapping the genetic basis of a disease phenotype, spurious associations can arise if genetic structure is not properly accounted for.

1.2.1. Population genetic studies with an epidemiological interest

Population genetic studies centered on disease traits are important for several reasons: i) to describe the population-wide distribution of disease-associated markers, ii) to explain population differences in specific disease prevalences , iii) to identify the possible role of natural selection in a specific disease trait, and vi) to identify the causal genetic factors associated to the disease.

Disease associated mutations are not randomly distributed across the genome. In general, SNPs associated with complex traits tend to cluster in regions of low recombination [49], and their frequency show a heterogeneous pattern across populations of different ancestry. A recent article stressed the non-homogeneous world-wide distribution of genetic risk variants analyzing 43 meta-analyses of gene-disease associations in 297.411 samples of various descents. The frequency of risk markers in controls often (58%) showed large heterogeneity between populations of different ancestry [50]. Despite this heterogeneity, there are some discrepancies about its causes. Some authors state that disease-associated SNPs do not show more population differentiation than random SNPs in the genome. They state that disease risk alleles follow an expected pattern of neutral drift among populations and are not strongly affected by natural selection [45 51 52]. In contrast, others authors recognize a putative role of natural selection as a likely explanation of the heterogeneous pattern of risk allele frequencies across populations. In support of this theory a recent article studied disease-associated gene clusters in regions of low recombination across the genome. This work identified several clusterings of disease-associated SNPs in regions that harbor genes involved in immunity, that is, the interleukin cluster on 5q31 or RhoA on 3p21, with high differences in allele frequency among populations and strong signatures of positive selection [49].

Many genes and variants implicated in disease traits such as blood pressure, infectious disease, immune response, autoimmune disease, cancer, diabetes, rheumatoid arthritis, or Crohn's disease show strong signals of selection in various studies [53] [54] [55] [56]. In general, it is well known that natural selection acts to remove harmful mutations so, the relatively high risk allele frequency, such as in the case of diabetes or heart diseases, is not easy to understand and generates controversial, and currently open questions. It is currently known that balancing selection, for example, may act in favor or against certain diseases. Mutations in the G6PD locus or in the α-globin gene in the homozygous state, for example, cause G6PD enzyme deficiency and sickle-cell anemia respectively, but confer partial protection against malaria in the heterozygous state. Another example concerns mutations in the CFTR locus, which causes cystic fibrosis in the homozygosity but protects against asthma in the heterozygous state [19]. Speculations to understand the high prevalence of risk variants in humans state that the genetic basis of common complex disease may have partially been shaped by positive selection events. A disease risk variant could be positively selected if it is in high LD with a relatively stronger still unknown beneficial polymorphism [55] related to the disease. At the moment the knowledge of complex genetic disease architecture needs of many other focused studies to absolutely detect or exclude natural selection.

1.3. Coronary Artery Disease

Cardiovascular disease (CVD) refers to any disease that involves the cardiovascular system, mainly coronary artery disease, cerebrovascular disease, high blood pressure, peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure. It is the leading cause of morbidity and mortality worldwide (Figure 9).

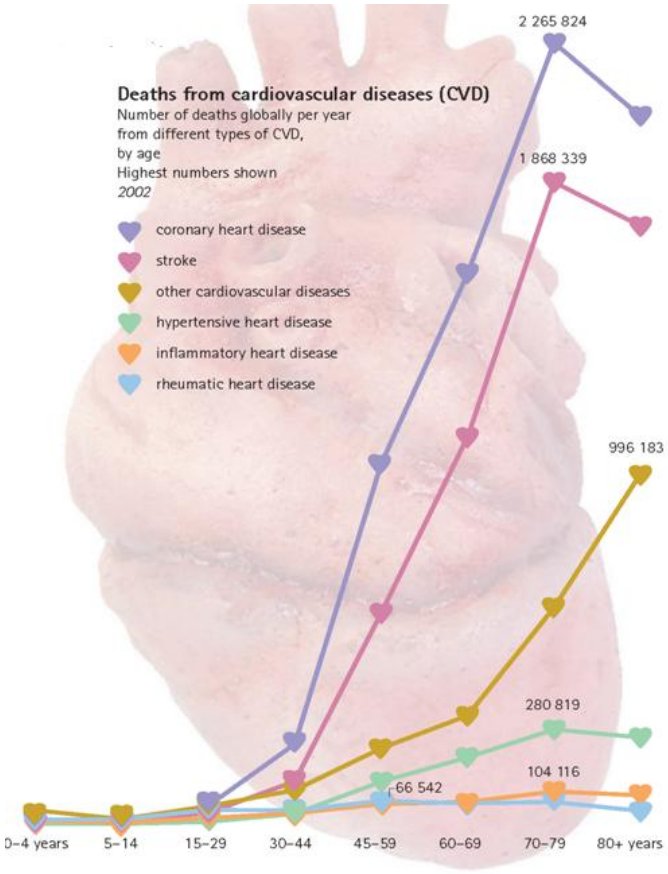


Figure 9. Number of deaths globally per year from different types of CVD by age. Figure reproduced from http://www.who.int/cardiovascular_diseases/en/.

Coronary Artery disease (CAD), also known as coronary heart disease or atherosclerotic heart disease, counts the higher number of deaths within the CVD group. Like any other complex multi-factorial disease, it is influenced by several environmental, lifestyle, and genetic factors which interact to determine the clinical phenotype. CAD typically occurs when part of the smooth and elastic lining inside a coronary artery develops a progressive and degenerative disease known as atherosclerosis. The key steps in this process are: i) the loss of the normal barrier function of the endothelium, ii) lipoprotein abnormalities that favor lipid entry, including high levels of low density lipoprotein cholesterol (LDL-C), and

iii) the recruitment of monocytes and lymphocytes to the artery wall (Figure 10). The atherosclerotic earliest lesions consist of sub-endothelial accumulations of cholesterol-engorged macrophages, called *foam cells*. These "fatty streak" lesions are not clinically significant, but they are the precursors of more advanced lesions, known as atherosclerotic plaques, or as atheromatous plaques. An atheroma is an accumulation of degenerative material in the tunica intima of the artery walls. Specifically, this material is formed by a "fibrous cap" consisting of smooth muscle cells, and an extracellular matrix that encloses lipid-rich necrotic debris. As plaque builds up, the arteries narrow, making more difficult for oxygen-rich blood to flow to the heart. Over time, advanced lesions can grow sufficiently large to block blood flow. The disease outcome changes depending on patient's clinical history: plaques can remain silent; can progressively narrow the lumen, restrict the flow and, consequently produce angina; or can precipitately occlude vessels through acute thrombosis, which leads to myocardial infarction. The most important clinical complication is an acute occlusion due to the formation of a thrombus, resulting in a myocardial infarction or stroke [57].

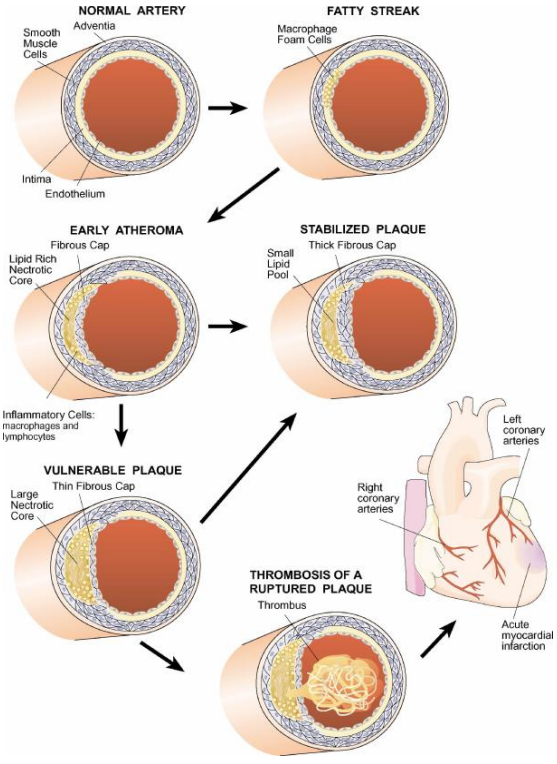


Figure 10. Stages of atherosclerosis. Figure reproduced from Luis et al., 2004.

Several genes, which in turn cooperate with each other and in conjunction with environmental factors, govern the processes that influence the disease outcome. Previous to 1948, year in which the Framingham Heart Study was born, little was known about the general causes of heart diseases. This longitudinal cohort study, carried out with 5209 residents of Framingham (Massachusetts), identified most of the risk factors currently approved for CAD.

The World Health Organization (WHO) divides CAD risk factors into 4 categories:

1. Major modifiable risk factors including:

    - High blood pressure
    - Abnormal blood lipids (high LDL-C and triglyceride levels, and low levels of high density lipoprotein (HDL) cholesterol)
    - Tobacco use
    - Physical inactivity
    - Obesity
    - Unhealthy diets
    - Diabetes mellitus

2. Other modifiable risk factors such as:

    - Low socioeconomic status
    - Mental ill-health
    - Psychosocial stress
    - Alcohol use
    - Use of certain medication (oral contraceptive and hormone replacement therapy)

3. Non-modifiable risk factors:

    - Advancing age
    - Heredity of family history
    - Gender (men are more likely to develop CAD than premenopausal women)
    - Ethnicity

4. Novel risk factors:

    - Inflammation (elevated C-reactive protein)
    - Excess of homocysteine in the blood
    - Abnormal blood coagulation

While modifiable risk factors can be altered to allow a decrease in the CAD individual risk, non-modifiable risk factors, including genetic predispositions, are immutable characteristics of each own person.

1.3.1. Genetic basis of CAD

The familial susceptibility of CAD has been assessed through several family and twin studies. The Swedish Twin Registry demonstrated that the relative risk to die from CAD was influenced by genetic factors that were evident up to the age of 75 years both in women and men, and that genetic effects decreased gradually at older ages [58]. In general, the heritability of fatal CAD events is higher in man (57%) with respect to woman (38%) (Zdravkovic et al., 2002), and around 96% of cardiovascular deaths occur after 50 years of age [60]. Data from traditional analysis of family pedigrees in twins indicate that the range of genetic variance in CAD ranges from 40% to 60% [61]. Regarding classical risk factors, such as hypertension, obesity and diabetes, it has been assessed that classical risk factors contribute to 25–39% of CAD population incidence and that their prevalence varies widely between different countries [62]. As a consequence, in the last years several genome-wide association studies (GWASs) have tried to ascertain the remaining part of genetic variance associated to CAD, which should explain the rest of the cardiovascular heritability. Currently153 DNA variants associated with CAD have been discovered through GWASs [63], 50 of which with genome wide significance confirmed in independent studies [64] (Table 1). The majority of these variants have an unknown mechanism of risk, whereas other are associated with LDL-C, HDL-C, triglycerides, or hypertension.

Chromosomal Location	SNP	Nearby Genes	Risk Allele Frequency (allele)	Odds Ratio	Delivery Route
Risk Variant Associated with LDL Cholesterol					
6q25.3	rs3798220	LPA	0.02 (C)	1.92 (1.48-2.49)	2009
2p24.1	rs515135	APOB	0.83 (G)	1.03	2012
1p13.3	rs599839	SORT1	0.78 (A)	1.29 (1.18-1.40)	2007
19p13.2	rs1122608	LDLR	0.77 (G)	1.14 (1.09-1.19)	2009
19q13.32	rs2075650	APOE	0.14 (G)	1.14 (1.09-1.19)	2011
2p21	rs6544713	ABCG5-ABCG8	0.29 (G)	1.07 (1.04-1.11)	2011
1p32.3	rs11206510	PCSK9	0.82 (T)	1.15 (1.10-1.21)	2009
Risk Variant Associated with HDL Cholesterol					
6p21.31	rs12205331	ANKS1A	0.81 (C)	1.04	2012
Risk Variant Associated with Triglycerides					
8q24.13	rs10808546	TRIB1	0.65 (A)	1.08 (1.04-1.12)	2011
11q23.3	rs964184	ZNF259, APOA5-A4-C3-A1	0.13 (G)	1.13 (1.10-1.16)	2011
Risk Variant Associated with Hypertension					
12q24.12	rs3184504	SH2B3	0.44 (T)	1.13 (1.08-1.18)	2009
10q24.32	rs12413409	CYP17A1, CNNM2, NT5C2	0.89 (G)	1.12 (1.08-1.16)	2011
4q31.1	rs7692387	GUCYA3	0.81 (G)	1.13	2012
15q26.1	rs17514846	FURIN-FES	0.44 (A)	1.04	2012
Risk Variant Associated with Myocardial Infarction					
9q34.2‡	rs579459	ABO	0.21 (C)	1.10 (1.07-1.13)	2011
Risk Variant Mechanism of Risk Unknown					
9p21.3	rs4977574	CDKN2A,CDKN2B	0.46 (G)	1.25 (1.18-1.31) to 1.37 (1.26-1.48)	2007
1q41	rs17465637	MIA3	0.74 (C)	1.20 (1.12-1.30)	2007
10q11.21	rs1746048	CXCL12	0.87 (C)	1.33 (1.20-1.48)	2007
2q33.1	rs6725887	WDR12	0.15 (C)	1.16 (1.10-1.22)	2009
6p24.1	rs12526453	PHACTR1	0.67 (C)	1.13 (1.09-1.17)	2009
21q22.11	rs9982601	MRPS6	0.15 (T)	1.19 (1.13-1.27)	2009
3q22.3	rs2306374	MRAS	0.18 (C)	1.15 (1.11-1.19)	2009
10p11.23	rs2505083	KIAA1462	0.42 (C)	1.07 (1.04-1.09)	2010
1p32.2	rs17114036	PPAP2B	0.91 (A)	1.17 (1.13-1.22)	2011
5q31.1	rs2706399	IL5	0.48 (A)	1.02 (1.01-1.03)	2011
6q23.2	rs12190287	TCF21	0.62 (C)	1.08 (1.06-1.10)	2011
7q22.3	rs10953541	BCAP29	0.75 (C)	1.08 (1.05-1.11)	2011
7q32.2	rs11556924	ZC3HC1	0.62 (C)	1.09 (1.07-1.12)	2011
10q23.31	rs1412444	LIPA	0.34 (T)	1.09 (1.07-1.12)	2011
11q22.3	rs974819	PDGF	0.29 (T)	1.07 (1.04-1.09)	2011
13q34	rs4773144	COL4A1, COL4A2	0.44 (G)	1.07 (1.05-1.09)	2011
14q32.2	rs2895811	HHIPL1	0.43 (C)	1.07 (1.05-1.10)	2011
15q25.1	rs3825807	ADAMTS7	0.57 (A)	1.08 (1.06-1.10)	2011
17p13.3	rs216172	SMG6, SRR	0.37 (C)	1.07 (1.05-1.09)	2011
17p11.2	rs12936587	RASD1, SMCR3, PEMT	0.56 (G)	1.07 (1.05-1.09)	2011
17q21.32	rs46522	UBE2Z, GIP, ATP5G1, SNF8	0.53 (T)	1.06 (1.04-1.08)	2011
5p13.3*	rs11748327	IRX1, ADAMTS16	0.76 (C)	1.25 [1.18-1.33]	2011
6p22.1*	rs6929846	BTN2A1	0.06 (T)	1.51 (1.28-1.77)	2011
6p24.1**	rs6903956	C6orf105	0.07 (A)	1.65 (1.44-1.90)	2011
6p21.3	rs3869109	HCG27 and HLA-C	0.60 (C)	1.15	2012
1q21	rs4845625	IL6R	0.47 (T)	1.09	2012
Chr4	rs1878406	EDNRA	0.15 (T)	1.09	2012
7p21.1	rs2023938	HDAC9	0.10 (G)	1.13	2012
2p11.2	rs1561198	VAMP5-VAMP8	0.45 (A)	1.07	2012
Chr2	rs2252641	ZEB2-AC074093.1	0.45 (A)	1	2012
Chr5	rs273909	SLC22A4-SLC22A5	0.14 (C)	1.11	2012
6p21	rs10947789	KCNK5	0.76 (T)	1.01	2012
6q26	rs4252120	PLG	0.73 (T)	1.07	2012
8p22	rs264	LPL	0.86 (G)	1.06	2012
13q12	rs9319428	FLT1	0.32 (A)	1.1	2012

Table 1. Chronological list of 50 genetic variants associated with CAD or myocardial infarction.*Variant identified only in Japanese; **Variant identified only in Han Chinese; ‡ The risk variant at 9q34.2 is associated with myocardial infarction but not with coronary atherosclerosis. A: adenine; C: cytosine; G: guanine; T: thymine; CI: confidence interval; OR: odds ratio. Table reproduced from Roberts, 2014.

In contrast to the candidate gene approach, GWASs simultaneously assess the association of hundreds of thousands of genetic variants distributed across the whole genome. The first two GWASs for CAD were published in 2007 [65] [66]. The main finding was a locus on chromosome *9p21*, which currently has a prominent position mainly because of the impressive robustness in replication efforts [64]. However, the responsible mechanism of CAD susceptibility in this genomic region still remains unclear. This risk region spans approximately 50 kb of DNA sequence (CAD associated loci in Figure 11). The nearest protein coding genes are *CDKN2A* (150 kb) and *CDKN2B* (118 kb), which encode inhibitors of cellular senescence involved in the control of cellular proliferation and apoptosis.

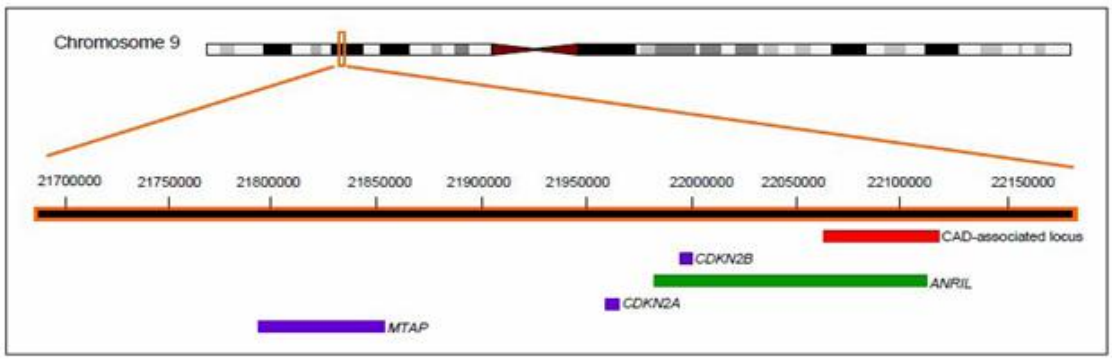


Figure 11. The 9p21 risk region. Figure reproduced from http://writepass.com/journal/2012/12/coronary-heart-disease/.

However, a potential role for CAD etiology has been attributed , to the *ANRIL* RNA non-coding region [67] [68]. The *ANRIL* region overlaps almost entirely the 9p21 CAD-associated locus (Figure 11), and there are high levels of *ANRIL* expression in tissues and cell types affected by atherosclerosis such as atheromatous vessels, abnormal aortic aneurism walls, or vascular endothelial cells [69]. A recent article reports a molecular mechanism through which *ARNIL* could increase cell adhesion and decrease apoptosis, two essential events of atherogenesis [70]. This study states that Alu elements in *ARNIL* RNA non-coding region likely modulate atherogenic cell function through trans-regulation of gene networks. Interestingly the 9p21 region is not only associated to atherosclerotic diseases, but also to diabetes [71], intracranial and abdominal aortic

aneurysms [72], and Alzheimer's disease [73]. In addition it has recently been associated also with periodontitis [74] and gout [75], both with a marked inflammatory component. The pleiotropic effect of this region is very common in human complex traits. A recent article analyzed the whole National Human Genome Research Institute (NHGRI) catalog of published GWASs finding abundant evidence of pleiotropy in 233 (16.9%) genes and 77 (4.6%) SNPs [76].

In any case, assuming a heritability of 40%, the 153 genome-wide significant SNPs only explain <10.6% of CAD variability [77]. In addition, these CAD-associated loci are strikingly pervasive across the population, but generally have weak effects. As recently reviewed [78], 50% of the CAD associated variants occur in over one-half of the population, and at least 25% occur in over 75% of the population. The fact that common variants detected by GWAS so far typically account for a minority of the heritability generates an issue known as *missing heritability*. Recent findings suggest that epigenetic mechanisms, gene-gene (GxG), and gene-environment interactions (GxE) may explain a substantial fraction of this missing heritability [79]. In support of this theory, a study [80] indicated that SNPs in the 9p21 locus have lower effect size among patients on diets rich in fruits, vegetables, nuts, desserts, and berries. This work demonstrated that the deleterious effect of genetic influences can be modulated by lifestyle factors. Another hypothesis is that much of the missing heritability may reside within the low frequency (MAF = 0.5%-5%) and rare (MAF > 0.5%) variants not included in GWASs. In this way, there are two theories: the *common disease common variant* (CDCV), and the *common disease rare variant* (CDRV) hypotheses. The first argues that common genetic variation with relatively low penetrance are the major contributors to genetic susceptibility to common diseases, while the second affirms that multiple rare DNA sequence variations, each with relatively high penetrance, may be the major contributors to genetic susceptibility to common diseases. But now, there are insufficient data to substantiate that multiple rare alleles are major components of missing heritability, and it is plausible to think that both type of variants contribute to CAD heritability. Currently, the unique clear matter is that a large component of CAD heritability remains unexplained and this situation will improve as we discover more about the genetic basis of CAD.

A bias inherent in GWAS regards the fact that common markers (MAF>0.05), selected to tag the most common haplotypes in the major continental populations, are based on people of European descent and consequently are more effective in European and Asian populations compared to African populations, because of differences in the LD patterns. Although an increasing number of association studies are now performed on other ancestral groups, currently 96% of GWASs are based on people of European ancestry [81]. LD patterns across loci may be different from population to population, and markers associated with a particular trait in a given population will often not be transferable to population of different ancestry. This seems the case of the SNP rs10757278 (Figure 12), located in the locus 9p21, and associated with myocardial infarction in several studies [66 65 72]. It is in strong LD with multiple SNPs in Europeans, whereas in Asians this SNP is in a singleton block, and in Africans it is in LD with only a subset of the same SNPs present in Europeans. Thus, rs10757278 probably tags so far undiscovered variants that are different in the three populations [82].

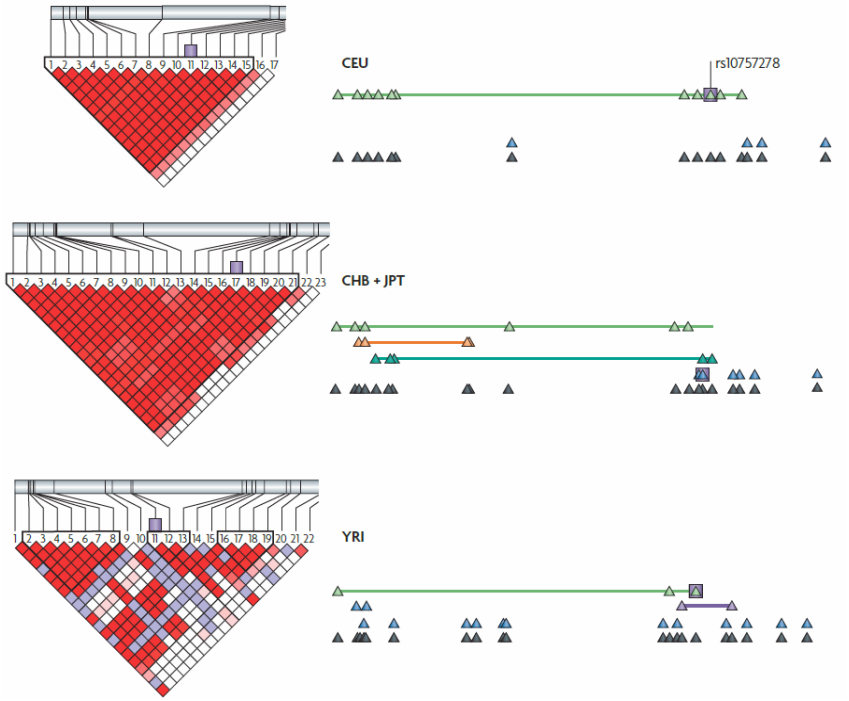


Figure 12. The LD structure of SNPs in a 13 kb interval of chromosome 9p21 is shown for the three HapMap populations: CEU, JPT + CHB and YRI. On the left of the figure, the LD structures of the interval are shown quantified using D'. On the right of the figure, all SNPs are shown on the bottom row as black triangles. Above this, SNPs are grouped together into bins at an r2 > 0.8. SNPs that are efficiently tagged by each other (r2 > 0.8) are shown in the same colour and are connected by a line. Singleton bins that do not tag any other SNPs are shown as individual blue triangles. Figure reproduced from Frazer, Murray, Schork, & Topol, 2009.

A recent investigation about consistency of GWAS results across major continental groups reports that odds ratios across ancestry groups correlate modestly, and point estimates of risk are opposite in direction or different by more than two-fold in 57%, 79% and 89% of Europe-Asia, Europe-Africa, and Asia-Africa comparisons, respectively [83]. Positive associations found in Europeans need to be confirmed or rejected analyzing populations of different ancestry, to identify the actual causal risk variants determining the outcome.

1.3.2. Population distribution of CAD

CAD incidence varies greatly according to geographical region, sex, and ethnic background. Several studies have been performed to evaluate the geographic distribution of incidence and CAD risk parameters. One of the most important contributions in this field was conducted by the ***Moni****toring Trends and* ***D****eterminants in* ***Ca****rdiovascular* ***D****isease (MONICA) project*. It was developed by the WHO as a monitoring system (from1980 to 1990) to assess trends and determinants of cardiovascular mortality, incidence and case fatality in 38 populations of 21 countries worldwide. Together with the *Framingham Heart Study*, the WHO MONICA Project contributed widely to increase epidemiology and prevention of cardiovascular diseases.

One of the most important discoveries was the gender difference in fatal CAD: it is higher in men than in women. This difference is also very country-dependent (Figure 13). In men, case fatality rates per 100,000 individuals vary 20-fold among countries (ranging from 35 in South Korea to >733 in the Ukraine), whereas in women rates vary nearly 30-fold (ranging from 11 in France to nearly 313 in the Ukraine) [84]. Although the burden of CAD was highest in Western countries during much of the 20th century, currently the greatest amount of heart diseases occurs in Asian and Middle-Eastern regions (Figure 13). In Europe, CAD prevalence is not homogeneously distributed but shows a four-fold North to South gradient with the highest incidences in Finland and the United Kingdom, and the lowest in Spain and France [85].

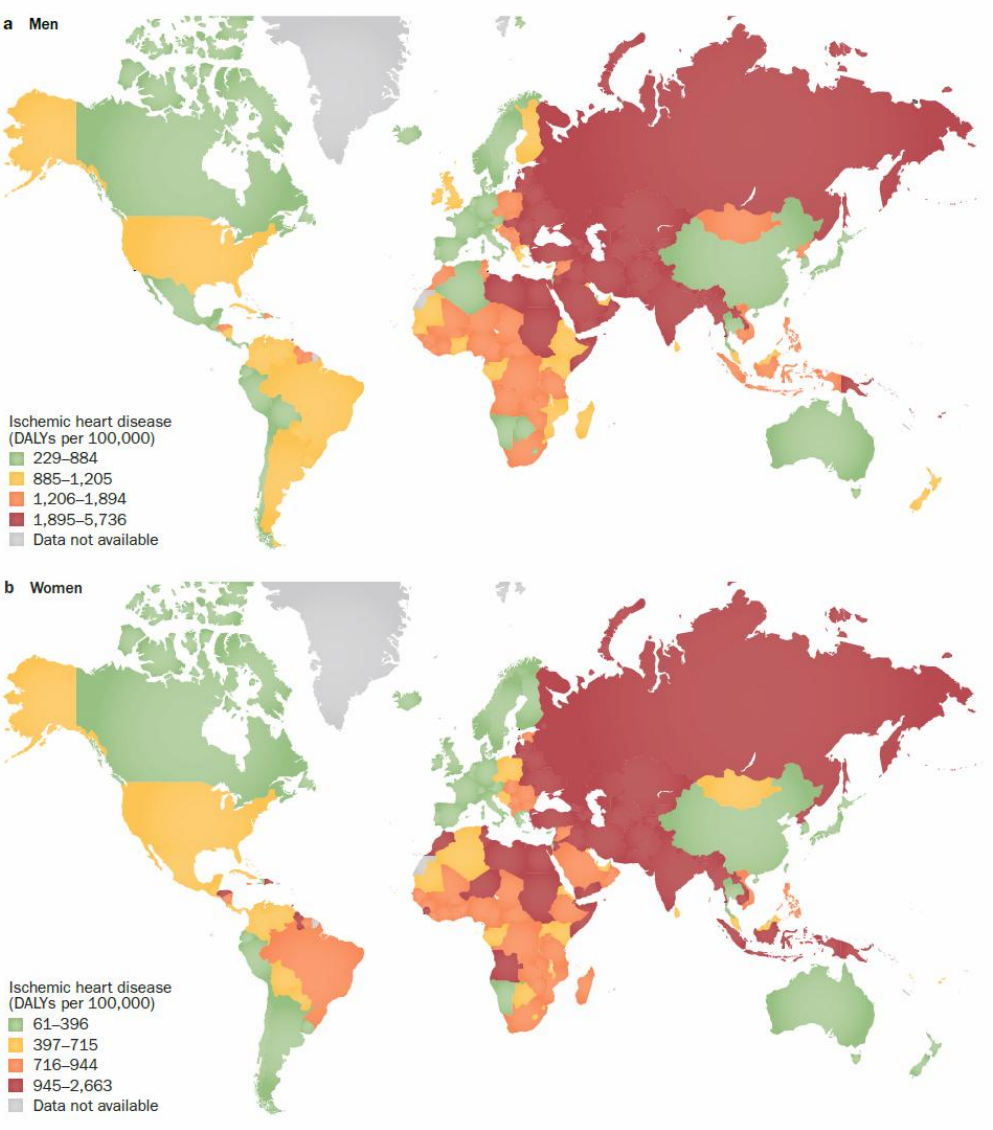


Figure 13. Global distribution of ischemic heart disease burden, in DALYs, in 2011.a Men. b Women. Data are age-standardized per 100,000 of the population. Abbreviation: DALYs, disability-adjusted life years. Figure reproduced from Wong et al., 2014.

Several studies have attempted to correlate CAD incidence variation with the distribution of both traditional and genetic risk factors, analyzing the geographic distribution of CAD genetic risk variants. Some of them affirmed that risk allele frequencies are clearly correlated with CAD incidence, showing a south to north increasing gradient. This is the case of the apolipoprotein (Apo) E4 [87], or the genetic risk score (GRS) of nitric oxide synthases (NOS) gene variants [88], both associated with susceptibility to CAD. This last study stated that GRS values across Europe are positively correlated with coronary events incidence, explaining 65–85% of the CAD inter-population variation. The geographic

distribution of GRS shows a concentric pattern from a center of lower risk in the North-West Mediterranean areas, especially in the islands of Corsica and Sardinia, and a gradual increase towards the North (UK, Poland and Finland) (Figure 14).

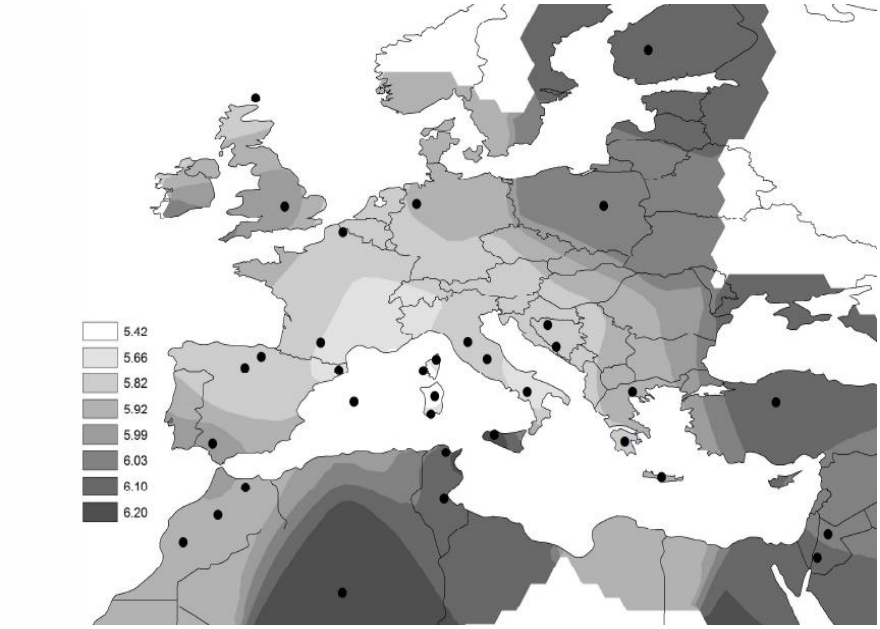


Figure 14. Contour map of NOS risk score in Europe and the Mediterranean. Figure reproduced from Carreras-Torres et al., 2014.

In contrast, another study [89] declared that genetic variants associated to CAD showed geographical patterns opposite and uncorrelated with the incidence of the disease. In this case, genetic risk factors in southern Europe show higher frequencies than in northern Europe. The observed north to south cline in frequency was explained likely due to the spatial distribution of the whole genome variation present in the European continent, which has been mainly shaped by the history of populations migrations.

As in the case of complex diseases in general, also population differences in CAD are, at the moment, not fully understood. The role that *natural selection* or *demographic events* may play in these differences is currently object of study. A recent article [90] analysed the frequency of 158 risk CVD SNPs in 52 different populations of the HGDP. This work found that the global mean FST value (a measure of the inter-population variation) for risk markers does not differ significantly from autosomal variants randomly sampled in the genome. Despite this fact, the authors detected eight CVD SNPs with higher global FST

values than putatively neutral SNPs in the pairwise comparisons. In addition, four of them showed additional evidences of recent positive selection in the integrated Haplotype Score test [20], which is a statistic measure of the amount of extended haplotype homozygosity (EHH) at a given SNP along the ancestral allele relative to the derived allele.

Several genes involved in the causal pathways of atherosclerosis, including blood pressure regulation, lipoprotein and glucose metabolism, coagulation, and inflammation, are suspected to be subject to various degrees of selective pressures resulting from climatic and dietary changes [91]. For examples, the *sodium hypothesis* posits that sodium conserving mechanisms conferred a survival advantage among our ancestors in the hot and humid climate of Africa but may lead to hypertension in temperate climates. The ancestral alleles (sodium-conserving alleles) show strong latitudinal gradients in allele frequency and are more prevalent in Africans than in populations from Northern Europe, in whom signatures of positive selection were noted for the derived allele [92]. Evolutionary hypotheses and models, such as the *thrifty-gene hypothesis*, which explain the predisposition of certain ethnic groups to obesity and diabetes, or the *ancestral-allele susceptibility model* [93], which affirms that the ancestral allele is the allele increasing risk, whereas the derived allele is protective, have been proposed to explain the epidemiology of complex diseases in an evolutionary context. Increasing genetic evidence supports these hypotheses [91]. It was postulated, for example, that several selective pressure, including climatic and dietary changes, may have influenced lipoprotein metabolism. Higher serum cholesterol may have been advantageous during the rapid increase in human size during human evolution for its role in steroid hormone synthesis. For this reason, the ancestral E4 allele in ApoE was a favorable '*thrifty*' allele in ancient populations with seasonally fluctuating food sources, but now it has subsequently become detrimental under contemporary environmental conditions. The absence of association of ApoE4 with CAD in Sub-Saharan Africans and its presence in African Americans seem to confirm this hypothesis [94].

Regarding the *ancestral-allele susceptibility model*, the ancestral variant in the angiotensinogen gene, associated with hypertension, is present at higher frequency in African populations than in non-African populations. It has been discovered that the derived allele had quickly risen to high frequency as a result of positive recent sweep in non-African populations [95]. Another example is the CYP3A5*3 ancestral allele, which is

associated with increased systolic blood pressure and mean arterial pressure in African Americans [96]. A sequence analysis of this gene revealed that the derived protective allele is associated with low levels of haplotypic variation as a result of a possible recent positive selection event [97].

Despite all these studies, mechanistic links between signals of natural selection and CAD have not been fully delineated. Further works are needed to address potential confounding effects caused by demographic processes and to detect clear evidences of selection in CAD risk loci. Such investigations could provide novel insights into the genetic epidemiology and pathophysiology of CAD, and potentially new strategies for prevention and treatment.

1.4. The population context

Genetic and paleoanthropological evidences point out that today's human populations are the result of a great demographic and geographic expansion that began approximately 60 thousand years ago (kya) in Africa, and rapidly resulted in the human occupation of almost all of the Earth's habitable regions (Figure 15). These demic events began with the expansion of a source population in southern Africa 60 to 100 kya and conclude with the settlement of South America approximately 12 to14 kya [98].

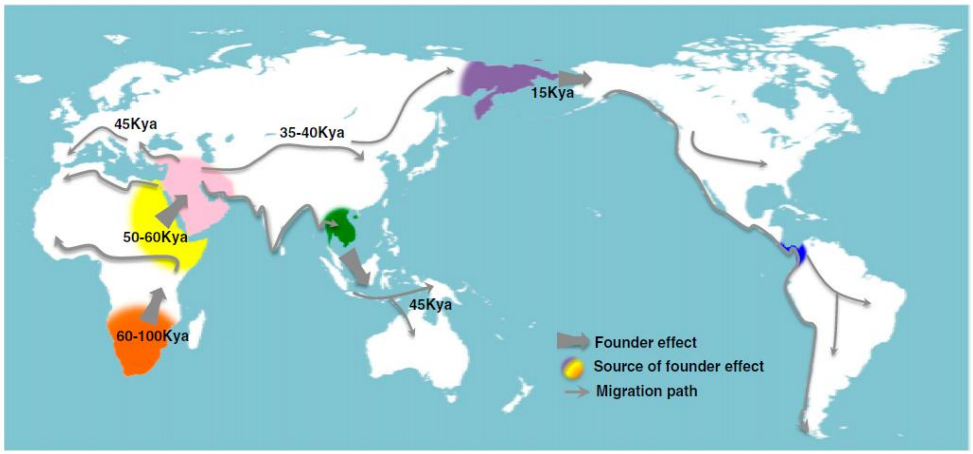


Figure 15. Ancient dispersal patterns of modern humans during the past 100,000 years. Wide arrows indicate major founder events during the demographic expansion into different continental regions. Colored arcs indicate the putative source for each of these founder events. Thin arrows indicate potential migration paths. Figure reproduced from BM Henn et al., 2012.

Different hypothesis have been formulated to explain the spatial and temporal distribution of modern human populations out of Africa, like as the eastward expansion (EE), that consists in a single dispersal event, with an iterative loss of diversity along a latitudinal axis in Eurasia [99]; or the multiple dispersals (MD) scenario, whereby humans expanded out of the African continent at different timescales and via distinct geographical routes [100]. The MD hypothesis predicts a first dispersal between 50 and 100 kya through the southern Arabian Peninsula reaching Southeast Asia, and a second dispersal through the Levant prompting the colonization of the rest of Eurasia between 40 and 50 kya. Given the discrepancies between the EE and the MD hypothesis, a reconciling view is that of a single wave bifurcation outside of Africa, likely in southwest Asia: the beachcomber single dispersal (BSD) hypothesis [101]. It suggests a single out of Africa event with a series of founding bottlenecks during the expansion. This hypothesis implies substantial migration

along a longitudinal axis: in addition to a dispersal along the Indian Ocean rim, it also includes the eastern Pacific Ocean rim. Furthermore, it allows for migration from southwest Asia back into Africa. Despite these different hypotheses, there is a growing consensus on a single southern dispersal of anatomically modern humans from Africa that led to the characteristic pattern of heterozygosity observed in today's populations. During the great expansion there was a continuous loss of genetic diversity resulting in the fact that genomes from African populations retained an exceptional number of unique variants, and there was a dramatic reduction in genetic diversity within populations living outside of Africa [98].

In the European continent, the prehistory of modern humans is commonly divided into five major episodes: i) the pioneer colonization of the Upper Paleolithic; ii) the Late Glacial re-colonization of much of the continent from southern refuges after the Last Glacial Maximum (LGM); iii) the post glacial recolonization by Mesolithic groups of deserted areas after the end of the Younger Dryas (marking the end of the Pleistocene and the beginning of the Holocene); iv) fresh dispersals of Near Easterners (Neolithic); and v) small-scale migrations along continent-wide economic exchange networks from the Copper Age onward [102].

The initial dispersal of anatomically and genetically modern populations across Europe in the *Upper Paleolithic* is usually placed around 50 kya. Data from mtDNA suggest dispersals from the Near East both north-west into Europe and south-west into North Africa, potentially marked by different sub-branches of haplogroup U:U5 in Europe [103] and U6 (together with M1) in North Africa [104]. The initial dispersal of modern populations, according to the distribution of the Aurignacian technologies, can be traced continuously from the adjacent areas of the Near East through most areas of eastern and central Europe, to the Atlantic coast of France and Spain, within the time range from around 40 kya to 35 kya [105].

The next major change occurred in the *LGM*, 25-19.5 kya. During this time human populations became concentrated in refuge areas in south-west Europe, along the Mediterranean, in the Balkans and the Levant, and on the eastern European plain [106]. The major signal in the modern European mtDNA pool is the re-expansion and resettlement in central and north Europe in the major warming phase after 15 kya. Haplogroup H, the

most frequent mtDNA haplogroup in Europe (45% in modern Europeans) seems likely to have arisen in the Near East around 18 kya. Its founder age in Europe is currently estimated at 15 kya, suggesting an entry after the LGM [102]. However, other analyses of the present database of almost 2000 complete mtDNA from European lineages suggest postglacial rather than Late Glacial expansion times for most of the lineages spreading from south-west Europe. Although H5 (13.9 ky) and U5b3 (13.0 ky) seem to date to the Late Glacial [107], haplogroups V, H1 and H3 all date to 11–11.5 kya, the end of the Younger Dryas glacial relapse, after which temperatures stabilized at levels similar to today.

Successively, the *Mesolithic* in Europe marked a new way of life: due to a much warmer climate, Europe became densely forested, and a new mode of subsistence took hold. Hunting, gathering as well as fishing became more important. Over time, coastal communities in particular became more sedentary and underwent considerable population growth. Central Europe Mesolithic communities appeared to be less dense and more mobile, although with some evidences of agriculture or horticulture [102].

The dynamics of the *Neolithic transition* in human prehistory is very well known in Europe and the Near East, because in this area hundreds of Early Neolithic sites have been dated. This transition can be defined as the shift from hunting–gathering into farming. About 9000 years ago, the Neolithic transition began to spread from the Near East into Europe, until it reached Northern Europe about 5500 years ago. There is continuing controversy about the relative contributions of European Paleolithic hunter-gatherers and of migrant Near Eastern Neolithic farmers, who brought agriculture to Europe. Two main models were used to describe this spread: the demic model and the cultural model. In the demic diffusion model [108] the spread of technologies involved a massive movement of people, which implies a significant genetic input of Near Eastern genes from Neolithic farmers. Under the cultural diffusion model [109 110] on the contrary, the transition to agriculture is regarded essentially as a cultural phenomenon, involving the movement of ideas and practices rather than people. Consequently, it would not imply major changes at the genetic level. The major geographic trends detected in allele frequencies at conventional marker loci, such as blood groups and enzymes [111 112] supported the demic diffusion model reveling a cline of allele frequency centered in the Near East (Figure 16). Conversely, mtDNA and Y chromosome data supported the cultural model, thereby generating a

controversy [113] [114]. In any case, the overall data seem to support both models: the cultural diffusion cannot be neglected, but demic diffusion was the most important mechanism in this major historical process at the continental scale [115].

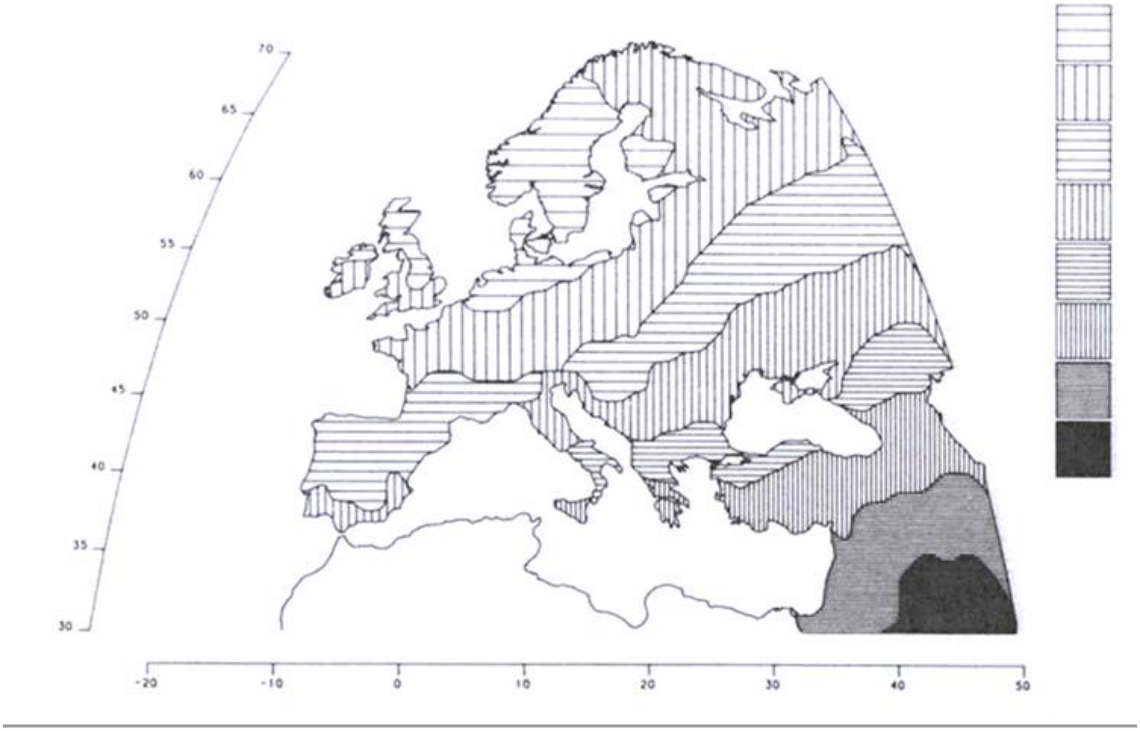


Figure 16. Synthetic map of Europe and Western Asia obtained using the first principal component of classical genetic data. Figure reproduced from Cavalli-Sforza et al., 1994.

Successively, in the Bronze Age (around 3000–1000 BC), Eurasia lived a period of major cultural changes. A recent study based on the low-coverage sequencing of 101 genomes from ancient humans across Eurasia showed that the Bronze Age was a highly dynamic period involving large-scale population migrations and replacements, responsible for shaping major parts of present-day demographic structure in both Europe and Asia [116]. Allentoft et al.[116] showed that ancient groups of Eurasia were genetically more structured than contemporary populations. The diverged ancestral genomic components spread further after the Bronze Age through population growth, combined with continuing gene flow between populations, to generate the low differentiation observed in contemporary West Eurasians.

The small-scale migrations along continent-wide economic exchange networks from the *Copper Age* onward consist of several different cultures and civilizations that invaded Europe during recent history. From the Minoan civilization in Crete (from approximately 2600 to 1400 BC), to the Arab invasion of North Africa and the Iberia peninsula (from 622 to 750), passing through the Roman Empire and the Barbarian invasions, all these civilization have contributed to create the current genetic composition of European and Mediterranean populations. In particular, regarding the Mediterranean area, a recent survey stated that recent migrations from North Africa contributed substantially to the higher genetic diversity in southwestern Europe [45]. In that study, based on SNP data, the haplotype sharing observed between Europe and the Near East followed a southeast to southwest gradient, whereas the sharing between Europe and North Africa followed an opposite pattern. As a consequence, gene flow from the Near East into Europe perhaps reflects more ancient migrations (Neolithic) and cannot account for the observed haplotype sharing between South Europe and North Africa.

1.4.1. Populations studied

This thesis explores the genetic variation of worldwide population samples giving special emphasis to the Mediterranean region. Lands surrounding the Mediterranean Sea were the starting point from which humans started great expansions. These lands represented a crossroads between three continents: Western Asia, North Africa, and Southern Europe.

Because of its position in the Middle East, *Jordan* represented one of the major pathways for human movements. Historically, Bedouins were the original settlers in the Middle East. From the Arabian Peninsula they spread out occupying the desert regions of all the countries between the Arabian Gulf and the Atlantic. The lack of information about their genetic background, and the fact that the unique previous published studies explored uniparental markers [117] [118] aimed us to perform a population genetic analysis in the Mediterranean area, centered on Bedouin and General Jordan populations. This analysis was carried out through autosomal Alu insertion polymorphisms.

Subsequently, the population study was extended to an epidemiological perspective using another kind of genetic variants: SNPs. The genetic variation present in the top 4 genomic

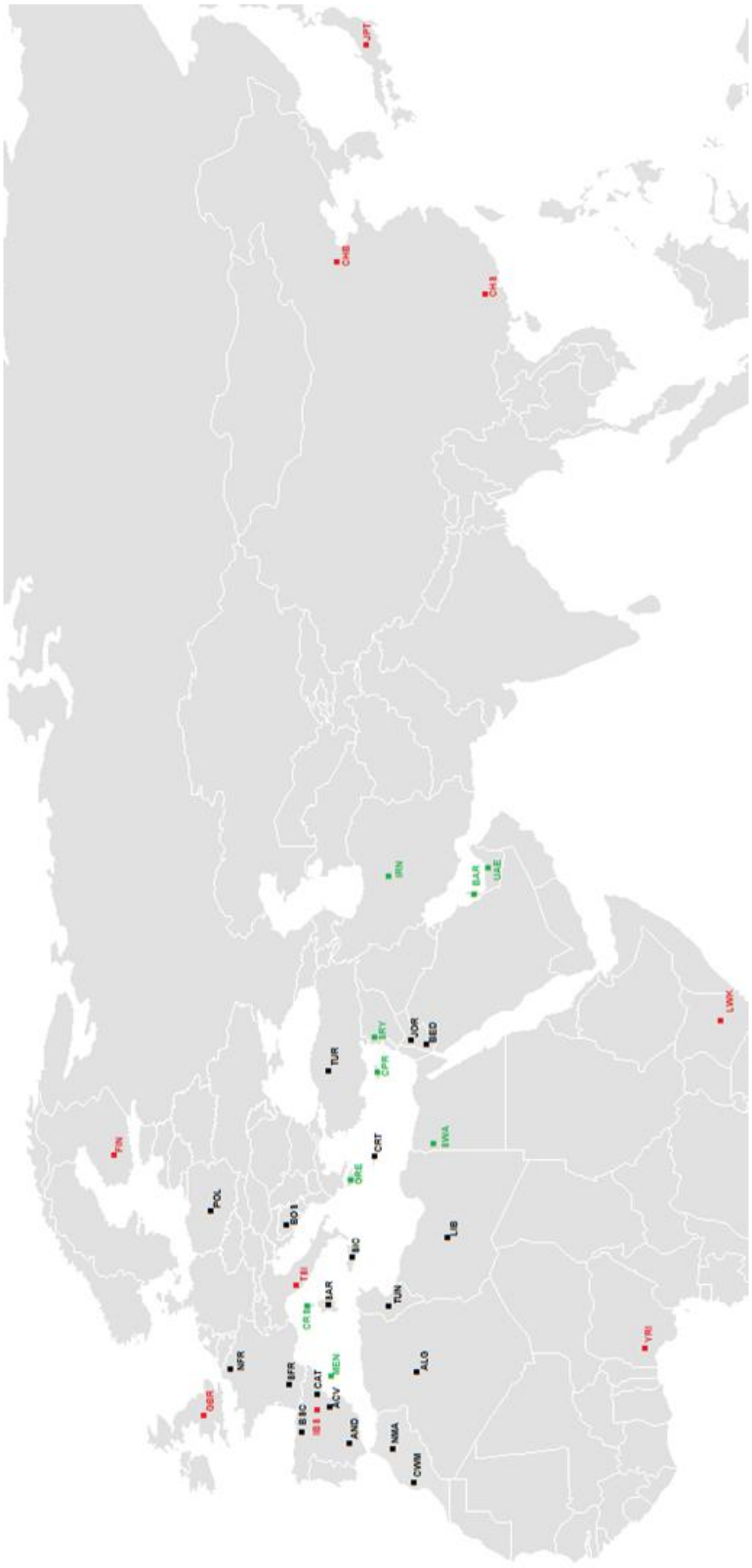
regions associate with *CAD* (*1p13*, *1q41*, *9p21*, and *10q11*) was analyzed for the first time using general population samples from South Europe, North Africa and Middle East, and also using Sub-Saharan African and Asian samples from the 1000 Genomes Project. The fine-structure analysis of these four genomic regions of epidemiological importance using general population samples had the double relevance to understand the demographic history of human populations and also to shed light on the genetic history of CAD.

These four CAD risk regions were also analyzed in an association study using a novel set of case control samples from North Africa, specifically from *Morocco* and *Tunisia*. For comparative purposes matched case-control samples from South Europe (Italy and Spain) were used from the Myocardial Infarction Genetics (MIGen) Consortium [119]. The relevance of this study lies in the fact that it was the first association study based on the regions 1p13, 1q41, 9p21, and 10q11 conducted on North African samples.

Finally, several case-control samples of European, Asian and Sub-Saharan African origin were *simulated* based on the haplotypes of the 1000 Genomes Project. Autosomal SNPs of the 1000 Genome Project Phase 1 were used as a dataset to randomly select one thousand variants in the whole genome in which to apply a specific multi-locus disease model. Then, logistic regression analysis and statistical comparisons were performed to evaluate the level of consistency across different continental populations using a consistent amount of simulated data.

A map of the whole populations studied is present below (Figure 17).

Figure 17. Geographic location of the populations analyzed in the study. Black dots represent the novel populations samples used. POL: Poland, NFR: North France, SFR: South France, BSC: Basque Country, CAT: Catalonia, ACV: Autonomous Community of Valencia, AND: Andalusia, SAR: Sardinia, SIC: Sicily, BOS: Bosnia Herzegovina, CRT: Crete, TUR: Turkey, JOR: General Jordanian, BED: Bedouins, NMA: North Morocco, CWM: Central-West Morocco, ALG: Algeria, TUN: Tunisia, LIB: Libya. Red dots represent 1000 Genomes Data: FIN: Finnish in Finland, GBR: British in England and Scotland, TSI: Toscani in Italia, IBS: Iberian Population in Spain, LWK: Luhya in Webuye, Kenya, YRI: Yoruba in Ibadan, Nigeria, CHB: Han Chinese in Beijing, China, CHS: Southern Han Chinese, JPT: Japanese in Tokyo, Japan. Green dots represent populations from other studies used for comparative purposes: MEN: Menorca, CRS: Corsica, GRE: Greece, CPR: Cyprus, SRY: Syria, IRN: Iran, BAR: Bahrain, UAE: United Arab Emirates, SWA: Siwa in Egypt.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TUN
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AND
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Aims

Evolutionary and demographic events throughout history have shaped the observed patterns of genetic differentiation between human populations. Previous studies lead researchers to consider the Mediterranean Sea, bringing together three continents, as a crucial point to study human genetic differences. In this way, a substantial part of this thesis is centered in this interesting population area.

The present thesis deals with a deep analysis of the genetic structure of extant human worldwide populations based in the analysis of different kinds of genetic markers, some of them with clear epidemiological implications, with a special focus on the Mediterranean region.

Specifically, the main objectives of the current work were the following:

- To contribute to the knowledge of the history of human populations from the Levant region through the genetic analysis of two population samples from Bedouins and general Jordanians. This analysis includes:

    i) the assessment of the genetic diversity within Jordan by means of a set of genetic "neutral" markers;
    ii) the definition of the relationships across present-day Middle Eastern, North African, and European populations;
    iii) the identification of the genetic traces of past human migrations between Africa and Eurasia.

- To analyze the genetic variation of the top four CAD risk regions (1p13, 1q41, 9p21, and 10q11) in 19 populations from Europe, Middle East and North Africa, together with data of Asian and African samples from the 1000 Genomes Project, in order to:

    i) explore the genetic variation and the LD patterns across these populations;
    ii) describe whether the genetic variability in these genomic regions is better explained by demography or by natural selection;

iii) assess if the signatures of selection eventually detected are shared across continents or belong to a specific population group.

- To study the genetic variation in these four CAD risk regions in an epidemiological context, in order to:

  i) evaluate if the associations found in previous GWAS, mainly conducted on people of European descent, could be transferable also to North Africa, specifically to Tunisian and Moroccan populations;
  iv) compare the associations and trends detected in North African samples with available data from South Europe;
  v) assess the combined effects (risk score) of the associated markers found in North Africa, and their ability to discriminate between cases and controls;

- To evaluate the level of consistency in the genetic effect of GWAS across populations of different continental ancestry. In this way, European, Asian and Sub-Saharan African case-control data were simulated to:

  i) evaluate the transferability of association signals in Europeans to populations from other continents;
  ii) assess if genetic risk variants are shared or not across European, Asian and Sub-Saharan African populations;
  iii) evaluate the potential role of allele frequencies in the trans-ethnic differences in GWAS signals.

Results

Supervisor's report on the quality of the published articles

The doctoral thesis "Genetics of human populations: evolutionary and epidemiological applications" is based on the original results obtained by Daniela Zanetti and published in three international peer-reviewed journals. The fourth article is currently under editorial consideration in the European Journal of Human Genetics.

In all four publications, genetic variation is used in order to address several issues regarding the demographic and biological history of various human groups. The large amount of data obtained (both in terms of populations and markers) and the variety of sophisticated statistical tests carried out are a considerable contribution to the scientific community.

The importance of the research conducted is demonstrated by the quality of the three journals:

1. *Human Biology* is the official publication of the American Association of Anthropological Genetics, an international, peer-reviewed journal that focuses on research to increase understanding of human biological variation. It is indexed in the Science Citation Index (SCI) and in the Social Science Citation Index (SSCI) with a current impact factor of 0.92 and classified in the second quartile of the area "Anthropology" (ranking: 38/83)

2. *PLoS One* is a peer-reviewed open access scientific journal published by the Public Library of Science (PLOS) since 2006. It features reports of original research from all disciplines within science and medicine. PLoS One is indexed in SCI and SSCI with a current impact factor of 3.23 and classified in the first quartile of the area "Multidisciplinary Science" (ranking: 8/56).

3. *Journal of Epidemiology* is the official open access scientific journal of the Japan Epidemiological Association. The Journal publishes a broad range of original research on epidemiology as it relates to human health. It is indexed in SCI and in SSCI with a current impact factor of 3.02, classified in the first quartile of the area "Public, Environmental & Occupational Health" (ranking: 32/162).

Signed by Dr. Pedro Moral Castrillo and Dr. Marc Via García
Barcelona, 1 September 2015

Result I

Zanetti et al., 2014

Human Diversity in Jordan: Polymorphic *Alu* Insertions in General Jordanian and Bedouin Groups

Daniela Zanetti, May Sadiq, Robert Carreras-Torres, Omar Khabour, Almuthanna Alkaraki, Esther Esteban, Marc Via, and Pedro Moral

Human Biology, Spring 2014, v. 86, no. 2, pp. 131 – 138

Resumen en castellano

Diversidad humana en Jordania: polimorfismos de inserción Alu en los jordanos generales y en los beduinos

Jordania, que se encuentra en la región de Levante, es un área crucial para investigar la migración humana entre África y Eurasia. Debido a su posición estratégica que conecta Asia, África y Europa, Jordania fue una zona de tránsito muy importante y por lo tanto objeto de rivalidad entre los imperios de la antigüedad como los persas, los griegos macedonios y muchos otros más. Históricamente, el término "beduino" denotaba un estilo de vida nómada y también una identidad de grupo. Los beduinos fueron los primeros pobladores del Oriente Medio. Desde la Península Arábica, su lugar de origen, extendieron sus rutas y ahora viven en las regiones desérticas situadas entre el Golfo Pérsico y el Atlántico.

La historia genética de los jordanos, incluyendo el origen de los beduinos actuales residentes en Jordania, aún no esta totalmente aclarada. La información genética anterior acerca de las poblaciones jordanas incluye dos estudios sobre marcadores uniparentales que apuntan a una clara diferenciación entre los dos grupos poblacionales considerados.

Este estudio ofrece nuevos datos genéticos de 18 inserciones autosómicas Alu en dos muestras poblacionales de Jordania (beduinos y población general) con el fin de examinar la diversidad genética dentro de este país y para proporcionar nueva información sobre la posición genética de estas poblaciones en el contexto de la zona del Mediterráneo y Oriente Medio. Las inserciones Alu fueron elegidas por su identidad por descendencia, su estado ancestral conocido (falta de inserción) y por su neutralidad selectiva aparente.

Los resultados indicaron significativas diferencias genéticas entre los beduinos y los jordanos generales (p=0,038). Mientras que los beduinos mostraron una mayor proximidad genética a los norteafricanos, los jordanos generales evidenciaron más similitudes genéticas con otras poblaciones de Oriente Medio. Considerando el tamaño de muestra relativamente pequeño, las diferencias genéticas encontradas apuntaron a una clara separación entre estos dos grupos. Esto podría estar relacionado con el hecho de que en los últimos años las zonas urbanas de Jordania han sido objeto de distintas y mayores influencias externas mientras que los beduinos han conservado su propia base genética debido a su estilo de vida nómada y aislada. Suponiendo que los beduinos representaron el sustrato original de los actuales jordanos, la diferenciación encontrada con el grupo de jordanos generales podría explicarse por una mayor influencia mediterránea en la población general debida a la posición de Jordania como cruce de caminos desde la antigüedad y/o a la contribución reciente de los inmigrantes en la última mitad del siglo XX. La mayor proximidad genética de los beduinos con los norte africanos podría explicarse por el impacto que la expansión árabe tuvo en el norte de África en el siglo VII. La proximidad genética encontrada entre los grupos del norte de África y los beduinos apoya la idea de que estos dos grupos poblacionales compartan los antecedentes genéticos de las poblaciones que propagaron la cultura árabe en el norte de Africa. En general, estos datos son consistentes con la hipótesis de que los beduinos tuvieron un papel importante en el poblamiento de Jordania y que probablemente constituyen el sustrato original de la población actual. Las migraciones recientes hacia Jordania probablemente contribuyeron a generar la diversidad observada entre la actual población general de Jordania y los beduinos.

Supervisor's report of the involvement of the PHD student in the development of this paper

Dr **Pedro Moral Castrillo**, Professor at the Department of Animal Biology of the University of Barcelona, and the Dr. **Marc Via García**, Professor at the Department of Psychiatry and Clinical Psychobiology of the University of Barcelona, both supervisors of the doctoral thesis "Genetics of human populations: evolutionary and epidemiological applications" by **Daniela Zanetti**, hereby certify that the participation of the above student in the article : "**Human Diversity in Jordan: Polymorphic Alu Insertions in General Jordanian and Bedouin Groups**", published in the *Human Biology*, consisted in the following tasks:

- Participation in the design of the study and selection of the analyzed markers
- Genotype determination of the Alu polymorphisms in the lab
- Creation of the genotype database and selection of available results in the literature for statistical comparison
- Statistical analysis of the data
- Redaction of the Manuscript

In addition, none of the co-authors of this article have used the results of this work in any implicit or explicit way to develop another doctoral thesis. As a consequence, this article forms part of the doctoral thesis of Daniela Zanetti exclusively.

Signed by Dr. Pedro Moral Castrillo and Dr. Marc Via García

Barcelona, 1 September 2015

Human Diversity in Jordan: Polymorphic *Alu* Insertions in General Jordanian and Bedouin Groups

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ABSTRACT

Jordan, located in the Levant region, is an area crucial for the investigation of human migration between Africa and Eurasia. However, the genetic history of Jordanians has yet to be clarified, including the origin of the Bedouins today resident in Jordan. Here, we provide new genetic data on autosomal independent markers in two Jordanian population samples (Bedouins and the general population) to begin to examine the genetic diversity inside this country and to provide new information about the genetic position of these populations in the context of the Mediterranean and Middle East area. The markers analyzed were 18 *Alu* polymorphic insertions characterized by their identity by descent, known ancestral state (lack of insertion), and apparent selective neutrality. The results indicate significant genetic differences between Bedouins and general Jordanians ($p = 0.038$). Whereas Bedouins show a close genetic proximity to North Africans, general Jordanians appear genetically more similar to other Middle East populations. In general, these data are consistent with the hypothesis that Bedouins had an important role in the peopling of Jordan and constitute the original substrate of the current population. However, migration into Jordan in recent years likely has contributed to the diversity among current Jordanian population groups.

The State of Jordan emerged in 1946 as the Hashemite Kingdom of Transjordan when Britain and France divided the Middle East after World War II. Since 1948 it has officially been known as the Hashemite Kingdom of Jordan. Jordan is a predominantly Arab nation, whose capital and largest city is Amman. It is located on the East Bank of the Jordan River and the Dead Sea and borders Palestine and Israel states to the west, Syria to the north, Saudi Arabia to the south and east, and Iraq to the northeast.

Because of its position in the Levant region, Jordan represents one of the major pathways for human movement. Since antiquity, traders traversed this area carrying products from the lands of the Indian Ocean basin to Syria, to be distributed from there to other parts of the Mediterranean world. Jordan was a crossroads for people from all over what is known today as the Middle East. Because of its strategic position connecting Asia, Africa, and Europe in the ancient world, Jordan was a major transit zone and thus an object of

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contention among the rival empires of ancient Persians, Macedonian Greeks, and many others (Salibi 1998).

Current inhabitants of Jordan are mostly Arab descendants of Transjordan or Palestine, and Bedouins, part of a predominantly desert-dwelling Arabian ethnic group traditionally divided into tribes. Historically, the inhabitants of this desert, which spreads northward into Syria, eastward into Iraq, and southward into Saudi Arabia, were Bedouin pastoralists (Salibi 1998). Today around 98% of the 7.9 million Jordanians are of Arab origin, along with other small minorities such as Circassians (1%) and Armenians (1%). Culturally, the official language is Arabic; in terms of religion, over 92% of the people are Sunni Muslims, around 6% are Christians (mostly Greek Orthodox, but some Greek and Roman Catholics, Syrian Orthodox, Coptic Orthodox, Armenian Orthodox, and Protestant denominations), and the remaining 2% are Shia Muslim and Druze populations (Central Intelligence Agency 2013–2014).

Historically, the term "Bedouin" has denoted both a nomadic way of life and a group identity. Bedouins were the original settlers in the Middle East. From the Arabian Peninsula, their original home, they spread out and now live in desert regions of all the countries between the Arabian Gulf and the Atlantic. The Arab conquest of North Africa in the seventh century AD caused a wide dispersion, such that today the Arab culture is extended over North Africa and beyond.

The availability of historical and ethnical information about Jordanian peoples (Salibi 1998) contrasts with the lack of information about the genetic background of these groups. As far as we know, previous genetic information about Jordanian populations includes two studies on uniparental markers analyzed in Bedouins and general Jordanians (Flores et al. 2005; González et al. 2008) and a survey of a reduced number of *Alu* insertions, fewer than those analyzed in this study, in a sample of the general Jordanian population (Bahri et al. 2011). Variation in the uniparental markers (Y-chromosome and mitochondrial DNA) underlines the genetic outlier position of Bedouins, whereas general Jordanians are relatively close to the neighboring Middle East groups.

To provide new insight from autosomal gene variation about the distinctiveness of Bedouins suggested by uniparental markers, this study genotyped 18 autosomal *Alu* insertions in two different Jordanian samples: one of individuals of Bedouin origin and the other of considered as representative of the general Jordanian population. The main objective was to test whether autosomal markers confirm the previous population differentiation within Jordan revealed by uniparental markers. The secondary objectives were to determine the degree of genetic heterogeneity in Jordan, the genetic position of Bedouins and general Jordanians in the general context of the Mediterranean and the Middle East areas, and to provide new data about the potential influence of Bedouins, as representatives of Arab origins, in North Africa.

In this study 18 *Alu* insertion markers were selected because they are a useful tool for population studies on the basis of their identity by descent, known ancestral state, and selective neutrality (Cordaux et al. 2006; Cordaux and Batzer 2009). The potential usefulness of specific *Alu* loci as ancestry-informative markers has been explored to detect differences between populations and to estimate biogeographical ancestry (Luizon et al. 2007). Polymorphic *Alu* insertions have also been used in several studies tackling many historical and demographical questions (González-Pérez et al. 2010; Terreros et al. 2009).

Materials and Methods

Samples and Markers

A total of 96 blood samples from healthy unrelated individuals of both sexes, collected from different regions of the north, center, and south of Jordan, were classified into two groups: Bedouins (n = 43) and general Jordanians (n = 53). Collection, classification, and DNA isolation of all samples were carried out by researchers at Yarmouk University. All participants were selected because their relatives were born in Jordan for at least three generations. The general Jordanian group was mostly sampled in Jordanian cities, such as Amman and Irbid. The Bedouin samples were collected from the Badia desert in collaboration with the Jordan Badia Research and Development Center. These samples were classified according to the towns or village in which the subject and the subject's parents and grandparents were born, as well as

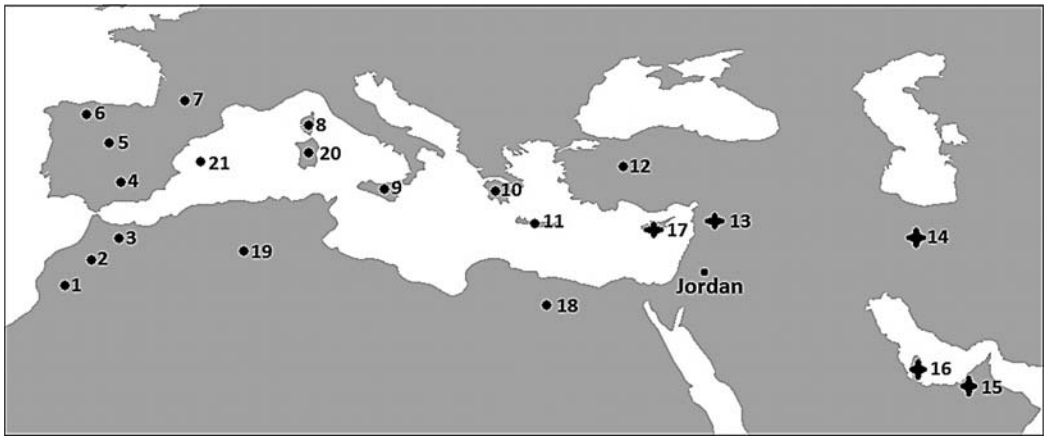

FIGURE 1. Geographic location of the populations analyzed in the study: populations analyzed using 18 *Alu* (circles) and populations analyzed using the only eight *Alu* insertion polymorphisms available in the literature (crosses). 1: Amizmiz Berbers (AMBE), 2: Middle Atlas Berbers (MABE), 3: Northeast Moroccan Berbers (NEBE), 4: Southern Spain, 5: Central Spain, 6: Northern Spain, 7: France, 8: Corsica, 9: Sicily, 10: Greece, 11: Crete, 12: Turkey, 13: Syria, 14: Iran, 15: United Arab Emirates, 16: Baharain, 17: Cyprus, 18: Siwa Berbers (Siwa), 19: Mzab Berbers (Mzab), 20: Sardinia, 21: Menorca.

the last names of the families and the tribes they belong to. All subjects signed an informed consent, and the study was approved by the ethical committees of the University of Barcelona and Yarmouk University. The protocols and procedures used in this research were in compliance with the Declaration of Helsinki.

Genomic DNA was extracted from blood cells using a Blood DNA Midi Kit (Omega Bio-Tek, Norcross, GA) according to the manufacturer's procedure. Eighteen human-specific *Alu* polymorphic elements (A25, ACE, APOA1, B65, CD4, D1, DM, FXIIIB, HS2.43, HS4.32, HS4.69, PV92, Sb19.12, Sb19.3, TPA25, Ya5NBC221, Yb8NBC120, and Yb8NBC125) located on 10 different chromosomes (Chr 1, 3, 8, 11, 12, 16, 17, 19, 21, and 22) were typed by PCR amplification and electrophoretic analysis. Primers and amplification conditions have been previously described (Batzer and Deininger 1991; González-Pérez et al. 2010; Stoneking et al. 1997). Positive and negative controls for the polymorphisms examined were included in all PCR runs.

Statistical Analyses

Standard human population genetic parameters were obtained. Allele frequencies were estimated by direct counting. Hardy–Weinberg equilibrium was assessed by an exact test based on the Markov chain method (Guo and Thompson 1992) using Genepop, version 4.2 (Rousset 2008). Heterozygosity values by locus and population according to Nei's formula (Saitou and Nei 1987) were calculated using Genetix version 4.05 (Belkhir et al. 1996–2004). Differences in allele frequency distribution between the two Jordanian samples and, in general, between all pairs of populations were assessed by an exact test based on Fisher's exact probability test using the Genepop software.

Genetic distances (Reynolds's distance) and hierarchical analyses of molecular variance (AMOVA) were estimated using Phylip, version 3.69 (Tuimala 2006), and Arlequin, version 3.5 (Excoffier et al. 2005). Genetic relationships among populations were assessed by a principal component (PC) plot using the FactoMineR package of R (Josse 2008).

Comparisons with Published Data Sets

To evaluate the genetic position of Bedouins and general Jordanians in the Mediterranean and the Middle East areas, two comparative analyses were carried out, based on population data available in the literature. The main analysis focused on the whole Mediterranean area using 18 polymorphic *Alu* insertions in 16 populations, as indicated in Figure 1. These populations comprised three Spanish regions (southern Spain: Andalusia; northern Spain: Asturias; central Spain: Sierra de Gredos), southern France (Toulouse), Turkey (Anatolia Peninsula), Greece (Attica region), five Mediterranean islands (Sardinia, Corsica, Sicily, Crete, and Minorca), and five Berber groups from Morocco, Algeria, and Egypt. The Moroccan samples came

Table 1. *Alu* Insertion Frequencies, Gene Diversities, and *p*-Values of Hardy-Weinberg (H-W) Equilibrium in Bedouins and General Jordanians

Locus	Bedouin				General_Jordan				Frequency Range	
	N	Insertion	Heterozygosity	H-W	N	Insertion	Heterozygosity	H-W	High	Low
DM	25	0.640	0.470	0.187	37	0.405	0.489	0.048	Siwa (0.356)	Sicily (0.674)
HS4.69	42	0.452	0.501	0.530	50	0.440	0.498	0.011	Mzab (0.287)	Bedouin (0.452)
HS4.32	38	0.776	0.352	0.059	51	0.824	0.294	0.638	Central Spain (0.493)	General_Jordan (0.824)
Ya5NBC221	34	0.941	0.112	1.000	41	0.939	0.116	0.121	Southern Spain (0.725)	Northern Spain (0.978)
Sb19.3	42	0.750	0.380	1.000	53	0.755	0.374	0.259	AMBE (0.613)	Sardinia (0.945)
HS2.43	38	0.000	0.000	<0.001	50	0.080	0.149	0.261	Bedouin (0)	Sardinia (0.171)
Sb19.12	43	0.267	0.396	0.133	53	0.274	0.401	1.000	Mzab (0.135)	Central Spain (0.4)
B65	40	0.500	0.506	0.536	48	0.563	0.497	0.140	Siwa (0.150)	Crete (0.647)
Yb8NBC120	33	0.394	0.485	0.270	43	0.430	0.496	1.000	Siwa (0.023)	AMBE (0.569)
YbNBC125	41	0.134	0.235	1.000	53	0.226	0.354	0.048	Siwa (0.065)	General Jordan (0.226)
PV92	27	0.241	0.373	0.613	35	0.143	0.248	0.526	Sicily (0.079)	MABE (0.368)
D1	39	0.385	0.479	0.005	51	0.412	0.489	<0.001	United Arab Emirates (0.08)	Sicily (0.474)
FXIIIB	43	0.302	0.427	1.000	52	0.298	0.423	t0.001	Iran (0.214)	Turkey (0.584)
A25	43	0.105	0.190	0.372	53	0.132	0.231	0.575	Syria (0)	Central Spain (0.175)
CD4	37	0.797	0.328	0.616	43	0.663	0.452	0.041	Crete (0.593)	Bedouin (0.797)
TPA25	38	0.487	0.506	0.204	49	0.551	0.500	0.251	Siwa (0.317)	NEBE (0.661)
APOA1	38	0.868	0.232	0.098	50	0.950	0.096	0.100	Siwa (0.84)	France (0.981)
ACE	42	0.202	0.327	0.657	53	0.387	0.479	0.772	Bedouin (0.202)	Central Spain (0.467
Average heterozygosity			0.349±0.146				0.366±0.142			

Abbreviations: N: number of chromosomes; AMBE: Amizmiz Berbers, MABE: Middle Atlas Berbers, NEBE: Northeast Moroccan Berbers, MZAB: Mzab Berbers. Variation ranges are given according to data from reviewed literature for populations represented in Figure 1.

from High Atlas (Amizmiz Berbers), Middle Atlas (Berbers from the Khenifra region), and northeast Moroccan Berbers (Bouhria area). Other Berber samples were Mzab from Algeria and Siwi from the Siwa Oasis in Egypt (González-Pérez et al. 2007, 2010).

To obtain a geographically more comprehensive data set in the Middle East, a second comparative analysis adding samples from Iran, Cyprus, United Arab Emirates, Syria, and Bahrain was performed. This analysis was based on data from only eight *Alu* markers available in the literature (Bahri et al. 2013; González-Pérez et al. 2010; Romualdi et al. 2002; Stoneking et al. 1997).

Results

Alu insertion frequencies and gene diversities in Bedouins and general Jordanians are shown in Table 1. The highest insertion frequencies correspond to the Ya5NBC221 locus in Bedouins (0.941) and to the APOA1 locus in general Jordanians (0.950); the lowest frequency values are found in the HS2.43 locus (0 in Bedouins and 0.08 in general Jordanians). As expected, the lowest gene diversity values correspond to loci showing extreme allele frequencies: Ya5NBC221 ($H = 0.112$) in Bedouins, APOA1 ($H = 0.096$) in general Jordanians, and HS2.43 in both Bedouins ($H = 0$) and general Jordanians ($H = 0.149$). The highest diversity values corresponding to loci with frequencies close to 0.5 were B65 and TPA25 ($H = 0.506$) in Bedouins and TPA25 ($H = 0.500$) in general Jordanians.

The test for Hardy-Weinberg equilibrium, after Bonferroni correction, indicates significant deviations only for D1 ($p = 0.0000$) and FXIIIB ($p = 0.0000$) in general Jordanians. Chance is the most likely explanation for this departure because there is no particular reason to expect a Hardy-Weinberg deviation for these markers, and the deviations are not shared by the two population samples.

Comparison of the two Jordanian samples shows that the average gene diversity in general Jordanians (0.366 ± 0.142) is only slightly higher than in Bedouins (0.349 ± 0.146). In general,

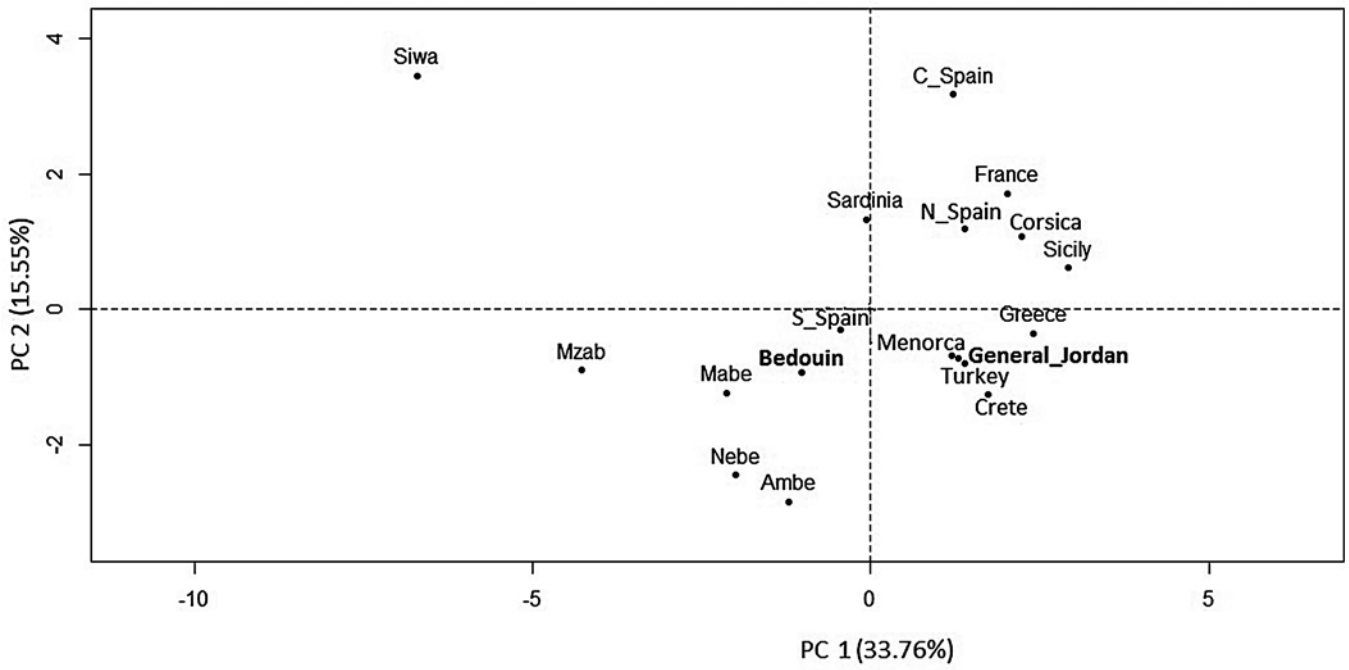

FIGURE 2. PC plot of 16 populations from the Mediterranean area based on the variation of 18 *Alu* insertion polymorphisms.

the Jordanian frequencies and gene diversities show values within the variation range of other Mediterranean populations. Extreme values were found only for HS2.43 and ACE in Bedouins, corresponding to the lowest frequencies in the literature revised, and for HS4.69 and CD4 in Bedouins and HS4.32 and Yb8NBC125 in general Jordanians, which are the highest values in the literature revised. Allele frequency comparisons show significant differences across all 18 loci (p = 0.038; 36 df) between Bedouins and general Jordanians. Locus-by-locus comparisons indicate significant differences for DM (p = 0.015), HS2.43 (p = 0.01), and ACE (p = 0.005) markers.

Concerning population relationships, the PC analysis based on the whole set of *Alu* insertion polymorphisms in 16 populations indicates that the two first axes account for 49.31% of the total genetic variance (Figure 2). The first axis (33.76% of the total variance) clusters Bedouins along with North African samples with a certain separation from the rest. Within this group, the Siwa Oasis sample appears in the most distant position. The second component underlines the separation of the Western Mediterranean samples (central Spain, France, north of Spain, Corsica, and Sicily) from Eastern Mediterranean groups (Greece, Turkey, Crete) and general Jordan. When the analysis was repeated to remove the effect of the Siwa Oasis sample (data not shown), the observed pattern was substantially the same. Population relationships within Jordan indicate that the Bedouins, closer to North Africans, show an intermediate position between these populations and Eastern Mediterraneans, whereas general Jordanians cluster with Eastern Mediterranean populations. Results from both genetic distance analysis and AMOVA support the distribution revealed by the PC analysis. Thus, the average Reynolds genetic distance of Bedouins to the remaining populations (31×10^{-3}) is of the same order of magnitude as the average distance among all the populations (32×10^{-3}), whereas the distance of general Jordanians to Middle Eastern populations (23×10^{-3}) is lower than that corresponding to Bedouins (28×10^{-3}; Table 2).

The hierarchical analysis of the allele frequency variance, classifying the populations into two groups (North Africa plus Bedouins, and all others) indicates a significant variation between the two groups, as plotted along the first PC axes (F_{ST} = 3.4%, $p < 0.001$; F_{CT} = 1.6%, $p \leq 0.001$; F_{SC} = 1.8%, $p < 0.001$). Likewise, the population distribution associated with the second PC component is also supported by the AMOVA results. In this case, the genetic variance between the three population groups formed by North Africa plus Bedouins, Middle East plus general Jordanians, and

Table 2. Reynolds's Genetic Distances Estimated among All 18 Populations using 18 Alu Insertion Markers

	Bedouin	GJ	Greece	Crete	Turkey	Asturias	C_Spain	Andalusia	Balearic_I	France	Corsica	Sardinia	Sicily	AMBE	MABE	NEBE	MZAB	Siwa
Bedouin	—																	
GJ	0.023	—																
Greece	0.028	0.023	—															
Crete	0.028	0.019	0.008	—														
Turkey	0.027	0.028	0.005	0.009	—													
Asturias	0.029	0.012	0.014	0.016	0.019	—												
C_Spain	0.039	0.034	0.024	0.029	0.035	0.017	—											
Andalusia	0.034	0.019	0.027	0.024	0.023	0.016	0.030	—										
Balearic_I	0.026	0.020	0.012	0.007	0.012	0.015	0.026	0.019	—									
France	0.020	0.018	0.011	0.014	0.014	0.009	0.016	0.021	0.016	—								
Corsica	0.028	0.026	0.008	0.012	0.011	0.016	0.018	0.024	0.008	0.011	—							
Sardinia	0.029	0.030	0.026	0.022	0.028	0.027	0.034	0.034	0.025	0.017	0.020	—						
Sicily	0.023	0.018	0.017	0.016	0.022	0.015	0.023	0.028	0.016	0.013	0.010	0.033	—					
AMBE	0.027	0.017	0.039	0.034	0.041	0.030	0.048	0.025	0.031	0.039	0.043	0.052	0.035	—				
MABE	0.028	0.020	0.025	0.023	0.026	0.022	0.033	0.019	0.027	0.028	0.036	0.033	0.040	0.018	—			
NEBE	0.024	0.022	0.024	0.023	0.024	0.023	0.042	0.023	0.022	0.031	0.030	0.038	0.036	0.017	0.012	—		
MZAB	0.034	0.036	0.045	0.037	0.042	0.042	0.050	0.033	0.036	0.045	0.049	0.035	0.059	0.027	0.010	0.020	—	
Siwa	0.076	0.085	0.105	0.101	0.102	0.087	0.084	0.077	0.091	0.091	0.094	0.075	0.100	0.102	0.065	0.083	0.057	—

Abbreviations: AMBE: Amizmiz Berbers, GJ, general Jordanians, MABE: Middle Atlas Berbers, NEBE: Northeast Moroccan Berbers, MZAB: Mzab Berbers.

Western Mediterranean also indicates statistically significant variation (F_{ST} = 3%, $p < 0.001$; F_{CT} = 1.2%, $p \leq 0.001$; F_{SC} = 1.8%, $p < 0.001$).

A second comparison, partial because it is based on the variation of only eight *Alu* markers but including a wider number of populations (21; PC analysis population plot not shown) also separates Bedouins from general Jordanians. However, in this case, the relative position of the two Jordanian samples versus other populations shows some differences compared with results of the previous analysis. For instance, the general Jordanian group tends to be closer to Western Mediterranean than to Middle East populations.

Discussion

This study provides the first comparative genetic analysis between two Jordanian ethnic groups selected according to strict and reliable criteria, Bedouins and general Jordanians, by analyzing 18 autosomal *Alu* insertion polymorphisms. In general, Jordanian allele frequencies and gene diversity estimates show intermediate values within the variation range of other Mediterranean populations. Compared with previous data, *Alu* frequencies in general Jordanians are substantially similar to those previously reported for a partial subset of *Alu* markers (10 of the 18) in a Jordanian sample (Bahri et al. 2011), except for two *Alu* markers: D1 (p = 0.02) and HS4.32 (p = 0.006). These few differences could be related to the potentially diverse origin of the individuals sampled in each case.

Concerning differentiation within Jordan, this study indicates a significant difference between Bedouins and urban inhabitants of Jordan (p = 0.038). Of the 18 autosomal insertion markers, three are statistically different: DM (p = 0.015), HS2.43 (p = 0.01), and ACE (p = 0.005). Considering the relatively small sample size, the genetic differences point to a clear separation between these two groups. This could be related to the fact that in recent times urban areas have been subject to several external influences but Bedouins have conserved their own genetic background because of their nomadic and isolated lifestyle. In fact, among all the considered populations in the comparative analyses, Bedouins appear to be the most diverse group, in contrast to general Jordanians, who cluster with other Middle Eastern groups. However, we should not ignore the fact that the

markers analyzed (number and/or low mutation rate) may be not powerful enough to uncover relatively recent demographic events. In this way, the small inconsistencies in the relative genetic position of the two Jordanian samples with respect to other populations found in the two analyses using different numbers of *Alu* loci (18 vs. 8) most likely reflect the role of chance when few markers are used to characterize human populations. In any case, the genetic differentiation observed between Bedouin and general Jordanians using 18 *Alu* insertions polymorphisms is consistent with the differentiation reported from the mitochondrial DNA and Y-chromosome uniparental loci in two recent studies (Flores et al. 2005; González et al. 2008). Assuming that Bedouins represent the original substrate of current-day Jordanians, the differentiation found between them and the general Jordanian group could be explained by a higher Mediterranean influence in the general population due to Jordan's position as a crossroads since ancient times and/or the recent contribution of immigrants in the last half of the twentieth century.

In a Mediterranean context, Bedouins seem to be closer to North African groups, whereas general Jordanians tend to group with North Mediterraneans, especially with the easternmost populations. Greater genetic proximity of Bedouins and North Africans could be explained by the impact of Arabic expansion into North Africa in the seventh century. However, the outlier position of the Egyptian sample from Siwa, also acknowledged in other studies (Athanasiadis et al. 2007), together with the significant lack of *Alu* data in most points of North Africa, does not allow definite conclusions.

In summary, this *Alu* population analysis reinforces the genetic distinctiveness of Bedouins, suggesting that they had an important role in the peopling of Jordan and probably constitute the original substrate of this population. Their relative genetic proximity to North African groups supports the idea that they share the genetic background of the populations that spread the Arab culture into North Africa. The genetic differentiation found between the two groups of current Jordanian population could be attributed to some extent to a relatively recent contribution of immigrants coming from neighboring areas. However, this conclusion needs to be confirmed with additional markers to avoid random effects associated with the use of a low number of markers.

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Result II

Zanetti et al., 2015

Potential signals of natural selection in the top risk loci for Coronary Artery Disease: 9p21 and 10q11

Daniela Zanetti, Robert Carreras-Torres, Esther Esteban, Marc Via, and Pedro Moral

PLoS One. 2015 Aug 7;10(8):e0134840.

Resumen en castellano

Potenciales señales de selección natural en los loci de riesgo de la enfermedad arterial coronaria: 9p21 y 10q11

La enfermedad arterial coronaria (CAD) es una enfermedad compleja y la principal causa de muerte en el mundo. Poblaciones de diferente ascendencia no siempre comparten los mismos marcadores de riesgo. Recientemente han sido detectadas diferencias poblacionales en los loci de susceptibilidad a la CAD. Procesos demograficos y/o de selección natural son las fuerzas evolutivas más importantes que podrían generar diferencias poblacionales respecto a mutaciones y a patrones de desequilibrio de ligamiento (LD).

Este estudio propuso estudiar 384 polimorfismos de nucleótido único (SNPs) localizados en cuatro regiones genómicas asociadas con CAD (1p13, 1q41, 9p21 y 10q11) en un conjunto de 19 poblaciones de Europa, Oriente Medio y África del Norte y también utilizando las muestras Asiáticas y Africanas Sub-Saharianas del Proyecto de los 1000 Genomas. El objetivo fue explorar por primera vez si la variabilidad genética en estas regiones genómicas podría explicarse mejor por demografía o por eventos de selección natural.

Los resultados indicaron diferencias significativas en la variación genética y en los patrones de LD entre las poblaciones estudiadas que probablemente explican las diferencias poblacionales encontradas en los marcadores de susceptibilidad a la CAD. La estructuración genética observada fue significativa en el contexto de los tres continentes (FST = 0,085; p <0,0001) y también en Europa y en el área mediterránea (FST = 0,017; p <0,0001). En cuanto a los bloques de LD, este estudio señaló una alta variabilidad interpoblacional en los niveles de LD y, a veces, una localización cromosómica diferente de marcadores de riesgo CAD en poblaciones de diferente ascendencia. Además los resultados

de este trabajo son consistentes con potenciales señales de selección positiva en la región 9p21 y de selección equilibradora en las regiones 9p21 y 10q11. En concreto, en Europa tres marcadores de riesgo CAD en la región 9p21 (rs9632884, rs1537371 y rs1333042) mostraron señales consistentes de selección positiva. Estos SNPs mostraron un gradiente de frecuencia de sur a norte, de acuerdo con las tasas de incidencia de la CAD.

Los polimorfismos seleccionados podrían estar en LD con un polimorfismo beneficioso aún desconocido que podría estar relacionado con CAD. Por otro lado, los loci seleccionados positivamente podrían estar relacionados con otros caracteres de riesgo. En el caso del locus 9p21, varios marcadores genéticos han sido asociados con distintos tipos de cáncer, glaucoma, aneurismas, y con Alzheimer. Debido a efectos de pleiotropía, las señales de selección encontradas podrían estar relacionadas con diferentes características de riesgo localizadas en la misma región genómica. Además, las señales encontradas han sido relativamente débiles y podrían explicarse a través de modelos de adaptación poligénica o de *soft sweep*, modelos especialmente relevantes para los rasgos complejos, como las enfermedades cardiovasculares, donde varios loci contribuyen en la determinación de la enfermedad.

Los resultados de este estudio son compatibles con un papel potencial de la selección natural en la CAD, pero el papel de los procesos demográficos no puede ser descartado y serían necesarios más análisis para comprobar o descartar las señales de selección natural observadas en este estudio.

Supervisor's report of the involvement of the PHD student in the development of this paper

Dr **Pedro Moral Castrillo**, Professor at the Department of Animal Biology of the University of Barcelona, and the Dr. **Marc Via García**, Professor at the Department of Psychiatry and Clinical Psychobiology of the University of Barcelona, both supervisors of the doctoral thesis "Genetics of human populations: evolutionary and epidemiological applications" by **Daniela Zanetti**, hereby certify that the participation of the above student in the article : "**Potential signals of natural selection in the top risk loci for Coronary Artery Disease: 9p21 and 10q11**", published in the *PLoS One*, consisted in the following tasks:

- Participation in the design of the study and selection of the analyzed markers
- Creation of the genotype database and selection of available results in the literature for statistical comparison
- Statistical analysis of the data
- Redaction of the Manuscript

In addition, none of the co-authors of this article have used the results of this work in any implicit or explicit way to develop another doctoral thesis. As a consequence, this article forms part of the doctoral thesis of Daniela Zanetti exclusively.

Signed by Dr. Pedro Moral Castrillo and Dr. Marc Via García

Barcelona, 1 September 2015

PLOS ONE

RESEARCH ARTICLE

Potential Signals of Natural Selection in the Top Risk Loci for Coronary Artery Disease: 9p21 and 10q11

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Abstract

Background

Coronary artery disease (CAD) is a complex disease and the leading cause of death in the world. Populations of different ancestry do not always share the same risk markers. Natural selective processes may be the cause of some of the population differences detected for specific risk mutations.

Objective

In this study, 384 single nucleotide polymorphisms (SNPs) located in four genomic regions associated with CAD (1p13, 1q41, 9p21 and 10q11) are analysed in a set of 19 populations from Europe, Middle East and North Africa and also in Asian and African samples from the 1000 Genomes Project. The aim of this survey is to explore for the first time whether the genetic variability in these genomic regions is better explained by demography or by natural selection.

Results

The results indicate significant differences in the structure of genetic variation and in the LD patterns among populations that probably explain the population disparities found in markers of susceptibility to CAD.

Conclusions

The results are consistent with potential signature of positive selection in the 9p21 region and of balancing selection in the 9p21 and 10q11. Specifically, in Europe three CAD risk markers in the 9p21 region (rs9632884, rs1537371 and rs1333042) show consistent signals of positive selection. The results of this study are consistent with a potential selective role of CAD in the configuration of genetic diversity in current human populations.

Introduction

Coronary artery disease (CAD) is a complex disease and the main cause of death in the world. In 2007, the first genome-wide significant risk region, 9p21, was simultaneously discovered by two independent groups [1, 2] and was subsequently confirmed by multiple investigators around the world. Currently, there are a total of 50 variants predisposing to CAD of genome-wide significance confirmed in independent populations [3]. Out of these 50 risk loci, 15 are associated with conventional risk factors for CAD: seven with low-density lipoprotein-cholesterol (LDL-C); one with high-density lipoprotein (HDL); two with triglycerides; four with hypertension, and one with coronary thrombosis. The remaining 35 variants operate through mechanisms yet to be determined [3].

Most genome wide association studies (GWAS) for CAD have been performed on populations of European descent, but increasing numbers of such investigations are now performed also on populations of Asian or African ancestry. In the literature currently available, some of the genetic effects observed are shared among ethnic groups but many times genetic effects are different across populations of different ancestry. The latter is the case of the 9p21 locus, which has been documented in Europeans and also in other ethnic groups including East and South Asians, but not among African Americans [4]. Demography and selection are the most important evolutionary forces that shape the population-specific patterns of mutations and linkage disequilibrium (LD) identified across populations of different ancestry. Demographic phenomena such as population expansions, subdivisions and bottleneck events could underlie differences among populations in a uniform way across genes. On the other hand, there are evolutionary processes with locus-specific effects. The genetic basis of common complex diseases may have partially been shaped by positive selection events, which simultaneously increased fitness and susceptibility to the disease. An additional difficulty to detect the role of selection is that methods to detect it have historically been challenged by the confounding effects of demography [5]. In any case, examples of positive selection have been identified in complex diseases such as type 1 diabetes, rheumatoid arthritis, or Crohn's disease [6].

Concerning CAD risk regions, in the current literature there are discrepancies regarding the role of natural selection. A recent survey proposed natural selection as a possible explanation for the observed differences between Africa, East Asia, America, and Oceania in risk allele frequencies (RAFs) for eight CAD risk single nucleotide polymorphisms (SNPs) [7]. Another study reported evidence for selection at several SNPs identified through GWAS on sets of genes implicated in cardiovascular diseases [8]. In addition, Soranzo et al. identified one haplotype in a region of long-range LD (12q24) that contains disease loci for CAD, hypertension and type I diabetes, and that recently spread by positive selection in Europeans [9]. On the contrary, a recent survey affirmed that genetic differences for CAD among world-wide populations are due to random and demographic processes [6]. However, the conclusions of this last paper were not demonstrated through the use of different methodological approaches. Indeed, the authors used two tests (iHS and LRH) exclusively based on the same class of analytical method (LD decay) to search for signals of selection in CAD risk loci. Despite all the studies performed so far, the genetic architecture of CAD is not completely understood yet. In CAD, as in any complex trait, risk variants at many different loci may contribute to the phenotype each with a small effect. By combining evidence from GWAS with evidence from selection scans, it may be possible to separate true causative regions from the background noise inherent in GWAS [8]. The role that natural selection plays in CAD population differentiation may be a good tool to improve the knowledge of this complex trait.

Population differences in risk loci associated to CAD were recently detected for the 1p13, 1q41, 9p13, and 10q11 regions. These genomic regions showed disparities in the specific risk markers associated with CAD between European and North African samples [10].

The present work is centred on these four genetic regions (1p13, 1q41, 9p21 and 10q11) to explore whether the population genetic diversity is better explained by demographic or by natural selection effects.

To do this, we have analysed these risk regions in a set of North European and Mediterranean populations. Several specific tests to detect positive and/or balancing selection were performed. In addition, these analyses were expanded to populations from Asia and Africa looking for signatures of selection shared across continents or belonging to a specific population group.

Materials and Methods

Ethics statement

The study has been specifically approved by the Ethical Committee of the University of Barcelona (Institutional Review Board: IRB00003099) and all the participants provided a written informed consent.

Sample description

Nineteen population samples from Europe, Middle East and North Africa were genetically tested. DNA samples of 868 healthy unrelated individuals of both sexes having their relatives for at least three generations born in the same geographical region were analyzed.

Population details of all samples, including sample size, geographic origin and coordinates are recorded in S1 Table. The geographic distribution of the analyzed samples is displayed in Fig 1. Europe is represented by samples from Poland, Spain (4 populations), France (2 populations), Italy (2 populations), Bosnia-Herzegovina, Greece, and Turkey. The Middle East is represented by two populations from Jordan and the North African area is represented by samples from Tunisia, Morocco (2 populations), Algeria and Libya. Genetic data from European (CEU, GBR, FIN, and TSI), Sub-Saharan African (LWK and YRI) and Asian (JPT and CHB) samples from the 1000 Genomes Project [11] were also included in the analyses (S1 Table).

Polymorphisms and genotyping

Genomic DNA was extracted from blood cells using a Blood Midi kit (Omega Biotek, USA) according to manufacturer's procedures. DNA samples were genotyped for a combined set of 384 SNPs using a Custom GoldenGate Panel (Illumina Inc., San Diego, CA). These polymorphisms were located in four loci previously associated and replicated in independent studies with CAD [12, 3, 13, 14, 15], specifically the 1p13 (61SNPs), 1q41 (38 SNPs), 9p21 (159 SNPs), and 10q11 (126 SNPs) chromosomal regions.

SNPs were selected as a representative set of the common variation in the four genomic regions, according to the following criteria: i) average coverage of 1 SNP every 1.5 kb, ii) minor allele frequency (MAF) higher than 0.05 in CEU and TSI HapMap populations, iii) given priority to markers not in linkage disequilibrium (LD) ($r^2<0.8$) in European populations, and iv) prioritizing markers previously associated with CAD [4]. These criteria were applied giving preference to tag SNPs. Genomic location of genetic variants is shown in S2 Table.

In addition, all the variation concerning these four genomic regions reported in the 1000 Genomes Project was used to perform three specific selection analyses: Tajima's D, Long Range Haplotype (LRH) test and F_{ST} tests.

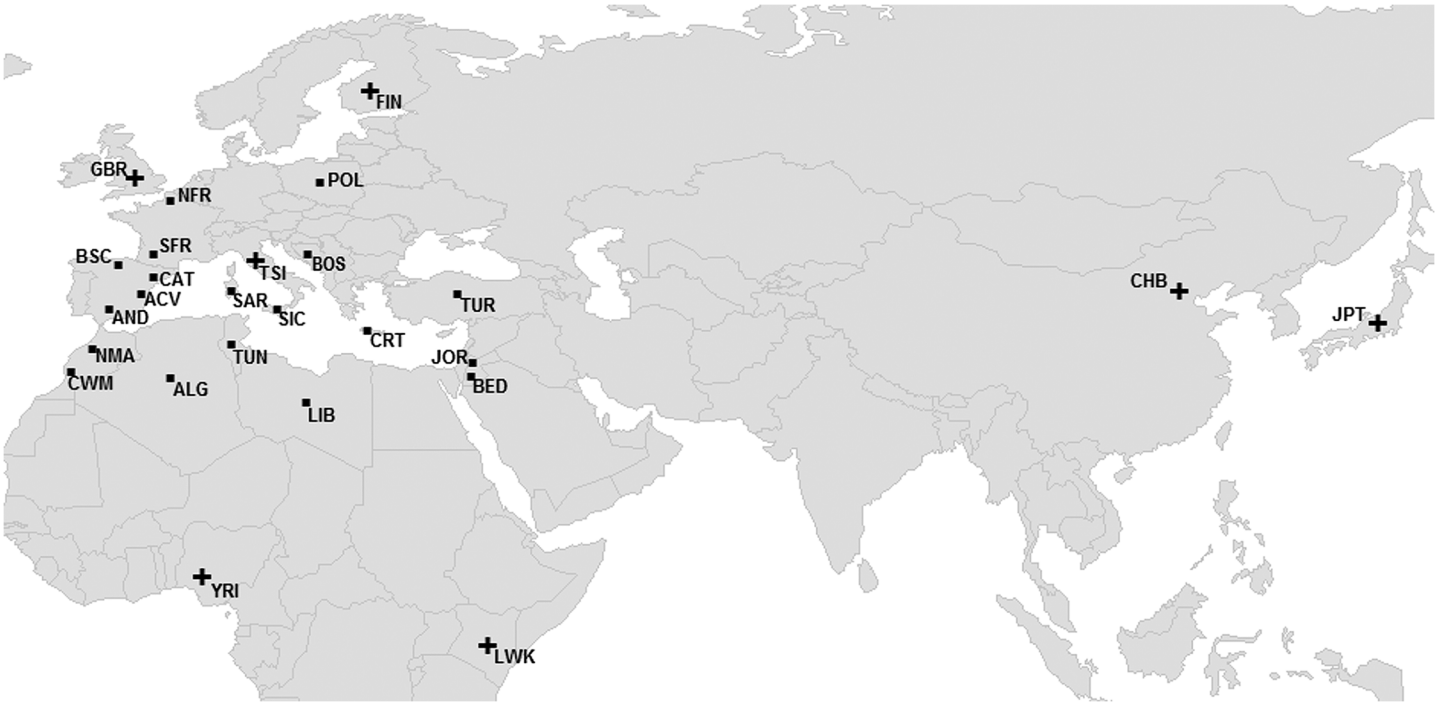

Fig 1. Geographic distribution of European, African and Asian samples. See S1 Table for abbreviation codes. Symbols: "■" samples genotyped in this study, "+" data from the 1000 Genomes Project.

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Data Cleaning and Quality Control

Genotyping rate per SNP and individual, cryptic relatedness, and LD pruning ($r^2 \geq 0.8$) were assessed using PLINK version 1.07 [16]. Individuals with more than 5% of missing genotypes were eliminated. Non-polymorphic SNPs or SNPs with genotyping rate lower than 0.95 were also removed from the analyses.

Population allele frequencies and heterozygosity calculations were performed using *PopGenkit* R software package [17]. Fitting to Hardy-Weinberg equilibrium in each population was calculated by means of Arlequin v3.5 software [18].

Population Structure Analyses

Genetic structure was assessed by molecular variance (AMOVA) using Wright's F-statistics in the European and Mediterranean area and, in a broader context, in the European, African and Asian continents. Populations were clustered according to geographic criteria. Middle Eastern samples were clustered into the South European group due to affinities in their genetic distances. The samples were clustered in: 1) North Europe, South Europe, and North Africa, and 2) North Europe, South Europe, North Africa, Sub-Saharan Africa and Asia. AMOVAs were carried out using Arlequin v3.5 [18].

Genetic relationships among populations were assessed by Reynolds genetic distance and by a principal component (PC) analysis calculated through the *Adegenet* [19] and *FactoMineR* R packages [20].

The LD blocks based on the LD measure D′ confidence interval [21] were performed in the four genomic regions using Haplot software [22]. These analyses were performed twice: first, considering all markers in all samples and, second, taking into account only the chromosomal fragments where markers previously associated in Europeans [21, 13, 22], Africans [10, 23, 24]

and Asians [25] are located. Permutation procedures to obtain a Monte Carlo statistical significance were used for each chromosomal region in order to evaluate population differences in LD structure through the VarLD software version 1.0 [26]. This analysis was carried out using 150 randomly selected individuals for each different population group (North Europe, South Europe, North Africa, Sub-Saharan Africa, and Asia) to avoid biases due to differences in sample size. The LD statistics (D' and r^2) for each pair of risk SNPs in each population analyzed were calculated through the Haploview software version 4.2 [27].

Selection Analyses

Detection of potential loci under selection was assessed using different methods. The first method used is based on the probability of observing locus by locus AMOVA statistics as a function of heterozygosity, given a null distribution generated under a hierarchically-structured island model of population differentiation [28]. This test detects loci under selection from genome scans that contrast patterns of genetic diversity within and between populations. A total of 20000 coalescent simulations in 50 groups, with 100 simulated demes per group were performed. The observed locus-specific measures of population differentiation (F_{ST}) were compared to a null distribution obtained by simulation samples. The P-value of each locus was estimated from the joint distribution of heterozygosity and F_{ST} using a kernel density estimation procedure. The null distribution generated was summarized by quantiles of the joint distribution. The 1% and 99% quantiles of the distribution correspond to markers potentially under balancing or directional selection, respectively, at the 1% level, without multiple-test correction and assuming one-tailed test. This method was performed using Arlequin v3.5 software [18].

Moreover, the spatial ancestry (SPA) analysis was used to detect positive signatures of selection [29]. In this analysis, SNP data were used to model allele frequency distributions in a geographic space. Applying the SPA approach, polymorphisms showing steep geographic gradients in allele frequencies can be identified through SPA scores reflecting the steepness of the geographic gradient. Large SPA scores are indicators of potential selection. In this study we focused on SPA scores above the 99th percentile, based on the 367 SNPs analysed. In order to detect continental adaptation events, analyses were performed only in Europe and North Africa. Asian and Sub-Saharan African samples were not tested for the SPA scores due to the low number of available populations for these geographic regions.

Spatial distribution of mean MAF for one of the three CAD SNPs potentially positively selected across populations was mapped using the geostatistical method known as kriging from the ArcGIS software (ESRI, Redlands, CA, USA). Since anisotropy was not detected in the semivariogram, we used the ordinary spherical interpolation kriging method [30]. Finally, the Tajima's D [31], the extended haplotype homozygosity (EHH) and the cross-continental F_{ST} tests were conducted in three populations of the larger dataset of the 1000 Genomes Project (CEU, CHB, and YRI) through the web tool 1000 Genome Selection Browser 1.0 [32]. The Tajima's D test was performed using windows of 3-kb to search signatures of balancing selection. The EHH test was applied to validate loci under positive selection found in previous tests, using a larger chromosome region of 20-Mb. The significance of the three tests was assessed by the rank score tracks, which provided a comparison to the rest of the genome, calculated by means of the web tool 1000 Genome Selection Browser 1.0 [32]. They were calculated by empirical comparisons sorting all the scores genome-wide and determining the-log10 of the rank divided by the number of values in the distribution, taking the upper tail for the F_{ST} and the EHH tests, and the lower tail for the Tajima's D test. The p-values were assigned on the basis of the rank score tracks. In this study, Tajima's D, EHH average and F_{ST} scores above the 95th percentile of the top extreme genome-wide distribution were considered as significant. All

p-values were corrected for multiple comparisons applying the false discovery rate (FDR) method [33] by means of the *stats* R package [17].

Results

Genotyping and quality control

After pruning, the average coverage was 1 SNP every 1.8 Kb. Genotyping rate for the 384 SNPs initially tested was 95.8%. Sixteen SNPs were not successfully genotyped and were removed from the study. One SNP showed a significant departure from Hardy-Weinberg equilibrium after Bonferroni correction. Thus, a total of 367 markers were included in the analyses after quality control: 59 SNPs in 1p13 (S1 Fig), 37 in 1q41 (S2 Fig), 155 in 9p21 (S3 Fig), and 116 in 10q11 (S4 Fig). Moreover, twenty individuals were removed for low genotyping rate (>5% of missing genotypes); consequently, 848 population samples were analysed. Individual genotypes are included in S1 Dataset. For PC and for Reynolds genetic distance analyses, a total of 176 SNPs were removed due to high LD (r^2>0.8) hence, only 190 SNPs were included in population relationship analyses.

Levels of diversity and population relationships

The SNP minor allele frequencies (MAF) in population samples and global heterozygosities per marker and population are presented in S2 Table. Mean heterozygosities per SNP were moderate-high, ranging from 0.038 to 0.495. Per population, heterozygosities ranged from 0.259 to 0.345.

Hierarchical AMOVA estimates when populations were clustered in North Europe, South Europe, North Africa, Sub-Saharan Africa and Asia were F_{ST} = 0.085 and F_{CT} = 0.080 (both p<0.0001). When Sub-Sahara African and Asian data were removed and the remaining populations were grouped in North Europe, South Europe and North Africa, AMOVA estimates were F_{ST} = 0.017 and F_{CT} = 0.012 (both p<0.0001). These values indicate a statistically significant geographic structure of genetic variation in the three continents, and also across Europe and North Africa.

Population genetic distances are indicated in S3 Table. The highest average genetic distance was among North African and European samples (0.170±0.031). The genetic distance between Middle East and North Africa was higher (0.156±0.032) with respect to Europe (0.141±0.023).

Concerning population relationships, in the PC analysis (Fig 2) of the European, North African and Middle East populations, the two first axes accounted for 38.31% of the total genetic variance. In the first axis (24.99% of the total variance) North African samples appeared clearly separated from the European ones. The second component underlined the separation of the Basque Country on one side, and the Middle Eastern samples on the other.

LD analyses

Different LD blocks were identified among populations. At first glance, Asian and Sub-Saharan African samples showed different and characteristic LD patterns when compared with other continental populations (S5–S8 Figs). Significant differences in LD structure for the 4 genomic regions were observed in pairwise comparisons between Europe, Africa, and Asia (Table 1). A more detailed analysis within continents indicated that only the 9p21 region showed significantly different LD patterns in all subcontinental groups. Between North and South Europe the LD blocks were not significantly different in the regions 1p13, 1q41 and 10q11.

Focusing only on SNPs previously associated with CAD, LD statistics (D' and r^2) for each pair of risk SNPs and for each analysed population are provided in S4 Table. Risk SNPs in the

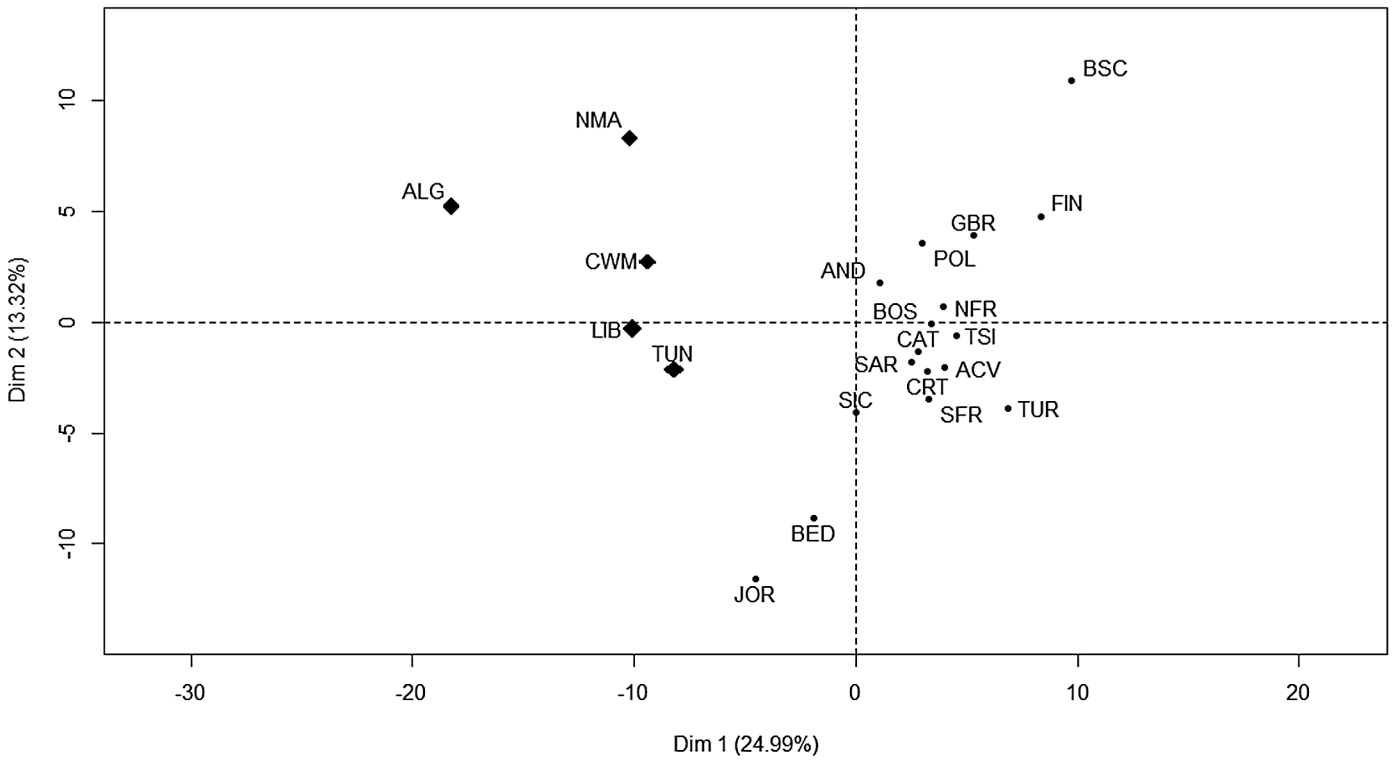

Fig 2. PC plot of the 22 population from Europe (circle), Middle East (circle) and North Africa (diamond) based on the variation of 190 independent SNPs located in the CAD risk regions 1p13, 1q41, 9p21 and 10q11.

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same haplotype block (red colour in S4 Table) showed a high degree of variation in LD ($0.35 \leq D' \leq 1$) in the populations analysed. The haplotype block information for these markers is provided in S5–S7 Tables for the 1p13, 9p21 and 10q11 regions, respectively.

The most remarkable differences in LD block structure were present in the 9p21 (Fig 3) and 10q11 regions (Fig 4). It is interesting to note the different positions shown by CAD associated markers in Europe and North Africa. In the 9p21 region, associated markers in Europe (blue) and in Caucasians together with African Americans or Chinese (black) laid at the beginning of the region, whereas markers associated in North Africa (red) were located at the end (Fig 3). In this region, the risk SNPs rs9632884, rs6475606, rs4977574, rs1537371, rs1333042, and

Table 1. LD difference p-values for the 4 genomic regions analysed. Pairwise comparisons between North Europe (NEUR), South Europe (SEUR), North Africa (NAFR), Sub-Saharan Africa (SAFR), and Asia.

1p13	NEUR	SEUR	NAFR	SAFR	1q41	NEUR	SEUR	NAFR	SAFR
SEUR	0.1740	-			**SEUR**	0.6001	-		
NAFR	0.0224	0.0005	-		**NAFR**	0.0016	0.0156	-	
SAFR	0.0096	0.0006	0.0328	-	**SAFR**	0.0001	0.0001	0.0001	-
ASIA	0.0001	0.0001	0.0001	0.0001	**ASIA**	0.0489	0.1060	0.0034	0.0001
9p21	**NEUR**	**SEUR**	**NAFR**	**SAFR**	**10q11**	**NEUR**	**SEUR**	**NAFR**	**SAFR**
SEUR	0.0179	-			**SEUR**	0.1193	-		
NAFR	0.0001	0.0001	-		**NAFR**	0.0001	0.0128	-	
SAFR	0.0001	0.0001	0.0001	-	**SAFR**	0.0001	0.0001	0.0001	-
ASIA	0.0001	0.0001	0.0001	0.0001	**ASIA**	0.0144	0.0032	0.0007	0.0001

doi:10.1371/journal.pone.0134840.t001

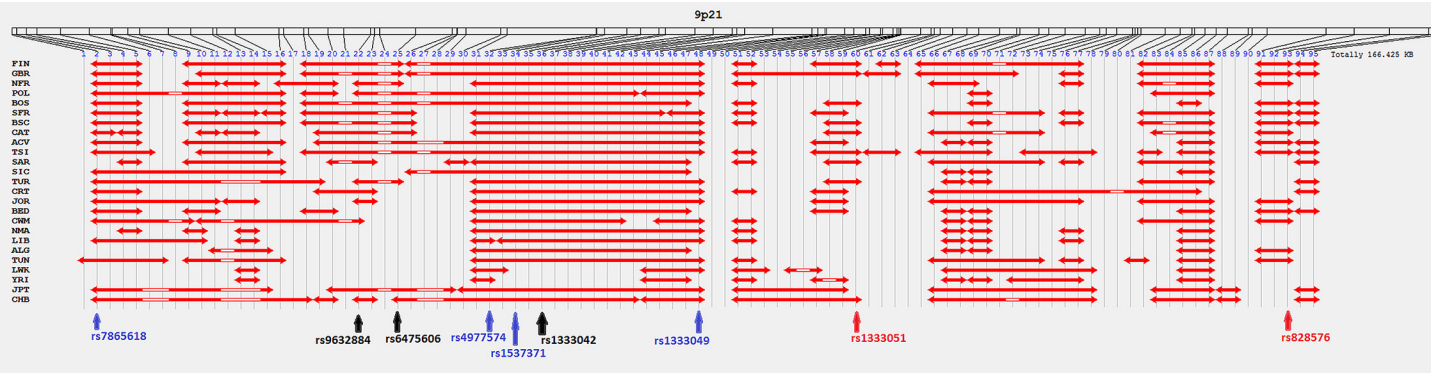

Fig 3. LD blocks for the region 9p21 in 26 populations from Europe, Africa and Asia. Markers previously associated with CAD only in Europe are highlighted in blue, in Caucasians together with African Americans and Chinese in black and in North Africa in red.

doi:10.1371/journal.pone.0134840.g003

rs1333049, located in the same haplotype block, were in tight LD in the European, North African and Middle Eastern populations studied (0.831≤ D'≤1) (S4 Table). On the other hand, in the Sub-Saharan African, and Asian samples LD values ranged from 0.091≤ D'≤1 (grey in S4 Table). These SNPs were located in different haplotype blocks except in Tuscany and Andalusia (S6 Table).

In the 10q11 genomic region, the three risk SNPs analysed (Fig 4) presented LD values in the range of 0.772≤ D'≤1 in all the populations studied except in Sub-Saharan African and Asian samples (0.035≤ D'≤1) (S4 Table). These three risk markers were located in the same haplotype block in all the populations analysed except in Yoruba samples (S7 Table). Regarding the 1p13 region (S9 Fig), the two risk markers, rs599839 and rs646776, presented high LD values in all the populations studied (D'>0.888) (S4 Table). These two risk factors were located in the same haplotype block except in African populations (S5 Table).

The 1q41 genomic region showed previous associations with CAD only in samples of European origin and not in North Africans [10]. The most representative associated SNP in this region was the rs17465637 [3] (S10 Fig).

Detection of potential signals of selection

The results of the locus by locus F_{ST} statistics and their significance as potential indicators of selection are presented in S8 Table. In the European/Mediterranean area, 16 loci were

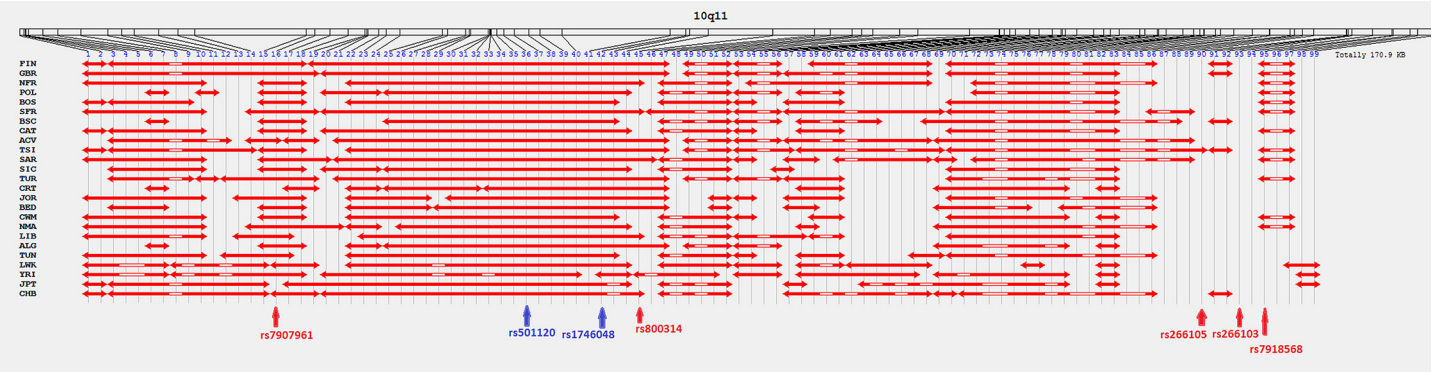

Fig 4. LD blocks for the region 10q11 in 26 populations from Europe, Africa and Asia. Markers previously associated with CAD only in Europe are highlighted in blue and in North Africa in red.

doi:10.1371/journal.pone.0134840.g004

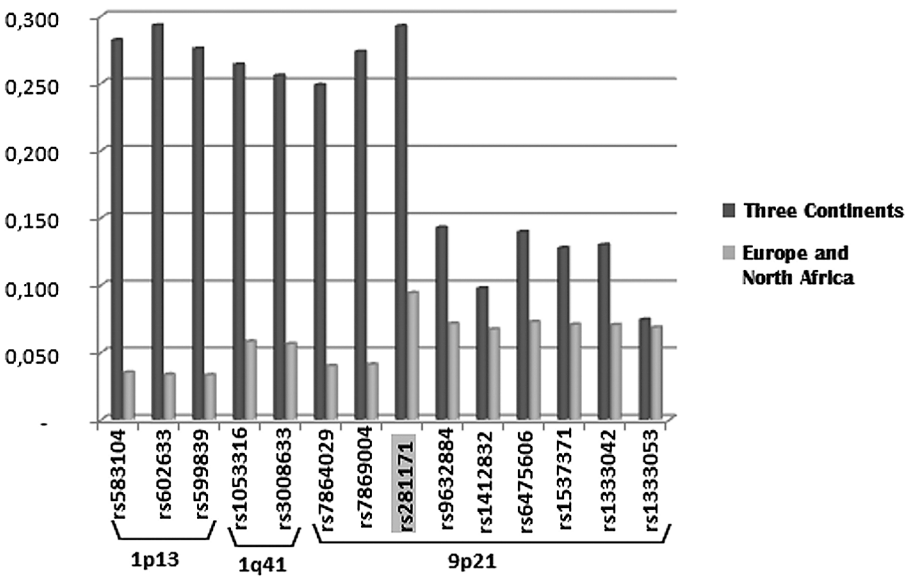

Fig 5. Plot of F_{ST} values of the markers under potential positive selection found in the F_{ST} vs heterozygosity analysis. On the left markers found only in the context of the three continents, on the right markers found only in Europe and North Africa and in the middle (grey) the SNPs identified in both analyses.

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potentially under selection (i.e. loci with significantly low or high F_{ST} values given their heterozygosity). Out of these 16 loci, seven had high F_{ST} values (F_{ST} range = 0.067–0.094) indicating potential positive selection and the other nine showed low F_{ST} values (F_{ST} range = <0.0001–0.0004) suggesting balancing selection. Regarding cross-continental analyses, 15 loci were potentially under selection, eight of which indicated potential positive selection (F_{ST} range = 0.248–0.293) and the other seven suggested balancing selection (F_{ST} range = <0.0001–0.007).

The potential positively selected markers found in the above analyses (F_{ST} vs heterozygosity) were a total of 14 and were located in regions 1p13, 1q41, and 9p21. Out of these 14 SNPs, seven were found only in the context of the three continents, six only in Europe and North Africa, and one in both groups (rs2811717 in the 9p21 region) (Fig 5). Fifteen markers located in chromosomes 9 and 10 were potentially under balancing selection: six in the context of the three continents, eight in Europe and North Africa and one in common (rs17155733 in the 10q11 region). The average allele frequency of these markers in the analysed populations is of 0.50±0.35 (S2 Table). Consequently the possible influence of negative selection can be discarded.

In the SPA analysis, three SNPs (rs9632884, rs1537371, and rs1333042) showed SPA scores above the 99th percentile in each one of the sample group: North Africa (SPA value in the 99th percentile: 0.87) and Europe (1.95) (S8 Table). None of these three North African markers showed association with CAD in previous studies or was identified as being under potential selective pressure in the previous tests. On the contrary, all three markers with the highest SPA score in Europe were among the SNPs that showed signs of positive selection in Europe and North Africa in the F_{ST}/H_O tests. Also, these SNPs have been associated with CAD in previous studies [34, 35, 36] and are located in the 9p21 genomic region: the CAD risk locus most studied [37]. These three risk markers are in strong LD in most populations analysed (S4 Table). A geographical distribution of the MAF of one of these three SNPs, the rs1333042, in the populations studied is represented in a smoothed spherical contour map in Fig 6.

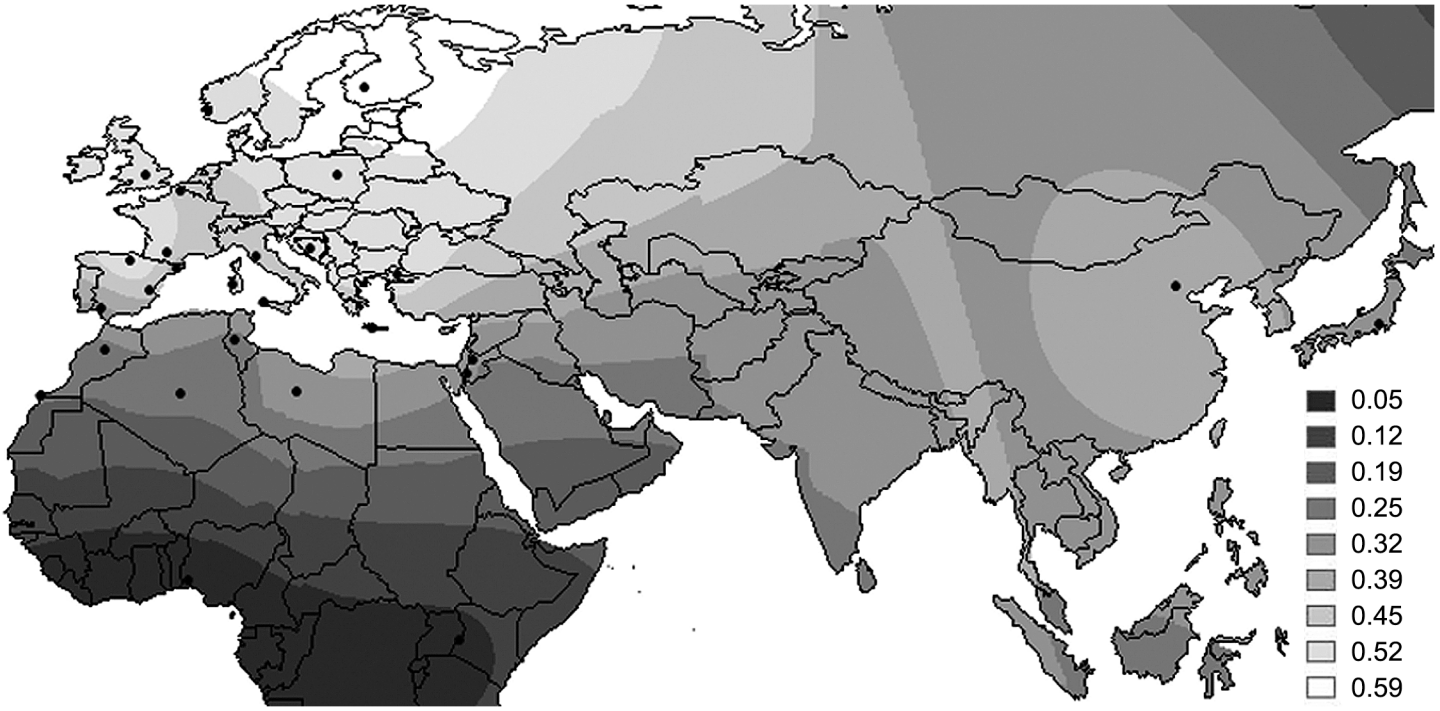

Fig 6. Contour map of the MAF of the CAD risk SNP rs1333042 potentially positive selected in the 9p21 region.

doi:10.1371/journal.pone.0134840.g006

The cross-continental F_{ST} and the EHH average tests, performed with the CEU, CHB and YRI samples from the 1000 Genomes Selection Browser, pointed out markers in the extreme 5% of the genome-wide distribution. Markers with high F_{ST} values indicating potential positive selection (top 2.5%) were identified in the four regions analysed (62 markers in the 1p13, 32 in the 1q41, 121 in the 9p21, and 63 in the 10q11). Markers with extremely low F_{ST} values (bottom 2.5%), indicating potential signatures of balancing selection, were also detected in all the regions studied (13 in the 1p13, 3 in the 1q41, 42 in the 9p21, and 53 in the 10q11) (S9 Table). After applying correction for multiple testing, seven markers with extremely high F_{ST} values in the 9p21 region maintained their significance (red in S9 Table). These markers were located in an 11-kb region (chr9: 21932366–21933125) and are not included in the 367 SNPs analysed in the 26 populations. Comparing the F_{ST} estimated in the 26 populations analysed with the 1000 Genomes Browser Data, it is noteworthy the common signals detected for the rs2811717 in the 9p21 region (S8 Table). For this SNP the differences in cross-continental F_{ST} values detected in the 26 population studied compared to the 1000 Genomes Browser data (0.29 vs. 0.65, respectively) are likely due to the different sets of populations included in each group (S8 Table). Regarding the region 1p13, F_{ST} values of the three common markers detected in both analyses (rs602633, rs583104, and rs599839) are very different comparing the 1000 Genomes data for CEU, CHB and YRI (0.57–0.59) with the 26 populations analysed (0.27–0.29). Also in this case, this is likely due to the different populations included in the analysis, mainly in the African continent (YRI alone versus 5 North African and 2 Sub-Saharan African populations together). The EHH average test, used to validate the results found in the 9p21 region, showed potential signals of positive selection ($p \leq 0.05$) in the three populations analysed (grey in S10 Table). It is noteworthy the fact that the CAD risk marker rs1333042, which showed potential signals of positive selection in the previous tests performed (F_{ST} vs $H_{O.}$ and SPA score), is located in one of the 3-kb regions that show significant EHH values (region

Table 2. Significant positive selection results in a minimum of two different tests. Observed (Obs) F_{ST} with selection significance (highlighted P value<0.01) for the three continents (Africa, Asia and Europe) and for Europe and North Africa. Global cross-continental F_{ST} scores in the CEU, CHB, and YRI samples from the 1000 Genomes Selection Browser. Significant high and low FST values (extreme top 5% values of the distribution of F_{ST} values across the genome) are highlighted in bold. P values were calculated on the basis of higher rank scores in the genomic distribution. SPA scores for continental European, and North African allele gradients (highlighted in bold SPA scores above 99th percentile).

			Three Continents		Europe and North Africa		1000 Genomes Browser		Europe	North Africa
Genomic region	Position	SNP_ID	Obs FST	FST P-value	Obs FST	FST P-value	FST	P_values	SPA scores	SPA scores
1p13	**109821307**	**rs583104**	0.282	**0.004**	0.035	0.136	0.594	**0.001**	0.655	0.300
1p13	**109821511**	**rs602633**	0.293	**0.002**	0.034	0.151	0.592	**0.001**	0.596	0.312
1p13	**109822166**	**rs599839**	0.276	**0.005**	0.033	0.160	0.578	**0.001**	0.651	0.278
1q41	**222839838**	**rs1053316**	0.264	**0.005**	0.058	0.019	0.416	**0.008**	0.376	0.534
1q41	**222844840**	**rs3008633**	0.256	**0.007**	0.056	0.023	0.412	**0.009**	0.310	0.484
9p21	**21920346**	**rs4977746**	0.236	0.011	0.051	0.032	0.342	**0.018**	0.425	**1.116**
9p21	**21930147**	**rs7864029**	0.249	**0.007**	0.040	0.085	0.350	**0.017**	0.373	0.517
9p21	**21931896**	**rs7869004**	0.273	**0.004**	0.041	0.077	0.389	**0.011**	0.480	0.592
9p21	**21946322**	**rs2811717**	0.292	**0.003**	0.094	**0.001**	0.648	**4.923E-04**	0.310	0.624
9p21	**22072301**	**rs9632884**	0.143	0.117	0.071	**0.008**	0.327	**0.021**	**2.075**	0.358
9p21	**22099568**	**rs1537371**	0.128	0.159	0.071	**0.008**	0.292	0.029	**2.046**	0.435
9p21	**22103813**	**rs1333042**	0.130	0.152	0.070	**0.008**	0.287	0.031	**2.043**	0.464

doi:10.1371/journal.pone.0134840.t002

highlighted in grey in S10 Table). However, no EHH average showed significant signals of positive selection after correcting for multiple comparisons. Finally, concerning potential signatures of balancing selection, the Tajima's D analysis pointed out ten, five, and fourteen windows with Tajima's D values above the 95th percentile ($p \leq 0.05$) of genome-wide distributions in CEU (9p21), CHB (10q11) and YRI (10q11), respectively (S8 Table). Two regions were found to overlap, a first between Asia and Sub-Saharan Africa in 10q11, for a 15 kb extension and a second one across European samples in 9p21 for a 24 kb (S8 Table). Even though, after applying corrections for multiple comparisons no windows showed significant signals of balancing selection.

The most relevant findings of positive selection regarding the 1p13, 1q41, and 9p21 genomic regions, and of balancing selection of the regions 9p21 and 10q11 are summarized in Tables 2 and 3.

Discussion

This study explores for the first time the genetic diversity in four genomic regions associated with CAD (1p13, 1q41, 9p21, and 10q11) through the genotyping of a set of European and Mediterranean populations and using European, Asian and Sub-Saharan African data from the 1000 Genomes Project [11]. The main aim was to evaluate the relative importance of demography and natural selection as a cause of population variability in some CAD risk regions identified in previous GWAS.

Diversity population indices indicate significant genetic structure in the context of the three continents ($F_{ST} = 0.085$; $p<0.0001$) and also in Europe and in the Mediterranean area ($F_{ST} = 0.017$; $p<0.0001$). The degree of genetic diversity observed in these four regions between continents is comparable to that obtained from genome-wide genotyping and sequencing studies [11, 38]. Moreover, in the European and Mediterranean context, these

Table 3. Significant balancing selection results in a minimum of two different tests. Observed (Obs) F_{ST} with selection significance (highlighted P value<0.01) for the three continents (Africa, Asia and Europe), and for Europe and North Africa. Global cross-continental F_{ST} scores and Tajima's D test results in the CEU, CHB, and YRI samples from the 1000 Genomes Selection Browser. Significant high and low F_{ST} values (extreme top 5% values of the distribution of F_{ST} values across the genome), and signals of potential balancing selection (P value≤0.05) are highlighted in bold. Both F_{ST} and Tajima D P values were calculated on the basis of higher rank scores in the genomic distribution.

				Three Continents		Europe and North Africa		1000 Genomes Browser		CEU		CHB		YRI	
Genomic region	chromStart	chromEnd	Significant SNPs in the window	Obs FST	FST P-value	Obs FST	FST P-value	FST	P_values	TajimaD	P_values	TajimaD	P_values	TajimaD	P_values
9p21	**22110605**	**22113605**								1.812	**0.044**	1.534	0.105	-0.878	0.776
9p21	**22113605**	**22116605**	**rs2383206**	0.028	0.075	0.018	0.394	-0.004	**0.997**	1.984	**0.030**	1.335	0.148	-0.756	0.705
9p21	**22116605**	**22119605**								1.819	**0.044**	1.198	0.183	-0.830	0.750
9p21	**22119605**	**22122605**								1.935	**0.034**	1.309	0.154	-0.721	0.684
9p21	**22122605**	**22125605**								1.947	**0.033**	1.227	0.175	-0.593	0.600
9p21	**22125605**	**22128605**								2.019	**0.028**	1.240	0.171	-0.451	0.503
9p21	**22128605**	**22131605**								2.056	**0.026**	1.056	0.223	-0.305	0.406
9p21	**22131605**	**22134605**	**rs1751449**	0.017	0.030	0.000	**0.005**	-0.005	**0.998**	1.837	**0.042**	0.980	0.247	-0.437	0.494
10q11			**rs11597731**	-0.001	**0.005**	-0.002	0.121	-0.003	**0.995**						
10q11	**44715700**	**44718700**	**rs2209067**	0.001	**0.001**	0.002	0.036	-0.001	**0.984**	0.194	0.507	0.932	0.262	-0.402	0.471
10q11			**rs17155733**	-0.000	**0.005**	0.000	**0.003**	0.002	0.748						
10q11	**44739700**	**44742700**								0.164	0.520	1.708	0.078	0.692	**0.046**
10q11	**44742700**	**44745700**								0.053	0.565	1.762	0.070	0.913	**0.026**
10q11	**44745700**	**44748700**								-0.050	0.606	1.757	0.071	0.959	**0.023**
10q11	**44748700**	**44751700**								-0.108	0.629	1.999	**0.044**	0.846	**0.031**
10q11	**44751700**	**44754700**								-0.087	0.621	2.102	**0.036**	1.008	**0.020**
10q11	**44754700**	**44757700**								0.011	0.582	2.209	**0.029**	1.081	**0.017**
10q11	**44757700**	**44760700**								-0.017	0.593	2.027	**0.042**	1.165	**0.013**
10q11	**44760700**	**44763700**								-0.153	0.645	1.964	**0.048**	1.185	**0.013**
10q11	**44763700**	**44766700**								-0.312	0.702	1.862	0.058	1.073	**0.017**
10q11	**44766700**	**44769700**								-0.545	0.774	1.490	0.115	0.844	**0.031**
10q11	**44769700**	**44772700**	**rs266088**	0.007	**0.009**	0.002	0.037	-0.002	0.990	-0.619	0.794	1.187	0.186	0.688	**0.047**

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regions of epidemiological importance exhibit the same genetic variation pattern described using sets of neutral markers (e.g. Alu insertion polymorphisms) and genome-wide arrays in previous population studies [39, 40, 41, 42].

Regarding the LD haplotype blocks, this survey pointed to high levels of variation in LD and sometimes to a different chromosomal location of CAD risk markers in populations of different ancestry. The significant differences in LD structure found across European, North African, Asian, and South African samples likely explain population differences in markers associated to CAD across populations. These LD differences can be explained by the previously observed trend of lower haplotype diversity and higher LD values when the geographic distance from Africa increases, [43], in agreement with the Recent-African-Origin hypothesis [44].

Even though the general patterns of genetic variation are in agreement with the genetic structure generated by demographic processes, we also observed potential signals of positive and balancing selection in some specific markers and haplotypes. Seven SNPs under potential positive selection showed association to diseases in previous studies [10, 24, 34, 35, 36, 45, 46, 47], whereas none of the markers under balancing selection was identified as a risk factor in previous GWAS. Regarding the seven risk markers under positive selection, three of them are located in the 1p13 region and four in 9p21. In the 1p13 region, two of the three markers (rs602633 and rs583104) were associated with LDL-C [45, 46]. The other positively selected SNP, rs599839, was associated with CAD in Caucasian populations [24]. These three markers were detected in two of the selection tests performed (F_{ST} vs H_O with 367 markers and F_{ST} with the 1000 Genomes Selection Browser) in the context of three continents. The F_{ST} value detected in the 1000 Genomes Data is in the same order of magnitude than recent positive selection signals ($F_{ST}>0.5$) detected in previous studies performed on the lactase gene [48] and on genome-wide scans [49].

The 9p21 genomic region, the most complex and studied CAD risk region [3], showed consistent signals of positive selection. Indeed positive signatures of selection were identified in each one of the four tests performed (F_{ST} vs H_O, SPA score, F_{ST} and LRH test). The consistency for selection signals in the 9p21 genomic region lies in the fact that these different tests are all based on the same aspect of the data, i.e. population differentiation. Briefly, four variants showed evidence of positive selection: rs9632884, rs6475606, rs1537371 and rs1333042. These SNPs were previously associated with CAD [34, 35, 36, 47] and showed slightly different patterns of LD blocks across populations.

Thanks to the high density of populations available for Europe and North Africa, we were able to do a spatial analysis of selection (SPA test) in these geographic areas. Thus, the positive signals of selection observed in the F_{ST} vs H_O tests could be mainly attributed to Europeans. In fact, the European SPA scores are higher than those detected in North Africans. Additionally, the confirmation of three markers in the 9p21 genomic region (rs9632884, rs1537371, and rs1333042) in two tests (F_{ST} vs H_O and SPA score in Europe) is a good indicator of consistency across our results. As an independent replication using the 1000 Genomes dataset, the region containing one of these 3 markers (rs1333042) has shown a significant EHH value (before correction for multiple testing) in the LRH test. Moreover, this SNP, used as representative of the other two risk markers, shows a South to North gradient of increase in MAF. The gradient observed is in agreement with CAD incidence [50] and with previous genetic studies based on the apolipoprotein E4 [51], or the genetic risk score of nitric oxide synthases [52], both associated with susceptibility to CAD. The South to North frequency gradient, in accordance with CAD incidence rates, may be correlated with a potential selective role of CAD in the configuration of genetic diversity in current human populations. On the contrary, another study showed a geographical pattern opposite and uncorrelated with the disease incidence for genetics variants correlated with CAD [53]. The observed North to South cline in frequency detected in

that work was likely due to the spatial distribution of the whole genome variation present in the European continent, mainly shaped by demography. The potential positive selection signals of the 9p21 region were also detected using the 1000 Genomes data. In fact, seven markers of this region passed the multiple testing corrections in the F_{ST} tests showing F_{ST} values >0.78. In addition is noteworthy the potential positive signal detected for the rs2811717 in the 26 population studied and also in the 1000 Genomes Browser data. The F_{ST} value of this SNP in Europe (0.094) is substantially higher than 0.028, value used to identify the most prominent genome-wide candidate regions in a recent selection scan in Europe [54].

Regarding signatures of balancing selection, only the 9p21 and 10q11 regions showed evidence of balancing selections in the Tajima's D and in the F_{ST} vs H_O tests. Although these regions did not pass the corrections for multiple testing, it is noteworthy that regions of 15 kb (encompassing five contiguous windows in 10q11) in Asian and African samples and 24 kb (corresponding to eight contiguous windows in 9p21) in European populations showed evidence of selection. The overlap in the signals observed for Asians and Africans in the 10q11 region suggests that this locus is likely subjected to selective processes in both populations, in agreement with Wang et al. [55], who estimated that 78% of selective events are shared by two or more populations. Regarding the 9p21 CAD risk region, the regions showing positive and balancing selection are physically separated by a minimum of 11kb (the last positive selected marker in the region: rs1333042 versus the first markers under balancing selection: rs2383206). The two different natural selection signals seem to have population specificity arguing for different evolutionary processes behind the positive and balancing selection in the same genomic region. While the plausible balancing selection signals found are acting mainly on European populations (Tajima's D test), the signals of positive selections in the region 9p21 involve the three continents (F_{ST} and EHH tests).

The heterogeneity observed in the potential signals of natural selection in the different populations analyzed might be correlated with environmental variables. A recent whole genome scan reported evidence for selection on two markers implicated in cardiovascular disease by identifying the SNPs with the strongest correlation between allele frequencies and climate, specifically with winter solar radiation and summer precipitation rate in African and Western Eurasian populations [56]. Another study enumerated several genes involved in the causal pathways of atherosclerosis, that may be subject to various degrees of selective pressures resulting from climatic and dietary changes and host response to pathogens [57]. These pathways may influence the genetic susceptibility to CAD and the heterogeneity observed in the signals of selection among the populations analyzed.

Regarding CAD risk loci, the selection of harmful mutations may be due to the fact that they are in LD with a relatively strong still unknown beneficial polymorphism [6] that could be related to CAD. On the other hand, the positively selected loci could be related to other risk traits since many GWAS SNPs are associated with more than one trait [58]. In the case of the 9p21 locus, several genetic variants had been associated with multiple cancers [59], glaucoma [60], intracranial and abdominal aortic aneurysms [61], vascular dementia and late onset Alzheimer's disease [62]. The response of a variant to selection is dependent also on the genetic background. Due to pleiotropy, the existence of selection at a specific locus may be related to different risk traits located in the same genomic region [58].

Although many selection scans have highlighted potentially interesting signals using genome-wide SNP data, it is currently difficult to assess how much confidence should be placed into them in the absence of clear signals of widespread, strong selection or of biological/functional information [63]. Recent data suggests that it is unusual for selection factors to drive new mutations rapidly to fixation in a specific population (the "hard sweep" model). A number of possible theories have been proposed to explain these potential genome-wide selective

signals. Among others, most selection on individual alleles may be relatively weak so that alleles have not had time to sweep to fixation within continental populations. Moreover, the strength of selection may vary temporally, and it may be rare for selection to be consistently strong for the 10,000 years or more required to drive an allele close to fixation. Finally, much of human adaptation may proceed by either polygenic adaptation or soft sweeps that can be difficult to detect using standard methods [64]. This latter explanation (polygenic adaptation and/or soft sweeps) may be especially relevant for complex traits, such as cardiovascular diseases, in which several loci contribute to generate the disease. Current GWAS identified several common variants associated to CAD but at the moment there is an open debate about causal variants and the role of rare variants [65, 66]. Consequently, the plausible signals of selection here found are expected to be weak and difficult to be clearly identified. In this way, different novel method to detect selection are needed to address potential confounding effects caused by population history and structure and to establish definitive evidence of selection, mechanism of selection, and functional effects of the allelic variants under selection in complex traits.

One possible limitation of this survey is related to the ascertainment bias in the selection of marker. The fact that these results were obtained by genotyping SNPs selected for specific criteria (MAF higher than 0.05 and giving priority to markers not in LD in European populations), and not through direct sequencing, could affect the found patterns of allele frequency, LD and population differentiation [5]. It has been reported that the ascertainment bias introduced by many methods of SNP discovery may have a large effect on the estimation of LD and recombination, influencing the decay of LD with distance [67]. Several studies reported significant LD over distances longer than those predicted by standard models, whereas some data from short, intergenic regions showed less LD than would be expected [68]. Indeed, loci containing high frequency alleles tend to have deeper than average genealogies, providing more opportunity for recombination, and thereby less LD. Regions in which many sequences are used for ascertainment show more SNPs at low frequencies and a higher number of haplotypes are represented in the data. In order to improve this bias, all the variation present in the 1000 Genomes Project [11] for these genomic regions was used to perform the F_{ST}, the LRH and the Tajima's D test. The correspondence in the results across these two datasets with different marker coverage (367 SNPs from our genotyping dataset and all the genetic variation from the 1000 Genomes Project) allow us to consider the 9p21 genomic region as a potential candidate for positive and balancing selection, and the 10q11 for balancing selection.

In the absence of additional functional information, our results are compatible with a potential selective role of CAD in shaping the genetic diversity observed in current human populations, but demographic processes cannot be discarded.

Supporting Information

S1 Dataset. Individual genotypes of the analysed data.
(XLSX)

S1 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 1p13.
(TIF)

S2 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 1q41.
(TIF)

S3 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 9p21.
(TIF)

S4 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 10q11.
(TIF)

S5 Fig. LD blocks for the risk region 1p13 in 26 populations from Europe, Africa and Asia.
(TIF)

S6 Fig. LD blocks for the risk region 1q41 in 26 populations from Europe, Africa and Asia.
(TIF)

S7 Fig. LD blocks for the risk region 9p21 in 26 populations from Europe, Africa and Asia.
(TIF)

S8 Fig. LD blocks for the risk region 10q11 in 26 populations from Europe, Africa and Asia.
(TIF)

S9 Fig. LD blocks for the risk region 1p13 in which markers previously associated with CAD are located in 26 populations from Europe, Africa and Asia. Markers previously associated in Europe are highlighted in blue.
(TIF)

S10 Fig. LD blocks for the risk region 1q41 in which markers previously associated with CAD are located in 26 populations from Europe, Africa and Asia. Markers previously associated in Europe are highlighted in blue.
(TIF)

S1 Table. Geographic origin, population codification, sample size and geographic coordinates in decimal degrees for the population samples.
(XLSX)

S2 Table. Allele frequencies and heterozygozities (mean and standard deviation (SD)) per marker and per population.
(XLSX)

S3 Table. Reynolds's genetic distances estimated among North European and Mediterranean populations based on the SNPs located in the 1p13, 1q41, 9p21, and 10q11 CAD risk regions.
(XLSX)

S4 Table. LD statistics (D' and r^2) for each pair of risk SNPs and for each population analysed. Risk SNPs in the same haplotype are highlighted in red. Risk SNPs in the same haplotype block in LD (D' = 1) are highlighted in grey.
(XLSX)

S5 Table. Haplotype block data for the 1p13 region based on the S9 Fig. CAD risk SNPs are highlighted in grey and their number corresponds to the risk markers in S9 Fig.
(XLSX)

S6 Table. Haplotype block data for the 9p21 region based on the Fig 3. CAD risk SNPs are highlighted in grey and their number corresponds to the risk markers in Fig 3.
(XLSX)

S7 Table. Haplotype block data for the 10q11 region based on the Fig 4. CAD risk SNPs are highlighted in grey and their number corresponds to the risk markers in Fig 4.
(XLSX)

S8 Table. Detection of selection results for the four genomic regions analysed (1p13, 1q41, 9p21 and 10q11). Observed (Obs) F_{ST} with selection significance (highlighted P value<0.01) for the three continents (Africa, Asia and Europe) and for Europe and North Africa. Global cross-continental F_{ST} scores in the CEU, CHB, and YRI samples from the 1000 Genomes Selection Browser. Significant high and low FST values (extreme top 5% values of the distribution of F_{ST} values across the genome) are highlighted in grey. P values were calculated on the basis of higher rank scores in the genomic distribution. SPA scores for continental European, and North African allele gradients (highlighted in grey SPA scores above 99th percentile). Tajima's D test results in the CEU, CHB, and YRI samples of the 1000 Genomes Project. Signals of potential balancing selection (P value≤0.05) are highlighted in grey. P-values were calculated on the basis of higher rank scores in the genomic distribution of Tajima's D values.
(XLSX)

S9 Table. Global cross-continental F_{ST} scores in the CEU, CHB, and YRI samples of the 1000 Genomes Project. Significant high and low F_{ST} values (above the top 5% extreme values of the distribution of F_{ST} values across de genome) are highlighted in grey. P values were calculated on the basis of higher rank scores in the genomic distribution. Significant F_{ST} values after applying correction for multiple testing are highlighted in red.
(XLSX)

S10 Table. EHH averages in the CEU, CHB, and YRI samples of the 1000 Genomes Project. Significant high EHH values (above the top 5% extreme values of the distribution of EHH values across de genome) are highlighted in grey. The region containing the CAD risk marker rs1333042 is highlighted in grey. P values were calculated on the basis of higher rank scores in the genomic distribution.
(XLSX)

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Author Contributions

Conceived and designed the experiments: PM MV RCT EE. Performed the experiments: DZ. Analyzed the data: DZ RCT MV. Contributed reagents/materials/analysis tools: PM. Wrote the paper: DZ PM MV. Revised the article critically: PM MV RCT EE.

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Result III

Zanetti et al., 2015b

Analysis of genomic regions associated with Coronary Artery Disease reveals continental-specific risk SNPs in North African populations

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Resumen en castellano

El análisis de regiones genéticas asociadas con la enfermedad arterial coronaria reveló SNPs de riesgo específicos de continete en poblaciones norte africanas

En los últimos años, varias regiones genómicas han sido fuertemente asociadas con la enfermedad arterial coronaria (CAD) en diferentes estudios de asociación del genoma completo (GWASs). El 96% de GWASs realizados hasta ahora han sido llevados a cabo principalmente en muestras de origen europeo. En la actualidad, este tipo de estudios son muy escasos en poblaciones africanas, aunque la enfermedad coronaria sea actualmente una importante causa de muerte prematura y de discapacidad en este continente.

Estudiar diferencias en las señales de asociación entre diferentes grupos poblacionales es un herramienta útil para validar los loci de riesgo ya detectados en Europa y también para identificar nuevas variantes de susceptibilidad en poblaciones específicas.

El presente trabajo consiste en un análisis detallado de las cuatro regiones de riesgo CAD más validadas en previos GWAS (1p13, 1q41, 9p21 y 10q11) en un nuevo conjunto de muestras de casos y controles del norte de África. El objetivo principal fue el de comprobar el nivel (regiones genómicas y/o marcadores individuales) en el cual los loci de riesgo CAD identificados previamente en Europa podrían transferirse tambien al norte de África, específicamente utilizando muestras de origen tunecino y marroquí.

Para hacerlo, se genotiparon 384 SNPs de estas cuatro regiones genómicas en muestras de casos y controles de Túnez y de Marruecos. Las asociaciones y las tendencias detectadas en las muestras del norte de África se compararon con los datos disponibles en el sur de Europa. Por último, se evaluaron los efectos combinados (la puntuación de riesgo) de los

marcadores asociados en el norte de África, así como su capacidad para discriminar entre casos y controles en el norte de África y en el sur de Europa.

Este trabajo mostró señales de asociación significativas en las cuatro regiones genómicas analizadas también en Marruecos y en Túnez. Sin embargo, en el meta-análisis realizado utilizando los casos y controles africanos, sólo las regiones 9p21 y 10q11 mostraron señales de asociación. Ninguno de los SNPs de riesgo del norte de África mostró asociación en las muestras europeas. Además, el modelo de riesgo calculado a partir de estos SNPs discriminó bien los casos y controles en África (AUC = 0,63), pero no en Europa (AUC = 0,52). Estos resultados sugieren la existencia de variantes de riesgo CAD específicas de continente en estas cuatro regiones cromosómicas. Las diferencias significativas detectadas en el LD ($p < 0,05$) y en los patrones haplotipicos entre los dos grupos poblacionales estudiados confirmaron un cierto grado de heterogeneidad en la estructura genómica entre norteafricanos y europeos en estas cuatro regiones cromosómicas. La disparidad encontrada en los marcadores de riesgo cardiovascular podría estar relacionada con las diferencias en la arquitectura cromosómica observadas en estas regiones de riesgo. Este estudio demuestra que los estudios epidemiológicos de enfermedades complejas deberían considerar las diferentes historias demográficas de las poblaciones analizadas porque los resultados encontrados en Europa pueden no ser siempre aplicables a otros grupos poblacionales.

Supervisor's report of the involvement of the PHD student in the development of this paper

Dr **Pedro Moral Castrillo**, Professor at the Department of Animal Biology of the University of Barcelona, and the Dr. **Marc Via García**, Professor at the Department of Psychiatry and Clinical Psychobiology of the University of Barcelona, both supervisors of the doctoral thesis "Genetics of human populations: evolutionary and epidemiological applications" by **Daniela Zanetti**, hereby certify that the participation of the above student in the article : "**Analysis of genomic regions associated with Coronary Artery Disease reveals continental-specific risk SNPs in North African populations**", published in the *Journal of Epidemiology*, consisted in the following tasks:

- Participation in the design of the study and selection of the analyzed markers
- Creation of the genotype database and selection of available results in the literature for statistical comparison
- Statistical analysis of the data
- Redaction of the Manuscript

In addition, none of the co-authors of this article have used the results of this work in any implicit or explicit way to develop another doctoral thesis. As a consequence, this article forms part of the doctoral thesis of Daniela Zanetti exclusively.

Signed by Dr. Pedro Moral Castrillo and Dr. Marc Via García

Barcelona, 1 September 2015

Analysis of genomic regions associated with Coronary Artery Disease reveals continental-specific risk SNPs in North African populations

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Abstract

Background: In recent years, several genomic regions have been robustly associated with coronary artery disease (CAD) in different genome-wide association studies (GWAS) mainly conducted on people of European descent. These kinds of data are lacking in African populations even though heart diseases are at present an important cause of premature death and disability.

Methods: Here 384 SNPs in the top four CAD risk regions (1p13, 1q41, 9p21, and 10q11) were genotyped in 274 case-control samples from Morocco and Tunisia with the aim of analysing for the first time if the associations found in European populations could be transferable also to North Africa.

Results: The results indicate that these four genetic regions are also important for CAD risk in North Africa. However, the individual SNPs associated with CAD in Africa are different from those identified in Europe in most cases (1p13, 1q41, and 9p21).

Moreover, the seven risk variants identified in North Africans are efficient in discriminating between cases and controls in North Africa, but not in Europe.

Conclusions: This study indicates a disparity in markers associated to CAD susceptibility between North Africa and Europe that may be related to population differences in the

chromosomal architecture of these risk regions.

Key Words

CAD genetic risk, North Africa, SNPs, Haplotype blocks, genetic association.

Introduction

Cardiovascular diseases (CVD) continue to be the leading cause of mortality and morbidity in Western populations [1]. According to WHO data, 17.3 million people died from CVDs in 2008, representing 30% of all global deaths (http://www.who.int/cardiovascular_diseases/about_cvd/en/). In North Africa and in the Middle East, non-communicable diseases are today an increasing cause of premature death and disability (Global Burden of Disease 2013). For example, ischemic heart disease and stroke have increased by 44% and 35%, respectively, during the last 20 years.

The most common type of heart disease is the coronary artery disease (CAD), a paradigm of complex disease, where environmental, lifestyle, and genetic factors interact to determine the clinical phenotype [2].

In the last years, several genetic variants robustly associated with CAD were detected mainly in people of European descent (96%) [3] through genome-wide association studies (GWAS). Previous surveys in non-European population suggested that markers associated in one population may not always easily translate to other populations. Associations found in Europeans must be investigated in other ethnic groups [3] to assess the replicability of association signals, or to detect new population-specific risk markers. For example, regarding Crohn's disease, three variants in the major susceptibility gene (NOD2) were associated to susceptibility in Europeans [4,5]. However, the same variants did not show evidence of association in Morocco and Tunisia [6, 7]. Regarding glaucoma, the genetic susceptibility alleles in European populations do not seem to play a substantial role in populations of African ancestry [8]. On the contrary, a recent study affirmed that Europeans and North Africans share the same 13 risk markers for type 2 diabetes [9].

Regarding the most studied CAD risk regions, the 9p21, the lack of replication of European association signals in African samples was previously reported for coronary artery calcification [10] and ischemic stroke [11].

These differences in association signals between different population groups is an intriguing question, and an increase in the number of epidemiological studies in different populations is required not only to validate the known risk loci, but also to identify new population-specific susceptibility variants.

In this way, the present study deals with a fine analysis of the four most validated CAD risk regions, 1p13, 1q41, 9p21 and 10q11, included among the labeled "top 12 golden loci" [2], in a novel set of case-control samples from North Africa. The main goal is to check the level (genomic regions and/or individual sites) to which the CAD associations previously found in Europe may also be transferable to North Africa, specifically to people of Tunisian and Moroccan origin. To do it, 384 SNPs on those four genomic regions were genotyped in case-control samples from North Africa. The associations and trends detected in North African samples were compared with available data from South Europe. Finally, the combined effects (risk score) of the associated markers found in North Africa, and their ability to discriminate between cases and controls were assessed.

Materials and Methods

Samples

A total of 142 cases and 132 controls from Morocco and Tunisia (52.05% males) were analysed in the present study. The Moroccan samples corresponded to 72 subjects from the area of Casablanca along with 51 controls from the Doukkala-Abda region in Central-West Morocco. The Tunisian case samples included 70 patients treated at the Department of Cardiology of the University Hospital Fattouma Bourguiba (Monastir, Tunisia). As a control group, 81 unrelated individuals, free from any CAD or any related disorders, were randomly selected from the same large geographical area to which belonged the patients (the centre of Tunisia). In both countries, CAD patients were diagnosed for ischemic heart disease complicated by myocardial infarction (MI), confirmed by electrocardiography and coronary angiography. All participants provided written informed consent and the study

was approved by the Ethical Committee of the University of Barcelona.

For comparative purposes, we used two South European matched case-control samples (Milan, ATVB, in North Italy, and Girona, Regicor, in North-East Spain) from the Myocardial Infarction Genetics (MIGen) Consortium [12] accessed through the database of Genotypes and Phenotypes (dbGAP; http://www.ncbi.nlm.nih.gov/gap). Baseline characteristics concerning the samples used in the study were included in Table 1.

		Morocco	Tunisia	Milan	Girona
N	**Cases**	**72**	**70**	**1693**	**312**
	Controls	**51**	**81**	**1668**	**317**
Mean Age (SD)	**Cases**	**56,5(10,8)**	**40,3 (10,1)**	**39,4 (4,9)**	**45,9 (5,9)**
	Controls	**23,0 (1,5)**	**23,8 (3,4)**	**39,3 (5,0)**	**46,0 (5,6)**
% Males	**Cases**	**68,0**	**55,7**	**88,3**	**79,5**
	Controls	**54,9**	**29,6**	**88,3**	**78,5**

Table 1. Baseline characteristics of the samples: sample size (N), mean age (SD), and % of males in case-control samples.

Polymorphisms and genotyping

Genomic DNA was extracted from blood cells using a Blood Midi kit (Omega Biotek, USA) according to manufacturer's procedures. DNA samples were genotyped for a set of 384 SNPs using a Custom GoldenGate Panel (Illumina Inc., San Diego, CA).

Out of the 384 SNPs, 61 are located in the 1p13.3 chromosomal region spanning 150 kb that includes the *CELSR2*, *PSRC1*, *MYBPHL* and *SORT1* genes; 38 SNPs are in 1q41, spanning 100 kb including the *TAF1A*, *MIA3* and *AIDA* genes; 159 SNPs in 9p21, spanning 300 kb that comprises the *CDKN2A* and *CDKN2B* genes; and finally, 126 in the 10q11 chromosomal region spanning 200 kb that embraces the *CXCL12* gene.

SNPs were selected as a representative set of the common variation in the four genomic regions according to the following criteria: i) average coverage of 1 SNP every 1.5 kb, ii) minor allele frequency (MAF) higher than 0.05 in European (CEU) HapMap populations, iii) given priority to markers not in linkage disequilibrium (LD) (r^2>0.8), and iv) prioritizing markers previously reported as associated with CAD [13]. These criteria were applied trying to give preference to tag SNPs.

Genotype data coming from the MIGen samples were generated in the corresponding original projects using the Affymetrix 6.0 GeneChip [12].

Statistical Analyses

Genotyping rate per SNP and individual, Hardy-Weinberg equilibrium (HWE), cryptic relatedness, MAF, and LD were checked using PLINK version 1.07 [14]. Individuals with more than 5% of missing genotypes were eliminated. SNPs with genotyping rate lower than 0.95 or with a MAF lower than 5% were also removed from the analyses.

In order to have the same genetic information, several SNPs not originally genotyped in MIGen samples were imputed simultaneously for cases and controls using MACH 1.0 software [15]. Phased chromosomes from the Tuscan (TSI) samples from the 1000 Genomes Project [16] were used as a reference panel. A standard single-step imputation approach, with 200 rounds of Markov Chain iterations, was used to estimate the crossover maps, error rate maps, and all missing genotypes.

Associations were tested by logistic-regression models adjusted for gender. Permutation tests (1000 permutations) were applied to assess the statistical significance (p-value$\leq$ 0.05) of the regression models. Permutation procedures provide a computationally intensive approach to generating significance levels empirically. Associations and permutations were calculated using PLINK [14]. In the case of the European case-control samples, logistic-regression models adjusted for gender were calculated using both the allelic dosage approach that accounts for imputation uncertainty and the most likely genotype approach. The mach2dat software version 119 [17] was used for the dosage approach. Statistical power of the North African samples was checked by the QUANTO software version 1.2 [18].

Haplotype structure and LD pattern analyses were performed by HaploView version 4.2 [19] using the algorithm proposed by Gabriel et al. 2002 [20]. Monte Carlo statistical significance was assessed for each chromosomal region in order to evaluate differences between populations in regional LD structure based on the r^2. This analysis was carried out using 100 random individuals for each different population group (North Africa and South Europe) through the VarLD software version 1.0 [21].

Genetic differentiation between Moroccans and Tunisians was calculated by means of the Fisher's exact probability test, using the algorithm described by Raymond & Rousset [22], through Genepop version 4.2 [23].

Considering that sample sizes of cases and controls from Morocco and Tunisia were not very large and to provide pooled allelic odd ratios (ORs), three random effect meta-analyses were performed with: i) samples from North Africa, ii) samples from South Europe, and iii) both populations together, paying special attention to markers found as

significantly associated in North Africa. Besides the statistical significance, an association was considered positive if the distribution pattern of the risk allele frequency was similar in the different case-control groups. The meta-analyses and the degree of heterogeneity in the different groups analysed (I^2) were calculated by means of the *Metafor* R package [24]. The I^2 index describes the percentage of total variation across studies due to true heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity.

The joint effect of multiple risk SNPs (risk score) was explored by a logistic-regression model including as independent variable the number of risk alleles. The increase in risk was quantified by adding supplementary risk alleles according to results of the North African meta-analysis. In this case, homozygotes for the protective allele were coded as 0, heterozygotes as 1, and homozygotes for the risk allele were coded as 2. Additionally, the overall score (i.e. the number of risk alleles) was calculated for each individual and compared between cases and controls. The ability of this model to discriminate between patients and healthy controls was evaluated through receiver operating characteristic (ROC) curves, using logistic-regression models. The area under the ROC curve (AUC) was calculated as a measure of discriminative accuracy. The risk score and the ROC curve were calculated using the *PredictABEL* R package [25].

A flowchart of all the analyses performed was included as Supplementary Figure 1.

Results

Genotyping, quality control, and imputation

According to the above criteria, the initial design included 1 SNP every 1.8 Kb and the genotyping rate for the 384 SNPs initially tested was 95.74%. However, fifteen SNPs were not successfully genotyped, one SNP showed a significant departure from Hardy-Weinberg equilibrium after Bonferroni correction, and nineteen SNPs failed the frequency criteria (MAF<0.05) and, hence, were removed from the study. Thus, a total of 349 markers were included in the analyses after quality control: 57 SNPs in 1p13, 36 in 1q41, 148 in 9p21, and 108 in 10q11 (a detailed list can be found in Supplementary Table 1). Moreover, one individual was removed for low genotyping rate (>5% of missing genotypes). The statistical power of the Moroccan and Tunisian samples was low when the two samples were analysed separately. For example, a SNP with a MAF of 0.25 had a statistical power of 37.7% and 45.8% for Moroccans and Tunisians respectively, to detect

an OR of 1.6 with a Type I error rate of 0.05. However, when we considered both samples together the statistical power substantially increased to 70.1% under the same assumptions as above.

Concerning comparison data from MIGen project, genotyping status and imputation quality index (r^2) are presented in the Supplementary Table 1. One hundred and seventy-four out of the 349 SNPs were imputed and only 14 of them showed an imputation quality lower than 0.3 in at least one case-control sample. So, 335 SNPs were considered consistent for this analytical epidemiologic analysis. Most of the imputed SNPs (79%) showed high accuracy ($r^2>0.75$), indicating a good quality of the imputation performed. After quality control per individual, a total of 4979 case-control samples from Europe were used for comparisons, with 3352 individuals from the ATVB (Italy) and 627 from the Regicor (Spain) studies.

Marker association analyses

A total of 5 SNPs were found associated with CAD in Morocco (two in the 1p13 chromosomal region and one in each one of the other three regions) whereas they were 26 in Tunisia (five in the 1p13 region, seven in the 9p21, and fourteen in the 10q11 region). Logistic regression results and genetic effects (OR) of these SNPs are shown in Supplementary Table 2. None of these SNPs was associated independently in Morocco and Tunisia, but most of them (24 out of 31) showed the same trend in the two African populations (i.e. OR values higher or lower than 1).

Preliminary comparisons of the results in North Africa with the two European samples from the MIGen Consortium pointed out to a low replicability of association signals between both groups of populations (Supplementary Table 2). For example, 12 out of 26 of the SNPs associated in the Tunisian sample were also associated in the ATVB study, but four of them showed an opposite effect.

The Fisher's exact probability test indicated a consistent genetic similarity between the two North African countries for both cases ($p=0.248$) and controls ($p=0.927$). In the meta-analysis of North African samples, seven SNPs showed significant associations with a remarkably low heterogeneity ($I^2=0\%$) (Table 2), two corresponding to 9p21, and five to 10q11 region. All these SNPs were located in intergenic regions. In the 1p13 and 1q41 regions, no association was detected.

The potential population specificity of the seven risk variants detected in North Africa was assessed by comparison with the results of the meta-analyses carried out in the European

populations. None of these seven SNPs showed significant associations in South European populations (Table 2). The heterogeneity among the South European samples was remarkably low except for the rs800314 marker (I^2=51%).

The third meta-analysis performed using the North Africans and the South Europeans case-control samples did not show significant associations for the seven SNPs previously identified in the African meta-analyses. The heterogeneity among African and European samples was medium to high (21%<I^2<74%) except for the rs7918568 (I^2=0%) (Table 2).

			North Africa				South Europe				All groups			
CHR	**BP**	**SNP**	**P**	**OR**	**CI**	**I^2**	**P**	**OR**	**CI**	**I^2**	**P**	**OR**	**CI**	**I^2**
9	22136489	rs1333051	0,016	0,470	(0,250-0,870)	0	0,726	1,020	(0,900-1,160)	0	0,410	0,840	(0,560-1,260)	74
9	22191189	rs828576	0,038	1,530	(1,020-2,290)	0	0,185	0,940	(0,860-1,030)	0	0,784	1,030	(0,850-1,230)	39
10	44730995	rs7907961	0,019	1,870	(1,110-3,140)	0	0,851	1,010	(0,910-1,120)	0	0,376	1,070	(0,920-1,260)	21
10	44786364	rs800314	0,013	0,380	(0,170-0,810)	0	0,410	0,870	(0,630-1,210)	51	0,152	0,740	(0,490-1,120)	56
10	44855663	rs266105	0,007	2,180	(1,240-3,850)	0	0,729	0,980	(0,860-1,110)	0	0,245	1,260	(0,850-1,860)	70
10	44856370	rs266103	0,019	1,890	(1,110-3,220)	0	0,601	0,970	(0,850-1,100)	0	0,369	1,150	(0,850-1,540)	53
10	44861220	rs7918568	0,047	1,600	(1,010-2,530)	0	0,300	1,060	(0,950-1,180)	0	0,144	1,080	(0,970-1,200)	0

Table 2. Results of the three meta-analyses performed in North Africans, South Europeans, and merging both continental groups. P: p-value. OR: Odds ratio. CI: 95% confidence interval. I^2: index to quantify the % of true heterogeneity (total heterogeneity / total variability).

Haplotype analyses

Haplotype structure was analyzed to better understand the patterns of associations observed in these two different populations groups. As expected, different patterns of haplotype blocks were identified in North Africa and South Europe (LD patterns and haplotype block structure are plotted in Supplementary Figures 2A, 2B, 2C, 2D). In general, a higher number of haplotype blocks in North Africans compared to South Europeans were observed in all 4 chromosomal regions: 6 vs 2 blocks in 1p13; 4 vs 2 in 1q41; 23 vs 21 in 9p21; and 12 vs 10 in 10q11. The two population groups showed statistically significant differences in LD patterns for all 4 chromosomal regions ($p<0.001$ for the 1p13 and 9p21, and $p<0.05$ for the 1q41 and 10q11 genomic regions). The comparison of the haplotype blocks that included the seven African-risk SNPs, indicate that these risk variants are not located in the same haplotype blocks in African and European individuals (Supplementary Figures 2C-D).

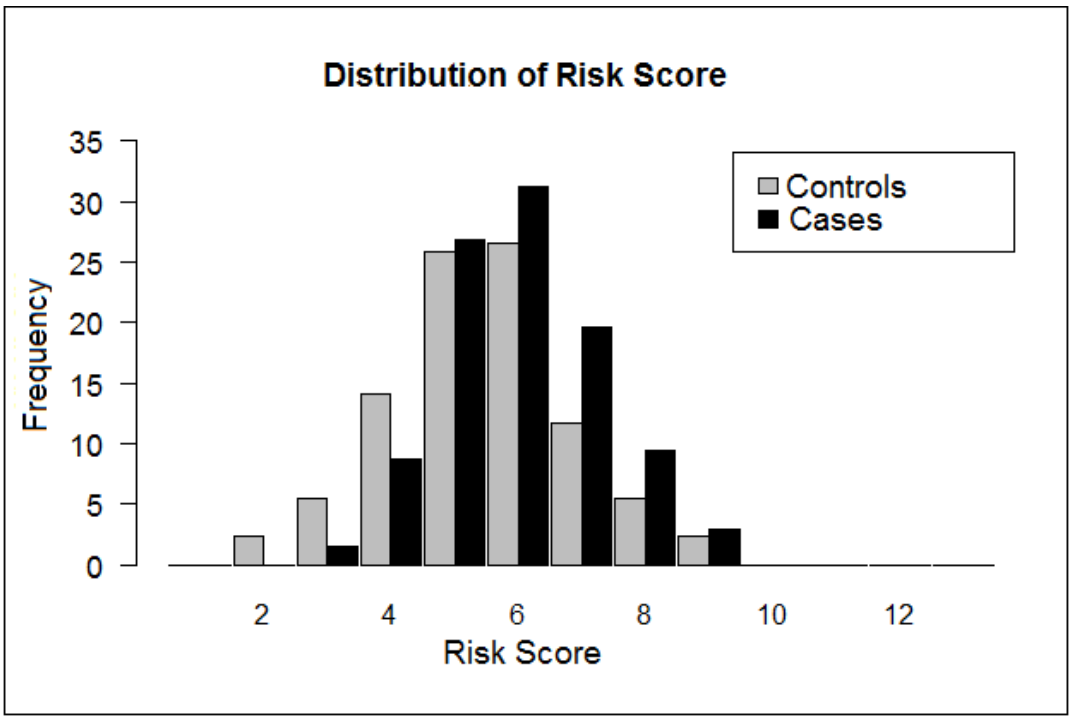
Risk Scores

The genomic risk-score was calculated using the information of SNPs associated in the North African meta-analysis. After applying LD pruning criteria in both European and

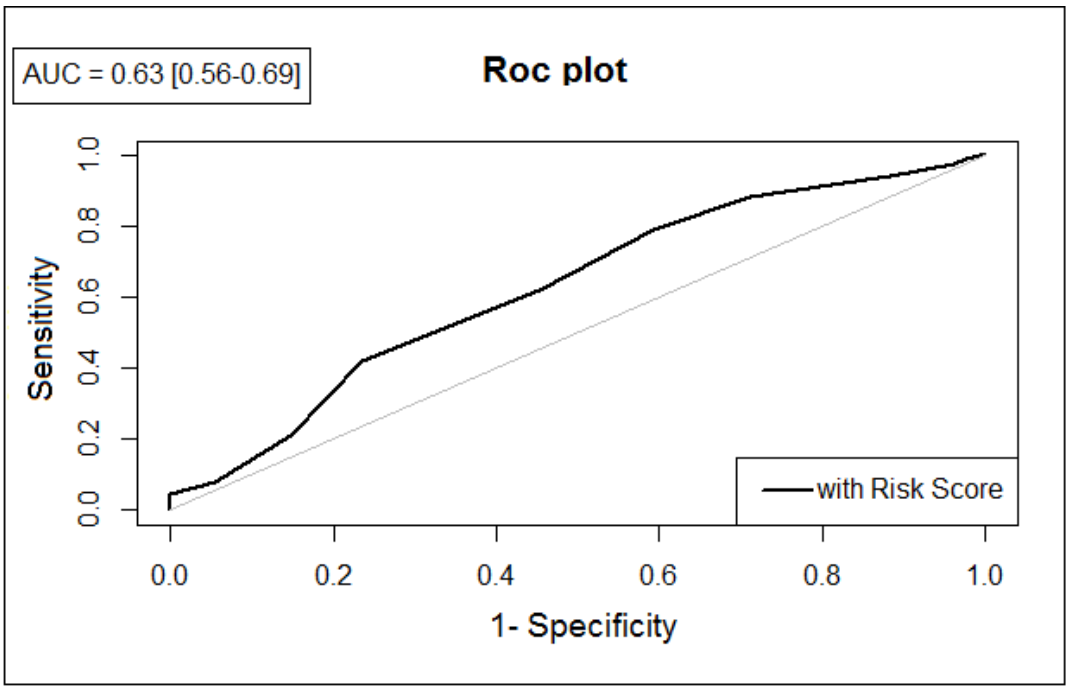
North African samples ($r^2 < 0.4$), six SNPs (making possible risk scores from 0 to 12 risk alleles) were considered in the analysis (Supplementary Table 3). In North Africa, the distribution of the risk score between patients and healthy individuals showed significant differences (Figure 1A). 32% of cases carried 6 risk alleles, whereas only 26% of controls showed the same amount of risk alleles. The risk score applied in North Africa pointed out a partial ability to discriminate between individuals with and without the disease (AUC=0.63; 95% CI: 0.56-0.69) (Figure 1B). In addition, in North Africa the risk for CAD increases with the amount of risk alleles included in the risk score. The susceptibility to develop CAD in North Africans shows a significant value from the group that had 6 risk alleles (p=0.04) and, as the number of risk alleles increases, also the OR value increases reaching a maximum for the individuals with 8-12 risk alleles (Figure 1C).

Comparatively, this risk score had remarkably lower ability to predict CAD risk in South Europeans [AUC=0.52; 95% CI: 0.50-0.54] (Supplementary Figure 3).

A



B



C

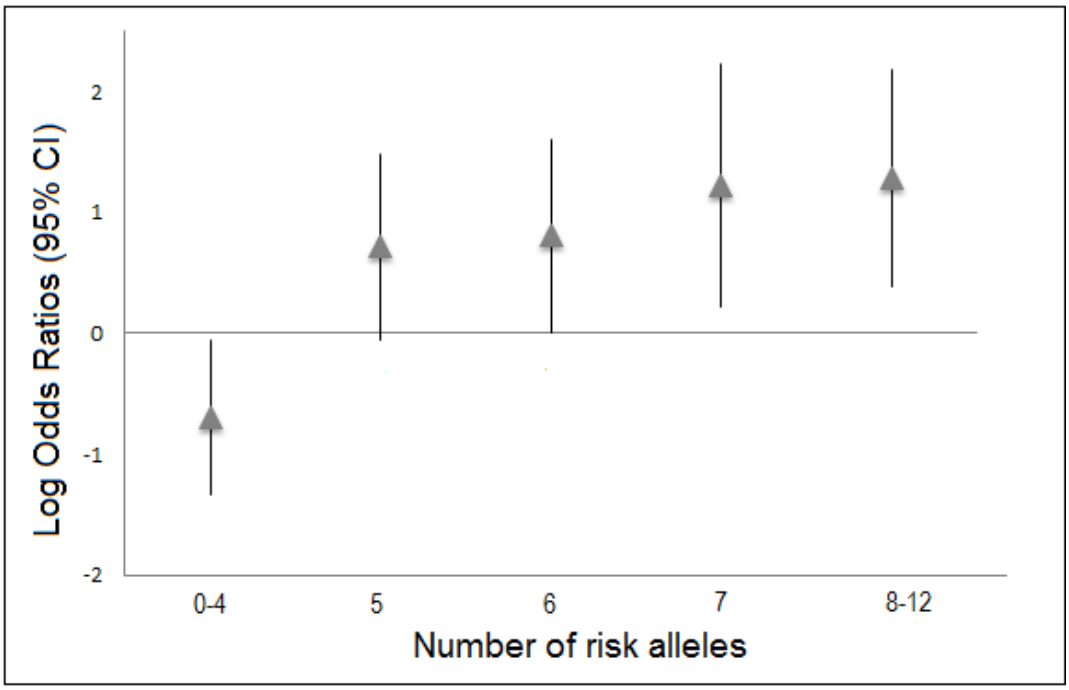


Figure 1. Results of the risk score analysis. The risk score was based on the six risk alleles associated with CAD in the North African meta-analysis. **A.** Distribution of North African individuals according to the number of risk alleles in the sample of cases and controls analyzed. **B.** Receiver operating characteristic (ROC) curves in North Africa. AUC: Area Under the ROC Curve with 95% confidence interval. **C.** Logarithm of the odds ratios with 95% confidence interval for CAD (adjusted by gender) in North African individuals carrying increasing numbers of risk alleles.

Discussion

This study provides novel genetic data of epidemiological interest in North Africa. The genomic variation of four CAD risk regions (1p13, 1q41, 9p21 and 10q11) is analysed through the genotyping of 384 SNPs in two North African case-control samples, specifically from Morocco and Tunisia. Previous studies of these genomic regions are based on populations of European descent and, to the best of our knowledge; these are the first results in populations from Africa.

Consequently, this study aims to assess whether findings about CAD risk variants in European populations can also be extended to North Africans.

This work shows significant association signals in the four genomic regions analysed also in Moroccan and Tunisian samples. However, in the meta-analyses performed with the African case-control samples, only the 9p21 and 10q11 regions showed association signals. None of the North African risk SNPs showed association in European samples. In addition, the calculated risk model had a partial ability to discriminate cases and controls in Africa (AUC=0.63) but not in Europe (AUC=0.52). These arguments suggest the existence of continental-specific CAD risk variants in these chromosomal regions.

Continent-specific risk markers within global risk regions

Among the several CAD risk loci identified so far, the 9p21 locus has a prominent position because of the impressive robustness of the association results [26, 27, 28]. In the North African meta-analysis, two SNPs in this genomic region showed association with CAD. A detailed analysis of the literature reveals that the rs1333051 marker was previously associated with type 2 diabetes in Mexican Americans [29].

The 10q11 genomic region shows the highest number of associated SNPs in North Africa (5 out of 7 of the associated SNPs). None of these five SNPs was found associated with CAD in previous studies.

Regarding the logistic association performed in the four populations analysed (Morocco, Tunisia, Italy, and Spain), the associated SNPs were not the same across populations even though association signals were present in all the regions studied. It is interesting to note that some associated SNPs are close to SNPs associated in other populations, while other SNPs are population-specific (i.e. physically distant or not in LD with SNPs associated in other populations).

The smaller samples size (and statistical power) of North African cases (N=142) compared to Europeans (N=2005) is a limitation inherent in this study that likely explain the

considerably larger number of SNPs associated in South Europe than in North Africa. The ability of the limited sample size to reach the significance threshold in the North African samples may be the cause of two results: i) the low number of associations found in Africa and, ii) the lack of replication in African samples of most associations found in Europe. Even though, the risk SNPs found in North Africa and not replicated in Europe underline the possible role of the genomic architecture in these results. Statistical power calculations indicate reduced power of the North African case-control samples to detect small genetic effects but a good power to detect a risk with an OR≥1.6. Although sample size biases cannot be fully discarded, the permutation test performed supports the associations detected in Africa but not in Europe.

These genetic differences could be partially related to the variation in determining factors of cardiovascular events in each country. Previous data reported elevated proportions of classical risk factors among urban Moroccans and Tunisians, with a prevalence of diabetes higher than that usually found in other European countries (7-10% compared to 2–4%) [30]. However, present data from the WHO do not point to striking differences in classical risk factors between the two North African countries (Tunisia: smoking 32%, total alcohol per capita consumption 1.5, hypertension 29%, and obesity 22.3%; Morocco: 17%, 0.9, 32.4%, and 16.4%, respectively) or between them and Europe (Italy: 25%, 6.7; 31.1%, and 19.8%; Spain: 30%, 11.2; 27%, and 26.6%). In the same way, currently there are not differences in CAD mortality between North Africa (Tunisia 49%, Morocco 34%) and Europe (Italy 37%, Spain 31%), according to WHO data. Thus, differences in the distribution of classical risk factors or in CAD incidence do not seem to explain the differences in genetic risk markers observed between North Africa and Europe.

The significant differences ($p<0.05$) in the LD and the haplotype patterns in the two population groups (Supplementary Figures 2A, 2B, 2C, 2D) confirm the heterogeneity in the genomic structure between North Africans and Europeans. This general trend of lower haplotype diversities and higher LD values when the geographic distance from Africa increases has been previously observed [31, 32]. Moreover, the haplotype blocks containing risk SNPs are different in North Africa compared to South Europe. This situation is especially evident in the 10q11 region where 3 out of the 5 associated SNPs are not located in any block in North Africa while in Europe only one of these SNPs is not located in a block (Supplementary Figures 2D). Differences in allele frequency and LD patterns may be related to the observed differences in the association tests. It is stated that

the higher LD, here illustrated by the different number of haplotype blocks, in populations of European origin with respect to Africans reduces the likelihood of finding a substantial number of associated SNPs in North Africa [33]. African populations are genetically more diverse than European and Asian populations, in agreement with the Recent-African-Origin hypothesis [34]. Consequently, replication studies across European populations have been largely successful because of the general genetic similarity across European populations. A failure to replicate an association signal in Africa may be influenced by variations in LD patterns between European and African populations [33]. Low levels of LD reduce the correlation among casual variants and nearby SNPs. As a consequence, the probability to detect association signals is lower among Africans than in Europe if the causal variants are not assayed directly.

The potential existence of ethnic-specific CAD risk markers is not an isolated case but is common in complex diseases. A recent study detected significant differences in association signals among African and European populations [35]. This work stressed a modest correlation in the risk allele frequencies between Europeans and Africans. The point estimates of risk were opposite in direction or differed more than twofold in 79% of the comparisons between European and African groups. Along with this fact, the under-representation of non-European population in GWAS suggests the need of extending epidemiological studies to a much broader ensemble of populations, including ethnic minorities [3].

Conclusion

This study shows that in North African populations, as in European populations, the regions 1p13, 1q41, 9p21 and 10q11 contain genetic risk variants associated with CAD. However Europeans and North Africans do not always share the same risk variants.

The differences obtained in CAD risk variants between Europeans with respect to North Africa, suggest that findings from one population cannot be directly applied to populations from other continents. That is, differences in the genomic architecture due to different demographic histories should be taken into account in epidemiological studies of complex disorders. These first evidences from four CAD risk genomic regions in North Africa populations need to be extended to additional larger analyses.

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Result IV

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Trans-ethnic differences in GWAS signals: a simulation study

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Resumen en castellano

Diferencias trans-étnicas en las señales GWAS: un estudio de simulación

Con el advenimiento de los estudios de asociación de genoma completo (GWASs), investigadores de distintos países han identificado cientos de variantes genéticas asociadas con determinados rasgos complejos. Sin embargo, el 96% de los individuos incluidos en los GWASs realizados hasta ahora han sido de origen europeo. En los últimos años el número de GWASs realizados en poblaciones no europeas incrementó sustancialmente. Como consecuencia, los estudios que compararon las señales de asociación entre poblaciones ancestrales también aumentaron. La literatura actual presenta algunos ejemplos en los que los efectos genéticos observados son consistentes entre distintos grupos ancestrales, en términos de la dirección del efecto o en la magnitud del mismo. Por otro lado, hay otros casos en los que las señales derivadas de los GWASs apuntan a patrones diferentes del efecto, o a una magnitud diferente en la señal de asociación en distintos grupos poblacionales.

Diferencias en los resultados GWASs pueden ser principalmente debidas a diferencias en el poder estadístico, en la frecuencia de los alelos de riesgo, en los patrones de disequilibrio de ligamiento o en las variantes causales. En el presente trabajo se simularon el mismo número de muestras de casos y controles de origen europeo, asiático y africano utilizando como referencia los datos del Proyecto de los 1000 Genomas. Variantes genéticas aleatorias en todo el genoma fueron seleccionadas para luego aplicar parámetros específicos de riesgo en los tres grupos poblacionales. Se realizaron análisis de regresión logística y comparaciones estadísticas en las diferentes poblaciones continentales para evaluar el nivel de consistencia entre los grupos, las posibles diferencias en las frecuencias alélicas, y la posible aplicabilidad de las señales de asociación detectadas en Europa a poblaciones de origen diferente. Se utilizó el Z-score para evaluar si el tamaño del efecto

difería significativamente en las comparaciones entre Europa, Asia y África subsahariana. Además, se evaluó cuán a menudo el tamaño del efecto difería en más del doble o en la dirección del mismo entre los grupos ancestrales. Estas comparaciones ancestrales se aplicaron cuatro veces utilizando diferentes SNPs de referencia: i) el SNP causal en el que se aplicó un modelo específico de riesgo, ii) el lead SNP, con el p-valor más bajo en Europa iii) el lead SNP , con el p-valor más bajo en Europa y con MAF> 1%, y finalmente vi) el lead SNP, con el p-valor más bajo en Europa, que también estaba incluido en el Human Omni Express Bead Chip array.

Este estudio subraya una replicabilidad substancial de los resultados de asociación entre los grupos ancestrales de Europa, Asia y África Subsahariana. Se detectó una consistencia global en la dirección del efecto genético entre las poblaciones estudiadas, específicamente entre los europeos y los asiáticos (SNP causal: 99,1%; lead SNP: 98,4%; lead SNP en el array de Illumina: 97,4%).

Comparaciones en el tamaño del efecto entre asiáticos y africanos mostraron las diferencias más altas utilizando los SNPs causales (6.6%) y los lead SNPs (12.3%), mientras que europeos y africanos mostraron los valores más altos utilizando los lead SNPs incluidos en el panel de Illumina (18.5%). Las diferencias observadas en las frecuencias allelicas podrían ser la razón de algunas de las discrepancias detectadas en el Z-score, pero hay casos en los que los SNPs con Z-score significativos mostraron valores parecidos de frecuencia alélica entre poblaciones. En estos casos, las variantes causales específicas de población podrían ser la causa principal de las diferencias significativas detectadas en el Z-score. Este trabajo muestra una falta de correspondencia en el 40.04% entre los SNPs causales y los lead SNPs, y en el 64.24% entre los SNPs causales y los lead SNPs incluidos en el panel de Illumina. Este resultado evidencia que los lead SNPs no siempre son los SNPs causales, y que una fracción de los SNPs causales podría haberse quedado fuera de los arrays utilizados en los actuales GWAS.

Este estudio confirma que una fracción importante de las señales de asociación se comparte entre poblaciones de diferente ascendencia continental. Sin embargo, algunas discrepancias detectadas en el tamaño del efecto entre poblaciones ponen de manifiesto la posible presencia de variantes causales específicas de población, y la importancia de tener en cuenta

la estructura poblacional en los estudios de asociación genética. Considerando que las simulaciones de este estudio no asumen diferencias en el tamaño del efecto genético entre poblaciones y que la tasa de diferencias detectadas en el efecto genético entre poblaciones (debidas a diferencias poblacionales en el poder estadístico, en la frecuencia alélica o en el desequilibrio de ligamiento) fue considerablemente más baja que la tasa reportada en estudios empíricos de datos reales, nuestro estudio apoya la existencia de diferencias reales entre poblaciones en la arquitectura del riesgo genético de caracteres complejos.

Supervisor's report of the involvement of the PHD student in the development of this paper

Dr **Pedro Moral Castrillo**, Professor at the Department of Animal Biology of the University of Barcelona, and the Dr. **Marc Via García**, Professor at the Department of Psychiatry and Clinical Psychobiology of the University of Barcelona, both supervisors of the doctoral thesis "Genetics of human populations: evolutionary and epidemiological applications" by **Daniela Zanetti**, hereby certify that the participation of the above student in the article : "**Trans-ethnic differences in GWAS signals: a simulation study**", submitted to the *European Journal of Human Genetics* consisted in the following tasks:

- Participation in the design of the study and selection of the analyzed markers
- Simulation work
- Statistical analysis of the data
- Redaction of the Manuscript

In addition, none of the co-authors of this article have used the results of this work in any implicit or explicit way to develop another doctoral thesis. As a consequence, this article forms part of the doctoral thesis of Daniela Zanetti exclusively.

Signed by Dr. Pedro Moral Castrillo and Dr. Marc Via García

Barcelona, 1 September 2015

Trans-ethnic differences in GWAS signals: a simulation study

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Abstract

With the advent of genome-wide association studies, researchers have identified hundreds of genetics variants associated with particular complex traits. Previous studies have compared the pattern of association signals across different populations in real data, and these have detected some level of discrepancy across populations of different ancestry.

In the present work, case-control samples of European, Asian and sub-Saharan African origin were simulated from the real linkage disequilibrium patterns present in the 1000 Genomes reference dataset. Logistic regression analyses and statistical comparisons were performed to evaluate the level of consistency across groups, possible differences in risk allele frequency (RAF), and the applicability of European association results to other populations. Pairwise population comparisons were applied using four different scenarios to select target SNPs: i) causal disease SNP assumed known, ii) lead SNPs, with the lowest p-value in Europe, iii) lead SNPs, with the lowest p-value in Europe and minor allele frequency (MAF)>1%, and iv) lead SNPs, with the lowest p-value in Europe and also contained in the Human Omni Express Bead Chip array.

We found that a substantial fraction of association signals are shared across people of different ancestry, especially between Europeans and Asians. However, some discrepancies in the effect size across populations highlight the possible presence of population-specific causal variants, and the importance of accounting for population structure in association studies. Because our simulations assumed no actual between-population differences in genetic effect size, and because the rate of between-population effect size differences generated by our study (generated due to between-population differences in power, allele

frequency or linkage disequilibrium) was considerably lower than the rate reported from empirical studies of real data, our study supports the existence of real between-population differences in the genetic risk architecture of complex traits.

Introduction

In the past decade, through collaborative efforts, the genetic basis of common complex diseases, such as Alzheimer's disease [1] or type 2 diabetes [2], and complex traits, such as height [3] or obesity [4], have been greatly clarified. With the advent of genome-wide association studies (GWASs) researchers have identified hundreds of genetics variants associated with particular complex traits. However, 96% of subjects included in the GWAS conducted so far are of European origin [5].

This Eurocentric bias in GWASs can lead to one-sided results that should be investigated in other ethnic groups to detect if genetic risk variants are shared or not across different population groups. Trans-ethnic replicability of GWAS signals could imply a common aetiology of complex diseases, and this would have important clinical implications [6 7]. The portability of GWAS results would also allow for 'trans-ethnic mapping' to help in the post-GWAS localization of the causal locus, by taking advantage of between-population differences in linkage disequilibrium (LD) [8].

In recent years the number of GWASs performed in non-European populations has substantially increased. As a consequence, studies that compare association signals across different continental populations have also been performed. The literature provides some examples in which the observed genetic effects show consistency across ancestral groups, either in terms of effect direction or in the magnitude of the effect [7 9 10 11]. On the other hand, there are also examples where GWAS-derived signals point to a pattern of population-specific risk effects [12 13], or to a different magnitude in the association signal across populations [14 15].

Recently, Ntzani and colleagues [16] used the catalog of published GWAS curated at the National Human Genome Research Institute (NHGRI) website to characterize the frequency and magnitude of between-population differences in GWAS signals. A total of 97 associations were evaluated in both European and Asian populations, 24 in both

European and African populations, and only 13 in all three groups. They found only a modest correlation in the frequency of risk alleles between Europeans, Asians and Africans, with absolute differences >10% in 75-89% of the three pairwise comparisons. Point estimates of risk were opposite in direction in 18%, 21%, and 39% in the European-Asian, European-African, and Asian-African comparisons, respectively.

The trans-ethnic differences in genetic risk effects catalogued by Ntzani and colleagues [16] could be due to one or a combination of the following explanations:

(1) Between-population genetic architectures are the same, but differences in power (say due to low sample sizes) prevent detection in other populations;
(2) The genetic *risk* architectures are the same, but differences in allele frequency prevent detection in other populations;
(3) The genetic *risk* architectures are the same, but differences in linkage disequilibrium patterns prevent detection in other populations (in cases where the 'lead' or most significantly associated SNP is not the truly causal SNP);
(4) The genetic *risk* architectures are different – in other words the truly causal SNP has a different true genetic effect size in different populations.

Biologically, the most interesting explanation is point (4), as this implies a truly different genetic risk architecture between populations. But because points (1)-(3) can also lead to apparent differences in GWAS signals between populations, it is very hard to distinguish between the four possible explanations based on studies of real GWAS (as in the study by Ntzani and colleagues [16]).

In the present work, we employed simulations to assess the relative importance of the four explanations listed above for generating trans-ethnic differences in GWAS signals. We generated simulated genomic data in the same number of case-control samples of European, Asian and Sub-Saharan African origin. Random genetic variants in the genome were selected to be 'truly causal', applying specific disease model parameters in the three population groups. Finally, logistic regression analyses and statistical comparisons across the different continental populations were performed to evaluate the level of consistency across groups, potential differences in allele frequency, and consequently the applicability of European association signals to other populations.

Materials and methods

Phased genotypes from the 1000 Genomes Phase 1 dataset [17], were used as input to simulate case-control genotype data. Specifically, Utah residents (from the CEPH collection) with Northern and Western European ancestry (CEU, n=85), Finns from Finland (FIN, n=93), British samples from England and Scotland (GBR, n=89), Iberians from Spain (IBS, n=14), and Tuscans from Italy (TSI, n=98) were used as input to simulate European samples (EUR, n=379). Han Chinese from Beijing, China (CHB, n=97), Han Chinese South (CHS, n=100), and Japanese from Tokyo, Japan (JPT, n=89) were used to simulate Asian samples (ASN, n=286). Finally, Yorubans from Ibadan, Nigeria (YRI, n=88) were used to simulate West African samples (only one population, YRI, was used for an African grouping, in recognition of the high degree of genetic heterogeneity among different African samples, making a pan-African "AFR" grouping of little relevance in simulating a typical GWAS). Simulated datasets were generated from SNPs with a 'global' MAF >1% (as calculated using all samples in the 1000 Genomes Phase 1 dataset). VCFtools [18] and Beagle [19] software were used to extract and transform 1000 Genomes phased data into a format suitable for GWAsimulator.

Simulations were performed via the GWAsimulator software version 2.1 [20]. This program implements a moving-window algorithm to simulate case-control genotype data based on a set of phased input data. It works outwards from the nominated disease locus to generate the case and control datasets, with patterns of LD similar to the input data. A window size of 5 was used for our simulations, meaning that a haplotype of 4 SNPs was used to propose the allele of the next adjacent SNP.

To mimic a Euro-centric bias in GWAS results, a simulated causal disease locus was selected at random for each simulation run from the set of all autosomal SNPs in the 1000 Genomes Project Phase 1 dataset with a minor allele frequency (MAF) >5% specifically in the EUR grouping. The Genotypic Relative Risk for this locus was set at 1.3, with a multiplicative effect, setting the minor allele as the risk allele. Genomic regions of 500 kb were simulated, 250 kb upstream and downstream of the randomly selected disease locus. For each simulation run, 2000 cases and 2000 controls were created with a disease prevalence of 1%. Logistic regression analyses were performed on the simulated data from the three continental groups (EUR, ASN and YRI), using Plink software version 1.07 [21].

Only markers with genome-wide significance ($p \leq 5 \times 10^{-8}$) in at least one continental grouping were considered for trans-ethnic GWAS comparisons. Following Ntzani and colleagues [16], the following metrics were recorded in order to assess the apparent differences in GWAS signals among the three continental groupings. Firstly, the Z-score, described previously by Ioannidis et al, 2001 [22], and by Cappelleri et al, 1996 [23], measures the difference in estimated log-odds-ratios between the two populations divided by the estimated standard error of the difference. A 'Z-score' flag was set 'on' (value=1) if the Z-score was nominally significant at the 5% level (abs(Z)>1.96), and set 'off' otherwise (value=0). Secondly, an 'opposite direction' flag was set 'on' (value=0) if the odds ratios deviated from 1 in different directions (value=1 otherwise). Finally, a 'two-fold difference' flag was set 'on' (value=1) if the odds ratios differed by more than two-fold between the two populations.

We assessed trans-ethic GWAS signal differences under the following scenarios:

(1) The causal disease SNP is assumed to be known, and so is assessed directly;
(2) The causal disease SNP is assumed not known. However, all SNPs are assumed to be imputed perfectly. Thus, the European lead SNP (with the lowest p-value in EUR) is assessed as the target SNP, regardless of its MAF;
(3) SNPs imputed with MAF<1% are assumed to be unreliable. Thus, the European lead SNP is defined based on SNPs with MAF>1% in EUR, and taken forwards for assessment as the target SNP;
(4) Imputation is not performed (mimicking an earlier GWAS study, or a study for which imputation is deemed unreliable). Thus the European lead SNP is defined based on SNPs present on a representable medium-coverage GWAS panel (here, the Illumina Human Omni Express Bead Chip array), and this SNP is taken forwards for assessment as the target SNP.

Results

A total of one thousand simulation runs, generating case-control genotype data in populations of European, Asian and Sub-Saharan African origin, were performed in this study. Logistic associations and trans-ethnic GWAS signal comparisons were carried out on each simulated dataset as described in the following paragraphs.

Eligible simulations and allele frequencies

Simulations containing monomorphic reference markers in at least one population (Asians or Sub-Saharan Africans) were not considered eligible. The number of eligible simulations varied according to the target SNP scenario considered (Table 1). Using *causal SNP*s, one hundred and forty-two simulations were eliminated due to the presence of monomorphic markers; as a consequence 858 simulations were considered in the subsequent analyses. Regarding the allele frequencies of the simulated causal SNP, the 858 simulations showed a similar average frequency in the three populations groups (Europeans=0.35±0.24; Asians=0.36±0.28; Africans=0.35±0.27). Considering *lead SNPs* with the lowest p-value in Europe as the target SNP, 807 simulations were considered eligible. The average frequency again showed similar values in the three populations groups (Europeans=0.39±0.23; Asians=0.39±0.28; Africans=0.38±0.28). The results based on *lead SNPs with MAF>1%* retrieved 809 eligible simulations, and again the average frequency was similar in the three populations groups (Europeans=0.39±0.23; Asians=0.40±0.28; Africans=0.38±0.28). Finally, considering *lead SNPs included in the Human Omni Express Bead Chip array*, the eligible simulations were a total of 797, again with similar average frequency in the three populations analysed (Europeans=0.39±0.24; Asians=0.41±0.28; Africans=0.38±0.27).

Genetic effect sizes

Logistic association analyses performed with *causal SNPs* showed genome-wide significant values ($p \leq 5 \times 10^{-8}$), in at least one of the three populations analysed, in 531 out of the 858 simulations performed (Table 1). A total of 284, 266 and 252 associations showed significant p-values in European, Asian and Sub-Saharan African case-control samples, respectively. The greater number of European signals reflects the bias generated by requiring a MAF>5% in the 1000 Genomes EUR grouping for all simulated causal SNPs. The common association signals across all continents totalled 55, while the common pairwise associations were 61, 53 and 47 for European-Asian, European-African, and Asian-African pairs, respectively. On average, considering only the significant associations detected in each group separately, genetic effects and the corresponding allele frequencies were substantially similar in European (beta=0.31±0.04; allele frequency=0.45±0.18),

Asian (beta=0.30±0.04; allele frequency=0.49±0.16), and African populations (beta=0.31±0.04, allele frequency=0.47±0.17).

Simulations based on *lead SNPs* showed genome-wide significant values in 447 out of the 807 simulations performed. A total of 297, 226 and 166 associations showed significant p-values in European, Asian and Sub-Saharan African case-control samples, respectively. The common association across continents were 49, while the common pairwise associations were 117, 91 and 80 for European-Asian, European-African, and Asian-African comparisons, respectively. On average, genetic effects and allele frequencies were similar in Europeans (beta=0.30±0.07; allele frequency=0.45±0.18), Asians (beta=0.29±0.08, allele frequency=0.50±0.15) and Africans (beta=0.31±0.04; allele frequency=0.48±0.16). Comparing the two reference SNP sets (*causal* versus *lead*), the 40.04% of the 447 genome-wide significant simulations were different. Interestingly, the genome-wide significant *lead SNPs with the lowest p-value in Europe and with MAF>1%* correspond exactly to the *lead SNPs* previously selected without considering the MAF. Consequently, *lead SNPs* and *lead SNPs with MAF>1%* were considered as a single group.

Finally, *lead SNPs included in the Illumina array* showed genome-wide significant values in at least one of the three populations analysed in 151 out of the 797 simulations performed. A total of 91, 75 and 45 associations showed significant p-values in the European, Asian and Sub-Saharan African case-control samples, respectively. The common association across continents were a total of 10, while the common pairwise associations were 31, 23 and 13 for European-Asian, European-African, and Asian-African comparisons, respectively. On average, genetic effect and corresponding allele frequencies were similar in European (beta=0.25±0.18; allele frequency=0.46±0.18), Asian (beta=0.28±0.13, allele frequency=0.47±0.16) and African populations (beta=0.29±0.10; allele frequency=0.50±0.16). Comparing the two reference SNP sets (*causal* versus *lead in the Illumina panel*), 64.24% of the 151 genome-wide significant simulations were different.

In general, the number of significant associations decreased considerably depending on the scenario used to determine the target SNP, and provide an insight into the how much power is degraded by imperfect imputation (simulated in the last scenario). The highest number of significant associations was detected using *causal SNPs* as the target SNP, followed by *lead SNPs*, and then by *lead SNPs included in the Illumina panel*. Beta values and

allele frequencies were in the range of 0.25≤beta≤0.31 and 0.45≤ allele frequency≤0.50 in the three different reference groups. Logistic association results and allele frequencies are included in Supplementary Tables 1-3.

	Eligible simulations / mean allele frequency (± SD)				GW significant associations							
Reference SNPs	**N**	**EUR**	**ASN**	**AFR**	**N**	**EUR**	**ASN**	**AFR**	**EUR-ASN**	**EUR-AFR**	**ASN-AFR**	**ALL**
Causal SNPs	858	0.35 ± 0.24	0.36 ± 0.28	0.35 ± 0.27	531	284	266	252	61	53	47	55
Lead SNPs	807	0.39 ± 0.23	0.39 ± 0.28	0.38 ± 0.28	447	297	226	166	117	91	80	49
Lead SNPs and MAF>1%	809	0.39 ± 0.23	0.40 ± 0.28	0.38 ± 0.28	447	297	226	166	117	91	80	49
Lead SNPs in the Illumina array	797	0.39 ± 0.24	0.41 ± 0.28	0.38 ± 0.27	151	91	75	45	31	23	13	10

Table 1. Eligible simulations and number of significant genome-wide association signals.

Z-score in the GW significant associations

Considering *causal SNPs* as the target SNP, between-population differences in estimated effect size were nominally significant (abs(Z)>1.96) in 6%, 5.8%, and 6.6% of the European-Asian, European-African, and Asian-African comparisons, respectively (Table 2). *Lead SNPs with MAF>1%* showed significant differences in 7.8%, 10.7%, and 12.3% of the European-Asian, European-African, and Asian-African comparisons, respectively. Considering *lead SNPs included in the Illumina array*, effect size estimates differed significantly in 11.9%, 18.5%, and 17.9% of the above comparisons.

In order to assess whether allele frequency differences might play a role in determining effect size differences, we investigated the allele frequencies of our SNPs showing significant between-population effect size differences (bearing in mind that our simulations were all generated under equal-true-causal-effect-size conditions, across all populations). Broadly the allele frequency patterns looked similar across populations. Allele frequency patterns of SNPs showing significantly different effect sizes between populations, and their averages, are shown in Supplementary Figures 1-3.

Opposite direction and two fold differences

The European versus Asian, European versus African and Asian versus African comparisons performed with *causal SNPs* showed opposite effect size direction in 0.9%, 0.9%, and 1.9%, respectively (Table 2). Moreover, 0.38%, 0%, and 0.38% of them were in the same direction but differed more than two-fold. Considering *lead SNPs*, 1.6%, 2.2%,

and 3.8% of the European-Asian, European-African and Asian-African comparisons, respectively, showed opposite direction. 0.28%, 0%, and 0.28% were in the same direction, but differed more than two-fold. Finally, considering *lead SNPs included in the Illumina panel* 2.6%, 5.3%, and 5.3% of the above comparisons showed opposite direction.

A list of the observed discrepancies for ancestral effect size is shown in Supplementary Tables 1-3.

	Z-scores			Opposite direction			Two-fold difference		
Reference SNPs	**EUR-ASN**	**EUR-AFR**	**ASN-AFR**	**EUR-ASN**	**EUR-AFR**	**ASN-AFR**	**EUR-ASN**	**EUR-AFR**	**ASN-AFR**
Causal SNPs	6.03%	5.84%	6.59%	0.94%	0.94%	1.88%	0.38%	0%	0.38%
Lead SNPs and MAF>1%	7.83%	10.74%	12.3%	1.57%	2.24%	3.8%	0.23%	0%	0.23%
Lead SNPs in the Illumina array	11.92%	18.54%	17.88%	2.65%	5.3%	5.3%	0%	0%	0%
Ntzani results	22%	42%	23%	18%	21%	39%	39%	58%	50%

Table 2. Differences in effect size and in the direction of effect across populations.

Comparison to Ntzani et al. study

Ntzani and colleagues [16] used the catalog of published GWAS curated at the National Human Genome Research Institute (NHGRI) website to characterize the frequency and magnitude of between-population differences in GWAS signals. A total of 97 associations were evaluated in both European and Asian populations, 24 in both European and African populations, and 13 in all three groups. The percentages of these signals displaying evidence for between-population differences are displayed in Table 2.

It is apparent that the rate at which trans-ethnic differences were found in the Ntzani et al study is considerably higher than what we found in our simulation study. A key constraint of our simulation study was that all our simulations were generated under equal-true-causal-effect-size conditions, across all populations. Thus, one plausible explanation for the considerable difference in the rate reported by Ntzani et al and our results is that true between-population differences in causal SNP genetic effect sizes do exist, and these true differences boost the rate seen in real empirical data.

Discussion

The evaluation of the simulated associations with genome-wide significance stresses Europeans as the population with the higher number of significant results. Specifically,

Europeans and Asians show the highest number of significant associations in common. This reflects the fact that the SNPs used to model the disease locus were selected from those common (MAF >5%) in Europe. SNPs across all eligible simulations showed lower average allele frequency than those with genome-wide significance (0.35≤allele frequency≤0.41 versus 0.45≤allele frequency≤0.50), reflecting a lower statistical power to reach genome-wide significance.

The current study highlights substantial replicability of association results across European, Asian and African ancestral groups. An overall consistency in the direction of effect across ancestries is detected, especially between Europeans and Asians (*causal SNPs*: 99.1%; *lead SNPs*: 98.4%; *lead SNPs in Illumina panel*: 97.4%). Regarding Z-scores, the three sets of target SNPs showed different patterns. Asian versus African comparisons showed the highest differences in effect size outside the setting of GWASs, using *causal* (6.6%) and *lead SNPs* (12.3%) approaches, while European versus African comparisons are the most different using *lead SNPs included in the Illumina panel* (18.5%). Differences in allele frequency may contribute to some of the discrepancies detected in the Z-scores but there are cases in which markers with significant Z-scores showed the same allele frequency between populations (Supplementary Figures 1-3). In these cases, population-specific causal variants are likely the main cause of the significant differences detected by Z-scores. Regarding African and Asian genetic differences, recent gene flow between Africans and Europeans [24] may explain the higher degree of differences in effect size observed between Africans and Asians compared to the differences between African and European populations. In addition, and in agreement with the Recent-African-Origin hypothesis [25], levels of haplotype diversity tend to decrease and LD patterns tend to increase proportionally to the geographic distance of a population from Africa. Asian populations in the 1000 Genomes Phase 1 release (CHB, CHS, and JPT) are all located in East Asia and consequently show the highest degree of discrepancies with the African samples. On the other hand, the higher level of differentiation detected between Europeans and Africans in the settings of current GWASs (using *lead SNPs included in the Illumina panel)* is in agreement with the low replicability rate detected between these two continental groups in a recent trans-ethnic comparison of GWAS results[7]. Lower lever of LD in Africans than in Eurasians reduce the correlation among causal variants and nearby SNPs. As a consequence, the probability to detect association signals is lower among

Africans than in Europe if the causal variants are not assayed directly. Despite this fact, comparing the three reference marker sets the proportion of differences decreases using *causal SNPs* then *lead SNPs included in the Illumina panel*, highlighting a possible shared genetic architecture of common diseases across continents.

The results of this simulation work may be relevant for one important open question in GWASs: the localization of causal variants. To evaluate the consistency of associations across continents might help to shortlist the noise inherent in current GWASs. In addition, in samples of African descent, it might be relatively easy to localize the causal SNP because it is in weak LD with neighbouring SNPs and will stand out at the peak of the association signal [26]. We have also detected differences in 40.04% of the detected genome-wide significant signals between *causal SNPs* and *lead SNPs*, and in 64.24% of the detected associations between *causal SNPs* and *lead SNPs in the Illumina panel*. Lead SNPs could be non-causal SNPs, and a fraction of causal SNPs is likely outside the setting of current GWASs. Consequently, considering also the substantial replicability of association results detected across populations, trans-ethnic mapping may be used as a powerful tool to identify causal risk variants.

Our study was designed to allow a direct comparison to the study of Ntzani et al [16], which investigated between-population differences in GWAS signals in real data (collated from the NHGRI GWAS Catalogue). There is a striking difference in the rate at which between-population differences were generated in our simulation study compared to the much higher rate observed in the Ntzani et al study. One plausible explanation for this considerable difference is that true between-population differences in causal SNP genetic effect sizes do exist, and these true differences boost the rate seen in real empirical data. Thus, our study supports the existence of true between-population differences in genetic risk architecture.

Conclusion

This study confirms that a substantial fraction of association signals are shared across people of different ancestry. However, some discrepancies detected in the effect size across populations highlight the potential presence of population-specific causal variants, and the

importance of accounting for population structure in association studies. Our study supports the existence of true between-population differences in genetic risk architecture.

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Supplementary Material

Supplementary Figure 1. Allele frequency patterns of SNPS showing significant different effect size across populations, and their averages using "casual SNPs".

Supplementary Figure 2. Allele frequency patterns of SNPs showing significant different effect size across populations, and their averages using "lead SNPs".

Supplementary Figure 3. Allele frequency patterns of SNPs showing significant different effect size across populations, and their averages using "Lead SNPs included in the Illumina Panel".

Supplementary Tables 1-3. Observed discrepancies for ancestral effect size for the different reference SNPs: the causal SNP (**Supplementary Table 1**); the lead SNP, with the lowest p-value in Europe and with MAF>1% (**Supplementary Table 2**); the lead SNP, with the lowest p-value in Europe and also in the Human Omni Express Bead Chip array (**Supplementary Table 3**). stdbeta: standard deviation of beta values; P: p-value of the logistic association; EUR= Europeans; ASN= Asians; YRI= Sub-Saharan Africans. Different Z-score: 1 grey; No different Z-score: 0 white. Opposite direction: 0 grey; same direction: 1 white. Two fold difference: 1 grey. nGWAS_SNPs: number of SNPs included in the Illumina panel in each simulation.

Discussion

4.1 General discussion

The genetics of current human worldwide populations, with a special focus on the Mediterranean region, was used as a raw material to shed light on their demographic history and on the genetic bases of complex diseases, specifically of CAD. Different genetic markers, 18 Alu insertions and 367 SNPs, were analysed for the first time in general populations and Bedouins from Jordan. The same SNPs were also genotyped in a consistent set of samples from the Mediterranean Basin. The use of different kinds of markers, some of them with clear epidemiological implications, had the main aim of exploring the genetic variation in the Mediterranean area. Specifically, Alu markers were used to assess the genetic diversity within Jordan and to define the relationships across present-day Middle Eastern, North African, and European populations. SNPs located in the top CAD risk regions (1p13, 1q41, 9p21, and 10q11) were used to explore the genetic variation and the LD patterns across 19 populations from Europe, Middle East and North Africa, together with the Asian and African samples from the 1000 Genomes Project, and to describe whether the genetic variability in these genomic regions is better explained by demography or by natural selection processes.

Furthermore, Tunisian and Moroccan case-control samples were genotyped to test for the first time the applicability of GWAS results, mainly detected on people of European descent, to North Africa populations.

Finally, simulated genomic data were used to evaluate the consistency of association results across European, Asian and Sub-Saharan African case-control samples.

The main findings of the current thesis are discussed and interpreted here by means of different sections.

The *first section* will focus on the Mediterranean area, and on the use of neutral and CAD risk markers to clarify the demographic history of South European, North African and Middle Eastern populations.

The *second section* will deal with the distribution of risk markers for CAD, at two geographic scales: from the Mediterranean Basin to three continents (Europe, Asia and

Africa). Specifically, a discussion about demography or natural selection as the main cause of the observed heterogeneity across continents of CAD risk loci will be conducted.

Finally, in the *third section*, similarities and differences in the signals of association across different population groups will be discussed. In addition, the level of consistency in the genetic effect size of GWASs across populations of different continental ancestry will be evaluated.

4.2 Demographic history in the Mediterranean area

One of the topics in the present thesis was to study the genetic differentiation in Mediterranean populations by means of different types of markers. Neutral and CAD risk markers analysed in this study pointed out a low but significant geographic structure in the Mediterranean area. Specifically, the two PC analyses based on neutral Alu insertion polymorphisms [120] and on SNPs located in four CAD risk loci (1p13, 1q41, 9p21, and 10q11) [121], clearly separated North African samples from South Europeans. These results were supported by the genetic distance analysis performed using both types of markers. In addition, AMOVA based on Alu insertion polymorphisms indicated a significant variation between North Africa (including Bedouins) and Europe (F_{ST} =0.034 and F_{CT}=0.016; both $p<0.001$). The apportionment of the genetic variance among North Europe, South Europe and North Africa groups was significant also using CAD risk markers: F_{ST}=0.017 and F_{CT}=0.012 (both $p<0.0001$). Differences in the amount of genetic differentiation between the two studies (genetic distances and F_{ST} values) are likely due to the different sets of markers and populations included in each project, on the one hand Mediterranean populations (using 18 Alu markers) and on the other hand Europeans and North Africans (using 367 SNPs).

These results are consistent with previous studies of population relationships in the Mediterranean Basin based on autosomal Alu polymorphisms [122] and on SNPs [47] [45] which reported a significant genetic structure in the Mediterranean area. Human genetic diversity in the Mediterranean is higher than in other regions of the European continent because of its particular demographic history. The genetic distinctiveness of this area has been attributed to several human movements of the past including postglacial expansions

from glacial refugia in southern Europe to the rest of the continent, and/or the genic gene flow from the Near East, associated with the diffusion of agriculture.

Regarding the differentiation between North Africa and South Europe, recent genetic data estimated that about 1–3% of recent Sub-Saharan African ancestry is present in southern European populations [123] and that recent shared ancestry between Europe and Africa is substantially higher when gene flow from North Africans, rather than Sub-Saharan Africans, is considered [45]. The geographic barrier imposed by the Sahara Desert between North Africa and Sub-Saharan Africa likely played a role in these results. Other previous studies indicated the Mediterranean Sea as a barrier to gene flow between the two Mediterranean shores [124] [125]. The low but significant differentiation between North Africa and South Europe detected in the present thesis suggests that gene flow through the Mediterranean Sea was, at least partially, impaired. Although the genomic variation analysed in this thesis do not provide enough information for a more detailed discussion into this issue, a clinal distribution of allele frequencies rather than abrupt changes in the Mediterranean seems to be more plausible. In agreement with this point, a recent work suggested that isolation-by-distance, rather than a barrier to gene flow, is a more likely mechanism of genetic differentiation in the Mediterranean area [126].

As a particular case in the Mediterranean context, Bedouins and general population from Jordan analysed by means of 18 Alu insertion polymorphisms showed statistical differences (p=0.038). In the PC analysis performed with Alu markers, Bedouins clustered with North African samples with a relative separation from the rest, whereas general Jordanians clustered with Eastern Mediterranean populations (i.e. Turkey and Crete). This separation was evident also in the genetic distance and the AMOVA. Indeed, the genetic distance of general Jordanians to Middle Eastern populations (0.023) was slightly lower than that corresponding to Bedouins (0.028) and the genetic variance between North Africa (including Bedouins), Middle East (including general Jordanians), and Western Mediterranean indicated a statistically significant structure (F_{ST}=0.030 and F_{CT}=0.012; both $p < 0.001$) [120].

The genetic heterogeneity detected between Bedouins and urban inhabitants of Jordan is likely related to the fact that urban areas have been subject to several external influences in recent times but Bedouins have preserved their own genetic background because of their

nomadic and isolated lifestyle. The Arabic name of the Bedouins is *Badoo* and means "desert dwellers". This name comes from the same Arabic root word, *badiya*, which means "desert" or "steppe". They are traditionally pastoral and nomadic people which live in family units within a tribe and make their living from their sheep and goats. Their communities are marked by characteristic black goat-hair tents. Bedouins were the only inhabitants of Jordan's land outside the East Bank just a few generations ago. Now they are a minority group and traditional anthropology distinguished Bedouins from other Arabs habiting Jordan by a set of general morphological traits such as "shorter, thinner bodies, smaller and pointed facial features; and their generally darker skin tones" [127]. Although the modern state of Jordan was founded in the 20th century, it can claim to have hosted some of the oldest civilizations in the world. Most of the great early civilizations passed through Jordan because of its strategic position: Egyptians, Assyrians, Babylonians, Hittites, Greeks, Romans, Arabs, Turks, and Crusaders all helped to shape the region [128]. The genetic picture from this study agrees with other two previous studies based on mitochondrial DNA and Y-chromosome uniparental loci [117] [118] . These surveys, carried out on these two populations groups, reinforced the genetic distinctiveness of Bedouins. These previous phylo-geographic analyses of male and female uniparental markers in Jordan indicated that general population from Jordan shows the typical features of other Levantine populations, while Bedouins appears as a genetic isolate. Although the Levant is a proven crossroad of bi-directional migrations between Africa and West Asia, some geographic, such as the Dead Sea area, and social isolates, such as the Bedouins, have genetically resisted that human traffic and probably constitute the original substrate of Jordan.

4.3 CAD risk markers in Europe, Asia and Africa: demography or selection?

The general patterns of genetic variation observed in the four CAD risk regions analysed, 1p13, 1q41, 9p21, and 10q11, are in agreement with the genetic structure generated by demographic processes. In the context of three continents (Europe, Asia, and Africa), the genetic results obtained here are similar to other data from genome-wide genotyping which revealed geographic structure of human populations at a trans-continental level [129]. As far as the European and Mediterranean area, the four genomic regions of

epidemiological importance point out a pattern of variation similar to the one previously described using Alu insertion polymorphisms [120] [122] and genome-wide arrays [42] [45]. In this point, the results of this thesis are consistent with the correspondence between genetics and geography such as reported in Novembre et al.[42] and between genetics and human migrations as in Botigue et al.[45].

Despite the role of the demographic processes detected, the present work also identifies potential signals of positive and balancing selection in some specific risk markers and haplotypes. Actually, potential signatures of positive selection in the 9p21 region and of balancing selection in 9p21 and 10q11 have been observed. The regions under positive or balancing selection are shared across continents but the specific markers under selection are in some cases continent-specific [121]. The heterogeneity observed in the potential signals of natural selection in populations of different ancestry might be correlated with environmental and climatic variables, dietary changes and/or host response to pathogens. A previous work reported evidence for selection on two markers implicated in cardiovascular disease by identifying the SNPs with the strongest correlation between allele frequencies and climate [54], while another study enumerated several genes involved in the causal pathways of atherosclerosis, that may be subject to various degrees of selective pressures resulting from climatic and dietary changes and host response to pathogens [130].
The 9p21 genomic region showed consistent signals of positive selection in three markers (rs6475606, rs1537371 and rs1333042) previously associated with CAD [131] [132] [133]. The rs1333042 marker, used as representative of the other two risk markers because of their high LD, shows a South to North gradient of increasing MAF. This gradient correlates with CAD incidence [85], similary to previous studies on the apolipoprotein (Apo) E4 allele [87] or the genetic risk score of nitric oxide synthases [88]. This South to North gradient may be correlated with a potential selective role of CAD in the configuration of genetic diversity in current human populations. On the other hand, a previous study showed North to South clines opposite and uncorrelated with CAD incidence in the frequency of other markers associated with CAD [89], likely shaped by demography. Consequently, also demographic processes should be taken into account to explain the genetic heterogeneity observed across current human populations in CAD risk loci.

The natural selection signals detected in this study are difficult to interpret and understand basically for two reasons: i) because they are not strong and widespread across

all populations and ii) because the signals of positive selection are associated to risk (i.e. potentially harmful) mutations. Regarding the former point, polygenic adaptation and/or soft sweep models, in which adaptation occurs through selective pressures acting simultaneously at different loci, may help to understand selection signals observed in complex traits. Indeed, in CAD and in all other complex traits, many different loci contribute to generate the disease and at the moment there is an open debate about the causal variants and the role of rare variants [134] [135]. Consequently, the plausible signals of selection here found are expected to be weak and difficult to be clearly identified. The current study is not an isolated case. Indeed, in the literature some recent studies have proposed natural selection as a potential explanation for the observed differences between populations in the loci implicated in CVD [90] [54] [136]. However, in these cases the plausible selective signals are also weak and the demographic processes cannot be discarded. Therefore, different methods to detect selection are needed to address potential confounding effects caused by population history and structure and functional studies should accompany selection scans to establish definitive evidences of selection, mechanisms of selection, and functional effects of the allelic variants under selection in complex traits.

Regarding the second point, LD patterns or pleiotropy may be involved in the positive selection signals observed in potentially harmful mutations. Indeed, the signals of selection detected may be in LD with a relatively strong still unknown beneficial polymorphism not related with CAD [55], or the positively selected loci could be related to different risk traits located in the same genomic region [53]. For example, the 9p21 locus is associated also with multiple cancers [137], glaucoma [138], intracranial and abdominal aortic aneurysms [72], vascular dementia, and late onset Alzheimer's disease [139]. Therefore, pleiotropic processes cannot be discarded.

One limitation inherent in this survey is related to the ascertainment bias in the selection of markers. The fact that these results were obtained by genotyping SNPs selected for specific criteria (MAF higher than 0.05 in Europe and giving priority to markers not in LD in European populations), and not through direct sequencing, could affect the observed patterns population differentiation [19]. Nevertheless, the correspondence in the results of the selection scans in two datasets with different marker coverage (367 SNPs from our

genotyping dataset and all the genetic variation from the 1000 Genomes Project) gives more consistency to the observed results. However, future studies should be performed to discard the influence of demography, and to confirm the potential selective role of CAD in shaping the genetic diversity in current human populations.

4.4 Differences in association signals across populations

In the last years, several genetic variants have been robustly associated with CAD mainly in people of European descent through GWASs. Previous surveys in non-European population suggested that markers associated in one population may not translate easily to other populations. Associations found in Europeans should be investigated in other ethnic groups [81] to assess the consistency in association signals across populations, or to detect new population-specific risk markers. The replicability of GWAS results across populations could be a major step forward for trans-ethnic mapping. In this way, trans-ethnic mapping may enable the identification of causal risk variants of disease susceptibility by taking advantage of natural differences in genomic LD across ethnically diverse populations [140].

In this context, one of the aims of the present study was to evaluate the level (genomic regions and/or individual sites) to which the four most validated CAD risk regions, (1p13, 1q41, 9p21, and 10q11) previously detected in Europe, were also transferable to North Africa, specifically to people from Tunisia and Morocco. The results of this work showed significant association signals in the four genomic regions analysed in Moroccan and Tunisian samples [141] confirming the trans-ethnic importance of these genomic regions for the risk of CAD. However, in the meta-analyses performed with the North African case-control samples, only the 9p21 and 10q11 regions showed association signals. None of the North African risk SNPs was associated with CAD in Europe and the corresponding risk-score model discriminated cases and controls substantially better in Africa (AUC=0.63) than in Europe (AUC=0.52). These arguments suggest the existence of continent-specific CAD risk variants in these chromosomal regions. Regarding the most studied CAD risk region, 9p21, the lack of replication of European association signals in populations of African descent has been previously reported for coronary artery calcification [142] and ischemic stroke [143].

In general, differences in GWAS results across populations may be explained by differences in LD patterns, in statistical power, in MAF, or in the causal variants. The failure to replicate an association signal in Africa may be linked to the differences in LD patterns between European and African populations [144]. LD decays more rapidly between SNPs in African populations than in non-African populations. Replication studies across European populations have been largely successful because of the general genetic similarity across Europeans. Moreover, the higher LD in populations of European origin with respect to Africans reduces the likelihood of finding a substantial number of associated SNPs in North African and Sub-Saharan African populations [145] if the causal variants are not assayed directly.

To examine this issue, differences in the patterns of LD blocks among populations in these four CAD risk loci were evaluated. First of all, comparing South Europe and North Africa, and then extending the analyses to populations from Europe, Asia, and Sub-Saharan Africa. Significant differences in the LD and in the haplotype patterns confirm the heterogeneity in the genomic structure between North Africans and Europeans [141]. In addition, differences in the LD structure persist even between pairwise comparisons of European, North African, Asian, and Sub-Saharan African samples [121]. This result is in agreement with the previously observed general trend of lower haplotype diversity and higher LD values as the geographic distance from Africa increases [41]. In addition, this survey also points to a different chromosomal location of continental-specific CAD risk markers between North Africa and South Europe [141], and across European, Asian and African samples [121]. Accounting for LD across different populations by means of different methods, such as VarLD and/or transethnic fine-mapping, may help to shed light on GWAS results, detecting the true causal variants and ensuring that results are not biased by false positive or false negative findings [146]. A recent GWAS replicated in African Americans 17 associations with CAD, previously discovered in individuals of European ancestry. Five of these 17 loci were then fine mapped in African Americans, using the different patterns of LD between populations of European and African ancestry to identify DNA sequence variants more strongly associated with phenotypes than the index SNPs previously found in Europeans. In the African American samples there were markers more strongly associated with the phenotype than the original European SNPs, suggesting smaller genomic intervals to search for causal alleles [147]. As an example, the European associated

SNP rs174547 is in strong LD with rs1535, the most strongly associated SNP in the locus among African Americans. The two markers are in strong LD in the HapMap CEU sample (r^2=1) but not in the HapMap YRI sample ($r^2 \geq 0.09$) [147].

Regarding statistical power, one of the main limitations inherent in the Zanetti et al, 2015a case-control study [141] concerns the smaller sample size of North Africans compared to the European case-control samples. The limited African sample size likely explains: i) the lower number of associations found in Africa and, ii) the lack of replication in African samples of many of the associations found in Europe. Nevertheless, the risk SNPs identified in North Africa that passed the permutation test and were not replicated in Europe, underline the importance of differences in the genomic architecture of association results, as well as the potential existence of ethnic-specific CAD risk markers.

In order to have the same sample size across the compared populations and to evaluate the level of consistency in the genetic effect of GWASs across populations of different ancestry, genome-wide data of case-control samples of European, Asian and Sub-Saharan African origin were simulated. The simulation study highlighted an overall consistency in effect direction across populations of different ancestry, specifically between Europeans and Asians (97.4-99.1%, depending on the reference SNPs). In agreement with the current work, two recent reports on the replicability of GWASs across major ancestral groups highlighted an overall consistency in effect direction between Eurasian populations [83 148]. Regarding Z-score, Asian versus African comparisons showed the highest differences in effect size using causal (6.6%) and lead SNPs (12.3%), while European versus African comparisons were the most different using lead SNPs included in the Illumina panel (18.5%). These discrepancies may be related to differences in allele frequency. There were also cases in which markers with significant Z-score showed the same allele frequency values across populations. In these cases, population-specific causal variants are likely the main cause of the detected differences.

This simulation work showed discrepancies in 40.04% of the association signals between causal SNPs and leads SNPs, and in 64.24% between causal and lead SNPs included in the Illumina panel, suggesting that lead SNPs could be non-causal, and that a fraction of causal SNPs could likely be outside the setting of current commercial arrays. Because our simulations assumed no actual between-population differences in genetic effect size, and

because the rate of between-population effect size differences generated by our study (generated due to between-population differences in power, allele frequency or linkage disequilibrium) was considerably lower than the rate reported from empirical studies of real data [83], our study supports the existence of real between-population differences in the genetic risk architecture of complex traits.

In general, this study confirmed that a substantial fraction of association signals are shared across people of different ancestry. However, some discrepancies in the effect size across populations highlighted the potential presence of population-specific causal variants, and the importance of accounting for population structure in association studies.

Conclusions

The main conclusions obtained in this thesis are the following:

1. From the distribution of Alu polymorphisms, the two population samples from the Levant region revealed a significant genetic heterogeneity. Bedouins appeared closer to North African groups, while general Jordanians tend to group with the easternmost populations in the Mediterranean.

2. The genetic distinctiveness of Bedouins suggests that they had an important role in the peopling of Jordan, probably constituting its original substrate.

3. The general pattern of genetic variation observed in the top four CAD risk regions analysed (1p13, 1q41, 9p21, and 10q11) is consistent with a genetic structure generated by demographic processes. However, there are also potential signals of positive and balancing selection in some specific risk markers and haplotypes. Specifically, potential signatures of positive selection in the 9p21 region and of balancing selection in the 9p21 and 10q11were observed.

4. Regions under positive or balancing selection are shared across continents but the specific markers under selection are in some cases continent-specific.

5. Significant association signals with CAD were detected in the four genomic regions analysed in Moroccan and Tunisian samples. However, only the 9p21 and 10q11 regions remained significant in the meta-analyses performed in the North African samples, confirming the important risk role of the 9p21 region.

6. Genetic risk models based on the associations identified in Africa for the four genomic regions under study have some ability to discriminate between cases and controls in Africa but not in Europe.

7. Differences in the specific markers associated with CAD in each region between North Africa and South Europe, as well as among samples from Europe, Asia and Africa, were detected. These differences suggest the existence of continent-specific CAD risk variants in these chromosomal regions.

8. Significant differences in LD and haplotype patterns explain the genetic heterogeneity in the four CAD risk loci between North Africans and Europeans and also across European, North African, Asian, and Sub-Saharan African samples.

9. The simulation study highlights an overall consistency in effect direction across populations of different ancestry, especially between Europeans and Asians.

10. In some cases differences in effect size across different populations may be related to the allele frequency, but in other cases population-specific causal variants are likely the main cause of the significant differences detected in association signals.

11. This work suggests that SNPs with the most significant p-value could not be always the causal SNPs, and that a fraction of causal SNPs is likely outside the setting of current GWAS arrays.

12. Despite the high trans-ethnic replicability of the detected association results, some discrepancies in the effect size across populations support the existence of real between-population differences in the genetic risk architecture of complex traits, and the importance of accounting for population structure in association studies.

Resumen en castellano

1. Introducción

• La variación genética

La secuencia de ADN nuclear es idéntica para casi el 99,9% de los seres humanos. El 0,01% de las diferencias en el ADN es la causa de toda la variabilidad genéticamente determinada en los seres humanos y, en consecuencia, de las enfermedades. La información genética entera que un organismo hereda constituye su *genotipo*, mientras que los caracteres observables, tales como la morfología, el desarrollo o el comportamiento, constituyen su *fenotipo*. Variaciones fenotípicas se deben principalmente a las interacciones entre el genotipo y los factores ambientales.

Los complejos patrones de diversidad genética poblacional son el producto de muchos eventos demográficos y evolutivos que actúan en diferentes escalas de tiempo. La *mutación*, generando nuevos alelos y la *recombinación*, produciendo nuevas combinaciones de alelos preexistentes en diferentes loci, son las principales fuentes de variabilidad genética en los seres humanos. La recombinación entre alelos en el mismo cromosoma es extremadamente rara si los alelos están muy cerca uno del otro. La combinación de alelos específicos en un conjunto de loci estrechamente vinculados genera una estructura conocida como *haplotipo*. En general, este conjunto de alelos suele heredarse junto. Sin embargo, a veces la recombinación puede actuar sobre los haplotipos generando nuevas combinaciones y aumentando la cantidad total de haplotipos en el genoma. El grado en el que están vinculados los loci se puede calcular estimando el desequilibrio de ligamiento (LD) que es una medida de la asociación no aleatoria de los alelos en dos o más loci. Las diferentes poblaciones humanas tienen diferentes grados y patrones de LD. Por ejemplo, las poblaciones afrodescendentes son las más ancestrales y tienen regiones más pequeñas de alto LD debido a la acumulación de más eventos de recombinación.

La transmisión de las variaciones genéticas de generación en generación se traduce en una compleja historia que se puede rastrear hacia atrás en el tiempo. Las principales fuerzas evolutivas que dan forma a las variaciones genéticas son tres: la *deriva genética*, la *selección natural* y la *migración*. Estos tres procesos actúan como modificadores de las frecuencias alélicas a nivel poblacional. Una nueva mutación puede ser eliminada o aumentar en frecuencia a través de procesos estocásticos, como la deriva genética. Reducciones severas

en el tamaño de la población, conocidos como cuellos de botella o efectos fundadores, pueden dar lugar a grandes cambios de frecuencia en las poblaciones. La deriva genética conduce a una reducción de la variación genética dentro de la población y a un aumento de la variación inter-poblacional. Asimismo, algunos loci, mayoritariamente funcionales, pueden ser sometidos a procesos selectivos en función de los efectos que ellos tienen sobre la supervivencia y la capacidad reproductiva de sus portadores. Las mutaciones que no confieren ninguna ventaja o desventaja a sus portadores se describen como mutaciónes neutras. Se distinguen tres tipos principales de selección que modelan la variación genética y afectan la distribución de las frecuencias alélicas en las poblaciones. Las mutaciones perjudiciales se seleccionan en contra y generan un tipo de selección conocida como *selección negativa* o *purificadora*. Otras veces una nueva mutación puede conferir una ventaja selectiva y aumentar la fitness de las personas que la llevan. Este es el caso de la *selección positiva*, también llamada selección ventajosa, en la que una nueva variante genética se eleva en frecuencia y se propaga a través de la población hasta llegar a la fijación. El tercer mecanismo de selección es la *selección equilibradora*. Este régimen selectivo, conocido como ventaja del heterocigoto, aumenta la variación genética debido al hecho de que los individuos heterocigotos presentan una fitness mayor en comparación con los homocigotos. Por último, *la migración* que afecta la distribución geográfica de la diversidad genética humana. La migración puede aumentar la diversidad dentro de la población, introduciendo nuevos alelos en una población y, a través del flujo génico, puede hacer que las diferentes poblaciones sean genéticamente similares reduciendo la diversidad inter-poblacional.

- **Categorías de marcadores moleculares que se han utilizado en este trabajo**

Inserciones Alu

Las secuencias Alu son secuencias cortas (~300 pares de bases), repetidas y dispersas en el genoma. Con aproximadamente más de un millón de copias, las secuencias Alu son los elementos móviles más abundantes en el genoma humano. Dichos polimorfismos Alu resultan de gran utilidad para los estudios de genética de poblaciones. Debido a su reciente introducción evolutiva en el genoma humano muchos de los elementos Alu son polimórficos (presencia o ausencia de inserción) entre los individuos y las poblaciones. En

los estudios poblacionales son una herramienta útil por varias razones: i) no hay mecanismos específicos para eliminar inserciones recientes; ii) son idénticas por descendencia; iii) tienen un estado ancestral conocido, la ausencia de inserción; iii) son los productos de eventos evolutivos únicos; y iv) tienen una tasa de mutación muy baja y, por tanto, pueden utilizarse para rastrear acontecimientos demográficos remotos.

Polimorfismos de un solo nucleótido (SNPs)

Los SNPs son la clase más común de variación genética entre los individuos y consisten en la sustitución de una base nucleotidica por otra. Generalmente, los SNPs se generan tras la incorporación errónea de nucleótidos durante la replicación por puro azar o como consecuencia de una mutagénesis química o física.

Son comúnmente bialélicos y pueden estar ubicados en diferentes regiones genómicas: dentro de las secuencias codificantes, en regiones no codificantes, o en regiones intergénicas. Actualmente son los marcadores más utilizados en los estudios epidemiológicos y de genética poblacional, principalmente por su baja tasa de mutación (aproximadamente en el orden de 10^{-7}-10^{-8} por generación), que hace que sean prácticamente idénticos por descendencia, y por su fácil caracterizacón a gran escala. Los SNPs que capturan la variación idéntica en sitios cercanos en el genoma se nombran *tag SNPs*. Los alelos de estos SNPs están en alto LD entre ellos y en consecuencia cualquier de ellos pueden predecir con alta resolución la información genética presente en los otros.

- **Estudios de genética poblacional basados en marcadores neutros**

Los estudios de genética poblacional consideran principalmente la distribución de las frecuencias alélicas en una población determinada o en diferentes poblaciones. Originalmente estos estudios tenían el objetivo de reconstruir la historia evolutiva humana. Actualmente se utilizan no sólo para estudiar las migraciones pasadas, sino también para analizar diferencias epidemiológicas entre poblaciones. En los últimos años muchos investigadores han colaborado para mejorar el conocimiento en estos campos. Estudios como el *Proyecto del Genoma Humano (HGP)* o recientemente el *Proyecto de los 1000*

Genomas nacieron con este objetivo. Estos proyectos aportaron un conjunto consistente de datos nuevos y útiles para la genética de poblaciones, así como paneles de imputación para los estudios epidemiológicos. Gracias a las modernas tecnologías utilizadas, en los últimos 30 años nuestro conocimiento de la historia y de las relaciones entre las poblaciones humanas ha aumentado dramáticamente revelando una fuerte correlación entre la distancia geográfica y la genética de las poblaciones humanas que confirman el origen africano de los humanos modernos. En Europa, una distribución clinal de Sur a Norte de diminución de la heterocigosidad media y de aumento de los valores de LD han sido detectados, en acuerdo con las expectativas basadas en la historia demográfica de la población europea. Respecto a la zona del Mediterráneo, en esta área se han encontrado las estimaciones más altas de diversidad genética en consonancia con la historia demográfica compleja de esta región. Según estudios recientes las poblaciones del Sur y del suroeste europeo muestran la mayor proporción de haplotipos compartidos con las poblaciones de África sub-sahariana. Si bien las migraciones iniciales en Europa llegaron a través de Oriente Medio, al menos un cierto grado de flujo genético posterior se produjo directamente desde África. Estudios genéticos y arqueológicos colocan el Oriente Medio y la Península Arábiga como el primer escalón de los humanos modernos fuera de África. Hay, sin embargo, un cierto desconocimiento de las relaciones genéticas que pudieron establecer estas poblaciones con sus vecinos. Según un estudio reciente, los cambios culturales de los últimos dos milenios facilitaron la unión entre las poblaciones culturalmente similares del Levante, de la Península Arábiga y de África. Sin embargo, los mismos cambios culturales propiciaron el aislamiento genético de otros grupos poblacionales, geográficamente más cercanos, pero culturalmente muy diferentes. En consecuencia, la expansión islámica desde la Península Arábiga en el siglo séptimo probablemente supuso la introducción de linajes genéticos específicos de esta península en el ámbito musulmán, mientras que la actividad de los cruzados en los siglos 11-13 favoreció la entrada de linajes europeos occidentales en los cristianos del Levante.

- **Estudios genéticos con interés epidemiológico**

Los estudios genéticos poblacionales centrados en rasgos asociados a enfermedades son importantes por varias razones: i) para describir la distribución poblacional de los marcadores de riesgo, ii) para explicar la prevalencia de enfermedades en una determinada población, iii) para detectar posible señales de selección natural en rasgos específicos de riesgo, y vi) para identificar los factores realmente causales asociados a la enfermedad.

Las mutaciones de riesgo asociadas a enfermedades no siempre se distribuyen al azar en el genoma. En general, los SNPs asociados a enfermedades complejas tienden a agruparse en regiones de baja recombinación, y su frecuencia muestra un patrón heterogéneo entre poblaciones de diferente ascendencia. Respecto a las causas de esta heterogeneidad, algunos autores afirman que los SNPs asociados a enfermedades siguen un patrón de deriva neutral entre las poblaciones y no se ven afectados por la selección natural. Por el contrario, otros autores reconocen a la selección natural un posible papel para explicar la heterogeneidad detectada en las frecuencias de los alelos de riesgo.

- **Base genética de las enfermedades cardiovasculares**

La enfermedad cardiovascular (CVD) incluye cualquier enfermedad que afecta al sistema cardiovascular. Es la principal causa de morbilidad y mortalidad en todo el mundo. La enfermedad arterial coronaria (CAD), también conocida como enfermedad coronaria o enfermedad cardíaca aterosclerótica, cuenta con el mayor número de muertes entre el grupo de las enfermedades cardiovasculares. Al igual que cualquier otra enfermedad multifactorial compleja, está influenciada por el ambiente, el estilo de vida y distintos factores genéticos que interactúan para determinar el fenotipo clínico.

La susceptibilidad familiar para la CAD se ha estimado a través de varios estudios familiares y de gemelos. En general, la heredabilidad de eventos fatales de CAD es mayor en los hombres (57%) con respecto a las mujeres (38%), y alrededor del 96% de las muertes cardiovasculares se producen después de los 50 años de edad. Los datos de análisis tradicionales basados en estudios de gemelos indican que la varianza genética por CAD varía del 40% al 60%. En cuanto a los factores de riesgo clásicos, como la hipertensión, la obesidad y la diabetes, se evaluó que contribuyen al 25-39% de la incidencia poblacional del

CAD y que su prevalencia varía ampliamente entre los diferentes países. En los últimos años varios estudios de asociación del genoma completo (GWAS) han tratado de determinar la parte restante de la varianza genética asociada a CAD, que debería explicar el resto de la heredabilidad cardiovascular. Actualmente se han descubierto 153 variantes asociadas a CAD, 50 de las cuales han sido confirmadas en estudios independientes. La mayoría de estas variantes tiene un mecanismo desconocido de riesgo, mientras que otras están asociadas con otros factores de riesgo como C-LDL, C-HDL, triglicéridos, o hipertensión.

Los 153 SNPs de riesgo descubiertos hasta ahora sólo explican <10% de la variabilidad total en la CAD. Este hecho genera un problema conocido como heredabilidad perdida (*missing heritability*). Recientes hallazgos sugieren que los mecanismos epigenéticos y las interacciones gen-ambiente (GxE) podrían explicar una fracción sustancial de la missing heritability. Otra hipótesis es que gran parte de esta heredabilidad faltante pueda residir en los alelos de baja frecuencia (MAF = 0,5 -5%) y/o en las variantes raras (MAF> 0,5%), no incluidos en los GWAS. De esta manera, hay dos teorías principales: la *common disease common variant* (CDCV), y la *common disease rare variant* hipótesis. La primera sostiene que variación genética común con una penetrancia relativamente baja es la principal contribuyente a la susceptibilidad genética para enfermedades comunes, mientras que la segunda afirma que son las variantes raras, cada una con una penetrancia relativamente alta las principales contribuyentes a la susceptibilidad genética para enfermedades comunes. Hasta ahora pero no hay datos suficientes para justificar que múltiples alelos raros sean los principales componentes de la missing heritability, y es plausible pensar que tanto las variantes raras como las comunes contribuyen a la heredabilidad para la CAD.

- **Distribución poblacional de la CAD**

La incidencia de la CAD varía mucho según la región geográfica, el sexo y el origen étnico. En Europa, la prevalencia de la CAD no se distribuye homogéneamente, y muestra un gradiente de Norte a Sur con las incidencias más altas en Finlandia y en el Reino Unido y las más bajas en España y en Francia. Varios estudios han tratado de correlacionar la variación en la incidencia de la CAD con la distribución de los factores de riesgo clásicos y genéticos. Algunos de ellos afirman que la frecuencia de los alelos de riesgo está

claramente correlacionada con la incidencia de la CAD, mostrando un gradiente de incremento de sur a norte. Por el contrario, otro estudio reportó que las variantes genéticas asociadas a la CAD muestran patrones geográficos contrarios y sin correlación con la incidencia a la enfermedad. En este caso, los factores genéticos de riesgo en el sur de Europa muestran frecuencias más altas que en el norte de Europa. El papel que la selección natural o los eventos demográficos puedan jugar en estas diferencias es actualmente objeto de estudio. Hipótesis y modelos evolutivos, como la hipótesis del gen ahorrador (*thrifty-gene*), que explica la predisposición de ciertos grupos étnicos a la obesidad y a la diabetes, o el modelo de *susceptibilidad del alelo ancestral*, que afirma que el alelo ancestral es el de riesgo, mientras que el alelo derivado es protector; se han propuesto para explicar la epidemiología de las enfermedades complejas en un contexto evolutivo. A pesar de todas estas hipótesis, los potenciales mecanismos entre las señales de selección y la CAD aún no se han identificado. Se necesitan más trabajos para esclarecer y distinguir los efectos de los porcesos demográficos de los atribuibles a selección.

- **El contexto poblacional**

La población humana actual es el resultado de una gran expansión demográfica que se inició hace aproximadamente 60.000 años (kya) en África y concluyó con la llegada a América del Sur alrededor de 12 a 14 kya.

En el continente europeo, la prehistoria de los humanos modernos se puede dividir en cinco episodios principales: i) la primera colonización del Paleolítico Superior; ii) la re-colonización de gran parte del continente a partir de los refugios del sur después del último máximo glacial (LGM); iii) la recolonización post glacial por los grupos mesolíticos (final del Pleistoceno y principios del Holoceno); iv) las dispersiones migratorias a partir de la zona de Oriente Medio (Neolítico); y v) las migraciones en pequeña escala a lo largo de las redes de intercambio económico en todo el continente a partir de la Edad del Cobre en adelante. Según el registro fósil y arqueológico, la colonización de Europa por los humanos anatómicamente modernos se produjo hace unos 40 kya años desde Oriente Próximo a través de los Balcanes y de allí al oeste. Semejantes dispersiones desde el Oriente Próximo se produjeron también en el norte de África. Durante el último máximo glacial (unos 19-25

kya años antes del presente), las poblaciones humanas buscaron refugio en el suroeste de Europa, a lo largo del Mediterráneo, en el Levante y en las llanuras de Europa oriental. Desde estos refugios, una vez que cesaron las circunstancias climáticas extremas, los humanos modernos volvieron a expandirse hacia el centro y norte de Europa. El comienzo del Neolítico fue marcado por la llegada de la agricultura (hace unos 10 kya) y constituye, sin duda, uno de los eventos más importantes en la historia de la humanidad. Con la llegada de la Edad del Cobre aparecieron las primeras rutas comerciales en el Mediterráneo. Primero los fenicios y luego los griegos, seguidos por los romanos, establecieron colonias comerciales a lo largo de las costas del Mediterráneo modelando la actual composición genética de las poblaciones mediterráneas.

- **Poblaciones estudiadas**

Esta tesis analiza la variación genética de muestras poblacionales europeas, africanas y asiáticas, con particular énfasis en la región mediterránea. Debido a su posición en el Oriente Medio, Jordania ha representado una de las principales vías para los movimientos humanos. La falta de información genética sobre esta población, específicamente sobre los beduinos y la población general jordana, nos animó a realizar un análisis genético centrado en estas poblaciones. Este análisis se llevó a cabo a través de 18 inserciones autosómicas Alu. Posteriormente, el estudio poblacional se extendió desde el punto de vista epidemiológico utilizando otro tipo de variante genética: los SNPs. La variación genética presente en 4 regiones genómicas asociadas a la CAD (1p13, 1q41, 9p21 y 10q11) se analizó por primera vez utilizando muestras del sur de Europa, norte de África y Oriente Medio, así como las muestras africanas subsaharianas y asiáticas del Proyecto de los 1000 Genomas.

Estas cuatro regiones de riesgo CAD fueron analizadas también en un conjunto de muestras de casos con CAD y controles sanos del norte de África, concretamente de Marruecos y Túnez.

Por último, se simularon varias muestras de casos y controles de origen africano, europeo, y asiático y se realizaron análisis de regresión logística. Sucesivamente se evaluó el nivel de consistencia en las asociaciones detectadas entre las diferentes poblaciones continentales.

2. Objetivos

En concreto, los principales objetivos de esta tesis fueron los siguientes:

- Contribuir al conocimiento de la historia de las poblaciones humanas de la región de Levante, gracias a un análisis genético de dos muestras poblacionales: beduinos y jordanos generales. Este análisis incluyó:

    i) la evaluación de la diversidad genética dentro de Jordania;
    ii) la definición de la relación poblacional de los dos grupos residentes en Jordania en el marco del Mediterráneo ;
    iii) la identificación de las huellas genéticas de las migraciones humanas.

- Analizar la variación genética de las cuatro regiones principales de riesgo CAD (1p13, 1q41, 9p21 y 10q11) en 19 poblaciones de Europa, Oriente Medio y África del Norte, y además utilizando los datos de las muestras de Asia y África del Proyecto de los 1000 Genomas, con el fin de :

    i) estudiar la variación genética y los patrones de LD en estas poblaciones;
    ii) describir si la variabilidad genética en estas regiones genómicas se explica mejor por demografía o por selección natural;
    iii) evaluar si las señales de selección detectadas se comparten en los distintos continentes o pertenecen a un grupo específico poblacional.

- Estudiar la variación genética en estas cuatro regiones de riesgo CAD en un contexto epidemiológico, con el fin de:

    i) evaluar si las asociaciones encontradas en los GWASs europeos podrían ser transferibles también al norte de África, concretamente a las poblaciones tunecinas y marroquíes;
    ii) comparar las asociaciones y las tendencias detectadas en las muestras del norte de África con los datos disponibles europeos;
    iii) evaluar los efectos combinados (puntuación de riesgo) de los marcadores asociados en el norte de África.

- Evaluar el grado de consistencia en los resultados de asociación entre poblaciones de diferente ascendencia continental, para:

    i) evaluar la posibilidad de transferir las señales de asociación detectadas en europeos a poblaciones de otros continentes;
    ii) evaluar si las variantes de riesgo genéticos se comparten o no entre europeos, asiáticos y africanos;
    iii) evaluar el papel potencial de la frecuencia alélica en las diferencias trans-étnicas de las señales GWAS.

3. Resultados y Discusión

Diferentes marcadores genéticos, 18 inserciones Alu y 367 SNPs, se analizaron en la población general y en los beduinos de Jordania, y también en un conjunto consistente de muestras mediterráneas. El uso de diferentes tipos de marcadores, algunos de ellos con una clara implicación epidemiológica, tuvo el objetivo principal de explorar la variación genética en el área mediterránea. Específicamente, se usaron marcadores Alu para evaluar la diversidad genética dentro de Jordania y para definir la relación entre las actuales poblaciones del Mediterráneo. Por otra parte, los SNPs localizados en cuatro regiones de riesgo CAD (1p13, 1q41, 9p21 y 10q11) se utilizaron para explorar la variación genética y los patrones de LD en 19 poblaciones de Europa, Oriente Medio y África del Norte, juntas a las muestras asiaticas y africanas del Proyecto de los 1000 Genomas.

- **Historia demográfica del Mediterráneo**

Los SNPs de riesgo CAD y las inserciones Alu analizadas en este estudio señalaron una estructuración geográfica significativa en el área mediterránea. En concreto, las dos PCA separaron claramente las muestras del norte de África y del Sur de Europa. La diversidad genética humana en el Mediterráneo es mayor que en otras regiones del continente europeo debido a su particular historia demográfica. La baja pero significativa diferenciación detectada entre Norte de África y Europa del Sur sugiere una distribución clinal de las frecuencias alélicas en lugar de cambios abruptos en el Mediterráneo.

Como caso particular en el contexto mediterráneo, los beduinos y la población general de Jordania mostraron diferencias genéticas estadísticamente significativas (p = 0,038). En los análisis de componentes principales (PCA) los beduinos aparecen agrupados con las muestras del norte de África, mientras que los jordanos generales se sitúan cerca de las poblaciones del Mediterráneo oriental. Estas agrupaciones son evidentes también en los análisis de distancias genéticas y AMOVA. La heterogeneidad genética detectada entre beduinos y los habitantes urbanos de Jordania está probablemente relacionada con el hecho de que las zonas urbanas fueron objeto de varias influencias externas en los últimos años, pero los beduinos conservaron su propia base genética debido a su aislamiento y a su estilo de vida nómada y aislado. Genéticamente, dos estudios previos basados en el ADN mitocondrial y en el cromosoma Y analizaron estos dos grupos poblacionales y resaltaron el carácter genéticamente distintivo de los beduinos.

- **Marcadores de riesgo CAD en Europa, Asia y África: ¿demografía o selección?**

Los patrones generales de variación genética observados en las cuatro regiones de riesgo CAD analizadas, 1p13, 1q41, 9p21 y 10q11, mostraron una estructura genética plausiblemente modelada por procesos demográficos. En el contexto de los tres continentes (Europa, Asia y África) y en la zona de Europa y del Mediterráneo, los resultados genéticos obtenidos revelaron una clara estructuración geográfica. A pesar de la importancia de los procesos demográficos detectados, el presente trabajo también mostró señales potenciales de selección positiva y equilibradora en algunos marcadores y haplotipos de riesgo específicos. Se observaron potenciales señales de selección positiva en la región 9p21 y de selección equilibradora en la 9p21 y 10q11.

La región genómica 9p21 mostró señales consistentes de selección positiva en tres marcadores (rs6475606, rs1537371 y rs1333042) previamente asociados a CAD, que mostraron un gradiente creciente de frecuencia del alelo menor (MAF) de Sur a Norte, en correlación con la incidencia de la CAD.

Las señales de selección natural detectadas en este estudio son difíciles de interpretar y entender, básicamente por dos razones: i) porque no son fuertes y generalizadas, y ii) porque la selección positiva aparece asociada a mutaciones de riesgo (potencialmente deletéreas). En cuanto al primer punto, los modelos de adaptación poligénica y/o soft

sweep, en los que la adaptación se produce a través de presiones selectivas débiles que actúan simultáneamente en diferentes loci, podrían ayudar a comprender las señales de selección aquí observadas. Respecto al segundo punto, las señales de selección detectadas podrían estar en LD con un polimorfismo desconocido con un papel beneficioso relativamente fuerte y no relacionado a la CAD, o los loci seleccionados positivamente podrían estar relacionados con diferentes marcadores de riesgo localizados en la misma región genómica. Por ejemplo, el locus 9p21 está asociado también a varios tipos de cánceres, glaucoma intracraneal, aneurismas aórticos abdominales, demencia vascular, y a la aparición tardía de la enfermedad de Alzheimer. Por lo tanto, los procesos pleiotrópicos no pueden ser descartados. Además, se deberían realizar futuros estudios para descartar la influencia de la demografía, y para confirmar la posible función selectiva de la CAD en la conformación de la diversidad genética de la población humana actual.

- **Diferencias en las señales de asociación entre poblaciones**

En los últimos años, diferentes variantes genéticas han sido fuertemente asociadas a la CAD principalmente en personas de ascendencia europea a través de varios GWASs. Uno de los objetivos del presente estudio fue el de evaluar el nivel (regiones genómicas y/o marcadores individuales) en el que las cuatro regiones de riesgo CAD estudiadas previamente en Europa (1p13, 1q41, 9p21 y 10q11) puedan ser transferibles al norte de África, específicamente a individuos de Túnez y de Marruecos. Los resultados de este trabajo mostraron señales significativos de asociación en las cuatro regiones genómicas analizadas también en Marruecos y Túnez. Sin embargo, en el meta-análisis realizado utilizando las muestras de casos y controles norteafricanos, sólo las regiones 9p21 y 10q11 mostraron señales de asociación. El modelo de puntuación de riesgo correspondiente discriminó casos y controles sustancialmente mejor en África (AUC=0,63) que en Europa (AUC=0,52). Estos argumentos sugieren la existencia de variantes de riesgo CAD específicas en los distintos continentes en las regiones cromosómicas analizadas.

En general, diferencias en los resultados GWASs entre poblaciones distintas pueden ser explicadas por diferencias en los patrones de LD, en el poder estadístico, en la MAF, o en las variantes causales. El fracaso en reproducir una señal de asociación en África puede

estar relacionado con diferencias en los patrones de LD entre las poblaciones europeas y africanas. Para examinar esta cuestión, se evaluaron las diferencias poblacionales en los patrones de LD en los cuatro loci de riesgo CAD. Diferencias significativas en el LD y en los patrones haplotípicos confirmaron la heterogeneidad en la estructura genómica entre norteafricanos y europeos, y también entre Europa, Norte de África, Asia, y África Subsahariana. Además, este estudio también apuntó a una localización cromosómica diferente de los marcadores de riesgo CAD entre distintos continentes.

En cuanto a la potencia estadística, esta fue una de las principales limitaciones inherente en el estudio de casos y controles norteafricanos. Con el fin de comparar poblaciones utilizando el mismo número de muestras y de evaluar el nivel de consistencia en los resultados de asociación entre poblaciones distintas, fueron simulados datos genómicos de casos y controles de origen europeo, africano subsahariano y asiático. El estudio de simulación destacó una alta replicabilidad global en las señales de asociación entre las poblaciones estudiadas, especialmente entre europeos y asiáticos. No obstante, en algunos casos se detectaron diferencias en el tamaño del efecto entre las poblaciones estudiadas que podrían estar relacionadas con la frecuencia alélica. También se evidenciaron casos en los que marcadores con Z score significativo mostraron parecidos valores de frecuencia alélica entre las poblaciones comparadas. En estos casos, variantes causales específicas de población podrían ser la causa principal de las diferencias significativas detectadas. Este trabajo sugirió que los SNPs con el p-valor más significativo no siempre son los SNPs causales, y que una fracción de los SNPs causales probablemente se quedó fuera de los paneles utilizados en los actuales GWASs.

En general, este estudio confirma que una fracción importante de las señales de asociación se comparte entre poblaciones de diferente ascendencia. Sin embargo, algunas discrepancias en el tamaño del efecto entre poblaciones revelan la posible existencia de diferencias reales interpoblacionales en la arquitectura del riesgo genético de caracteres complejos, y la importancia de tener en cuenta la estructura poblacional en los estudios de asociación.

4. Conclusiones

Las principales conclusiones obtenidas en esta tesis son las siguientes:

1. Las dos muestras de Jordania revelan una heterogeneidad genética significativa. Los beduinos parecen estar más cerca de los grupos del norte de África, mientras que los jordanos generales tienden a agruparse con las poblaciones más orientales del Mediterráneo.

2. El carácter distintivo genético de los beduinos sugiere que tuvieron un papel importante en el poblamiento de Jordania, probablemente constituyendo su sustrato inicial.

3. El patrón general de la variación genética observada en las cuatro regiones de riesgo CAD analizadas (1p13, 1q41, 9p21 y 10q11) evidencia una estructuración genética probablemente modelada por procesos demográficos. A pesar de este hecho, se detectaron potenciales señales de selección positiva y equilibradora en algunos marcadores y haplotipos de riesgo. Específicamente, fueron observados potenciales señales de selección positiva en la región 9p21 y equilibradora en la 9p21 y 10q11.

4. Las regiones bajo selección positiva o equilibradora están compartidas en todos los continentes, pero los marcadores específicos son en algunos casos específicos de cada continente.

5. Se detectaron señales de asociación significativa a la CAD en las cuatro regiones genómicas analizadas en Marruecos y Túnez. Sin embargo, sólo las regiones 9p21 y 10q11 se mantuvieron significativas en el meta-análisis realizado utilizando las muestras del norte de África, confirmando el papel de riesgo de la región 9p21.

6. El modelo de puntuación de riesgo genético basado en las asociaciones identificadas en África para las cuatro regiones genómicas estudiadas evidencia una cierta capacidad para discriminar entre los casos y controles en África, pero no en Europa.

7. Se detectaron diferencias en los marcadores específicos asociados a la CAD entre el norte de África y el Sur de Europa, y también entre las muestras de Europa, Asia y África. Estas diferencias sugieren la existencia de variantes de riesgo CAD específicas de cada continente.

8. Diferencias significativas en los patrones de LD pueden explican la heterogeneidad genética relativa en los loci de riesgo para la CAD observadas entre norteafricanos y europeos y también entre Europa, Norte de África, Asia y África Subsahariana.

9. El estudio de simulación destaca una replicabilidad global en las señales de asociación entre poblaciones de diferente ascendencia, específicamente entre europeos y asiáticos.

10. En algunos casos diferencias en el tamaño del efecto entre diferentes poblaciones podrían estar relacionadas con la frecuencia alélica, pero en otros casos variantes causales específicas de población podrían ser la causa principal de las diferencias detectadas.

11. Este trabajo sugiere que los SNPs que muestran los p-valores más significativos no siempre son los SNPs causales, y que una fracción de los SNPs causales podría haberse quedad fuera de los actuales paneles GWAS.

12. A pesar de la alta replicabilidad trans-étnica detectada en las señales de asociación, algunas discrepancias en el tamaño del efecto entre poblaciones revelan la posible existencia de diferencias reales entre poblaciones en la arquitectura del riesgo genético de caracteres complejos y la importancia de tener en cuenta la estructura poblacional en los estudios de asociación.

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Appendix

Appendix 1:

Digital object identification (DOI) for the additional files provided in article: "Potential Signals of Natural Selection in the Top Risk Loci for Coronary Artery Disease: 9p21 and 10q11".

- **S1 Dataset. Individual genotypes of the analysed data.**
  doi:10.1371/journal.pone.0134840.s001
- **S1 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 1p13.**
  doi:10.1371/journal.pone.0134840.s002
- **S2 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 1q41.**
  doi:10.1371/journal.pone.0134840.s003
- **S3 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 9p21.**
  doi:10.1371/journal.pone.0134840.s004
- **S4 Fig. Genomic coordinates, genes included and genotyped SNPs for the region 10q11.**
  doi:10.1371/journal.pone.0134840.s005
- **S5 Fig. LD blocks for the risk region 1p13 in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s006
- **S6 Fig. LD blocks for the risk region 1q41 in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s007
- **S7 Fig. LD blocks for the risk region 9p21 in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s008
- **S8 Fig. LD blocks for the risk region 10q11 in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s009
- **S9 Fig. LD blocks for the risk region 1p13 in which markers previously associated with CAD are located in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s010

- **S10 Fig. LD blocks for the risk region 1q41 in which markers previously associated with CAD are located in 26 populations from Europe, Africa and Asia.**
  doi:10.1371/journal.pone.0134840.s011

- **S1 Table. Geographic origin, population codification, sample size and geographic coordinates in decimal degrees for the population samples.**
  doi:10.1371/journal.pone.0134840.s012

- **S2 Table. Allele frequencies and heterozygozities (mean and standard deviation (SD)) per marker and per population.**
  doi:10.1371/journal.pone.0134840.s013

- **S3 Table. Reynolds's genetic distances estimated among North European and Mediterranean populations based on the SNPs located in the 1p13, 1q41, 9p21, and 10q11 CAD risk regions.**
  doi:10.1371/journal.pone.0134840.s014

- **S4 Table. LD statistics (D' and r^2) for each pair of risk SNPs and for each population analysed.**
  doi:10.1371/journal.pone.0134840.s015

- **S5 Table. Haplotype block data for the 1p13 region based on the S9 Fig.**
  doi:10.1371/journal.pone.0134840.s016

- **S6 Table. Haplotype block data for the 9p21 region based on the Fig 3.**
  doi:10.1371/journal.pone.0134840.s017

- **S7 Table. Haplotype block data for the 10q11 region based on the Fig 4.**
  doi:10.1371/journal.pone.0134840.s018

- **S8 Table. Detection of selection results for the four genomic regions analysed (1p13, 1q41, 9p21 and 10q11).**
  doi:10.1371/journal.pone.0134840.s019

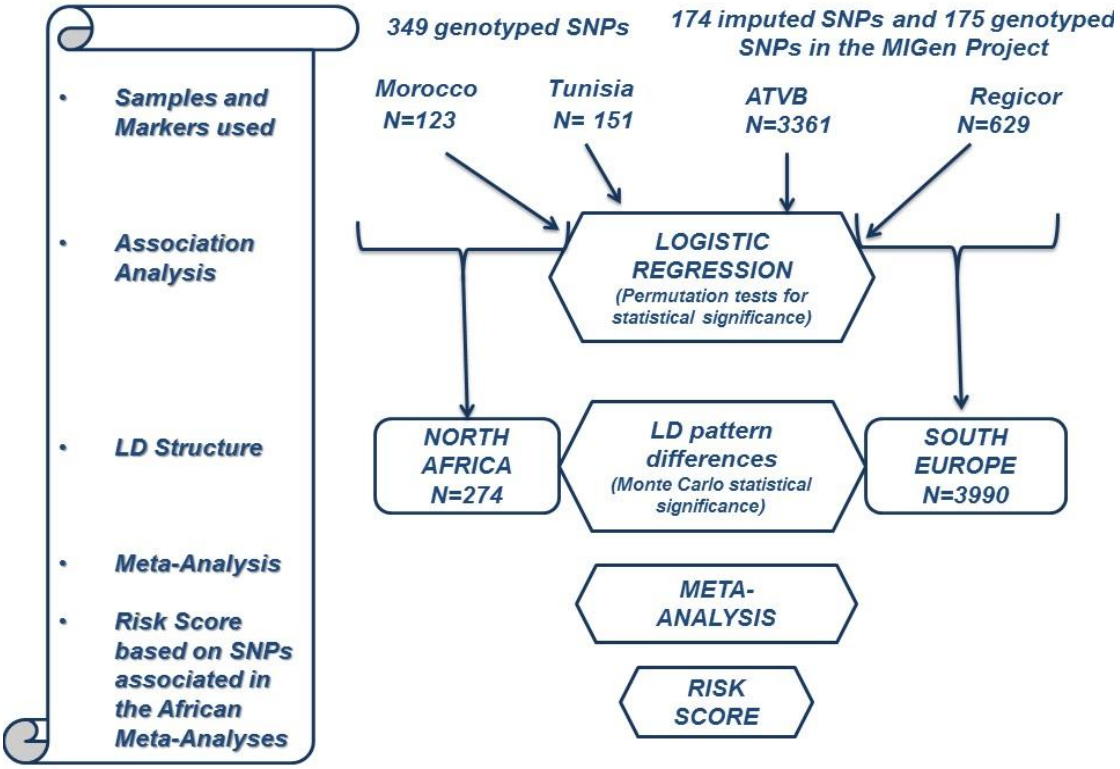
- **S9 Table. Global cross-continental F_{ST} scores in the CEU, CHB, and YRI samples of the 1000 Genomes Project.**
  doi:10.1371/journal.pone.0134840.s020

- **S10 Table. EHH averages in the CEU, CHB, and YRI samples of the 1000 Genomes Project.**
  doi:10.1371/journal.pone.0134840.s021

Appendix 2:

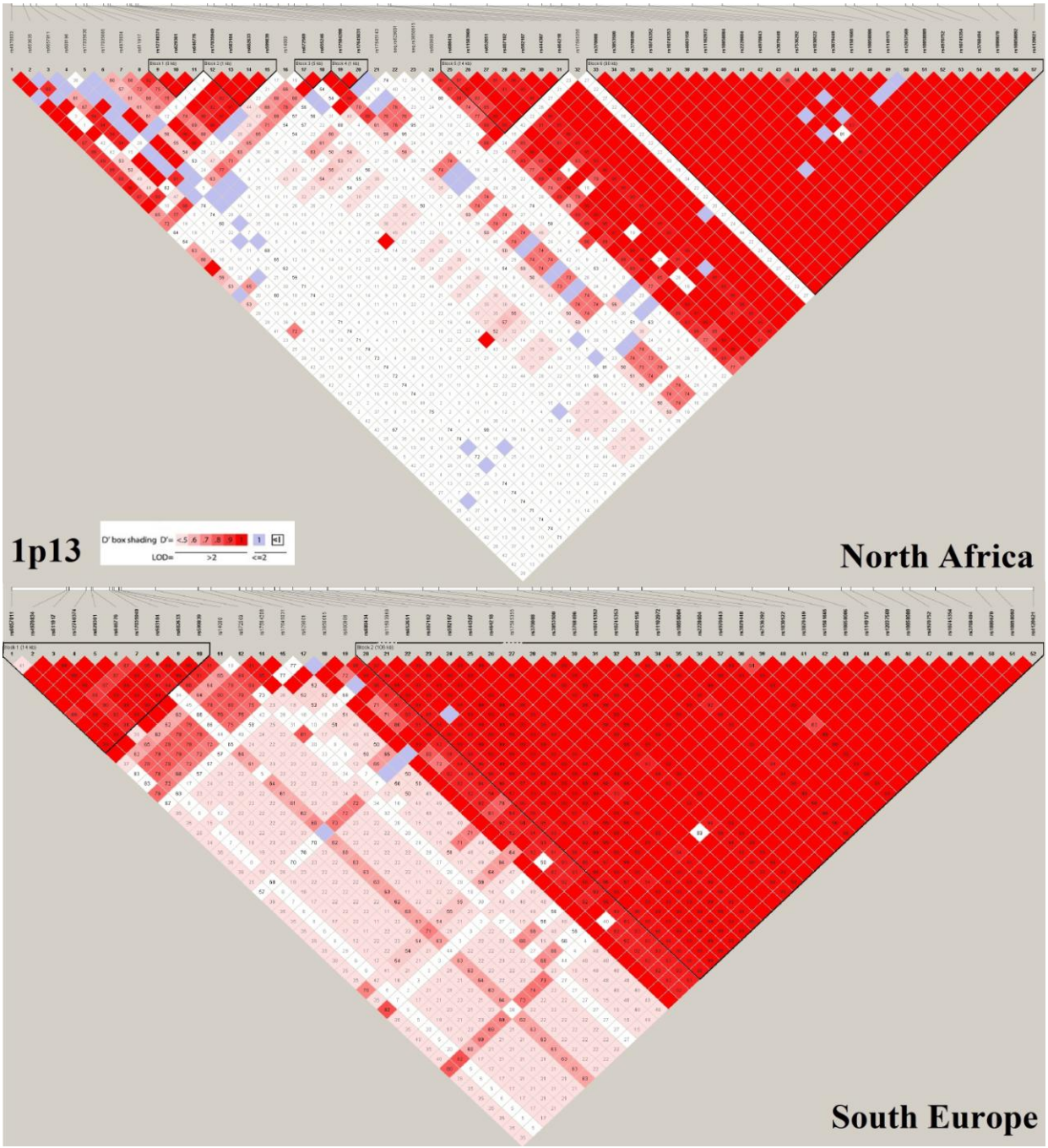
Additional files to the article: "Analysis of genomic regions associated with Coronary Artery Disease reveals continental-specific risk SNPs in North African populations".

- **Figure S1. Flowchart of the analyses performed in the study.**

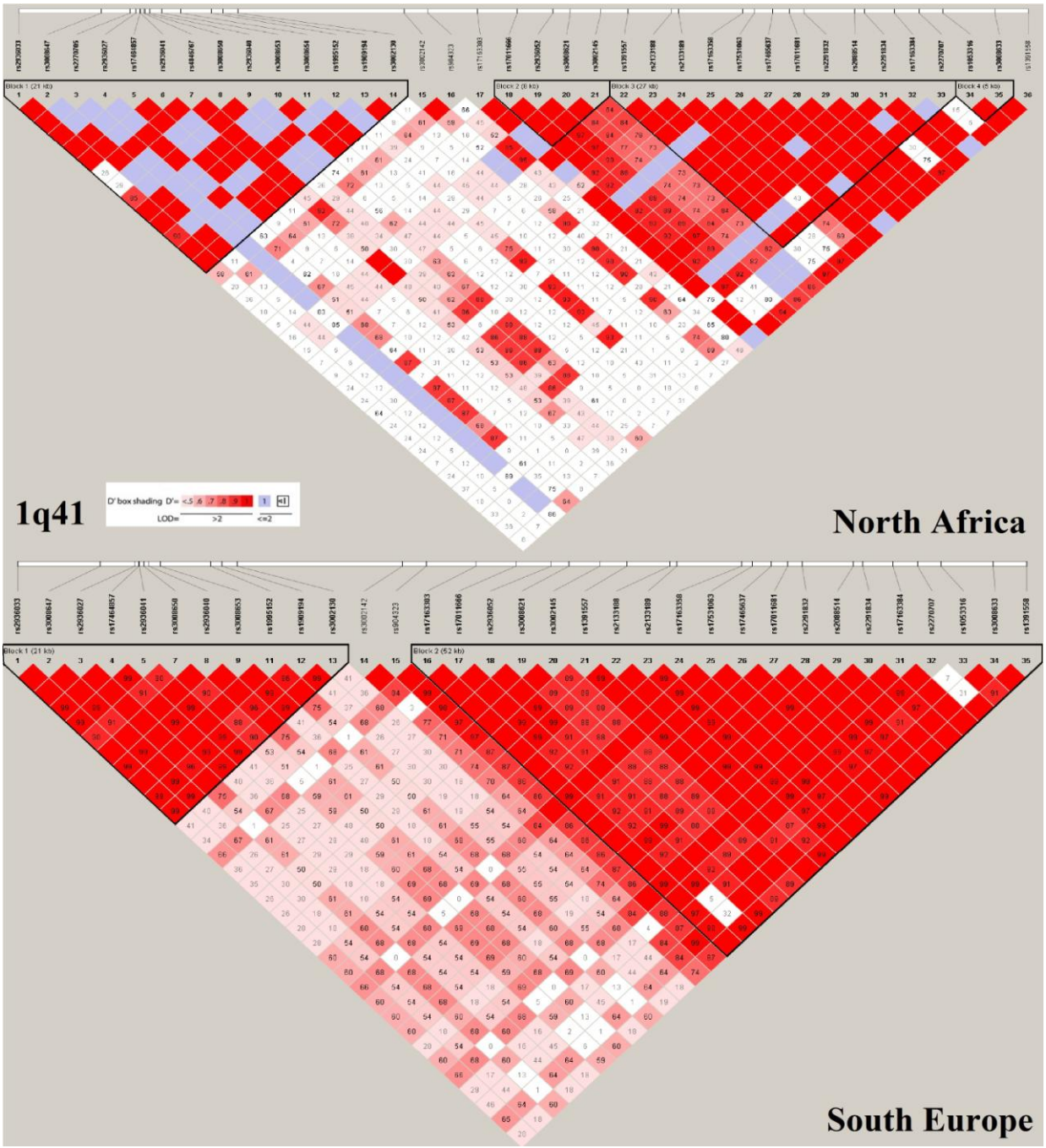


- **Figure S2A-D. LD patterns and haplotype block structure observed in North Africa and in South Europe for the region 1p13 (Figure S2A), 1q41 (Figure S2B), 9p21 (Figure S2C) and 10q11 (Figure S2D).** LD colors and values are based on D'. The 7 SNPs associated in the North Africa meta-analysis are marked with a black circle. D'-values represent percentages and appeared inside each diamond; values of 100% are not labeled.

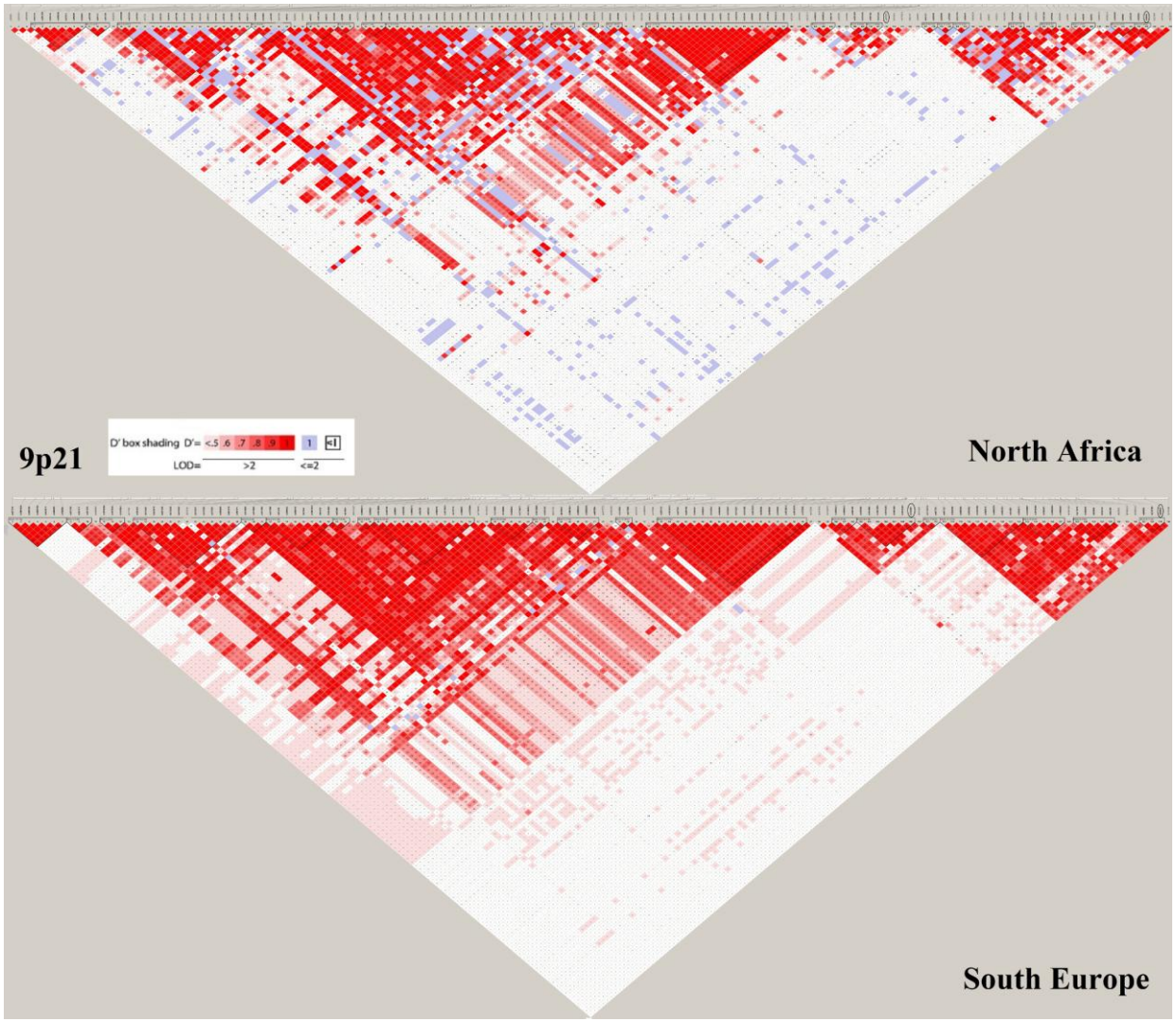
A



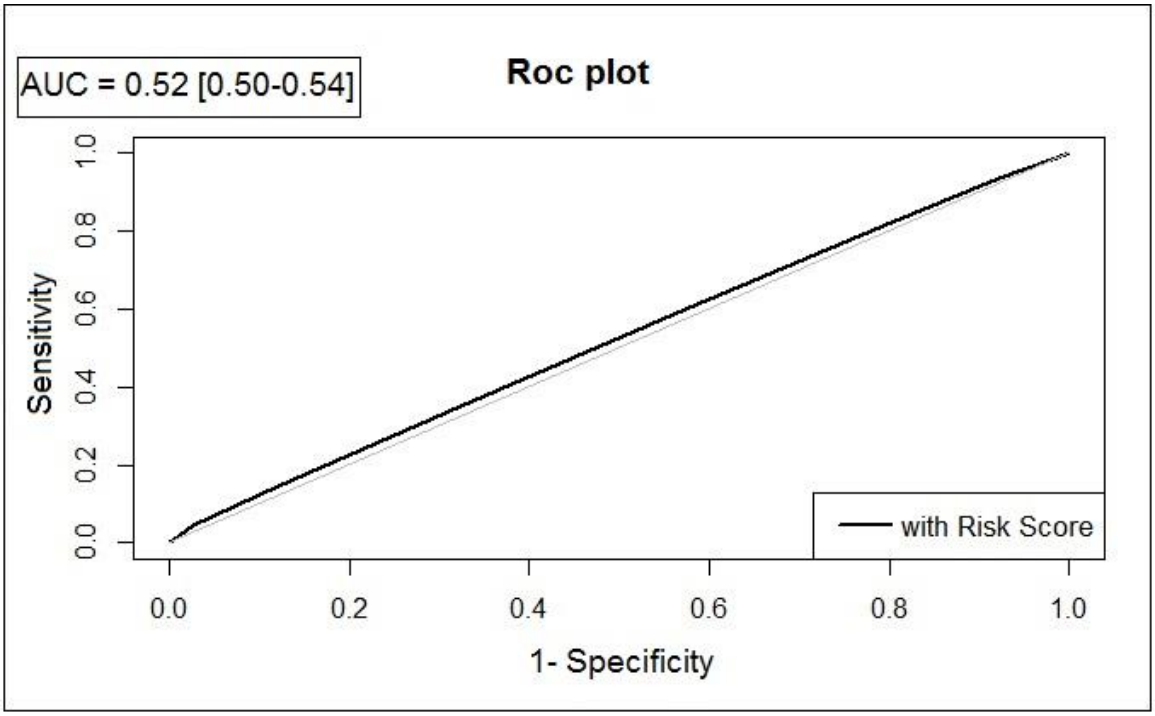
B



C


9p21
D' box shading D'= <.5 .6 .7 .8 .9 1 =1
LOD= >2 <=2
North Africa
South Europe

- **Figure S3. Receiver operating characteristic (ROC) curves in South Europe.** The number of risk alleles was based on the 6 independent risk alleles associated with CAD in North Africans. AUC: Area Under the ROC Curve with 95% confidence interval.



- **Table S1.Genomic location of the genetic variants, genotyping and imputation details.** Chromosome positions from Genome Reference Consortium human build 37 (GRCh37). GENOT: Genotyped; IMPUT: Imputed. MAF: minor allele frequency. Quality: the average posterior probability for the most likely genotype. Rsq: MACH quality metric (R2). SNPs with low imputation quality (R2<0.3) are highlighted in grey.

							ATVB				Regicor			
CHR	BP	SNP	Region	Status	Al1	Al2	FreqAl1	MAF	Quality	Rsq	FreqAl1	MAF	Quality	Rsq
1	109804646	rs4970833	1p13	IMPUT	A	G	0,529	0,471	0,565	0,244	0,517	0,483	0,569	0,251
1	109806313	rs653635	1p13	IMPUT	T	C	0,919	0,082	0,858	0,265	0,909	0,091	0,850	0,308
1	109807283	rs6657811	1p13	IMPUT	A	T	0,907	0,093	0,924	0,646	0,901	0,099	0,914	0,616
1	109808117	rs608196	1p13	IMPUT	C	T	0,918	0,082	0,859	0,268	0,909	0,091	0,850	0,311
1	109810981	rs17035630	1p13	IMPUT	G	A	0,914	0,086	0,835	0,057	0,919	0,081	0,844	0,049
1	109813719	rs17035665	1p13	IMPUT	C	T	0,802	0,198	0,736	0,277	0,796	0,204	0,724	0,263
1	109814880	rs4970834	1p13	IMPUT	C	T	0,879	0,121	0,960	0,848	0,865	0,135	0,960	0,866
1	109815252	rs611917	1p13	IMPUT	A	G	0,755	0,245	0,837	0,649	0,734	0,266	0,834	0,669
1	109817590	rs12740374	1p13	IMPUT	G	T	0,819	0,181	0,997	0,990	0,806	0,194	0,998	0,993
1	109818306	rs629301	1p13	GENOT	T	G	0,820	0,181	1	1	0,806	0,194	1	1
1	109818530	rs646776	1p13	IMPUT	T	C	0,819	0,181	0,999	0,996	0,806	0,194	0,999	0,998
1	109820919	rs17035949	1p13	GENOT	T	G	0,948	0,052	1	1	0,946	0,054	1	1
1	109821307	rs583104	1p13	GENOT	T	G	0,806	0,194	1	1	0,790	0,210	1	1
1	109821511	rs602633	1p13	IMPUT	G	T	0,823	0,177	0,970	0,919	0,809	0,191	0,966	0,915

1	109822166	rs599839	1p13	GENOT	A	G	0,807	0,193	1	1	0,790	0,210	1	1
1	109822509	rs14000	1p13	GENOT	T	C	0,889	0,111	1	1	0,881	0,119	1	1
1	109827253	rs672569	1p13	GENOT	G	A	0,892	0,108	1	1	0,882	0,118	1	1
1	109832283	rs655246	1p13	IMPUT	G	A	0,568	0,432	0,656	0,394	0,555	0,445	0,649	0,391
1	109833187	rs17584208	1p13	GENOT	G	A	0,956	0,044	1	1	0,948	0,053	1	1
1	109834938	rs17645031	1p13	IMPUT	C	T	0,956	0,044	0,998	0,980	0,948	0,052	0,998	0,977
1	109835757	rs17645143	1p13	IMPUT	T	C	0,680	0,320	0,665	0,338	0,684	0,316	0,661	0,332
1	109838918	rs629001	1p13	IMPUT	T	C	0,960	0,040	0,978	0,789	0,950	0,051	0,971	0,800
1	109839738	rs3850615	1p13	IMPUT	C	A	0,921	0,079	0,905	0,396	0,913	0,087	0,901	0,428
1	109840629	rs600806	1p13	GENOT	G	A	0,219	0,219	1	1	0,239	0,239	1	1
1	109842271	rs680434	1p13	IMPUT	C	T	0,263	0,263	0,939	0,851	0,278	0,278	0,941	0,857
1	109843775	rs11583969	1p13	GENOT	T	C	0,049	0,049	1	1	0,064	0,064	1	1
1	109844532	rs652651	1p13	IMPUT	A	G	0,242	0,242	0,963	0,921	0,261	0,261	0,961	0,919
1	109846278	rs407102	1p13	IMPUT	C	T	0,253	0,253	0,948	0,872	0,268	0,268	0,949	0,874
1	109848726	rs592107	1p13	IMPUT	A	T	0,253	0,253	0,948	0,870	0,268	0,268	0,949	0,873
1	109851127	rs444387	1p13	IMPUT	A	G	0,252	0,252	0,922	0,813	0,269	0,269	0,924	0,821
1	109856306	rs464218	1p13	IMPUT	G	A	0,421	0,421	0,968	0,931	0,453	0,453	0,968	0,929
1	109857815	rs17585355	1p13	GENOT	A	C	0,970	0,030	1	1	0,965	0,035	1	1
1	109858119	rs370088	1p13	IMPUT	T	C	0,247	0,247	0,932	0,834	0,263	0,263	0,934	0,843
1	109864269	rs3853500	1p13	IMPUT	T	C	0,245	0,245	0,933	0,837	0,261	0,261	0,937	0,847
1	109866569	rs3768496	1p13	IMPUT	T	A	0,249	0,249	0,981	0,948	0,267	0,267	0,983	0,954
1	109871787	rs10745352	1p13	IMPUT	T	C	0,249	0,249	0,982	0,951	0,267	0,267	0,984	0,956
1	109877506	rs10745353	1p13	IMPUT	A	G	0,248	0,248	0,985	0,961	0,267	0,267	0,986	0,963
1	109879549	rs4603158	1p13	IMPUT	C	T	0,248	0,248	0,987	0,964	0,266	0,266	0,988	0,966
1	109880721	rs11102972	1p13	IMPUT	C	T	0,209	0,209	0,939	0,829	0,222	0,222	0,942	0,838
1	109882250	rs10858084	1p13	IMPUT	T	A	0,248	0,248	0,992	0,978	0,266	0,266	0,990	0,973
1	109884775	rs2228604	1p13	IMPUT	T	G	0,247	0,247	0,995	0,986	0,266	0,266	0,996	0,990
1	109887191	rs4970843	1p13	GENOT	T	C	0,455	0,455	1	1	0,502	0,498	1	1
1	109891423	rs3879448	1p13	GENOT	G	C	0,255	0,255	1	1	0,279	0,279	1	1
1	109894693	rs7536292	1p13	GENOT	T	C	0,826	0,174	1	1	0,810	0,190	1	1
1	109900707	rs1030522	1p13	IMPUT	C	G	0,246	0,246	0,994	0,983	0,266	0,266	0,995	0,985
1	109904971	rs3879449	1p13	IMPUT	A	T	0,246	0,246	0,992	0,978	0,266	0,266	0,993	0,981
1	109910013	rs11581665	1p13	IMPUT	T	C	0,135	0,135	0,994	0,973	0,145	0,145	0,995	0,978
1	109915075	rs10858086	1p13	IMPUT	C	A	0,246	0,246	0,991	0,975	0,266	0,266	0,992	0,978
1	109922377	rs1149175	1p13	GENOT	A	G	0,134	0,134	1	1	0,144	0,144	1	1
1	109923677	rs12037569	1p13	IMPUT	G	T	0,863	0,137	0,907	0,661	0,851	0,149	0,893	0,651
1	109926828	rs10858089	1p13	IMPUT	T	C	0,246	0,246	0,993	0,980	0,265	0,265	0,993	0,981
1	109930852	rs4970752	1p13	IMPUT	C	T	0,246	0,246	0,993	0,982	0,266	0,266	0,994	0,983
1	109931908	rs10745354	1p13	IMPUT	C	T	0,246	0,246	0,994	0,982	0,266	0,266	0,994	0,983
1	109935427	rs3768494	1p13	IMPUT	A	G	0,246	0,246	0,995	0,985	0,266	0,266	0,995	0,985
1	109941133	rs1880670	1p13	IMPUT	C	T	0,246	0,246	0,998	0,994	0,266	0,266	0,998	0,994
1	109943893	rs10858092	1p13	GENOT	C	T	0,246	0,246	1	1	0,266	0,266	1	1
1	109949008	rs4120621	1p13	IMPUT	A	G	0,249	0,249	0,958	0,889	0,267	0,267	0,981	0,947
1	222751034	rs2936033	1q41	IMPUT	C	T	0,721	0,279	0,772	0,494	0,725	0,276	0,771	0,491
1	222759007	rs3008647	1q41	IMPUT	C	T	0,841	0,159	0,973	0,902	0,841	0,159	0,976	0,913

1	222761771	rs2270705	1q41	IMPUT	A	G	0,876	0,124	0,767	0,062	0,878	0,123	0,770	0,053
1	222762316	rs2936027	1q41	IMPUT	C	T	0,886	0,115	0,998	0,991	0,866	0,134	0,999	0,995
1	222762709	rs17464857	1q41	GENOT	T	G	0,839	0,161	1	1	0,839	0,161	1	1
1	222762773	rs2936041	1q41	GENOT	A	T	0,841	0,159	1	1	0,839	0,161	1	1
1	222763026	rs4846767	1q41	IMPUT	T	C	0,771	0,229	0,856	0,661	0,750	0,251	0,858	0,675
1	222763215	rs3008650	1q41	GENOT	C	G	0,882	0,118	1	1	0,858	0,142	1	1
1	222763661	rs2936040	1q41	GENOT	T	A	0,886	0,115	1	1	0,866	0,134	1	1
1	222764791	rs3008653	1q41	GENOT	C	G	0,839	0,161	1	1	0,839	0,161	1	1
1	222766609	rs3008654	1q41	IMPUT	G	A	0,869	0,131	0,909	0,702	0,869	0,131	0,912	0,708
1	222769593	rs1995152	1q41	IMPUT	A	C	0,886	0,115	0,998	0,988	0,866	0,134	0,998	0,991
1	222770703	rs1909194	1q41	GENOT	A	G	0,839	0,161	1	1	0,839	0,161	1	1
1	222772139	rs3002130	1q41	GENOT	T	C	0,839	0,162	1	1	0,839	0,161	1	1
1	222788062	rs3002142	1q41	GENOT	T	C	0,876	0,124	1	1	0,880	0,120	1	1
1	222790366	rs904323	1q41	IMPUT	G	A	0,834	0,166	0,865	0,599	0,823	0,177	0,852	0,579
1	222795118	rs17163303	1q41	GENOT	G	T	0,932	0,068	1	1	0,926	0,074	1	1
1	222798965	rs17011666	1q41	IMPUT	A	G	0,795	0,205	0,959	0,883	0,788	0,212	0,955	0,880
1	222802376	rs2936052	1q41	IMPUT	A	G	0,822	0,179	0,963	0,886	0,817	0,183	0,959	0,878
1	222804046	rs3008621	1q41	IMPUT	G	A	0,856	0,144	0,996	0,984	0,846	0,155	0,997	0,989
1	222807013	rs3002145	1q41	GENOT	C	T	0,855	0,145	1	1	0,845	0,155	1	1
1	222809616	rs1391557	1q41	IMPUT	C	T	0,824	0,176	0,998	0,993	0,819	0,181	0,997	0,992
1	222813753	rs2133188	1q41	GENOT	G	T	0,824	0,176	1	1	0,818	0,182	1	1
1	222814442	rs2133189	1q41	GENOT	T	C	0,729	0,271	1	1	0,716	0,284	1	1
1	222820639	rs17163358	1q41	GENOT	A	G	0,729	0,271	1	1	0,717	0,283	1	1
1	222821709	rs17531063	1q41	IMPUT	T	G	0,933	0,068	1,000	0,997	0,927	0,073	1,000	0,997
1	222823529	rs17465637	1q41	GENOT	C	A	0,731	0,269	1	1	0,717	0,283	1	1
1	222825088	rs17011681	1q41	IMPUT	G	C	0,730	0,270	1,000	0,999	0,716	0,284	0,999	0,998
1	222826481	rs2291832	1q41	IMPUT	A	G	0,730	0,270	0,999	0,998	0,716	0,284	0,999	0,997
1	222831372	rs2088514	1q41	IMPUT	A	G	0,824	0,176	0,998	0,995	0,819	0,182	0,998	0,993
1	222832295	rs2291834	1q41	IMPUT	C	T	0,730	0,270	0,998	0,996	0,716	0,284	0,998	0,995
1	222835222	rs17163384	1q41	IMPUT	A	C	0,933	0,068	0,999	0,994	0,927	0,073	0,999	0,994
1	222837594	rs2270707	1q41	GENOT	A	G	0,797	0,203	1	1	0,788	0,212	1	1
1	222839838	rs1053316	1q41	GENOT	G	A	0,905	0,095	1	1	0,897	0,103	1	1
1	222844840	rs3008633	1q41	IMPUT	C	T	0,918	0,082	0,974	0,860	0,907	0,093	0,974	0,877
1	222848029	rs1391558	1q41	IMPUT	T	C	0,827	0,174	0,976	0,916	0,822	0,179	0,973	0,911
9	21902354	rs756641	9p21	IMPUT	A	C	0,150	0,150	0,744	0,166	0,146	0,146	0,736	0,105
9	21905379	rs10811634	9p21	IMPUT	T	C	0,144	0,144	0,750	0,151	0,142	0,142	0,742	0,095
9	21909979	rs16938590	9p21	IMPUT	A	G	0,938	0,062	0,887	0,183	0,942	0,058	0,889	0,111
9	21920346	rs4977746	9p21	IMPUT	T	C	0,834	0,166	0,936	0,791	0,843	0,157	0,938	0,796
9	21923279	rs10811638	9p21	IMPUT	A	G	0,834	0,166	0,943	0,818	0,843	0,157	0,944	0,819
9	21925855	rs7852128	9p21	IMPUT	T	G	0,823	0,177	0,972	0,912	0,834	0,167	0,974	0,915
9	21927913	rs10965186	9p21	IMPUT	G	A	0,823	0,177	0,980	0,938	0,834	0,167	0,978	0,932
9	21929666	rs2518713	9p21	GENOT	A	G	0,824	0,176	1	1	0,833	0,167	1	1
9	21930147	rs7864029	9p21	GENOT	G	C	0,820	0,180	1	1	0,828	0,173	1	1
9	21931896	rs7869004	9p21	GENOT	G	T	0,820	0,180	1	1	0,828	0,173	1	1
9	21944317	rs4977750	9p21	IMPUT	A	C	0,865	0,135	0,952	0,821	0,890	0,111	0,962	0,832

9	**21946322**	**rs2811717**	**9p21**	**IMPUT**	**T**	**C**	0,869	0,131	0,974	0,909	0,896	0,104	0,985	0,933
9	**21947957**	**rs2811720**	**9p21**	**GENOT**	**C**	**G**	0,861	0,139	1	1	0,890	0,110	1	1
9	**21948666**	**rs10965197**	**9p21**	**GENOT**	**C**	**T**	0,604	0,396	1	1	0,632	0,368	1	1
9	**21953137**	**rs10757260**	**9p21**	**IMPUT**	**A**	**G**	0,596	0,405	0,994	0,989	0,645	0,355	0,993	0,986
9	**21954953**	**rs10757261**	**9p21**	**GENOT**	**G**	**A**	0,596	0,405	1	1	0,645	0,355	1	1
9	**21955669**	**rs12335941**	**9p21**	**IMPUT**	**A**	**G**	0,595	0,405	0,994	0,988	0,644	0,356	0,996	0,992
9	**21958524**	**rs717326**	**9p21**	**GENOT**	**T**	**C**	0,919	0,081	1	1	0,932	0,068	1	1
9	**21961866**	**rs7041637**	**9p21**	**IMPUT**	**C**	**A**	0,690	0,311	0,792	0,605	0,674	0,326	0,755	0,530
9	**21966221**	**rs3731257**	**9p21**	**IMPUT**	**G**	**A**	0,737	0,263	0,755	0,509	0,718	0,282	0,723	0,454
9	**21970427**	**rs2518719**	**9p21**	**IMPUT**	**A**	**G**	0,851	0,149	0,977	0,923	0,837	0,163	0,965	0,889
9	**21973422**	**rs2811708**	**9p21**	**IMPUT**	**G**	**T**	0,669	0,331	0,974	0,952	0,702	0,298	0,962	0,925
9	**21974218**	**rs3731239**	**9p21**	**IMPUT**	**G**	**A**	0,314	0,314	0,775	0,590	0,340	0,340	0,747	0,552
9	**21983914**	**rs3731222**	**9p21**	**IMPUT**	**T**	**C**	0,855	0,145	0,991	0,968	0,841	0,159	0,987	0,958
9	**21986218**	**rs3731213**	**9p21**	**GENOT**	**C**	**T**	0,979	0,021	1	1	0,991	0,009	1	1
9	**21986847**	**rs3731211**	**9p21**	**IMPUT**	**A**	**T**	0,687	0,313	0,991	0,982	0,710	0,290	0,988	0,974
9	**21987584**	**rs3731204**	**9p21**	**IMPUT**	**T**	**C**	0,855	0,145	0,993	0,977	0,841	0,159	0,989	0,965
9	**21988896**	**rs3731201**	**9p21**	**GENOT**	**T**	**C**	0,829	0,171	1	1	0,867	0,134	1	1
9	**21990457**	**rs7036656**	**9p21**	**IMPUT**	**T**	**C**	0,686	0,314	1,00	0,99	0,71	0,29	0,99	0,98
9	**21991923**	**rs2811710**	**9p21**	**GENOT**	**C**	**T**	0,598	0,402	1	1	0,646	0,355	1	1
9	**21993964**	**rs2811711**	**9p21**	**GENOT**	**T**	**C**	0,854	0,146	1	1	0,835	0,165	1	1
9	**21997872**	**rs3218020**	**9p21**	**IMPUT**	**A**	**G**	0,440	0,440	0,975	0,957	0,441	0,441	0,974	0,949
9	**22000841**	**rs3218002**	**9p21**	**IMPUT**	**G**	**A**	0,875	0,125	0,996	0,983	0,906	0,094	0,994	0,974
9	**22003223**	**rs3217992**	**9p21**	**GENOT**	**T**	**C**	0,481	0,481	1	1	0,474	0,474	1	1
9	**22005330**	**rs3217986**	**9p21**	**GENOT**	**T**	**G**	0,927	0,073	1	1	0,942	0,058	1	1
9	**22006348**	**rs974336**	**9p21**	**IMPUT**	**C**	**T**	0,875	0,125	0,997	0,986	0,906	0,094	0,994	0,976
9	**22008026**	**rs2069422**	**9p21**	**IMPUT**	**T**	**G**	0,872	0,128	0,994	0,979	0,904	0,096	0,993	0,970
9	**22009698**	**rs2069418**	**9p21**	**IMPUT**	**C**	**G**	0,657	0,343	0,992	0,985	0,606	0,394	0,991	0,985
9	**22011477**	**rs575427**	**9p21**	**GENOT**	**A**	**G**	0,920	0,081	1	1	0,894	0,106	1	1
9	**22013411**	**rs10811640**	**9p21**	**IMPUT**	**T**	**G**	0,534	0,467	0,995	0,992	0,513	0,487	0,993	0,988
9	**22017836**	**rs643319**	**9p21**	**GENOT**	**C**	**A**	0,620	0,380	1	1	0,591	0,409	1	1
9	**22018781**	**rs7044859**	**9p21**	**GENOT**	**A**	**T**	0,533	0,467	1	1	0,514	0,486	1	1
9	**22019129**	**rs523096**	**9p21**	**GENOT**	**A**	**G**	0,662	0,338	1	1	0,614	0,386	1	1
9	**22019673**	**rs518394**	**9p21**	**GENOT**	**G**	**C**	0,664	0,336	1	1	0,615	0,386	1	1
9	**22019732**	**rs10757264**	**9p21**	**GENOT**	**G**	**A**	0,580	0,420	1	1	0,561	0,439	1	1
9	**22023795**	**rs10965212**	**9p21**	**GENOT**	**A**	**T**	0,569	0,431	1	1	0,544	0,456	1	1
9	**22024351**	**rs496892**	**9p21**	**GENOT**	**C**	**T**	0,378	0,378	1	1	0,406	0,406	1	1
9	**22025493**	**rs10738604**	**9p21**	**IMPUT**	**A**	**G**	0,460	0,460	0,991	0,980	0,458	0,458	0,993	0,982
9	**22026834**	**rs1591136**	**9p21**	**IMPUT**	**C**	**G**	0,563	0,437	0,985	0,972	0,537	0,463	0,985	0,970
9	**22027551**	**rs598664**	**9p21**	**IMPUT**	**T**	**C**	0,875	0,125	0,995	0,983	0,906	0,094	0,995	0,979
9	**22028801**	**rs7049105**	**9p21**	**GENOT**	**G**	**A**	0,570	0,430	1	1	0,544	0,456	1	1
9	**22029445**	**rs10965215**	**9p21**	**GENOT**	**A**	**G**	0,563	0,438	1	1	0,537	0,463	1	1
9	**22029547**	**rs564398**	**9p21**	**GENOT**	**T**	**C**	0,697	0,303	1	1	0,642	0,359	1	1
9	**22030438**	**rs662463**	**9p21**	**GENOT**	**G**	**A**	0,881	0,119	1	1	0,908	0,092	1	1
9	**22031005**	**rs7865618**	**9p21**	**GENOT**	**A**	**G**	0,691	0,309	1	1	0,635	0,365	1	1
9	**22032119**	**rs10115049**	**9p21**	**IMPUT**	**G**	**A**	0,568	0,432	0,997	0,995	0,543	0,457	0,998	0,996

9	**22033366**	**rs2157719**	**9p21**	**IMPUT**	**T**	**C**	0,691	0,309	0,997	0,993	0,634	0,366	0,996	0,992
9	**22036112**	**rs1008878**	**9p21**	**IMPUT**	**T**	**G**	0,691	0,309	0,996	0,990	0,634	0,366	0,994	0,988
9	**22039426**	**rs12376000**	**9p21**	**IMPUT**	**C**	**T**	0,917	0,083	0,991	0,951	0,894	0,106	0,990	0,952
9	**22041998**	**rs17694493**	**9p21**	**GENOT**	**C**	**G**	0,858	0,142	1	1	0,874	0,126	1	1
9	**22042086**	**rs12352425**	**9p21**	**GENOT**	**G**	**A**	0,925	0,075	1	1	0,940	0,060	1	1
9	**22043926**	**rs1412829**	**9p21**	**IMPUT**	**A**	**G**	0,692	0,308	0,985	0,972	0,634	0,367	0,989	0,978
9	**22045317**	**rs1360589**	**9p21**	**IMPUT**	**T**	**C**	0,691	0,309	0,988	0,979	0,636	0,364	0,993	0,987
9	**22048683**	**rs7028570**	**9p21**	**IMPUT**	**A**	**G**	0,566	0,434	0,983	0,976	0,545	0,455	0,989	0,983
9	**22053895**	**rs17756311**	**9p21**	**GENOT**	**G**	**A**	0,895	0,105	1	1	0,919	0,081	1	1
9	**22054356**	**rs17694572**	**9p21**	**GENOT**	**G**	**A**	0,896	0,104	1	1	0,917	0,084	1	1
9	**22056499**	**rs10120688**	**9p21**	**GENOT**	**A**	**G**	0,574	0,426	1	1	0,554	0,446	1	1
9	**22061614**	**rs1537378**	**9p21**	**IMPUT**	**G**	**A**	0,708	0,292	0,992	0,984	0,657	0,343	0,993	0,987
9	**22062134**	**rs1011970**	**9p21**	**IMPUT**	**G**	**T**	0,817	0,184	0,983	0,955	0,856	0,144	0,981	0,946
9	**22064465**	**rs8181047**	**9p21**	**GENOT**	**G**	**A**	0,785	0,215	1	1	0,750	0,250	1	1
9	**22065002**	**rs10811647**	**9p21**	**IMPUT**	**G**	**C**	0,515	0,485	0,987	0,979	0,510	0,490	0,984	0,975
9	**22067276**	**rs10965224**	**9p21**	**GENOT**	**A**	**T**	0,707	0,293	1	1	0,657	0,343	1	1
9	**22069144**	**rs16905599**	**9p21**	**GENOT**	**G**	**A**	0,931	0,069	1	1	0,943	0,057	1	1
9	**22072301**	**rs9632884**	**9p21**	**GENOT**	**C**	**G**	0,623	0,377	1	1	0,600	0,400	1	1
9	**22072719**	**rs10757270**	**9p21**	**GENOT**	**G**	**A**	0,516	0,484	1	1	0,514	0,486	1	1
9	**22073334**	**rs16923583**	**9p21**	**GENOT**	**T**	**A**	0,977	0,023	1	1	0,989	0,011	1	1
9	**22077543**	**rs1412832**	**9p21**	**IMPUT**	**T**	**C**	0,781	0,220	0,961	0,912	0,750	0,250	0,963	0,926
9	**22081850**	**rs6475606**	**9p21**	**GENOT**	**T**	**C**	0,609	0,391	1	1	0,595	0,405	1	1
9	**22082340**	**rs1547704**	**9p21**	**GENOT**	**G**	**A**	0,982	0,018	1	1	0,987	0,013	1	1
9	**22082380**	**rs10965228**	**9p21**	**GENOT**	**A**	**G**	0,911	0,089	1	1	0,902	0,098	1	1
9	**22083404**	**rs1333040**	**9p21**	**IMPUT**	**T**	**C**	0,687	0,313	0,984	0,969	0,687	0,314	0,987	0,974
9	**22087473**	**rs7857345**	**9p21**	**IMPUT**	**C**	**T**	0,798	0,202	0,919	0,808	0,767	0,233	0,920	0,821
9	**22088260**	**rs10757272**	**9p21**	**GENOT**	**T**	**C**	0,591	0,409	1	1	0,575	0,425	1	1
9	**22098574**	**rs4977574**	**9p21**	**GENOT**	**G**	**A**	0,593	0,407	1	1	0,575	0,425	1	1
9	**22098619**	**rs2891168**	**9p21**	**GENOT**	**G**	**A**	0,592	0,408	1	1	0,575	0,425	1	1
9	**22099568**	**rs1537371**	**9p21**	**IMPUT**	**A**	**C**	0,604	0,396	0,997	0,995	0,582	0,419	0,995	0,992
9	**22102165**	**rs7859727**	**9p21**	**IMPUT**	**T**	**C**	0,594	0,406	0,997	0,994	0,576	0,424	0,996	0,993
9	**22103813**	**rs1333042**	**9p21**	**GENOT**	**G**	**A**	0,629	0,371	1	1	0,603	0,397	1	1
9	**22105927**	**rs7859362**	**9p21**	**IMPUT**	**C**	**T**	0,610	0,390	0,980	0,963	0,589	0,412	0,978	0,960
9	**22106731**	**rs1333043**	**9p21**	**IMPUT**	**A**	**T**	0,610	0,390	0,979	0,959	0,588	0,412	0,977	0,957
9	**22110131**	**rs1412834**	**9p21**	**IMPUT**	**C**	**T**	0,609	0,391	0,976	0,953	0,588	0,412	0,974	0,950
9	**22112241**	**rs7341786**	**9p21**	**IMPUT**	**C**	**A**	0,615	0,385	0,961	0,927	0,595	0,405	0,957	0,919
9	**22114469**	**rs10733376**	**9p21**	**IMPUT**	**C**	**G**	0,611	0,389	0,969	0,944	0,590	0,410	0,965	0,936
9	**22115026**	**rs2383206**	**9p21**	**IMPUT**	**G**	**A**	0,611	0,389	0,970	0,944	0,590	0,410	0,965	0,936
9	**22115959**	**rs2383207**	**9p21**	**IMPUT**	**G**	**A**	0,611	0,389	0,970	0,945	0,591	0,410	0,966	0,937
9	**22119195**	**rs1333045**	**9p21**	**IMPUT**	**C**	**T**	0,586	0,414	0,962	0,931	0,558	0,442	0,965	0,937
9	**22123766**	**rs10738610**	**9p21**	**IMPUT**	**C**	**A**	0,599	0,401	0,991	0,984	0,582	0,418	0,993	0,985
9	**22124477**	**rs10757278**	**9p21**	**IMPUT**	**G**	**A**	0,566	0,435	0,982	0,969	0,550	0,451	0,987	0,975
9	**22125347**	**rs1333048**	**9p21**	**GENOT**	**C**	**A**	0,597	0,403	1	1	0,579	0,421	1	1
9	**22125503**	**rs1333049**	**9p21**	**GENOT**	**C**	**G**	0,562	0,438	1	1	0,548	0,452	1	1
9	**22127613**	**rs10757281**	**9p21**	**IMPUT**	**C**	**T**	0,864	0,136	0,802	0,310	0,849	0,151	0,825	0,419

9	22128709	rs12347779	9p21	GENOT	C	G	0,946	0,054	1	1	0,922	0,078	1	1
9	22130065	rs10965243	9p21	IMPUT	A	G	0,921	0,079	0,995	0,967	0,894	0,106	0,998	0,989
9	22130515	rs10965245	9p21	GENOT	G	A	0,921	0,079	1	1	0,893	0,107	1	1
9	22131825	rs2891169	9p21	GENOT	A	G	0,572	0,428	1	1	0,553	0,448	1	1
9	22132076	rs2383208	9p21	GENOT	A	G	0,798	0,202	1	1	0,799	0,201	1	1
9	22133251	rs7045889	9p21	GENOT	G	A	0,334	0,334	1	1	0,356	0,356	1	1
9	22133716	rs10811659	9p21	GENOT	T	C	0,756	0,244	1	1	0,776	0,224	1	1
9	22133984	rs10757282	9p21	GENOT	T	C	0,529	0,471	1	1	0,522	0,479	1	1
9	22134094	rs10811661	9p21	GENOT	T	C	0,803	0,197	1	1	0,807	0,193	1	1
9	22134172	rs10757283	9p21	GENOT	C	T	0,527	0,473	1	1	0,525	0,475	1	1
9	22136489	rs1333051	9p21	GENOT	A	T	0,844	0,156	1	1	0,842	0,158	1	1
9	22137685	rs7018475	9p21	GENOT	T	G	0,700	0,300	1	1	0,708	0,293	1	1
9	22138105	rs11791416	9p21	GENOT	G	A	0,297	0,297	1	1	0,275	0,275	1	1
9	22138762	rs4977761	9p21	GENOT	T	C	0,283	0,283	1	1	0,305	0,305	1	1
9	22140224	rs2065501	9p21	IMPUT	C	A	0,565	0,435	0,559	0,213	0,594	0,406	0,550	0,190
9	22141875	rs4977577	9p21	IMPUT	C	T	0,273	0,273	0,704	0,418	0,292	0,292	0,708	0,452
9	22143293	rs7849199	9p21	IMPUT	T	A	0,703	0,297	0,916	0,804	0,714	0,287	0,946	0,873
9	22145694	rs2065500	9p21	IMPUT	A	G	0,781	0,219	0,946	0,863	0,775	0,225	0,961	0,902
9	22147715	rs7022662	9p21	GENOT	C	G	0,778	0,222	1	1	0,775	0,226	1	1
9	22148055	rs12341394	9p21	GENOT	C	T	0,701	0,299	1	1	0,715	0,285	1	1
9	22150261	rs7856219	9p21	IMPUT	T	C	0,696	0,304	0,989	0,977	0,707	0,293	0,979	0,954
9	22151465	rs10965256	9p21	GENOT	G	A	0,926	0,074	1	1	0,930	0,070	1	1
9	22153360	rs7853123	9p21	IMPUT	A	G	0,448	0,448	0,891	0,821	0,459	0,459	0,887	0,807
9	22155709	rs944802	9p21	IMPUT	C	T	0,789	0,211	0,958	0,907	0,777	0,223	0,956	0,906
9	22157360	rs7028213	9p21	IMPUT	T	G	0,695	0,305	0,972	0,939	0,709	0,291	0,967	0,928
9	22158168	rs12238587	9p21	IMPUT	T	A	0,780	0,220	0,986	0,968	0,771	0,229	0,987	0,969
9	22159416	rs10757288	9p21	IMPUT	C	T	0,404	0,404	0,955	0,928	0,427	0,427	0,950	0,919
9	22161212	rs7864275	9p21	GENOT	C	T	0,626	0,374	1	1	0,660	0,340	1	1
9	22161494	rs10965266	9p21	GENOT	T	G	0,782	0,218	1	1	0,774	0,226	1	1
9	22161828	rs10965267	9p21	GENOT	T	G	0,917	0,083	1	1	0,941	0,059	1	1
9	22164991	rs10811668	9p21	GENOT	C	A	0,726	0,274	1	1	0,751	0,249	1	1
9	22166769	rs2779748	9p21	IMPUT	T	C	0,379	0,379	0,877	0,791	0,411	0,411	0,864	0,782
9	22168128	rs7863846	9p21	GENOT	C	T	0,708	0,292	1	1	0,723	0,277	1	1
9	22168464	rs828580	9p21	GENOT	A	T	0,926	0,074	1	1	0,949	0,051	1	1
9	22169700	rs1537377	9p21	GENOT	T	C	0,635	0,365	1	1	0,673	0,327	1	1
9	22170983	rs954399	9p21	GENOT	C	A	0,708	0,292	1	1	0,728	0,272	1	1
9	22172259	rs828582	9p21	IMPUT	T	A	0,615	0,385	0,953	0,909	0,655	0,345	0,955	0,915
9	22174712	rs10965278	9p21	GENOT	G	A	0,728	0,272	1	1	0,733	0,267	1	1
9	22175188	rs10965279	9p21	GENOT	G	C	0,931	0,069	1	1	0,932	0,068	1	1
9	22176961	rs10757292	9p21	IMPUT	C	T	0,963	0,037	0,937	0,243	0,969	0,031	0,944	0,186
9	22183781	rs866666	9p21	IMPUT	C	T	0,340	0,340	0,639	0,335	0,368	0,368	0,629	0,337
9	22184997	rs2767409	9p21	IMPUT	G	A	0,627	0,373	0,649	0,369	0,653	0,347	0,646	0,342
9	22187074	rs1095904	9p21	IMPUT	G	T	0,656	0,344	0,629	0,317	0,680	0,320	0,632	0,298
9	22191189	rs828576	9p21	IMPUT	T	C	0,341	0,341	0,631	0,315	0,367	0,367	0,622	0,321
9	22195820	rs2219849	9p21	IMPUT	T	C	0,531	0,469	0,604	0,309	0,539	0,461	0,595	0,293

9	**22196863**	**rs1751449**	**9p21**	**IMPUT**	**A**	**G**	0,599	0,401	0,635	0,343	0,620	0,380	0,634	0,331
9	**22198149**	**rs12375458**	**9p21**	**IMPUT**	**G**	**A**	0,898	0,102	0,812	0,115	0,904	0,096	0,819	0,085
10	**44682973**	**rs1482472**	**10q11**	**IMPUT**	**T**	**C**	0,624	0,376	0,858	0,721	0,624	0,376	0,831	0,677
10	**44686664**	**rs12415866**	**10q11**	**IMPUT**	**A**	**G**	0,867	0,133	0,959	0,857	0,895	0,105	0,958	0,804
10	**44688587**	**rs7917089**	**10q11**	**IMPUT**	**G**	**A**	0,868	0,132	0,963	0,881	0,899	0,101	0,960	0,819
10	**44691241**	**rs1623851**	**10q11**	**GENOT**	**A**	**G**	0,814	0,186	1	1	0,836	0,165	1	1
10	**44691633**	**rs1627329**	**10q11**	**GENOT**	**T**	**C**	0,813	0,187	1	1	0,836	0,165	1	1
10	**44693544**	**rs10508883**	**10q11**	**GENOT**	**A**	**C**	0,976	0,024	1	1	0,981	0,019	1	1
10	**44693742**	**rs7900182**	**10q11**	**GENOT**	**T**	**G**	0,829	0,171	1	1	0,807	0,193	1	1
10	**44694201**	**rs11597731**	**10q11**	**GENOT**	**C**	**T**	0,822	0,178	1	1	0,801	0,200	1	1
10	**44695308**	**rs7902040**	**10q11**	**GENOT**	**A**	**G**	0,889	0,111	1	1	0,917	0,084	1	1
10	**44695862**	**rs11238911**	**10q11**	**GENOT**	**G**	**A**	0,891	0,110	1	1	0,917	0,083	1	1
10	**44695973**	**rs11238913**	**10q11**	**GENOT**	**T**	**C**	0,667	0,333	1	1	0,661	0,339	1	1
10	**44696034**	**rs2802477**	**10q11**	**IMPUT**	**G**	**A**	0,418	0,418	0,781	0,665	0,419	0,419	0,775	0,660
10	**44696352**	**rs11594522**	**10q11**	**GENOT**	**G**	**A**	0,833	0,168	1	1	0,808	0,192	1	1
10	**44698075**	**rs2054620**	**10q11**	**IMPUT**	**T**	**C**	0,667	0,333	0,994	0,987	0,661	0,339	0,995	0,990
10	**44699910**	**rs11238921**	**10q11**	**IMPUT**	**G**	**T**	0,667	0,333	0,991	0,980	0,662	0,339	0,992	0,983
10	**44702681**	**rs768676**	**10q11**	**GENOT**	**T**	**A**	0,938	0,062	1	1	0,941	0,060	1	1
10	**44705969**	**rs3865770**	**10q11**	**IMPUT**	**G**	**A**	0,832	0,168	0,990	0,960	0,807	0,193	0,991	0,972
10	**44707598**	**rs1482473**	**10q11**	**IMPUT**	**G**	**C**	0,845	0,155	0,990	0,963	0,861	0,139	0,992	0,968
10	**44709171**	**rs3851257**	**10q11**	**IMPUT**	**G**	**T**	0,668	0,333	0,983	0,957	0,662	0,339	0,985	0,967
10	**44712128**	**rs12573558**	**10q11**	**IMPUT**	**C**	**A**	0,818	0,182	0,978	0,927	0,797	0,203	0,982	0,948
10	**44714402**	**rs11238935**	**10q11**	**IMPUT**	**C**	**T**	0,891	0,109	0,992	0,961	0,918	0,082	0,994	0,962
10	**44716469**	**rs2209067**	**10q11**	**IMPUT**	**G**	**A**	0,818	0,183	0,977	0,926	0,796	0,204	0,982	0,947
10	**44729958**	**rs1704219**	**10q11**	**GENOT**	**G**	**C**	0,682	0,318	1	1	0,676	0,324	1	1
10	**44730995**	**rs7907961**	**10q11**	**IMPUT**	**T**	**C**	0,791	0,209	0,994	0,985	0,757	0,243	0,993	0,984
10	**44732825**	**rs1746043**	**10q11**	**IMPUT**	**T**	**C**	0,679	0,321	0,990	0,983	0,677	0,323	0,987	0,980
10	**44734995**	**rs647419**	**10q11**	**IMPUT**	**G**	**A**	0,639	0,361	0,990	0,979	0,638	0,362	0,983	0,971
10	**44737036**	**rs88796**	**10q11**	**GENOT**	**T**	**C**	0,722	0,278	1	1	0,735	0,266	1	1
10	**44737246**	**rs617019**	**10q11**	**GENOT**	**G**	**A**	0,886	0,114	1	1	0,921	0,080	1	1
10	**44737433**	**rs17155733**	**10q11**	**GENOT**	**A**	**G**	0,837	0,163	1	1	0,817	0,183	1	1
10	**44738688**	**rs583489**	**10q11**	**GENOT**	**C**	**G**	0,876	0,124	1	1	0,913	0,087	1	1
10	**44739594**	**rs676966**	**10q11**	**GENOT**	**C**	**T**	0,884	0,116	1	1	0,919	0,081	1	1
10	**44741256**	**rs494207**	**10q11**	**IMPUT**	**G**	**A**	0,876	0,124	0,999	0,994	0,913	0,087	0,998	0,987
10	**44746395**	**rs541483**	**10q11**	**IMPUT**	**A**	**G**	0,826	0,174	1,000	0,999	0,864	0,136	1,000	0,998
10	**44747059**	**rs535176**	**10q11**	**GENOT**	**C**	**T**	0,826	0,174	1	1	0,864	0,136	1	1
10	**44749211**	**rs622472**	**10q11**	**GENOT**	**A**	**C**	0,826	0,174	1	1	0,864	0,136	1	1
10	**44749708**	**rs513391**	**10q11**	**GENOT**	**A**	**C**	0,826	0,174	1	1	0,864	0,136	1	1
10	**44749854**	**rs11238956**	**10q11**	**GENOT**	**C**	**T**	0,339	0,339	1	1	0,329	0,329	1	1
10	**44751910**	**rs687175**	**10q11**	**GENOT**	**T**	**C**	0,827	0,173	1	1	0,867	0,133	1	1
10	**44752078**	**rs559580**	**10q11**	**GENOT**	**T**	**C**	0,829	0,171	1	1	0,872	0,128	1	1
10	**44752118**	**rs559469**	**10q11**	**GENOT**	**T**	**C**	0,826	0,174	1	1	0,867	0,133	1	1
10	**44752268**	**rs2437935**	**10q11**	**GENOT**	**A**	**G**	0,614	0,386	1	1	0,624	0,376	1	1
10	**44752330**	**rs535949**	**10q11**	**GENOT**	**G**	**T**	0,828	0,172	1	1	0,867	0,133	1	1
10	**44752976**	**rs671765**	**10q11**	**GENOT**	**A**	**G**	0,828	0,172	1	1	0,867	0,133	1	1

10	**44753867**	**rs501120**	**10q11**	**IMPUT**	**T**	**C**	0,828	0,173	0,999	0,997	0,867	0,133	0,999	0,996
10	**44755104**	**rs579058**	**10q11**	**IMPUT**	**A**	**G**	0,828	0,173	0,999	0,996	0,867	0,133	0,999	0,995
10	**44756894**	**rs604674**	**10q11**	**IMPUT**	**G**	**T**	0,828	0,172	0,995	0,985	0,867	0,133	0,997	0,986
10	**44758197**	**rs487465**	**10q11**	**IMPUT**	**A**	**C**	0,828	0,172	0,995	0,984	0,867	0,133	0,997	0,986
10	**44760887**	**rs475926**	**10q11**	**IMPUT**	**T**	**G**	0,678	0,322	0,984	0,970	0,687	0,313	0,986	0,972
10	**44773984**	**rs1632484**	**10q11**	**GENOT**	**C**	**T**	0,833	0,168	1	1	0,872	0,128	1	1
10	**44775824**	**rs1746048**	**10q11**	**GENOT**	**C**	**T**	0,830	0,170	1	1	0,868	0,132	1	1
10	**44776310**	**rs1746049**	**10q11**	**GENOT**	**C**	**T**	0,832	0,168	1	1	0,869	0,131	1	1
10	**44778546**	**rs1746052**	**10q11**	**GENOT**	**A**	**C**	0,838	0,162	1	1	0,871	0,129	1	1
10	**44786364**	**rs800314**	**10q11**	**IMPUT**	**A**	**G**	0,915	0,085	0,994	0,970	0,932	0,068	0,990	0,940
10	**44791433**	**rs11598523**	**10q11**	**IMPUT**	**T**	**A**	0,841	0,160	0,995	0,983	0,812	0,188	0,992	0,979
10	**44793299**	**rs2505734**	**10q11**	**GENOT**	**T**	**C**	0,631	0,369	1	1	0,655	0,345	1	1
10	**44797087**	**rs754713**	**10q11**	**GENOT**	**C**	**T**	0,717	0,283	1	1	0,726	0,274	1	1
10	**44798482**	**rs800320**	**10q11**	**GENOT**	**C**	**T**	0,956	0,044	1	1	0,967	0,033	1	1
10	**44801673**	**rs800323**	**10q11**	**GENOT**	**A**	**G**	0,717	0,284	1	1	0,724	0,276	1	1
10	**44803925**	**rs2437934**	**10q11**	**GENOT**	**C**	**G**	0,632	0,368	1	1	0,654	0,346	1	1
10	**44810205**	**rs11238983**	**10q11**	**GENOT**	**A**	**G**	0,165	0,165	1	1	0,135	0,135	1	1
10	**44813738**	**rs2146807**	**10q11**	**GENOT**	**C**	**T**	0,164	0,164	1	1	0,139	0,139	1	1
10	**44813777**	**rs2146808**	**10q11**	**GENOT**	**A**	**C**	0,959	0,041	1	1	0,970	0,030	1	1
10	**44814336**	**rs7082209**	**10q11**	**GENOT**	**G**	**A**	0,168	0,168	1	1	0,134	0,134	1	1
10	**44815048**	**rs800310**	**10q11**	**GENOT**	**A**	**T**	0,232	0,232	1	1	0,179	0,179	1	1
10	**44815709**	**rs2505735**	**10q11**	**GENOT**	**C**	**A**	0,790	0,210	1	1	0,835	0,165	1	1
10	**44817419**	**rs977754**	**10q11**	**GENOT**	**T**	**G**	0,803	0,197	1	1	0,847	0,153	1	1
10	**44818563**	**rs812889**	**10q11**	**GENOT**	**C**	**G**	0,912	0,088	1	1	0,936	0,064	1	1
10	**44820157**	**rs2476351**	**10q11**	**IMPUT**	**T**	**C**	0,807	0,194	0,989	0,976	0,853	0,147	0,992	0,977
10	**44821220**	**rs11238987**	**10q11**	**GENOT**	**G**	**A**	0,967	0,033	1	1	0,968	0,032	1	1
10	**44821387**	**rs10508884**	**10q11**	**GENOT**	**C**	**T**	0,731	0,269	1	1	0,711	0,289	1	1
10	**44821772**	**rs1111259**	**10q11**	**GENOT**	**C**	**T**	0,887	0,113	1	1	0,915	0,085	1	1
10	**44823136**	**rs2505741**	**10q11**	**GENOT**	**A**	**G**	0,525	0,475	1	1	0,553	0,448	1	1
10	**44826376**	**rs2028100**	**10q11**	**GENOT**	**G**	**A**	0,754	0,246	1	1	0,728	0,272	1	1
10	**44827164**	**rs1836982**	**10q11**	**GENOT**	**C**	**G**	0,787	0,214	1	1	0,841	0,159	1	1
10	**44828234**	**rs982097**	**10q11**	**IMPUT**	**A**	**G**	0,537	0,463	0,998	0,997	0,567	0,433	0,998	0,998
10	**44830727**	**rs7918046**	**10q11**	**GENOT**	**C**	**T**	0,705	0,296	1	1	0,719	0,281	1	1
10	**44831379**	**rs11815919**	**10q11**	**GENOT**	**C**	**T**	0,817	0,183	1	1	0,805	0,195	1	1
10	**44832884**	**rs928565**	**10q11**	**GENOT**	**A**	**G**	0,490	0,490	1	1	0,529	0,471	1	1
10	**44833031**	**rs11599561**	**10q11**	**GENOT**	**T**	**C**	0,892	0,108	1	1	0,889	0,111	1	1
10	**44833894**	**rs266080**	**10q11**	**GENOT**	**A**	**G**	0,978	0,022	1	1	0,983	0,017	1	1
10	**44835963**	**rs1144482**	**10q11**	**GENOT**	**T**	**C**	0,477	0,477	1	1	0,516	0,484	1	1
10	**44837267**	**rs1360724**	**10q11**	**IMPUT**	**A**	**G**	0,682	0,318	0,999	0,999	0,698	0,303	0,999	0,998
10	**44838019**	**rs10900025**	**10q11**	**GENOT**	**A**	**G**	0,593	0,407	1	1	0,603	0,398	1	1
10	**44838464**	**rs7069891**	**10q11**	**GENOT**	**C**	**T**	0,891	0,109	1	1	0,889	0,111	1	1
10	**44838530**	**rs77839**	**10q11**	**GENOT**	**A**	**G**	0,571	0,429	1	1	0,586	0,414	1	1
10	**44839865**	**rs17390084**	**10q11**	**GENOT**	**A**	**G**	0,042	0,042	1	1	0,034	0,034	1	1
10	**44842048**	**rs10793536**	**10q11**	**IMPUT**	**G**	**C**	0,562	0,438	0,996	0,993	0,582	0,418	0,993	0,989
10	**44844381**	**rs266076**	**10q11**	**IMPUT**	**A**	**G**	0,560	0,440	0,997	0,995	0,580	0,420	0,996	0,993

10	**44848921**	**rs1144480**	**10q11**	**IMPUT**	**A**	**T**	0,462	0,462	0,979	0,965	0,502	0,498	0,988	0,979
10	**44850424**	**rs266109**	**10q11**	**GENOT**	**A**	**G**	0,878	0,122	1	1	0,900	0,100	1	1
10	**44851737**	**rs1144477**	**10q11**	**GENOT**	**T**	**C**	0,478	0,478	1	1	0,512	0,488	1	1
10	**44855663**	**rs266105**	**10q11**	**GENOT**	**G**	**A**	0,862	0,139	1	1	0,889	0,111	1	1
10	**44855740**	**rs11595588**	**10q11**	**GENOT**	**T**	**C**	0,603	0,397	1	1	0,612	0,388	1	1
10	**44855927**	**rs17391002**	**10q11**	**GENOT**	**A**	**G**	0,801	0,199	1	1	0,767	0,233	1	1
10	**44856370**	**rs266103**	**10q11**	**GENOT**	**C**	**T**	0,855	0,145	1	1	0,890	0,111	1	1
10	**44858840**	**rs185545**	**10q11**	**IMPUT**	**G**	**C**	0,793	0,207	0,894	0,752	0,799	0,201	0,868	0,706
10	**44861220**	**rs7918568**	**10q11**	**GENOT**	**C**	**T**	0,829	0,171	1	1	0,814	0,186	1	1
10	**44863434**	**rs7915848**	**10q11**	**GENOT**	**T**	**C**	0,828	0,172	1	1	0,816	0,184	1	1
10	**44864300**	**rs266094**	**10q11**	**GENOT**	**C**	**T**	0,854	0,146	1	1	0,875	0,125	1	1
10	**44866208**	**rs266093**	**10q11**	**IMPUT**	**G**	**C**	0,639	0,361	0,997	0,994	0,658	0,342	0,993	0,988
10	**44867146**	**rs1029153**	**10q11**	**GENOT**	**A**	**G**	0,725	0,275	1	1	0,721	0,279	1	1
10	**44868257**	**rs1801157**	**10q11**	**GENOT**	**T**	**C**	0,246	0,246	1	1	0,215	0,215	1	1
10	**44869427**	**rs266089**	**10q11**	**GENOT**	**G**	**A**	0,847	0,153	1	1	0,859	0,141	1	1
10	**44870015**	**rs266088**	**10q11**	**GENOT**	**C**	**T**	0,853	0,147	1	1	0,814	0,186	1	1
10	**44871062**	**rs266087**	**10q11**	**IMPUT**	**A**	**G**	0,399	0,399	0,934	0,875	0,403	0,403	0,951	0,904
10	**44871548**	**rs2297630**	**10q11**	**IMPUT**	**G**	**A**	0,731	0,269	0,918	0,812	0,730	0,270	0,936	0,848
10	**44875166**	**rs2839690**	**10q11**	**IMPUT**	**A**	**G**	0,833	0,167	0,927	0,759	0,824	0,176	0,922	0,750
10	**44878713**	**rs3780891**	**10q11**	**IMPUT**	**G**	**A**	0,915	0,085	0,925	0,605	0,890	0,110	0,896	0,581

- **Table S2. Case-control allelic frequencies and association parameters adjusted for gender in the genotype and imputed case-control samples.** Genomic location of the genetic variants. F_A: allele frequency in cases (Affected), F_U: allele frequency in controls (Unaffected), OR: odd ratio for the reference allele (A1). L_95: Lower bound of 95% confidence interval for odds ratio. U_95: Upper bound of 95% confidence interval for odds ratio. P: p-value after a permutation test (1000 permutations).

				Morocco						
CHR	SNP	BP	Region	A1	F_A	F_U	OR	L95	U95	P
1	rs4970833	109804646	1p13	A	0,493	0,418	1,268	0,792	2,032	0,330
1	rs653635	109806313	1p13	G	0,069	0,214	0,257	0,110	0,598	0,003
1	rs6657811	109807283	1p13	T	0,142	0,085	1,828	0,746	4,483	0,208
1	rs608196	109808117	1p13	A	0,028	0,082	0,317	0,089	1,129	0,055
1	rs17035630	109810981	1p13	A	0,070	0,122	0,589	0,250	1,390	0,253
1	rs17035665	109813719	1p13	T	0,220	0,167	1,334	0,695	2,563	0,386
1	rs4970834	109814880	1p13	T	0,215	0,229	0,928	0,519	1,659	0,777
1	rs611917	109815252	1p13	C	0,236	0,245	0,974	0,540	1,755	0,977
1	rs12740374	109817590	1p13	T	0,190	0,177	1,088	0,566	2,091	0,788
1	rs629301	109818306	1p13	C	0,201	0,194	1,038	0,563	1,917	0,988
1	rs646776	109818530	1p13	G	0,201	0,194	1,038	0,563	1,917	0,988
1	rs17035949	109820919	1p13	G	0,118	0,174	0,585	0,274	1,246	0,148
1	rs583104	109821307	1p13	C	0,319	0,378	0,769	0,457	1,293	0,306
1	rs602633	109821511	1p13	A	0,319	0,357	0,838	0,496	1,415	0,515
1	rs599839	109822166	1p13	G	0,319	0,367	0,805	0,480	1,351	0,403
1	rs14000	109822509	1p13	C	0,083	0,153	0,483	0,209	1,117	0,049
1	rs672569	109827253	1p13	A	0,188	0,255	0,710	0,398	1,266	0,265
1	rs655246	109832283	1p13	A	0,493	0,490	1,034	0,621	1,724	0,897
1	rs17584208	109833187	1p13	A	0,049	0,051	0,974	0,288	3,294	0,979
1	rs17645031	109834938	1p13	T	0,049	0,051	0,974	0,288	3,294	0,979
1	rs17645143	109835757	1p13	C	0,236	0,235	1,022	0,559	1,869	0,885
1	rs629001	109838918	1p13	C	0,097	0,163	0,532	0,236	1,200	0,140
1	rs3850615	109839738	1p13	A	0,104	0,082	1,307	0,524	3,256	0,641
1	rs600806	109840629	1p13	C	0,264	0,250	1,081	0,570	2,052	0,831
1	rs680434	109842271	1p13	G	0,285	0,255	1,193	0,649	2,194	0,553
1	rs11583969	109843775	1p13	T	0,063	0,092	0,599	0,217	1,656	0,291
1	rs652651	109844532	1p13	T	0,285	0,245	1,269	0,688	2,339	0,445
1	rs407102	109846278	1p13	G	0,243	0,235	1,077	0,570	2,032	0,809
1	rs592107	109848726	1p13	T	0,257	0,214	1,314	0,691	2,499	0,371
1	rs444387	109851127	1p13	A	0,304	0,260	1,284	0,691	2,388	0,431
1	rs464218	109856306	1p13	T	0,493	0,439	1,263	0,767	2,080	0,374
1	rs17585355	109857815	1p13	C	0,310	0,255	1,448	0,719	2,919	0,303
1	rs370088	109858119	1p13	T	0,264	0,214	1,348	0,718	2,531	0,354
1	rs3853500	109864269	1p13	A	0,292	0,255	1,236	0,671	2,277	0,460
1	rs3768496	109866569	1p13	A	0,257	0,214	1,314	0,691	2,499	0,371

1	rs10745352	109871787	1p13	T	0,292	0,255	1,236	0,671	2,277	0,460
1	rs10745353	109877506	1p13	A	0,208	0,163	1,403	0,710	2,775	0,323
1	rs4603158	109879549	1p13	C	0,292	0,255	1,236	0,671	2,277	0,460
1	rs11102972	109880721	1p13	C	0,193	0,104	2,199	0,982	4,928	0,062
1	rs10858084	109882250	1p13	T	0,292	0,255	1,236	0,671	2,277	0,460
1	rs2228604	109884775	1p13	A	0,292	0,255	1,236	0,671	2,277	0,460
1	rs4970843	109887191	1p13	C	0,472	0,388	1,449	0,862	2,435	0,191
1	rs3879448	109891423	1p13	G	0,299	0,255	1,296	0,701	2,395	0,376
1	rs7536292	109894693	1p13	C	0,160	0,235	0,572	0,291	1,124	0,102
1	rs1030522	109900707	1p13	G	0,289	0,255	1,216	0,660	2,241	0,535
1	rs3879449	109904971	1p13	A	0,292	0,255	1,236	0,671	2,277	0,460
1	rs11581665	109910013	1p13	T	0,056	0,061	0,892	0,287	2,771	0,807
1	rs10858086	109915075	1p13	C	0,257	0,219	1,280	0,672	2,438	0,476
1	rs1149175	109922377	1p13	A	0,063	0,061	1,007	0,332	3,058	0,968
1	rs12037569	109923677	1p13	T	0,125	0,194	0,571	0,286	1,137	0,095
1	rs10858089	109926828	1p13	T	0,292	0,255	1,236	0,671	2,277	0,460
1	rs4970752	109930852	1p13	C	0,299	0,277	1,123	0,604	2,088	0,720
1	rs10745354	109931908	1p13	C	0,292	0,255	1,236	0,671	2,277	0,460
1	rs3768494	109935427	1p13	T	0,257	0,214	1,314	0,691	2,499	0,371
1	rs1880670	109941133	1p13	C	0,282	0,255	1,164	0,624	2,172	0,640
1	rs10858092	109943893	1p13	C	0,292	0,255	1,236	0,671	2,277	0,460
1	rs4120621	109949008	1p13	T	0,257	0,214	1,314	0,691	2,499	0,371
1	rs2936033	222751034	1q41	A	0,493	0,469	1,072	0,653	1,759	0,803
1	rs3008647	222759007	1q41	T	0,271	0,163	1,915	0,962	3,811	0,064
1	rs2270705	222761771	1q41	C	0,042	0,102	0,339	0,113	1,015	0,036
1	rs2936027	222762316	1q41	A	0,049	0,071	0,697	0,226	2,154	0,578
1	rs17464857	222762709	1q41	G	0,257	0,153	1,902	0,952	3,802	0,065
1	rs2936041	222762773	1q41	A	0,271	0,163	1,915	0,962	3,811	0,064
1	rs4846767	222763026	1q41	C	0,424	0,357	1,355	0,785	2,339	0,272
1	rs3008650	222763215	1q41	G	0,153	0,194	0,789	0,381	1,637	0,525
1	rs2936040	222763661	1q41	T	0,056	0,082	0,717	0,263	1,954	0,598
1	rs3008653	222764791	1q41	G	0,257	0,163	1,756	0,888	3,473	0,101
1	rs3008654	222766609	1q41	A	0,254	0,163	1,720	0,870	3,399	0,111
1	rs1995152	222769593	1q41	C	0,097	0,122	0,818	0,351	1,909	0,654
1	rs1909194	222770703	1q41	G	0,243	0,153	1,747	0,879	3,473	0,098
1	rs3002130	222772139	1q41	C	0,257	0,163	1,756	0,888	3,473	0,101
1	rs3002142	222788062	1q41	C	0,188	0,225	0,821	0,454	1,486	0,537
1	rs904323	222790366	1q41	A	0,250	0,194	1,347	0,730	2,483	0,354
1	rs17163303	222795118	1q41	T	0,132	0,122	1,190	0,541	2,616	0,683
1	rs17011666	222798965	1q41	G	0,257	0,255	0,959	0,514	1,791	0,907
1	rs2936052	222802376	1q41	C	0,222	0,194	1,148	0,578	2,282	0,688
1	rs3008621	222804046	1q41	A	0,118	0,082	1,456	0,564	3,758	0,449
1	rs3002145	222807013	1q41	T	0,118	0,083	1,406	0,543	3,639	0,479
1	rs1391557	222809616	1q41	T	0,208	0,194	1,080	0,546	2,135	0,837
1	rs2133188	222813753	1q41	T	0,204	0,188	1,103	0,553	2,200	0,796

1	rs2133189	222814442	1q41	C	0,333	0,327	1,029	0,605	1,751	0,977
1	rs17163358	222820639	1q41	G	0,375	0,367	1,048	0,603	1,821	0,824
1	rs17531063	222821709	1q41	G	0,063	0,051	1,257	0,427	3,704	0,648
1	rs17465637	222823529	1q41	A	0,361	0,367	0,989	0,560	1,745	0,983
1	rs17011681	222825088	1q41	C	0,368	0,367	1,019	0,582	1,783	0,898
1	rs2291832	222826481	1q41	G	0,375	0,367	1,048	0,603	1,821	0,824
1	rs2088514	222831372	1q41	G	0,201	0,194	1,033	0,523	2,043	0,984
1	rs2291834	222832295	1q41	T	0,368	0,367	1,019	0,582	1,783	0,898
1	rs17163384	222835222	1q41	C	0,125	0,092	1,548	0,645	3,716	0,321
1	rs2270707	222837594	1q41	G	0,236	0,250	0,906	0,488	1,684	0,766
1	rs1053316	222839838	1q41	A	0,194	0,225	0,861	0,446	1,663	0,659
1	rs3008633	222844840	1q41	T	0,194	0,194	1,041	0,543	1,995	0,878
1	rs1391558	222848029	1q41	G	0,167	0,143	1,184	0,561	2,496	0,687
9	rs756641	21902354	9p21	A	0,340	0,357	0,922	0,562	1,513	0,716
9	rs10811634	21905379	9p21	T	0,347	0,347	0,990	0,608	1,613	0,929
9	rs16938590	21909979	9p21	G	0,194	0,122	1,611	0,777	3,342	0,170
9	rs4977746	21920346	9p21	C	0,375	0,327	1,240	0,701	2,192	0,465
9	rs10811638	21923279	9p21	G	0,125	0,061	2,134	0,795	5,728	0,122
9	rs7852128	21925855	9p21	G	0,347	0,296	1,260	0,706	2,249	0,449
9	rs10965186	21927913	9p21	A	0,111	0,061	1,857	0,688	5,007	0,221
9	rs2518713	21929666	9p21	G	0,097	0,061	1,562	0,575	4,245	0,396
9	rs7864029	21930147	9p21	C	0,333	0,296	1,169	0,659	2,075	0,612
9	rs7869004	21931896	9p21	T	0,333	0,296	1,169	0,659	2,075	0,612
9	rs4977750	21944317	9p21	C	0,347	0,306	1,147	0,668	1,971	0,611
9	rs2811717	21946322	9p21	C	0,438	0,388	1,187	0,690	2,041	0,513
9	rs2811720	21947957	9p21	G	0,299	0,225	1,369	0,765	2,450	0,281
9	rs10965197	21948666	9p21	T	0,345	0,375	0,860	0,507	1,459	0,552
9	rs10757260	21953137	9p21	A	0,389	0,418	0,921	0,534	1,588	0,783
9	rs10757261	21954953	9p21	G	0,389	0,418	0,921	0,534	1,588	0,783
9	rs12335941	21955669	9p21	A	0,382	0,418	0,896	0,521	1,542	0,719
9	rs717326	21958524	9p21	G	0,042	0,010	4,254	0,493	36,730	0,197
9	rs7041637	21961866	9p21	A	0,181	0,225	0,809	0,414	1,579	0,528
9	rs3731257	21966221	9p21	T	0,162	0,184	0,893	0,434	1,840	0,774
9	rs2518719	21970427	9p21	G	0,111	0,163	0,626	0,293	1,337	0,206
9	rs2811708	21973422	9p21	T	0,444	0,429	0,996	0,572	1,737	0,998
9	rs3731239	21974218	9p21	C	0,207	0,204	1,060	0,524	2,145	0,878
9	rs3731222	21983914	9p21	G	0,104	0,163	0,588	0,273	1,266	0,196
9	rs3731213	21986218	9p21	A	0,083	0,082	1,079	0,462	2,524	0,856
9	rs3731211	21986847	9p21	A	0,444	0,408	1,108	0,628	1,956	0,714
9	rs3731204	21987584	9p21	G	0,111	0,163	0,626	0,293	1,337	0,206
9	rs3731201	21988896	9p21	G	0,326	0,245	1,433	0,787	2,606	0,233
9	rs7036656	21990457	9p21	C	0,444	0,408	1,108	0,628	1,956	0,714
9	rs2811710	21991923	9p21	C	0,417	0,449	0,900	0,515	1,574	0,721
9	rs2811711	21993964	9p21	C	0,194	0,194	0,964	0,495	1,876	0,915
9	rs3218020	21997872	9p21	T	0,389	0,388	0,995	0,590	1,679	0,968

9	rs3218002	22000841	9p21	T	0,250	0,184	1,471	0,784	2,763	0,233
9	rs3217992	22003223	9p21	A	0,410	0,418	0,972	0,587	1,609	0,973
9	rs3217986	22005330	9p21	C	0,042	0,000	1,32E+09	0	inf	0,959
9	rs974336	22006348	9p21	A	0,243	0,184	1,402	0,749	2,625	0,360
9	rs2069422	22008026	9p21	C	0,222	0,135	1,861	0,910	3,807	0,079
9	rs2069418	22009698	9p21	C	0,201	0,296	0,586	0,319	1,076	0,082
9	rs575427	22011477	9p21	C	0,076	0,115	0,618	0,242	1,578	0,288
9	rs10811640	22013411	9p21	G	0,438	0,429	1,035	0,620	1,728	0,912
9	rs643319	22017836	9p21	T	0,382	0,316	1,275	0,767	2,118	0,349
9	rs7044859	22018781	9p21	T	0,438	0,429	1,035	0,620	1,728	0,912
9	rs523096	22019129	9p21	C	0,188	0,245	0,710	0,382	1,319	0,287
9	rs518394	22019673	9p21	G	0,188	0,245	0,710	0,382	1,319	0,287
9	rs10757264	22019732	9p21	A	0,409	0,388	1,084	0,648	1,815	0,800
9	rs10965212	22023795	9p21	T	0,417	0,388	1,103	0,667	1,825	0,695
9	rs496892	22024351	9p21	A	0,382	0,323	1,239	0,744	2,064	0,391
9	rs10738604	22025493	9p21	A	0,319	0,367	0,816	0,468	1,421	0,490
9	rs1591136	22026834	9p21	C	0,417	0,388	1,103	0,667	1,825	0,695
9	rs598664	22027551	9p21	G	0,203	0,133	1,676	0,821	3,422	0,142
9	rs7049105	22028801	9p21	A	0,417	0,388	1,103	0,667	1,825	0,695
9	rs10965215	22029445	9p21	A	0,493	0,448	1,188	0,710	1,986	0,514
9	rs564398	22029547	9p21	G	0,167	0,204	0,767	0,401	1,466	0,432
9	rs662463	22030438	9p21	T	0,211	0,133	1,782	0,872	3,640	0,105
9	rs7865618	22031005	9p21	G	0,167	0,214	0,716	0,375	1,367	0,307
9	rs10115049	22032119	9p21	A	0,479	0,490	0,962	0,577	1,603	0,908
9	rs2157719	22033366	9p21	G	0,167	0,204	0,767	0,401	1,466	0,432
9	rs1008878	22036112	9p21	G	0,167	0,225	0,692	0,369	1,298	0,240
9	rs12376000	22039426	9p21	T	0,076	0,133	0,532	0,224	1,267	0,175
9	rs17694493	22041998	9p21	G	0,215	0,125	1,962	0,944	4,076	0,068
9	rs12352425	22042086	9p21	A	0,069	0,041	1,821	0,533	6,220	0,340
9	rs1412829	22043926	9p21	C	0,167	0,214	0,716	0,375	1,367	0,307
9	rs1360589	22045317	9p21	G	0,160	0,174	0,870	0,448	1,689	0,686
9	rs7028570	22048683	9p21	A	0,500	0,500	1,007	0,610	1,665	0,928
9	rs17756311	22053895	9p21	A	0,215	0,122	1,975	0,953	4,092	0,066
9	rs17694572	22054356	9p21	A	0,215	0,122	1,975	0,953	4,092	0,066
9	rs10120688	22056499	9p21	A	0,500	0,480	1,102	0,655	1,855	0,711
9	rs1537378	22061614	9p21	T	0,155	0,174	0,846	0,435	1,646	0,629
9	rs1011970	22062134	9p21	T	0,299	0,174	2,155	1,106	4,198	0,021
9	rs8181047	22064465	9p21	A	0,090	0,071	1,218	0,466	3,180	0,701
9	rs10811647	22065002	9p21	G	0,431	0,459	0,909	0,537	1,539	0,743
9	rs10965224	22067276	9p21	T	0,236	0,327	0,636	0,359	1,127	0,124
9	rs16905599	22069144	9p21	A	0,090	0,041	2,490	0,756	8,203	0,163
9	rs9632884	22072301	9p21	G	0,188	0,174	1,052	0,554	2,001	0,885
9	rs10757270	22072719	9p21	G	0,465	0,510	0,865	0,517	1,447	0,585
9	rs16923583	22073334	9p21	A	0,085	0,143	0,547	0,243	1,233	0,132
9	rs1412832	22077543	9p21	C	0,104	0,082	1,277	0,513	3,180	0,624

9	rs6475606	22081850	9p21	C	0,194	0,194	0,969	0,522	1,797	0,920
9	rs1547704	22082340	9p21	A	0,104	0,102	1,000	0,423	2,363	0,997
9	rs10965228	22082380	9p21	G	0,063	0,102	0,576	0,225	1,473	0,264
9	rs1333040	22083404	9p21	C	0,208	0,204	1,000	0,517	1,935	0,999
9	rs7857345	22087473	9p21	T	0,097	0,092	1,009	0,430	2,368	0,980
9	rs10757272	22088260	9p21	C	0,417	0,429	0,919	0,541	1,561	0,765
9	rs4977574	22098574	9p21	A	0,451	0,500	0,797	0,477	1,331	0,409
9	rs2891168	22098619	9p21	A	0,471	0,521	0,762	0,444	1,307	0,349
9	rs1537371	22099568	9p21	C	0,188	0,194	0,931	0,495	1,753	0,826
9	rs7859727	22102165	9p21	C	0,271	0,316	0,779	0,440	1,381	0,399
9	rs1333042	22103813	9p21	A	0,188	0,194	0,931	0,495	1,753	0,826
9	rs7859362	22105927	9p21	T	0,188	0,194	0,931	0,495	1,753	0,826
9	rs1333043	22106731	9p21	T	0,188	0,194	0,931	0,495	1,753	0,826
9	rs1412834	22110131	9p21	T	0,188	0,194	0,931	0,495	1,753	0,826
9	rs7341786	22112241	9p21	A	0,188	0,194	0,931	0,495	1,753	0,826
9	rs10733376	22114469	9p21	G	0,188	0,194	0,931	0,495	1,753	0,826
9	rs2383206	22115026	9p21	A	0,347	0,357	0,922	0,530	1,602	0,783
9	rs2383207	22115959	9p21	A	0,190	0,194	0,946	0,502	1,783	0,865
9	rs1333045	22119195	9p21	T	0,417	0,347	1,306	0,774	2,201	0,347
9	rs10738610	22123766	9p21	A	0,451	0,490	0,828	0,498	1,377	0,485
9	rs10757278	22124477	9p21	G	0,493	0,459	1,173	0,699	1,968	0,566
9	rs1333048	22125347	9p21	A	0,424	0,418	0,980	0,576	1,667	0,928
9	rs1333049	22125503	9p21	C	0,493	0,449	1,220	0,723	2,059	0,454
9	rs10757281	22127613	9p21	T	0,243	0,265	0,770	0,392	1,510	0,472
9	rs12347779	22128709	9p21	G	0,152	0,188	0,767	0,370	1,586	0,529
9	rs10965243	22130065	9p21	G	0,076	0,112	0,617	0,253	1,506	0,272
9	rs10965245	22130515	9p21	A	0,070	0,112	0,552	0,221	1,378	0,190
9	rs2891169	22131825	9p21	G	0,437	0,531	0,589	0,336	1,034	0,070
9	rs2383208	22132076	9p21	G	0,160	0,194	0,751	0,359	1,567	0,367
9	rs7045889	22133251	9p21	G	0,375	0,316	1,350	0,779	2,341	0,264
9	rs10811659	22133716	9p21	C	0,201	0,184	1,224	0,620	2,417	0,574
9	rs10757282	22133984	9p21	C	0,451	0,520	0,650	0,366	1,153	0,141
9	rs10811661	22134094	9p21	C	0,153	0,174	0,806	0,380	1,711	0,561
9	rs10757283	22134172	9p21	T	0,409	0,510	0,608	0,350	1,056	0,075
9	rs1333051	22136489	9p21	T	0,125	0,184	0,557	0,257	1,208	0,131
9	rs7018475	22137685	9p21	G	0,319	0,378	0,721	0,416	1,249	0,258
9	rs11791416	22138105	9p21	G	0,229	0,204	1,279	0,663	2,467	0,498
9	rs4977761	22138762	9p21	T	0,410	0,337	1,355	0,806	2,278	0,232
9	rs2065501	22140224	9p21	A	0,250	0,265	0,947	0,531	1,689	0,827
9	rs4977577	22141875	9p21	C	0,444	0,469	0,877	0,516	1,490	0,623
9	rs7849199	22143293	9p21	A	0,181	0,188	1,003	0,530	1,899	0,990
9	rs2065500	22145694	9p21	G	0,174	0,102	1,925	0,843	4,395	0,099
9	rs7022662	22147715	9p21	G	0,174	0,102	1,925	0,843	4,395	0,099
9	rs12341394	22148055	9p21	T	0,194	0,214	0,946	0,512	1,747	0,839
9	rs7856219	22150261	9p21	C	0,150	0,167	0,971	0,492	1,919	0,934

9	rs10965256	22151465	9p21	A	0,028	0,071	0,348	0,095	1,272	0,062
9	rs7853123	22153360	9p21	G	0,458	0,438	1,140	0,665	1,955	0,617
9	rs944802	22155709	9p21	A	0,111	0,051	2,344	0,825	6,657	0,079
9	rs7028213	22157360	9p21	G	0,201	0,214	0,979	0,523	1,833	0,950
9	rs12238587	22158168	9p21	A	0,174	0,112	1,744	0,808	3,765	0,148
9	rs10757288	22159416	9p21	T	0,438	0,418	1,128	0,669	1,900	0,638
9	rs7864275	22161212	9p21	T	0,236	0,271	0,874	0,475	1,608	0,653
9	rs10965266	22161494	9p21	G	0,215	0,143	1,789	0,865	3,701	0,091
9	rs10965267	22161828	9p21	G	0,035	0,061	0,531	0,151	1,861	0,239
9	rs10811668	22164991	9p21	A	0,243	0,204	1,260	0,670	2,369	0,425
9	rs2779748	22166769	9p21	G	0,444	0,459	0,976	0,586	1,624	0,925
9	rs7863846	22168128	9p21	T	0,194	0,204	0,995	0,522	1,897	0,983
9	rs828580	22168464	9p21	T	0,104	0,102	1,092	0,459	2,597	0,844
9	rs1537377	22169700	9p21	C	0,250	0,296	0,826	0,440	1,553	0,553
9	rs954399	22170983	9p21	T	0,194	0,204	0,995	0,522	1,897	0,983
9	rs828582	22172259	9p21	A	0,347	0,357	1,009	0,578	1,763	0,978
9	rs10965278	22174712	9p21	A	0,194	0,174	1,090	0,554	2,145	0,817
9	rs10965279	22175188	9p21	C	0,056	0,061	0,892	0,287	2,771	0,784
9	rs10757292	22176961	9p21	T	0,111	0,082	1,482	0,576	3,814	0,362
9	rs866666	22183781	9p21	T	0,507	0,429	1,368	0,800	2,338	0,239
9	rs2767409	22184997	9p21	A	0,265	0,239	1,179	0,640	2,172	0,587
9	rs1095904	22187074	9p21	T	0,222	0,174	1,364	0,724	2,569	0,329
9	rs828576	22191189	9p21	C	0,529	0,438	1,482	0,848	2,590	0,153
9	rs2219849	22195820	9p21	C	0,493	0,490	1,010	0,616	1,655	0,993
9	rs1751449	22196863	9p21	G	0,292	0,265	1,149	0,640	2,061	0,540
9	rs12375458	22198149	9p21	A	0,104	0,061	1,749	0,655	4,671	0,350
10	rs1482472	44682973	10q11	C	0,444	0,365	1,399	0,805	2,432	0,252
10	rs12415866	44686664	10q11	G	0,201	0,174	1,216	0,616	2,398	0,507
10	rs7917089	44688587	10q11	A	0,201	0,174	1,216	0,616	2,398	0,507
10	rs1623851	44691241	10q11	G	0,229	0,194	1,252	0,651	2,407	0,452
10	rs1627329	44691633	10q11	C	0,229	0,194	1,252	0,651	2,407	0,452
10	rs10508883	44693544	10q11	C	0,056	0,041	1,276	0,393	4,143	0,755
10	rs7900182	44693742	10q11	G	0,149	0,094	1,655	0,716	3,823	0,244
10	rs11597731	44694201	10q11	T	0,215	0,153	1,530	0,779	3,006	0,206
10	rs7902040	44695308	10q11	G	0,083	0,102	0,760	0,324	1,782	0,521
10	rs11238911	44695862	10q11	A	0,063	0,092	0,637	0,245	1,655	0,358
10	rs11238913	44695973	10q11	C	0,354	0,265	1,534	0,853	2,760	0,169
10	rs2802477	44696034	10q11	C	0,354	0,427	0,720	0,417	1,242	0,273
10	rs11594522	44696352	10q11	A	0,139	0,102	1,397	0,622	3,134	0,423
10	rs2054620	44698075	10q11	C	0,354	0,265	1,534	0,853	2,760	0,169
10	rs11238921	44699910	10q11	T	0,354	0,265	1,534	0,853	2,760	0,169
10	rs768676	44702681	10q11	A	0,076	0,092	0,849	0,355	2,031	0,814
10	rs3865770	44705969	10q11	T	0,139	0,102	1,397	0,622	3,134	0,423
10	rs1482473	44707598	10q11	C	0,160	0,143	1,090	0,515	2,307	0,819
10	rs3851257	44709171	10q11	T	0,229	0,167	1,330	0,739	2,393	0,356

10	rs12573558	44712128	10q11	A	0,139	0,102	1,397	0,622	3,134	0,423
10	rs11238935	44714402	10q11	T	0,099	0,122	0,736	0,327	1,658	0,461
10	rs2209067	44716469	10q11	A	0,207	0,143	1,571	0,776	3,179	0,198
10	rs1704219	44729958	10q11	C	0,347	0,255	1,527	0,848	2,752	0,182
10	rs7907961	44730995	10q11	C	0,243	0,133	2,166	1,054	4,451	0,044
10	rs1746043	44732825	10q11	C	0,347	0,255	1,527	0,848	2,752	0,182
10	rs647419	44734995	10q11	T	0,347	0,276	1,412	0,779	2,558	0,264
10	rs88796	44737036	10q11	C	0,319	0,255	1,312	0,737	2,335	0,370
10	rs617019	44737246	10q11	T	0,090	0,112	0,750	0,327	1,717	0,504
10	rs17155733	44737433	10q11	G	0,194	0,122	1,589	0,781	3,232	0,214
10	rs583489	44738688	10q11	C	0,208	0,184	1,129	0,597	2,136	0,725
10	rs676966	44739594	10q11	A	0,111	0,133	0,763	0,347	1,677	0,517
10	rs494207	44741256	10q11	T	0,208	0,184	1,129	0,597	2,136	0,725
10	rs541483	44746395	10q11	C	0,208	0,235	0,834	0,449	1,552	0,538
10	rs535176	44747059	10q11	A	0,264	0,276	0,930	0,527	1,641	0,792
10	rs622472	44749211	10q11	G	0,261	0,276	0,917	0,520	1,618	0,775
10	rs513391	44749708	10q11	G	0,264	0,276	0,930	0,527	1,641	0,792
10	rs11238956	44749854	10q11	C	0,299	0,327	0,896	0,520	1,542	0,703
10	rs687175	44751910	10q11	G	0,264	0,276	0,930	0,527	1,641	0,792
10	rs559580	44752078	10q11	C	0,204	0,235	0,818	0,439	1,522	0,523
10	rs559469	44752118	10q11	G	0,264	0,276	0,930	0,527	1,641	0,792
10	rs2437935	44752268	10q11	C	0,465	0,449	1,047	0,630	1,738	0,891
10	rs535949	44752330	10q11	A	0,271	0,271	0,992	0,566	1,738	0,956
10	rs671765	44752976	10q11	C	0,264	0,265	0,981	0,556	1,732	0,911
10	rs501120	44753867	10q11	G	0,268	0,276	0,946	0,536	1,671	0,847
10	rs579058	44755104	10q11	C	0,264	0,276	0,930	0,527	1,641	0,792
10	rs604674	44756894	10q11	A	0,264	0,276	0,930	0,527	1,641	0,792
10	rs487465	44758197	10q11	G	0,264	0,276	0,930	0,527	1,641	0,792
10	rs475926	44760887	10q11	C	0,380	0,354	1,078	0,623	1,866	0,783
10	rs1632484	44773984	10q11	A	0,229	0,255	0,843	0,467	1,523	0,593
10	rs1746048	44775824	10q11	T	0,264	0,276	0,930	0,527	1,641	0,792
10	rs1746049	44776310	10q11	T	0,264	0,276	0,930	0,527	1,641	0,792
10	rs1746052	44778546	10q11	C	0,174	0,225	0,726	0,383	1,379	0,328
10	rs800314	44786364	10q11	G	0,063	0,112	0,470	0,176	1,250	0,116
10	rs11598523	44791433	10q11	A	0,120	0,102	1,130	0,499	2,561	0,779
10	rs2505734	44793299	10q11	C	0,438	0,417	1,062	0,632	1,787	0,833
10	rs754713	44797087	10q11	T	0,375	0,313	1,288	0,757	2,191	0,368
10	rs800320	44798482	10q11	T	0,076	0,092	0,855	0,340	2,147	0,757
10	rs800323	44801673	10q11	G	0,340	0,316	1,086	0,643	1,836	0,788
10	rs2437934	44803925	10q11	G	0,438	0,429	1,011	0,605	1,688	0,969
10	rs11238983	44810205	10q11	A	0,217	0,192	1,138	0,576	2,250	0,711
10	rs2146807	44813738	10q11	C	0,167	0,163	1,003	0,485	2,076	0,992
10	rs2146808	44813777	10q11	C	0,059	0,092	0,620	0,219	1,757	0,387
10	rs7082209	44814336	10q11	G	0,201	0,184	1,097	0,561	2,146	0,809
10	rs800310	44815048	10q11	A	0,306	0,296	1,031	0,593	1,795	0,970

10	rs2505735	44815709	10q11	A	0,285	0,286	0,983	0,542	1,784	0,895
10	rs977754	44817419	10q11	G	0,257	0,225	1,194	0,647	2,203	0,640
10	rs812889	44818563	10q11	G	0,076	0,071	1,118	0,420	2,976	0,825
10	rs2476351	44820157	10q11	C	0,229	0,194	1,223	0,648	2,309	0,565
10	rs11238987	44821220	10q11	A	0,069	0,102	0,598	0,236	1,516	0,286
10	rs10508884	44821387	10q11	T	0,285	0,286	0,950	0,515	1,752	0,861
10	rs1111259	44821772	10q11	T	0,132	0,102	1,236	0,561	2,724	0,582
10	rs2505741	44823136	10q11	A	0,424	0,439	0,995	0,571	1,732	0,995
10	rs2028100	44826376	10q11	A	0,257	0,265	0,906	0,479	1,714	0,739
10	rs1836982	44827164	10q11	G	0,264	0,235	1,138	0,633	2,048	0,657
10	rs982097	44828234	10q11	T	0,493	0,500	1,022	0,596	1,752	0,939
10	rs7918046	44830727	10q11	T	0,299	0,276	1,075	0,604	1,913	0,774
10	rs11815919	44831379	10q11	T	0,167	0,174	0,939	0,468	1,882	0,862
10	rs928565	44832884	10q11	T	0,430	0,439	1,008	0,597	1,701	0,970
10	rs11599561	44833031	10q11	C	0,090	0,102	0,884	0,367	2,126	0,804
10	rs266080	44833894	10q11	G	0,063	0,061	1,006	0,357	2,837	0,979
10	rs1144482	44835963	10q11	A	0,389	0,388	1,066	0,620	1,833	0,829
10	rs1360724	44837267	10q11	G	0,299	0,286	1,018	0,572	1,812	0,949
10	rs10900025	44838019	10q11	G	0,431	0,429	0,951	0,554	1,633	0,863
10	rs7069891	44838464	10q11	T	0,099	0,102	0,966	0,406	2,299	0,986
10	rs77839	44838530	10q11	G	0,486	0,490	0,927	0,540	1,592	0,792
10	rs17390084	44839865	10q11	A	0,042	0,073	0,536	0,167	1,715	0,268
10	rs10793536	44842048	10q11	C	0,472	0,480	0,905	0,528	1,552	0,712
10	rs266076	44844381	10q11	A	0,472	0,459	1,141	0,656	1,983	0,629
10	rs1144480	44848921	10q11	A	0,410	0,418	1,027	0,604	1,748	0,927
10	rs266109	44850424	10q11	G	0,169	0,133	1,268	0,619	2,596	0,532
10	rs1144477	44851737	10q11	A	0,424	0,439	0,995	0,589	1,681	0,996
10	rs266105	44855663	10q11	A	0,194	0,102	2,134	0,976	4,666	0,064
10	rs11595588	44855740	10q11	C	0,528	0,417	1,554	0,919	2,630	0,096
10	rs17391002	44855927	10q11	G	0,278	0,255	1,110	0,611	2,017	0,739
10	rs266103	44856370	10q11	T	0,215	0,133	1,854	0,896	3,836	0,101
10	rs185545	44858840	10q11	C	0,278	0,225	1,418	0,741	2,711	0,269
10	rs7918568	44861220	10q11	T	0,306	0,235	1,409	0,790	2,515	0,244
10	rs7915848	44863434	10q11	C	0,285	0,235	1,294	0,715	2,342	0,449
10	rs266094	44864300	10q11	T	0,141	0,133	1,112	0,541	2,286	0,779
10	rs266093	44866208	10q11	C	0,479	0,429	1,241	0,759	2,027	0,381
10	rs1029153	44867146	10q11	C	0,208	0,265	0,738	0,409	1,330	0,329
10	rs1801157	44868257	10q11	A	0,167	0,194	0,821	0,429	1,574	0,482
10	rs266089	44869427	10q11	A	0,139	0,133	1,082	0,528	2,217	0,823
10	rs266088	44870015	10q11	T	0,153	0,112	1,378	0,659	2,882	0,401
10	rs266087	44871062	10q11	A	0,340	0,347	0,952	0,551	1,645	0,835
10	rs2297630	44871548	10q11	A	0,153	0,204	0,681	0,346	1,339	0,268
10	rs2839690	44875166	10q11	C	0,285	0,235	1,294	0,715	2,342	0,449
10	rs3780891	44878713	10q11	A	0,097	0,061	1,644	0,604	4,474	0,341

				Tunisia						
CHR	SNP	BP	Region	A1	F_A	F_U	OR	L95	U95	P
1	rs4970833	109804646	1p13	A	0,533	0,493	1,426	0,741	2,744	0,288
1	rs653635	109806313	1p13	G	0,120	0,092	0,884	0,323	2,417	0,841
1	rs6657811	109807283	1p13	T	0,076	0,112	1,050	0,345	3,196	0,912
1	rs608196	109808117	1p13	A	0,098	0,033	2,188	0,585	8,188	0,243
1	rs17035630	109810981	1p13	A	0,098	0,072	1,031	0,386	2,752	0,981
1	rs17035665	109813719	1p13	T	0,174	0,224	0,866	0,401	1,873	0,718
1	rs4970834	109814880	1p13	T	0,087	0,197	0,314	0,118	0,835	0,020
1	rs611917	109815252	1p13	C	0,207	0,243	0,772	0,353	1,690	0,526
1	rs12740374	109817590	1p13	T	0,120	0,224	0,541	0,228	1,285	0,171
1	rs629301	109818306	1p13	C	0,141	0,270	0,475	0,206	1,095	0,063
1	rs646776	109818530	1p13	G	0,141	0,270	0,475	0,206	1,095	0,063
1	rs17035949	109820919	1p13	G	0,065	0,105	0,601	0,192	1,882	0,364
1	rs583104	109821307	1p13	C	0,174	0,342	0,358	0,156	0,821	0,010
1	rs602633	109821511	1p13	A	0,163	0,322	0,354	0,153	0,819	0,014
1	rs599839	109822166	1p13	G	0,174	0,336	0,365	0,159	0,837	0,011
1	rs14000	109822509	1p13	C	0,120	0,059	1,214	0,405	3,645	0,733
1	rs672569	109827253	1p13	A	0,141	0,243	0,382	0,159	0,918	0,028
1	rs655246	109832283	1p13	A	0,500	0,513	0,874	0,457	1,670	0,676
1	rs17584208	109833187	1p13	A	0,033	0,066	0,357	0,080	1,585	0,151
1	rs17645031	109834938	1p13	T	0,033	0,066	0,357	0,080	1,585	0,151
1	rs17645143	109835757	1p13	C	0,304	0,224	1,529	0,747	3,131	0,233
1	rs629001	109838918	1p13	C	0,109	0,171	1,054	0,410	2,709	0,895
1	rs3850615	109839738	1p13	A	0,054	0,099	0,744	0,230	2,411	0,648
1	rs600806	109840629	1p13	C	0,228	0,296	0,845	0,421	1,697	0,645
1	rs680434	109842271	1p13	G	0,261	0,283	0,944	0,473	1,885	0,871
1	rs11583969	109843775	1p13	T	0,022	0,039	0,335	0,056	2,001	0,236
1	rs652651	109844532	1p13	T	0,261	0,263	0,924	0,454	1,879	0,861
1	rs407102	109846278	1p13	G	0,261	0,290	0,820	0,407	1,652	0,560
1	rs592107	109848726	1p13	T	0,261	0,296	0,811	0,405	1,625	0,502
1	rs444387	109851127	1p13	A	0,272	0,329	0,743	0,370	1,493	0,396
1	rs464218	109856306	1p13	C	0,500	0,513	0,783	0,408	1,502	0,461
1	rs17585355	109857815	1p13	C	0,304	0,224	1,926	0,915	4,056	0,081
1	rs370088	109858119	1p13	T	0,261	0,296	0,811	0,405	1,625	0,502
1	rs3853500	109864269	1p13	A	0,272	0,329	0,743	0,370	1,493	0,396
1	rs3768496	109866569	1p13	A	0,261	0,296	0,811	0,405	1,625	0,502
1	rs10745352	109871787	1p13	T	0,272	0,329	0,743	0,370	1,493	0,396
1	rs10745353	109877506	1p13	A	0,261	0,263	0,987	0,491	1,981	0,984
1	rs4603158	109879549	1p13	C	0,272	0,329	0,743	0,370	1,493	0,396
1	rs11102972	109880721	1p13	C	0,217	0,204	1,327	0,628	2,805	0,458
1	rs10858084	109882250	1p13	T	0,272	0,329	0,743	0,370	1,493	0,396
1	rs2228604	109884775	1p13	A	0,272	0,329	0,743	0,370	1,493	0,396
1	rs4970843	109887191	1p13	C	0,457	0,454	1,196	0,644	2,221	0,579
1	rs3879448	109891423	1p13	G	0,294	0,342	0,758	0,385	1,492	0,417

1	rs7536292	109894693	1p13	C	0,185	0,151	0,954	0,410	2,219	0,912
1	rs1030522	109900707	1p13	G	0,272	0,329	0,743	0,370	1,493	0,396
1	rs3879449	109904971	1p13	A	0,272	0,329	0,743	0,370	1,493	0,396
1	rs11581665	109910013	1p13	T	0,054	0,105	0,479	0,141	1,632	0,219
1	rs10858086	109915075	1p13	C	0,261	0,296	0,811	0,405	1,625	0,502
1	rs1149175	109922377	1p13	A	0,065	0,112	0,558	0,175	1,778	0,329
1	rs12037569	109923677	1p13	T	0,196	0,118	1,583	0,654	3,831	0,308
1	rs10858089	109926828	1p13	T	0,272	0,329	0,743	0,370	1,493	0,396
1	rs4970752	109930852	1p13	C	0,283	0,336	0,817	0,409	1,631	0,560
1	rs10745354	109931908	1p13	C	0,272	0,329	0,743	0,370	1,493	0,396
1	rs3768494	109935427	1p13	T	0,261	0,296	0,811	0,405	1,625	0,502
1	rs1880670	109941133	1p13	C	0,272	0,329	0,743	0,370	1,493	0,396
1	rs10858092	109943893	1p13	C	0,272	0,329	0,743	0,370	1,493	0,396
1	rs4120621	109949008	1p13	T	0,261	0,296	0,811	0,405	1,625	0,502
1	rs2936033	222751034	1q41	A	0,359	0,408	0,786	0,414	1,490	0,489
1	rs3008647	222759007	1q41	T	0,163	0,171	1,221	0,537	2,780	0,628
1	rs2270705	222761771	1q41	C	0,152	0,053	2,794	0,929	8,410	0,070
1	rs2936027	222762316	1q41	A	0,076	0,086	1,046	0,322	3,402	0,998
1	rs17464857	222762709	1q41	G	0,163	0,171	1,221	0,537	2,780	0,628
1	rs2936041	222762773	1q41	A	0,163	0,171	1,221	0,537	2,780	0,628
1	rs4846767	222763026	1q41	C	0,283	0,342	1,025	0,539	1,949	0,941
1	rs3008650	222763215	1q41	G	0,120	0,171	0,849	0,367	1,965	0,720
1	rs2936040	222763661	1q41	T	0,076	0,086	1,046	0,322	3,402	0,998
1	rs3008653	222764791	1q41	G	0,163	0,171	1,221	0,537	2,780	0,628
1	rs3008654	222766609	1q41	A	0,163	0,171	1,221	0,537	2,780	0,628
1	rs1995152	222769593	1q41	C	0,087	0,132	0,816	0,307	2,168	0,693
1	rs1909194	222770703	1q41	G	0,163	0,171	1,221	0,537	2,780	0,628
1	rs3002130	222772139	1q41	C	0,163	0,171	1,221	0,537	2,780	0,628
1	rs3002142	222788062	1q41	C	0,087	0,118	1,132	0,388	3,307	0,812
1	rs904323	222790366	1q41	A	0,152	0,197	0,802	0,347	1,849	0,611
1	rs17163303	222795118	1q41	T	0,109	0,105	1,249	0,474	3,288	0,658
1	rs17011666	222798965	1q41	G	0,185	0,283	0,690	0,302	1,577	0,385
1	rs2936052	222802376	1q41	C	0,174	0,250	0,845	0,363	1,964	0,696
1	rs3008621	222804046	1q41	A	0,120	0,138	1,052	0,389	2,847	0,875
1	rs3002145	222807013	1q41	T	0,120	0,138	1,052	0,389	2,847	0,875
1	rs1391557	222809616	1q41	T	0,207	0,237	1,303	0,567	2,994	0,530
1	rs2133188	222813753	1q41	T	0,200	0,237	1,225	0,522	2,872	0,656
1	rs2133189	222814442	1q41	C	0,294	0,355	1,045	0,533	2,048	0,909
1	rs17163358	222820639	1q41	G	0,315	0,375	1,035	0,523	2,045	0,943
1	rs17531063	222821709	1q41	G	0,076	0,059	1,229	0,386	3,915	0,812
1	rs17465637	222823529	1q41	A	0,315	0,375	1,035	0,523	2,045	0,943
1	rs17011681	222825088	1q41	C	0,315	0,375	1,035	0,523	2,045	0,943
1	rs2291832	222826481	1q41	G	0,315	0,375	1,035	0,523	2,045	0,943
1	rs2088514	222831372	1q41	G	0,207	0,237	1,303	0,567	2,994	0,530
1	rs2291834	222832295	1q41	T	0,315	0,375	1,035	0,523	2,045	0,943

1	rs17163384	222835222	1q41	C	0,098	0,099	1,040	0,378	2,860	0,813
1	rs2270707	222837594	1q41	G	0,217	0,270	1,044	0,465	2,344	0,913
1	rs1053316	222839838	1q41	A	0,120	0,171	0,713	0,308	1,647	0,404
1	rs3008633	222844840	1q41	T	0,109	0,151	0,744	0,301	1,839	0,494
1	rs1391558	222848029	1q41	G	0,196	0,204	1,521	0,642	3,604	0,348
9	rs756641	21902354	9p21	A	0,359	0,296	1,077	0,576	2,017	0,808
9	rs10811634	21905379	9p21	T	0,348	0,280	1,083	0,575	2,041	0,814
9	rs16938590	21909979	9p21	G	0,130	0,112	1,136	0,442	2,918	0,827
9	rs4977746	21920346	9p21	C	0,272	0,237	1,175	0,583	2,369	0,643
9	rs10811638	21923279	9p21	G	0,130	0,053	1,669	0,548	5,081	0,363
9	rs7852128	21925855	9p21	G	0,283	0,217	1,466	0,728	2,952	0,285
9	rs10965186	21927913	9p21	A	0,130	0,053	1,669	0,548	5,081	0,363
9	rs2518713	21929666	9p21	G	0,120	0,046	1,900	0,589	6,125	0,278
9	rs7864029	21930147	9p21	C	0,283	0,237	1,403	0,695	2,833	0,356
9	rs7869004	21931896	9p21	T	0,283	0,230	1,520	0,751	3,079	0,279
9	rs4977750	21944317	9p21	C	0,294	0,283	0,862	0,446	1,665	0,659
9	rs2811717	21946322	9p21	C	0,348	0,342	0,815	0,433	1,533	0,554
9	rs2811720	21947957	9p21	G	0,207	0,171	0,948	0,441	2,039	0,896
9	rs10965197	21948666	9p21	T	0,289	0,384	0,762	0,401	1,449	0,402
9	rs10757260	21953137	9p21	A	0,478	0,395	1,412	0,798	2,499	0,234
9	rs10757261	21954953	9p21	G	0,478	0,395	1,412	0,798	2,499	0,234
9	rs12335941	21955669	9p21	A	0,478	0,395	1,412	0,798	2,499	0,234
9	rs717326	21958524	9p21	G	0,043	0,059	0,797	0,225	2,829	0,791
9	rs7041637	21961866	9p21	A	0,283	0,243	1,052	0,566	1,956	0,875
9	rs3731257	21966221	9p21	T	0,261	0,230	0,999	0,526	1,897	1
9	rs2518719	21970427	9p21	G	0,120	0,151	0,664	0,272	1,625	0,363
9	rs2811708	21973422	9p21	T	0,370	0,401	0,751	0,399	1,414	0,385
9	rs3731239	21974218	9p21	C	0,217	0,132	1,992	0,946	4,198	0,072
9	rs3731222	21983914	9p21	G	0,087	0,151	0,493	0,188	1,297	0,130
9	rs3731213	21986218	9p21	A	0,076	0,112	0,691	0,246	1,940	0,510
9	rs3731211	21986847	9p21	A	0,370	0,408	0,745	0,398	1,397	0,362
9	rs3731204	21987584	9p21	G	0,098	0,151	0,550	0,215	1,403	0,192
9	rs3731201	21988896	9p21	G	0,272	0,250	1,072	0,519	2,215	0,861
9	rs7036656	21990457	9p21	C	0,370	0,395	0,795	0,419	1,509	0,482
9	rs2811710	21991923	9p21	C	0,489	0,395	1,554	0,862	2,802	0,129
9	rs2811711	21993964	9p21	C	0,141	0,184	0,715	0,308	1,661	0,489
9	rs3218020	21997872	9p21	T	0,413	0,434	0,804	0,442	1,462	0,502
9	rs3218002	22000841	9p21	T	0,207	0,178	1,005	0,463	2,181	0,999
9	rs3217992	22003223	9p21	A	0,435	0,447	0,850	0,474	1,525	0,587
9	rs3217986	22005330	9p21	C	0,043	0,059	0,797	0,225	2,829	0,750
9	rs974336	22006348	9p21	A	0,207	0,178	1,005	0,463	2,181	0,999
9	rs2069422	22008026	9p21	C	0,174	0,138	1,019	0,442	2,349	0,956
9	rs2069418	22009698	9p21	C	0,294	0,211	1,864	0,942	3,688	0,072
9	rs575427	22011477	9p21	C	0,033	0,072	0,423	0,095	1,881	0,229
9	rs10811640	22013411	9p21	G	0,511	0,368	1,760	0,962	3,219	0,068

9	rs643319	22017836	9p21	T	0,413	0,290	1,496	0,812	2,755	0,199
9	rs7044859	22018781	9p21	T	0,511	0,362	1,773	0,971	3,238	0,070
9	rs523096	22019129	9p21	C	0,304	0,191	2,072	1,030	4,165	0,042
9	rs518394	22019673	9p21	G	0,294	0,191	1,981	0,987	3,977	0,065
9	rs10757264	22019732	9p21	A	0,424	0,342	1,360	0,736	2,515	0,321
9	rs10965212	22023795	9p21	T	0,446	0,347	1,423	0,782	2,592	0,250
9	rs496892	22024351	9p21	A	0,370	0,287	1,261	0,673	2,361	0,475
9	rs10738604	22025493	9p21	A	0,413	0,408	0,879	0,483	1,600	0,700
9	rs1591136	22026834	9p21	C	0,446	0,349	1,420	0,779	2,588	0,252
9	rs598664	22027551	9p21	G	0,174	0,138	1,019	0,442	2,349	0,956
9	rs7049105	22028801	9p21	A	0,446	0,349	1,420	0,779	2,588	0,252
9	rs10965215	22029445	9p21	G	0,446	0,434	1,069	0,603	1,897	0,813
9	rs564398	22029547	9p21	G	0,239	0,171	1,703	0,803	3,610	0,162
9	rs662463	22030438	9p21	T	0,185	0,145	1,067	0,466	2,442	0,862
9	rs7865618	22031005	9p21	G	0,239	0,171	1,703	0,803	3,610	0,162
9	rs10115049	22032119	9p21	A	0,457	0,434	1,106	0,621	1,972	0,729
9	rs2157719	22033366	9p21	G	0,233	0,171	1,652	0,779	3,503	0,225
9	rs1008878	22036112	9p21	G	0,239	0,171	1,703	0,803	3,610	0,162
9	rs12376000	22039426	9p21	T	0,054	0,072	0,728	0,226	2,343	0,526
9	rs17694493	22041998	9p21	G	0,185	0,138	1,194	0,517	2,758	0,691
9	rs12352425	22042086	9p21	A	0,065	0,112	0,707	0,246	2,031	0,528
9	rs1412829	22043926	9p21	C	0,239	0,171	1,703	0,803	3,610	0,162
9	rs1360589	22045317	9p21	G	0,228	0,165	1,648	0,776	3,498	0,205
9	rs7028570	22048683	9p21	G	0,435	0,421	1,057	0,594	1,879	0,915
9	rs17756311	22053895	9p21	A	0,174	0,138	1,019	0,442	2,349	0,956
9	rs17694572	22054356	9p21	A	0,174	0,138	1,019	0,442	2,349	0,956
9	rs10120688	22056499	9p21	G	0,457	0,428	1,066	0,609	1,868	0,803
9	rs1537378	22061614	9p21	T	0,228	0,165	1,648	0,776	3,498	0,205
9	rs1011970	22062134	9p21	T	0,261	0,243	0,923	0,485	1,755	0,822
9	rs8181047	22064465	9p21	A	0,185	0,099	2,574	1,020	6,499	0,041
9	rs10811647	22065002	9p21	G	0,457	0,461	0,975	0,555	1,710	0,902
9	rs10965224	22067276	9p21	T	0,239	0,243	1,137	0,560	2,308	0,720
9	rs16905599	22069144	9p21	A	0,087	0,105	0,909	0,327	2,525	0,822
9	rs9632884	22072301	9p21	G	0,272	0,230	1,325	0,672	2,613	0,384
9	rs10757270	22072719	9p21	A	0,522	0,520	0,910	0,511	1,619	0,729
9	rs16923583	22073334	9p21	A	0,033	0,072	0,604	0,160	2,276	0,460
9	rs1412832	22077543	9p21	C	0,185	0,105	2,096	0,874	5,024	0,086
9	rs6475606	22081850	9p21	C	0,250	0,257	1,076	0,552	2,096	0,807
9	rs1547704	22082340	9p21	A	0,054	0,086	0,540	0,156	1,872	0,363
9	rs10965228	22082380	9p21	G	0,022	0,092	0,350	0,078	1,577	0,157
9	rs1333040	22083404	9p21	C	0,250	0,257	1,074	0,556	2,075	0,806
9	rs7857345	22087473	9p21	T	0,163	0,099	1,608	0,669	3,864	0,313
9	rs10757272	22088260	9p21	C	0,402	0,434	0,878	0,465	1,657	0,681
9	rs4977574	22098574	9p21	A	0,391	0,474	0,757	0,409	1,402	0,398
9	rs2891168	22098619	9p21	A	0,391	0,474	0,757	0,409	1,402	0,398

9	rs1537371	22099568	9p21	C	0,239	0,243	0,941	0,479	1,849	0,882
9	rs7859727	22102165	9p21	C	0,283	0,316	0,871	0,459	1,652	0,676
9	rs1333042	22103813	9p21	A	0,239	0,237	0,954	0,486	1,875	0,885
9	rs7859362	22105927	9p21	T	0,239	0,237	0,954	0,486	1,875	0,885
9	rs1333043	22106731	9p21	T	0,239	0,237	0,954	0,486	1,875	0,885
9	rs1412834	22110131	9p21	T	0,239	0,237	0,954	0,486	1,875	0,885
9	rs7341786	22112241	9p21	A	0,239	0,237	0,954	0,486	1,875	0,885
9	rs10733376	22114469	9p21	G	0,239	0,237	0,954	0,486	1,875	0,885
9	rs2383206	22115026	9p21	A	0,348	0,375	0,890	0,467	1,697	0,770
9	rs2383207	22115959	9p21	A	0,239	0,237	0,954	0,486	1,875	0,885
9	rs1333045	22119195	9p21	T	0,402	0,428	0,883	0,460	1,696	0,804
9	rs10738610	22123766	9p21	A	0,391	0,467	0,768	0,416	1,418	0,432
9	rs10757278	22124477	9p21	A	0,424	0,540	0,676	0,361	1,267	0,252
9	rs1333048	22125347	9p21	A	0,380	0,421	0,827	0,434	1,574	0,590
9	rs1333049	22125503	9p21	G	0,424	0,533	0,682	0,363	1,282	0,251
9	rs10757281	22127613	9p21	T	0,109	0,211	0,386	0,155	0,964	0,046
9	rs12347779	22128709	9p21	G	0,152	0,099	1,623	0,632	4,172	0,307
9	rs10965243	22130065	9p21	G	0,043	0,118	0,198	0,055	0,711	0,011
9	rs10965245	22130515	9p21	A	0,033	0,118	0,150	0,037	0,609	0,004
9	rs2891169	22131825	9p21	G	0,435	0,447	0,815	0,423	1,571	0,556
9	rs2383208	22132076	9p21	G	0,141	0,204	0,520	0,234	1,155	0,087
9	rs7045889	22133251	9p21	G	0,380	0,428	0,879	0,483	1,599	0,673
9	rs10811659	22133716	9p21	C	0,207	0,217	1,232	0,567	2,678	0,595
9	rs10757282	22133984	9p21	C	0,435	0,395	0,965	0,532	1,751	0,888
9	rs10811661	22134094	9p21	C	0,130	0,171	0,617	0,277	1,375	0,229
9	rs10757283	22134172	9p21	T	0,457	0,415	1,002	0,544	1,847	0,993
9	rs1333051	22136489	9p21	T	0,076	0,138	0,344	0,123	0,968	0,035
9	rs7018475	22137685	9p21	G	0,367	0,276	1,397	0,708	2,756	0,342
9	rs11791416	22138105	9p21	G	0,217	0,250	1,096	0,512	2,346	0,821
9	rs4977761	22138762	9p21	T	0,380	0,408	0,823	0,449	1,510	0,573
9	rs2065501	22140224	9p21	A	0,304	0,329	0,851	0,422	1,713	0,649
9	rs4977577	22141875	9p21	C	0,478	0,388	1,352	0,742	2,464	0,317
9	rs7849199	22143293	9p21	A	0,152	0,243	0,583	0,269	1,263	0,158
9	rs2065500	22145694	9p21	G	0,141	0,197	0,640	0,282	1,453	0,308
9	rs7022662	22147715	9p21	G	0,141	0,197	0,640	0,282	1,453	0,308
9	rs12341394	22148055	9p21	T	0,163	0,250	0,617	0,289	1,319	0,212
9	rs7856219	22150261	9p21	C	0,163	0,237	0,713	0,322	1,581	0,369
9	rs10965256	22151465	9p21	A	0,109	0,086	1,381	0,513	3,719	0,518
9	rs7853123	22153360	9p21	A	0,554	0,441	1,675	0,906	3,097	0,098
9	rs944802	22155709	9p21	A	0,109	0,158	0,640	0,254	1,614	0,344
9	rs7028213	22157360	9p21	G	0,174	0,270	0,579	0,272	1,235	0,146
9	rs12238587	22158168	9p21	A	0,141	0,184	0,693	0,290	1,656	0,448
9	rs10757288	22159416	9p21	C	0,587	0,434	1,910	1,021	3,574	0,037
9	rs7864275	22161212	9p21	T	0,261	0,362	0,635	0,321	1,254	0,191
9	rs10965266	22161494	9p21	G	0,174	0,211	0,746	0,328	1,694	0,491

9	rs10965267	22161828	9p21	G	0,109	0,099	1,137	0,433	2,982	0,689
9	rs10811668	22164991	9p21	A	0,250	0,296	0,732	0,370	1,448	0,335
9	rs2779748	22166769	9p21	A	0,565	0,447	1,580	0,852	2,930	0,149
9	rs7863846	22168128	9p21	T	0,152	0,263	0,560	0,260	1,207	0,136
9	rs828580	22168464	9p21	T	0,109	0,105	1,088	0,448	2,643	0,860
9	rs1537377	22169700	9p21	C	0,228	0,349	0,653	0,336	1,271	0,211
9	rs954399	22170983	9p21	T	0,144	0,263	0,536	0,246	1,164	0,107
9	rs828582	22172259	9p21	A	0,304	0,420	0,554	0,284	1,080	0,083
9	rs10965278	22174712	9p21	A	0,174	0,191	0,727	0,352	1,499	0,405
9	rs10965279	22175188	9p21	C	0,043	0,105	0,385	0,104	1,420	0,130
9	rs10757292	22176961	9p21	T	0,120	0,112	0,938	0,396	2,226	0,917
9	rs866666	22183781	9p21	C	0,511	0,434	1,404	0,793	2,487	0,197
9	rs2767409	22184997	9p21	A	0,311	0,342	1,023	0,543	1,931	0,926
9	rs1095904	22187074	9p21	T	0,272	0,237	1,155	0,593	2,249	0,667
9	rs828576	22191189	9p21	T	0,500	0,399	1,590	0,882	2,867	0,119
9	rs2219849	22195820	9p21	T	0,500	0,493	1,103	0,617	1,970	0,754
9	rs1751449	22196863	9p21	G	0,326	0,395	0,769	0,416	1,422	0,385
9	rs12375458	22198149	9p21	A	0,163	0,072	1,954	0,769	4,965	0,164
10	rs1482472	44682973	10q11	C	0,367	0,415	0,703	0,378	1,308	0,278
10	rs12415866	44686664	10q11	G	0,141	0,197	0,419	0,177	0,991	0,032
10	rs7917089	44688587	10q11	A	0,141	0,197	0,419	0,177	0,991	0,032
10	rs1623851	44691241	10q11	G	0,185	0,250	0,496	0,239	1,030	0,056
10	rs1627329	44691633	10q11	C	0,185	0,250	0,496	0,239	1,030	0,056
10	rs10508883	44693544	10q11	C	0,043	0,072	0,380	0,099	1,460	0,133
10	rs7900182	44693742	10q11	G	0,144	0,100	2,103	0,746	5,931	0,193
10	rs11597731	44694201	10q11	T	0,207	0,138	1,942	0,833	4,530	0,099
10	rs7902040	44695308	10q11	G	0,043	0,079	0,255	0,068	0,951	0,024
10	rs11238911	44695862	10q11	A	0,033	0,079	0,188	0,045	0,789	0,007
10	rs11238913	44695973	10q11	C	0,294	0,263	1,066	0,541	2,101	0,862
10	rs2802477	44696034	10q11	C	0,391	0,401	1,088	0,610	1,940	0,796
10	rs11594522	44696352	10q11	A	0,141	0,105	1,991	0,710	5,584	0,184
10	rs2054620	44698075	10q11	C	0,304	0,283	1,007	0,527	1,923	0,988
10	rs11238921	44699910	10q11	T	0,304	0,263	1,110	0,573	2,152	0,772
10	rs768676	44702681	10q11	A	0,120	0,105	1,065	0,428	2,651	0,848
10	rs3865770	44705969	10q11	T	0,141	0,105	1,991	0,710	5,584	0,184
10	rs1482473	44707598	10q11	C	0,109	0,158	0,496	0,213	1,158	0,109
10	rs3851257	44709171	10q11	T	0,163	0,204	0,656	0,343	1,257	0,220
10	rs12573558	44712128	10q11	A	0,141	0,105	1,991	0,710	5,584	0,184
10	rs11238935	44714402	10q11	T	0,065	0,099	0,373	0,125	1,117	0,071
10	rs2209067	44716469	10q11	A	0,196	0,132	1,801	0,785	4,132	0,150
10	rs1704219	44729958	10q11	C	0,294	0,276	0,978	0,513	1,865	0,909
10	rs7907961	44730995	10q11	C	0,228	0,178	1,589	0,750	3,365	0,259
10	rs1746043	44732825	10q11	C	0,294	0,276	0,978	0,513	1,865	0,909
10	rs647419	44734995	10q11	T	0,272	0,250	1,365	0,679	2,741	0,395
10	rs88796	44737036	10q11	C	0,250	0,237	0,938	0,469	1,875	0,854

10	rs617019	44737246	10q11	T	0,065	0,105	0,367	0,123	1,092	0,059
10	rs17155733	44737433	10q11	G	0,185	0,132	1,829	0,747	4,478	0,177
10	rs583489	44738688	10q11	C	0,120	0,132	0,643	0,288	1,433	0,254
10	rs676966	44739594	10q11	A	0,065	0,118	0,356	0,127	0,997	0,046
10	rs494207	44741256	10q11	T	0,120	0,132	0,643	0,288	1,433	0,254
10	rs541483	44746395	10q11	C	0,163	0,158	0,780	0,364	1,674	0,508
10	rs535176	44747059	10q11	A	0,163	0,171	0,718	0,345	1,496	0,365
10	rs622472	44749211	10q11	G	0,163	0,171	0,718	0,345	1,496	0,365
10	rs513391	44749708	10q11	G	0,163	0,171	0,718	0,345	1,496	0,365
10	rs11238956	44749854	10q11	C	0,304	0,322	0,984	0,516	1,875	0,920
10	rs687175	44751910	10q11	G	0,163	0,171	0,718	0,345	1,496	0,365
10	rs559580	44752078	10q11	C	0,156	0,158	0,750	0,348	1,618	0,464
10	rs559469	44752118	10q11	G	0,163	0,171	0,718	0,345	1,496	0,365
10	rs2437935	44752268	10q11	C	0,457	0,421	1,093	0,590	2,024	0,773
10	rs535949	44752330	10q11	A	0,163	0,187	0,706	0,344	1,447	0,339
10	rs671765	44752976	10q11	C	0,163	0,171	0,718	0,345	1,496	0,365
10	rs501120	44753867	10q11	G	0,163	0,171	0,718	0,345	1,496	0,365
10	rs579058	44755104	10q11	C	0,163	0,178	0,678	0,334	1,378	0,283
10	rs604674	44756894	10q11	A	0,163	0,178	0,678	0,334	1,378	0,283
10	rs487465	44758197	10q11	G	0,163	0,178	0,678	0,334	1,378	0,283
10	rs475926	44760887	10q11	C	0,294	0,273	0,951	0,497	1,818	0,875
10	rs1632484	44773984	10q11	A	0,163	0,171	0,687	0,337	1,399	0,302
10	rs1746048	44775824	10q11	T	0,163	0,171	0,687	0,337	1,399	0,302
10	rs1746049	44776310	10q11	T	0,163	0,171	0,687	0,337	1,399	0,302
10	rs1746052	44778546	10q11	C	0,087	0,145	0,416	0,175	0,989	0,034
10	rs800314	44786364	10q11	G	0,043	0,086	0,262	0,075	0,917	0,022
10	rs11598523	44791433	10q11	A	0,120	0,099	1,754	0,601	5,118	0,282
10	rs2505734	44793299	10q11	C	0,457	0,434	0,970	0,536	1,755	0,920
10	rs754713	44797087	10q11	T	0,413	0,322	1,618	0,880	2,975	0,114
10	rs800320	44798482	10q11	T	0,163	0,151	1,182	0,530	2,640	0,720
10	rs800323	44801673	10q11	G	0,413	0,355	1,326	0,729	2,410	0,342
10	rs2437934	44803925	10q11	G	0,457	0,434	0,970	0,536	1,755	0,920
10	rs11238983	44810205	10q11	A	0,239	0,165	1,720	0,807	3,665	0,164
10	rs2146807	44813738	10q11	C	0,239	0,132	2,644	1,121	6,237	0,039
10	rs2146808	44813777	10q11	C	0,152	0,138	1,267	0,560	2,864	0,601
10	rs7082209	44814336	10q11	G	0,239	0,165	1,720	0,807	3,665	0,164
10	rs800310	44815048	10q11	A	0,348	0,290	1,559	0,802	3,029	0,198
10	rs2505735	44815709	10q11	A	0,300	0,287	1,004	0,524	1,925	0,997
10	rs977754	44817419	10q11	G	0,283	0,250	1,048	0,533	2,059	0,902
10	rs812889	44818563	10q11	G	0,087	0,086	0,760	0,272	2,129	0,585
10	rs2476351	44820157	10q11	C	0,272	0,204	1,344	0,667	2,709	0,423
10	rs11238987	44821220	10q11	A	0,065	0,087	0,576	0,211	1,569	0,287
10	rs10508884	44821387	10q11	T	0,294	0,355	0,737	0,397	1,368	0,312
10	rs1111259	44821772	10q11	T	0,174	0,125	1,702	0,717	4,041	0,190
10	rs2505741	44823136	10q11	A	0,402	0,388	1,051	0,596	1,853	0,890

10	rs2028100	44826376	10q11	A	0,228	0,303	0,609	0,312	1,190	0,177
10	rs1836982	44827164	10q11	G	0,348	0,250	1,797	0,916	3,524	0,099
10	rs982097	44828234	10q11	T	0,424	0,447	0,942	0,534	1,662	0,809
10	rs7918046	44830727	10q11	T	0,326	0,336	0,945	0,524	1,704	0,805
10	rs11815919	44831379	10q11	T	0,152	0,211	0,574	0,256	1,288	0,193
10	rs928565	44832884	10q11	T	0,402	0,375	1,215	0,688	2,147	0,475
10	rs11599561	44833031	10q11	C	0,043	0,105	0,204	0,056	0,740	0,011
10	rs266080	44833894	10q11	G	0,087	0,033	6,354	1,398	28,870	0,003
10	rs1144482	44835963	10q11	A	0,380	0,342	1,197	0,679	2,109	0,530
10	rs1360724	44837267	10q11	G	0,326	0,336	0,945	0,524	1,704	0,805
10	rs10900025	44838019	10q11	G	0,424	0,474	0,770	0,438	1,355	0,401
10	rs7069891	44838464	10q11	T	0,043	0,112	0,201	0,056	0,725	0,010
10	rs77839	44838530	10q11	G	0,511	0,507	1,022	0,582	1,795	0,889
10	rs17390084	44839865	10q11	A	0,076	0,072	0,794	0,244	2,582	0,738
10	rs10793536	44842048	10q11	C	0,446	0,507	0,789	0,455	1,369	0,402
10	rs266076	44844381	10q11	G	0,522	0,540	1,004	0,579	1,742	0,984
10	rs1144480	44848921	10q11	A	0,370	0,329	1,191	0,668	2,124	0,557
10	rs266109	44850424	10q11	G	0,196	0,138	1,758	0,769	4,018	0,165
10	rs1144477	44851737	10q11	A	0,424	0,349	1,423	0,793	2,554	0,245
10	rs266105	44855663	10q11	A	0,185	0,118	2,241	0,975	5,152	0,057
10	rs11595588	44855740	10q11	C	0,421	0,426	1,103	0,618	1,969	0,739
10	rs17391002	44855927	10q11	G	0,196	0,237	0,743	0,372	1,484	0,391
10	rs266103	44856370	10q11	T	0,196	0,171	1,944	0,885	4,272	0,093
10	rs185545	44858840	10q11	C	0,261	0,204	1,609	0,812	3,191	0,166
10	rs7918568	44861220	10q11	T	0,294	0,191	1,954	0,932	4,097	0,086
10	rs7915848	44863434	10q11	C	0,272	0,184	1,906	0,875	4,151	0,120
10	rs266094	44864300	10q11	T	0,163	0,105	1,852	0,753	4,557	0,153
10	rs266093	44866208	10q11	C	0,533	0,388	2,084	1,086	4,001	0,026
10	rs1029153	44867146	10q11	C	0,228	0,263	0,836	0,397	1,762	0,642
10	rs1801157	44868257	10q11	A	0,152	0,243	0,368	0,153	0,889	0,026
10	rs266089	44869427	10q11	A	0,185	0,145	1,343	0,608	2,966	0,465
10	rs266088	44870015	10q11	T	0,130	0,151	0,808	0,348	1,877	0,573
10	rs266087	44871062	10q11	A	0,304	0,428	0,400	0,194	0,827	0,014
10	rs2297630	44871548	10q11	A	0,141	0,165	0,902	0,373	2,179	0,808
10	rs2839690	44875166	10q11	C	0,283	0,197	1,611	0,764	3,396	0,211
10	rs3780891	44878713	10q11	A	0,065	0,099	0,653	0,224	1,899	0,516

				ATVB						
CHR	**SNP**	**BP**	**Region**	**A1**	**F_A**	**F_U**	**OR**	**L95**	**U95**	**P**
1	rs4970833	109804646	1p13							
1	rs653635	109806313	1p13							
1	rs6657811	109807283	1p13	T	0,084	0,096	0,868	0,735	1,025	0,096
1	rs608196	109808117	1p13							
1	rs17035630	109810981	1p13							

1	rs17035665	109813719	1p13							
1	rs4970834	109814880	1p13	T	0,121	0,143	0,831	0,721	0,956	0,013
1	rs611917	109815252	1p13	G	0,217	0,232	0,912	0,809	1,027	0,130
1	rs12740374	109817590	1p13	T	0,170	0,191	0,870	0,769	0,985	0,029
1	rs629301	109818306	1p13	G	0,170	0,191	0,870	0,769	0,985	0,029
1	rs646776	109818530	1p13	C	0,170	0,191	0,870	0,769	0,985	0,029
1	rs17035949	109820919	1p13	G	0,053	0,052	1,020	0,826	1,261	0,863
1	rs583104	109821307	1p13	G	0,184	0,203	0,885	0,784	0,999	0,055
1	rs602633	109821511	1p13	T	0,180	0,201	0,870	0,771	0,983	0,023
1	rs599839	109822166	1p13	G	0,184	0,202	0,892	0,790	1,007	0,073
1	rs14000	109822509	1p13	C	0,120	0,100	1,227	1,052	1,432	0,013
1	rs672569	109827253	1p13	A	0,103	0,114	0,897	0,768	1,046	0,166
1	rs655246	109832283	1p13	A	0,354	0,365	0,949	0,853	1,056	0,313
1	rs17584208	109833187	1p13	A	0,044	0,043	1,014	0,802	1,281	0,921
1	rs17645031	109834938	1p13	T	0,044	0,043	1,014	0,802	1,281	0,921
1	rs17645143	109835757	1p13	C	0,228	0,218	1,067	0,946	1,204	0,300
1	rs629001	109838918	1p13	C	0,030	0,045	0,653	0,506	0,843	0,002
1	rs3850615	109839738	1p13	A	0,041	0,031	1,343	1,036	1,740	0,023
1	rs600806	109840629	1p13	G	0,224	0,213	1,067	0,951	1,197	0,280
1	rs680434	109842271	1p13	C	0,255	0,238	1,093	0,979	1,221	0,114
1	rs11583969	109843775	1p13	T	0,054	0,044	1,229	0,988	1,529	0,068
1	rs652651	109844532	1p13	A	0,259	0,238	1,117	1,000	1,247	0,050
1	rs407102	109846278	1p13	C	0,252	0,232	1,112	0,995	1,242	0,059
1	rs592107	109848726	1p13	A	0,252	0,232	1,112	0,995	1,242	0,059
1	rs444387	109851127	1p13	A	0,253	0,234	1,104	0,989	1,234	0,080
1	rs464218	109856306	1p13	G	0,427	0,413	1,062	0,964	1,170	0,202
1	rs17585355	109857815	1p13	C	0,034	0,026	1,362	1,024	1,813	0,032
1	rs370088	109858119	1p13	T	0,252	0,234	1,103	0,987	1,232	0,087
1	rs3853500	109864269	1p13	T	0,251	0,232	1,111	0,994	1,242	0,061
1	rs3768496	109866569	1p13	T	0,258	0,236	1,121	1,004	1,252	0,042
1	rs10745352	109871787	1p13	T	0,258	0,236	1,121	1,004	1,252	0,042
1	rs10745353	109877506	1p13	A	0,258	0,236	1,121	1,004	1,252	0,042
1	rs4603158	109879549	1p13	C	0,258	0,236	1,121	1,004	1,252	0,042
1	rs11102972	109880721	1p13	C	0,210	0,191	1,123	0,996	1,266	0,053
1	rs10858084	109882250	1p13	T	0,257	0,236	1,120	1,002	1,251	0,045
1	rs2228604	109884775	1p13	T	0,257	0,236	1,120	1,002	1,251	0,045
1	rs4970843	109887191	1p13	T	0,455	0,455	0,999	0,908	1,099	0,989
1	rs3879448	109891423	1p13	G	0,265	0,244	1,114	0,998	1,243	0,057
1	rs7536292	109894693	1p13	C	0,170	0,177	0,953	0,840	1,081	0,444
1	rs1030522	109900707	1p13	C	0,257	0,235	1,120	1,003	1,251	0,049
1	rs3879449	109904971	1p13	A	0,257	0,235	1,120	1,003	1,251	0,049
1	rs11581665	109910013	1p13	T	0,134	0,133	1,012	0,880	1,163	0,879
1	rs10858086	109915075	1p13	C	0,257	0,235	1,120	1,003	1,251	0,049
1	rs1149175	109922377	1p13	A	0,135	0,133	1,017	0,884	1,169	0,826
1	rs12037569	109923677	1p13	T	0,142	0,143	0,991	0,863	1,137	0,893

1	rs10858089	109926828	1p13	T	0,257	0,235	1,122	1,004	1,253	0,041
1	rs4970752	109930852	1p13	C	0,257	0,235	1,122	1,004	1,253	0,041
1	rs10745354	109931908	1p13	C	0,257	0,235	1,122	1,004	1,253	0,041
1	rs3768494	109935427	1p13	A	0,257	0,235	1,122	1,004	1,253	0,041
1	rs1880670	109941133	1p13	C	0,257	0,235	1,122	1,004	1,253	0,041
1	rs10858092	109943893	1p13	C	0,257	0,235	1,122	1,004	1,253	0,041
1	rs4120621	109949008	1p13	A	0,257	0,235	1,122	1,004	1,253	0,041
1	rs2936033	222751034	1q41	T	0,192	0,189	1,021	0,905	1,150	0,751
1	rs3008647	222759007	1q41	T	0,162	0,158	1,028	0,902	1,171	0,694
1	rs2270705	222761771	1q41							
1	rs2936027	222762316	1q41	T	0,098	0,132	0,718	0,617	0,836	0,001
1	rs17464857	222762709	1q41	G	0,162	0,159	1,028	0,902	1,170	0,700
1	rs2936041	222762773	1q41	T	0,161	0,158	1,021	0,896	1,165	0,777
1	rs4846767	222763026	1q41	C	0,192	0,225	0,808	0,714	0,914	0,001
1	rs3008650	222763215	1q41	G	0,101	0,136	0,720	0,620	0,835	0,001
1	rs2936040	222763661	1q41	A	0,098	0,132	0,718	0,617	0,836	0,001
1	rs3008653	222764791	1q41	G	0,163	0,159	1,030	0,904	1,173	0,673
1	rs3008654	222766609	1q41	A	0,148	0,150	0,985	0,856	1,133	0,828
1	rs1995152	222769593	1q41	C	0,098	0,132	0,718	0,617	0,836	0,001
1	rs1909194	222770703	1q41	G	0,162	0,159	1,028	0,902	1,171	0,702
1	rs3002130	222772139	1q41	C	0,164	0,158	1,046	0,918	1,192	0,522
1	rs3002142	222788062	1q41	C	0,134	0,115	1,197	1,034	1,386	0,017
1	rs904323	222790366	1q41	A	0,116	0,149	0,743	0,644	0,858	0,001
1	rs17163303	222795118	1q41	T	0,068	0,067	1,023	0,845	1,238	0,818
1	rs17011666	222798965	1q41	G	0,197	0,231	0,815	0,724	0,917	0,003
1	rs2936052	222802376	1q41	G	0,169	0,206	0,785	0,694	0,889	0,001
1	rs3008621	222804046	1q41	A	0,127	0,163	0,748	0,652	0,859	0,001
1	rs3002145	222807013	1q41	T	0,127	0,163	0,748	0,652	0,859	0,001
1	rs1391557	222809616	1q41	T	0,160	0,192	0,801	0,705	0,909	0,003
1	rs2133188	222813753	1q41	T	0,160	0,192	0,804	0,709	0,913	0,003
1	rs2133189	222814442	1q41	C	0,257	0,285	0,870	0,781	0,969	0,017
1	rs17163358	222820639	1q41	G	0,257	0,285	0,870	0,781	0,969	0,016
1	rs17531063	222821709	1q41	G	0,069	0,066	1,048	0,865	1,269	0,632
1	rs17465637	222823529	1q41	A	0,256	0,283	0,873	0,783	0,972	0,016
1	rs17011681	222825088	1q41	C	0,257	0,284	0,871	0,782	0,971	0,016
1	rs2291832	222826481	1q41	G	0,257	0,284	0,871	0,782	0,971	0,016
1	rs2088514	222831372	1q41	G	0,160	0,193	0,798	0,703	0,905	0,003
1	rs2291834	222832295	1q41	T	0,257	0,284	0,871	0,782	0,971	0,016
1	rs17163384	222835222	1q41	C	0,069	0,066	1,048	0,865	1,269	0,632
1	rs2270707	222837594	1q41	G	0,188	0,218	0,829	0,735	0,934	0,006
1	rs1053316	222839838	1q41	A	0,097	0,093	1,047	0,890	1,233	0,555
1	rs3008633	222844840	1q41	T	0,075	0,073	1,037	0,865	1,243	0,674
1	rs1391558	222848029	1q41	C	0,160	0,193	0,796	0,701	0,903	0,002
9	rs756641	21902354	9p21							
9	rs10811634	21905379	9p21							

9	rs16938590	21909979	9p21							
9	rs4977746	21920346	9p21	C	0,166	0,170	0,971	0,856	1,102	0,669
9	rs10811638	21923279	9p21	G	0,166	0,171	0,967	0,852	1,097	0,629
9	rs7852128	21925855	9p21	G	0,172	0,174	0,987	0,871	1,118	0,863
9	rs10965186	21927913	9p21	A	0,172	0,174	0,987	0,871	1,118	0,863
9	rs2518713	21929666	9p21	G	0,175	0,177	0,989	0,873	1,120	0,882
9	rs7864029	21930147	9p21	C	0,179	0,182	0,977	0,864	1,105	0,727
9	rs7869004	21931896	9p21	T	0,178	0,181	0,983	0,868	1,112	0,796
9	rs4977750	21944317	9p21	C	0,137	0,131	1,048	0,908	1,209	0,525
9	rs2811717	21946322	9p21	C	0,137	0,132	1,047	0,908	1,208	0,527
9	rs2811720	21947957	9p21	G	0,140	0,138	1,021	0,888	1,175	0,762
9	rs10965197	21948666	9p21	T	0,396	0,395	1,008	0,914	1,112	0,884
9	rs10757260	21953137	9p21	G	0,413	0,397	1,068	0,969	1,177	0,178
9	rs10757261	21954953	9p21	A	0,413	0,397	1,068	0,969	1,177	0,178
9	rs12335941	21955669	9p21	G	0,414	0,398	1,067	0,968	1,175	0,184
9	rs717326	21958524	9p21	C	0,076	0,086	0,872	0,729	1,043	0,135
9	rs7041637	21961866	9p21	A	0,370	0,338	1,154	1,042	1,277	0,007
9	rs3731257	21966221	9p21	A	0,323	0,288	1,201	1,077	1,340	0,001
9	rs2518719	21970427	9p21	G	0,159	0,134	1,215	1,062	1,391	0,004
9	rs2811708	21973422	9p21	T	0,346	0,314	1,156	1,045	1,279	0,004
9	rs3731239	21974218	9p21	G	0,242	0,298	0,747	0,670	0,834	0,001
9	rs3731222	21983914	9p21	C	0,155	0,136	1,166	1,019	1,334	0,025
9	rs3731213	21986218	9p21	T	0,018	0,024	0,730	0,523	1,020	0,056
9	rs3731211	21986847	9p21	T	0,329	0,296	1,161	1,048	1,286	0,003
9	rs3731204	21987584	9p21	C	0,155	0,136	1,166	1,019	1,334	0,025
9	rs3731201	21988896	9p21	C	0,178	0,164	1,107	0,974	1,258	0,107
9	rs7036656	21990457	9p21	C	0,330	0,298	1,159	1,047	1,284	0,003
9	rs2811710	21991923	9p21	T	0,411	0,393	1,079	0,979	1,189	0,107
9	rs2811711	21993964	9p21	C	0,155	0,138	1,144	1,000	1,310	0,049
9	rs3218020	21997872	9p21	A	0,467	0,420	1,211	1,099	1,333	0,001
9	rs3218002	22000841	9p21	A	0,131	0,119	1,113	0,963	1,288	0,151
9	rs3217992	22003223	9p21	T	0,502	0,458	1,192	1,084	1,312	0,001
9	rs3217986	22005330	9p21	G	0,068	0,079	0,847	0,703	1,022	0,091
9	rs974336	22006348	9p21	T	0,131	0,118	1,120	0,968	1,296	0,131
9	rs2069422	22008026	9p21	G	0,133	0,122	1,107	0,957	1,281	0,181
9	rs2069418	22009698	9p21	G	0,320	0,364	0,824	0,745	0,911	0,001
9	rs575427	22011477	9p21	G	0,083	0,078	1,075	0,902	1,280	0,408
9	rs10811640	22013411	9p21	G	0,451	0,483	0,879	0,799	0,967	0,013
9	rs643319	22017836	9p21	A	0,370	0,390	0,917	0,832	1,012	0,090
9	rs7044859	22018781	9p21	T	0,451	0,484	0,879	0,800	0,967	0,012
9	rs523096	22019129	9p21	G	0,317	0,361	0,821	0,742	0,909	0,001
9	rs518394	22019673	9p21	C	0,315	0,359	0,822	0,743	0,910	0,001
9	rs10757264	22019732	9p21	A	0,408	0,433	0,902	0,819	0,993	0,044
9	rs10965212	22023795	9p21	T	0,417	0,447	0,888	0,807	0,978	0,022
9	rs496892	22024351	9p21	C	0,368	0,389	0,913	0,827	1,007	0,070

9	rs10738604	22025493	9p21	A	0,484	0,439	1,195	1,086	1,315	0,002
9	rs1591136	22026834	9p21	G	0,417	0,446	0,889	0,808	0,978	0,026
9	rs598664	22027551	9p21	C	0,129	0,120	1,094	0,945	1,267	0,219
9	rs7049105	22028801	9p21	A	0,415	0,447	0,881	0,801	0,969	0,016
9	rs10965215	22029445	9p21	G	0,422	0,455	0,876	0,797	0,964	0,010
9	rs564398	22029547	9p21	C	0,282	0,324	0,823	0,742	0,914	0,002
9	rs662463	22030438	9p21	A	0,124	0,113	1,111	0,957	1,289	0,163
9	rs7865618	22031005	9p21	G	0,289	0,331	0,823	0,742	0,912	0,001
9	rs10115049	22032119	9p21	A	0,417	0,448	0,882	0,802	0,971	0,021
9	rs2157719	22033366	9p21	C	0,288	0,330	0,821	0,741	0,911	0,002
9	rs1008878	22036112	9p21	G	0,288	0,330	0,821	0,741	0,911	0,002
9	rs12376000	22039426	9p21	T	0,084	0,079	1,061	0,892	1,262	0,502
9	rs17694493	22041998	9p21	G	0,147	0,138	1,080	0,941	1,241	0,254
9	rs12352425	22042086	9p21	A	0,070	0,081	0,855	0,711	1,028	0,101
9	rs1412829	22043926	9p21	G	0,286	0,327	0,827	0,745	0,917	0,003
9	rs1360589	22045317	9p21	C	0,288	0,329	0,828	0,746	0,917	0,003
9	rs7028570	22048683	9p21	G	0,418	0,448	0,887	0,806	0,976	0,017
9	rs17756311	22053895	9p21	A	0,110	0,100	1,113	0,952	1,301	0,194
9	rs17694572	22054356	9p21	A	0,111	0,098	1,140	0,974	1,333	0,103
9	rs10120688	22056499	9p21	G	0,410	0,442	0,881	0,801	0,970	0,016
9	rs1537378	22061614	9p21	A	0,268	0,312	0,811	0,730	0,900	0,001
9	rs1011970	22062134	9p21	T	0,184	0,181	1,023	0,903	1,159	0,710
9	rs8181047	22064465	9p21	A	0,192	0,239	0,764	0,680	0,858	0,001
9	rs10811647	22065002	9p21	C	0,464	0,508	0,839	0,762	0,923	0,001
9	rs10965224	22067276	9p21	T	0,270	0,316	0,806	0,726	0,894	0,001
9	rs16905599	22069144	9p21	A	0,064	0,075	0,834	0,689	1,010	0,066
9	rs9632884	22072301	9p21	G	0,350	0,406	0,791	0,717	0,873	0,001
9	rs10757270	22072719	9p21	A	0,463	0,506	0,842	0,765	0,927	0,002
9	rs16923583	22073334	9p21	A	0,022	0,023	0,946	0,685	1,306	0,718
9	rs1412832	22077543	9p21	C	0,203	0,242	0,803	0,717	0,900	0,001
9	rs6475606	22081850	9p21	C	0,370	0,414	0,836	0,758	0,922	0,001
9	rs1547704	22082340	9p21	A	0,015	0,021	0,738	0,513	1,062	0,105
9	rs10965228	22082380	9p21	G	0,091	0,087	1,056	0,893	1,249	0,555
9	rs1333040	22083404	9p21	C	0,286	0,338	0,792	0,714	0,877	0,001
9	rs7857345	22087473	9p21	T	0,188	0,227	0,796	0,708	0,894	0,002
9	rs10757272	22088260	9p21	C	0,383	0,437	0,805	0,731	0,887	0,001
9	rs4977574	22098574	9p21	A	0,382	0,435	0,808	0,733	0,889	0,001
9	rs2891168	22098619	9p21	A	0,383	0,435	0,809	0,735	0,891	0,001
9	rs1537371	22099568	9p21	C	0,372	0,423	0,816	0,741	0,898	0,001
9	rs7859727	22102165	9p21	C	0,382	0,434	0,808	0,734	0,890	0,001
9	rs1333042	22103813	9p21	A	0,346	0,398	0,804	0,728	0,887	0,001
9	rs7859362	22105927	9p21	T	0,372	0,423	0,816	0,741	0,898	0,001
9	rs1333043	22106731	9p21	T	0,372	0,423	0,816	0,741	0,898	0,001
9	rs1412834	22110131	9p21	T	0,372	0,423	0,816	0,741	0,898	0,001
9	rs7341786	22112241	9p21	A	0,372	0,423	0,816	0,742	0,899	0,001

9	rs10733376	22114469	9p21	G	0,371	0,418	0,832	0,756	0,916	0,001
9	rs2383206	22115026	9p21	A	0,372	0,418	0,833	0,757	0,917	0,001
9	rs2383207	22115959	9p21	A	0,372	0,418	0,833	0,757	0,917	0,001
9	rs1333045	22119195	9p21	T	0,396	0,438	0,845	0,768	0,931	0,001
9	rs10738610	22123766	9p21	A	0,378	0,427	0,820	0,745	0,904	0,001
9	rs10757278	22124477	9p21	A	0,418	0,458	0,852	0,774	0,937	0,003
9	rs1333048	22125347	9p21	A	0,379	0,428	0,817	0,741	0,900	0,001
9	rs1333049	22125503	9p21	G	0,417	0,459	0,846	0,768	0,931	0,001
9	rs10757281	22127613	9p21	T	0,093	0,083	1,154	0,968	1,376	0,118
9	rs12347779	22128709	9p21	G	0,057	0,052	1,087	0,880	1,343	0,461
9	rs10965243	22130065	9p21	G	0,082	0,077	1,073	0,898	1,282	0,458
9	rs10965245	22130515	9p21	A	0,082	0,077	1,073	0,898	1,282	0,458
9	rs2891169	22131825	9p21	G	0,433	0,423	1,040	0,943	1,147	0,434
9	rs2383208	22132076	9p21	G	0,204	0,200	1,028	0,914	1,157	0,644
9	rs7045889	22133251	9p21	G	0,331	0,338	0,967	0,872	1,072	0,525
9	rs10811659	22133716	9p21	C	0,241	0,247	0,967	0,864	1,081	0,557
9	rs10757282	22133984	9p21	C	0,474	0,469	1,019	0,925	1,123	0,703
9	rs10811661	22134094	9p21	C	0,199	0,195	1,024	0,908	1,155	0,710
9	rs10757283	22134172	9p21	T	0,475	0,471	1,018	0,924	1,122	0,715
9	rs1333051	22136489	9p21	T	0,156	0,156	1,001	0,877	1,144	0,987
9	rs7018475	22137685	9p21	G	0,302	0,298	1,019	0,918	1,132	0,711
9	rs11791416	22138105	9p21	G	0,290	0,302	0,944	0,850	1,048	0,278
9	rs4977761	22138762	9p21	T	0,285	0,282	1,017	0,914	1,131	0,763
9	rs2065501	22140224	9p21							
9	rs4977577	22141875	9p21	C	0,275	0,278	0,984	0,877	1,104	0,781
9	rs7849199	22143293	9p21	A	0,292	0,303	0,952	0,857	1,057	0,373
9	rs2065500	22145694	9p21	G	0,216	0,219	0,984	0,877	1,104	0,782
9	rs7022662	22147715	9p21	G	0,221	0,223	0,992	0,884	1,113	0,896
9	rs12341394	22148055	9p21	T	0,293	0,304	0,950	0,855	1,054	0,347
9	rs7856219	22150261	9p21	C	0,297	0,309	0,946	0,852	1,050	0,305
9	rs10965256	22151465	9p21	A	0,075	0,072	1,042	0,868	1,252	0,684
9	rs7853123	22153360	9p21	A	0,420	0,413	1,032	0,936	1,138	0,520
9	rs944802	22155709	9p21	T	0,201	0,204	0,983	0,874	1,105	0,773
9	rs7028213	22157360	9p21	G	0,294	0,305	0,949	0,855	1,054	0,337
9	rs12238587	22158168	9p21	A	0,219	0,221	0,989	0,882	1,109	0,843
9	rs10757288	22159416	9p21	C	0,414	0,405	1,040	0,943	1,148	0,412
9	rs7864275	22161212	9p21	T	0,371	0,378	0,973	0,881	1,075	0,611
9	rs10965266	22161494	9p21	G	0,218	0,218	1,001	0,892	1,123	0,977
9	rs10965267	22161828	9p21	G	0,085	0,081	1,057	0,888	1,257	0,540
9	rs10811668	22164991	9p21	A	0,279	0,270	1,046	0,939	1,165	0,406
9	rs2779748	22166769	9p21	T	0,421	0,416	1,022	0,926	1,127	0,693
9	rs7863846	22168128	9p21	T	0,286	0,298	0,942	0,848	1,047	0,294
9	rs828580	22168464	9p21	T	0,077	0,072	1,078	0,899	1,292	0,433
9	rs1537377	22169700	9p21	C	0,363	0,368	0,976	0,883	1,079	0,646
9	rs954399	22170983	9p21	A	0,286	0,297	0,951	0,856	1,056	0,365

9	rs828582	22172259	9p21	A	0,380	0,382	0,992	0,899	1,095	0,877
9	rs10965278	22174712	9p21	A	0,272	0,269	1,017	0,913	1,132	0,748
9	rs10965279	22175188	9p21	C	0,068	0,070	0,971	0,803	1,174	0,724
9	rs10757292	22176961	9p21							
9	rs866666	22183781	9p21	C	0,321	0,334	0,935	0,841	1,040	0,208
9	rs2767409	22184997	9p21	A	0,352	0,349	1,016	0,915	1,130	0,756
9	rs1095904	22187074	9p21							
9	rs828576	22191189	9p21	T	0,320	0,331	0,944	0,848	1,051	0,283
9	rs2219849	22195820	9p21							
9	rs1751449	22196863	9p21	G	0,374	0,371	1,012	0,910	1,125	0,810
9	rs12375458	22198149	9p21							
10	rs1482472	44682973	10q11	C	0,375	0,395	0,915	0,827	1,013	0,076
10	rs12415866	44686664	10q11	G	0,124	0,143	0,841	0,729	0,970	0,015
10	rs7917089	44688587	10q11	A	0,121	0,145	0,815	0,707	0,940	0,005
10	rs1623851	44691241	10q11	G	0,177	0,197	0,876	0,774	0,991	0,036
10	rs1627329	44691633	10q11	C	0,177	0,197	0,878	0,776	0,993	0,040
10	rs10508883	44693544	10q11	C	0,026	0,021	1,260	0,918	1,729	0,152
10	rs7900182	44693742	10q11	G	0,175	0,168	1,046	0,922	1,187	0,468
10	rs11597731	44694201	10q11	T	0,178	0,178	1,003	0,885	1,137	0,971
10	rs7902040	44695308	10q11	G	0,102	0,121	0,820	0,704	0,954	0,008
10	rs11238911	44695862	10q11	A	0,100	0,120	0,816	0,700	0,951	0,008
10	rs11238913	44695973	10q11	C	0,324	0,343	0,913	0,824	1,011	0,059
10	rs2802477	44696034	10q11	G	0,428	0,417	1,052	0,950	1,165	0,321
10	rs11594522	44696352	10q11	A	0,170	0,165	1,039	0,914	1,179	0,546
10	rs2054620	44698075	10q11	C	0,324	0,343	0,914	0,825	1,012	0,063
10	rs11238921	44699910	10q11	T	0,323	0,343	0,911	0,822	1,010	0,060
10	rs768676	44702681	10q11	A	0,067	0,058	1,166	0,956	1,423	0,125
10	rs3865770	44705969	10q11	A	0,170	0,165	1,039	0,914	1,179	0,546
10	rs1482473	44707598	10q11	C	0,144	0,166	0,847	0,743	0,967	0,016
10	rs3851257	44709171	10q11	T	0,323	0,343	0,912	0,823	1,011	0,059
10	rs12573558	44712128	10q11	A	0,179	0,178	1,005	0,887	1,138	0,924
10	rs11238935	44714402	10q11	T	0,099	0,119	0,815	0,699	0,950	0,008
10	rs2209067	44716469	10q11	A	0,179	0,179	1,001	0,884	1,134	0,981
10	rs1704219	44729958	10q11	C	0,308	0,328	0,912	0,821	1,012	0,068
10	rs7907961	44730995	10q11	C	0,209	0,209	0,998	0,887	1,124	0,966
10	rs1746043	44732825	10q11	C	0,310	0,333	0,895	0,807	0,994	0,026
10	rs647419	44734995	10q11	A	0,353	0,372	0,919	0,831	1,016	0,075
10	rs88796	44737036	10q11	C	0,267	0,290	0,889	0,797	0,990	0,021
10	rs617019	44737246	10q11	A	0,103	0,127	0,792	0,681	0,921	0,003
10	rs17155733	44737433	10q11	G	0,163	0,162	1,005	0,883	1,143	0,951
10	rs583489	44738688	10q11	G	0,111	0,138	0,779	0,673	0,902	0,003
10	rs676966	44739594	10q11	T	0,105	0,127	0,803	0,691	0,934	0,005
10	rs494207	44741256	10q11	A	0,111	0,138	0,779	0,672	0,902	0,003
10	rs541483	44746395	10q11	G	0,159	0,189	0,809	0,712	0,918	0,002
10	rs535176	44747059	10q11	T	0,159	0,189	0,809	0,712	0,918	0,002

10	rs622472	44749211	10q11	C	0,159	0,189	0,809	0,712	0,918	0,002
10	rs513391	44749708	10q11	C	0,159	0,190	0,807	0,710	0,917	0,002
10	rs11238956	44749854	10q11	C	0,348	0,329	1,085	0,981	1,200	0,095
10	rs687175	44751910	10q11	C	0,157	0,188	0,802	0,706	0,911	0,002
10	rs559580	44752078	10q11	C	0,155	0,187	0,794	0,698	0,903	0,002
10	rs559469	44752118	10q11	C	0,159	0,189	0,808	0,711	0,918	0,002
10	rs2437935	44752268	10q11	G	0,378	0,395	0,933	0,845	1,030	0,162
10	rs535949	44752330	10q11	T	0,157	0,188	0,803	0,707	0,913	0,002
10	rs671765	44752976	10q11	G	0,157	0,188	0,803	0,707	0,913	0,002
10	rs501120	44753867	10q11	C	0,157	0,188	0,803	0,707	0,913	0,002
10	rs579058	44755104	10q11	G	0,157	0,188	0,803	0,707	0,913	0,002
10	rs604674	44756894	10q11	T	0,157	0,188	0,803	0,707	0,913	0,002
10	rs487465	44758197	10q11	C	0,157	0,188	0,803	0,707	0,913	0,002
10	rs475926	44760887	10q11	G	0,309	0,334	0,890	0,803	0,987	0,025
10	rs1632484	44773984	10q11	T	0,152	0,183	0,799	0,703	0,910	0,002
10	rs1746048	44775824	10q11	T	0,154	0,186	0,797	0,701	0,906	0,002
10	rs1746049	44776310	10q11	T	0,152	0,183	0,800	0,703	0,910	0,002
10	rs1746052	44778546	10q11	C	0,148	0,177	0,807	0,708	0,919	0,002
10	rs800314	44786364	10q11	G	0,076	0,096	0,778	0,656	0,923	0,005
10	rs11598523	44791433	10q11	A	0,164	0,156	1,055	0,926	1,201	0,415
10	rs2505734	44793299	10q11	C	0,360	0,379	0,922	0,835	1,019	0,111
10	rs754713	44797087	10q11	T	0,283	0,283	1,002	0,901	1,114	0,970
10	rs800320	44798482	10q11	T	0,047	0,040	1,176	0,931	1,486	0,184
10	rs800323	44801673	10q11	G	0,283	0,284	0,995	0,894	1,106	0,924
10	rs2437934	44803925	10q11	G	0,358	0,378	0,920	0,833	1,016	0,106
10	rs11238983	44810205	10q11	A	0,156	0,174	0,876	0,769	0,998	0,041
10	rs2146807	44813738	10q11	C	0,155	0,173	0,879	0,771	1,002	0,049
10	rs2146808	44813777	10q11	C	0,043	0,039	1,102	0,867	1,400	0,422
10	rs7082209	44814336	10q11	G	0,159	0,176	0,881	0,773	1,003	0,044
10	rs800310	44815048	10q11	A	0,224	0,240	0,914	0,815	1,026	0,123
10	rs2505735	44815709	10q11	A	0,203	0,217	0,917	0,814	1,033	0,139
10	rs977754	44817419	10q11	G	0,191	0,203	0,922	0,816	1,041	0,183
10	rs812889	44818563	10q11	G	0,089	0,087	1,030	0,869	1,221	0,748
10	rs2476351	44820157	10q11	C	0,185	0,198	0,921	0,814	1,041	0,171
10	rs11238987	44821220	10q11	A	0,029	0,036	0,798	0,611	1,042	0,096
10	rs10508884	44821387	10q11	T	0,272	0,268	1,021	0,917	1,137	0,683
10	rs1111259	44821772	10q11	T	0,106	0,121	0,860	0,740	1,000	0,042
10	rs2505741	44823136	10q11	G	0,472	0,480	0,969	0,880	1,066	0,527
10	rs2028100	44826376	10q11	A	0,249	0,245	1,019	0,913	1,138	0,740
10	rs1836982	44827164	10q11	G	0,209	0,218	0,947	0,841	1,065	0,361
10	rs982097	44828234	10q11	G	0,461	0,466	0,977	0,888	1,075	0,635
10	rs7918046	44830727	10q11	T	0,293	0,299	0,975	0,879	1,081	0,615
10	rs11815919	44831379	10q11	T	0,188	0,179	1,062	0,938	1,201	0,324
10	rs928565	44832884	10q11	A	0,493	0,487	1,025	0,931	1,128	0,632
10	rs11599561	44833031	10q11	C	0,106	0,112	0,939	0,804	1,096	0,419

10	rs266080	44833894	10q11	G	0,024	0,020	1,190	0,862	1,642	0,300
10	rs1144482	44835963	10q11	T	0,480	0,473	1,031	0,936	1,135	0,529
10	rs1360724	44837267	10q11	G	0,317	0,320	0,985	0,889	1,091	0,765
10	rs10900025	44838019	10q11	G	0,402	0,413	0,955	0,867	1,052	0,362
10	rs7069891	44838464	10q11	T	0,107	0,112	0,945	0,810	1,103	0,478
10	rs77839	44838530	10q11	G	0,426	0,433	0,969	0,880	1,067	0,535
10	rs17390084	44839865	10q11	A	0,041	0,043	0,934	0,734	1,189	0,576
10	rs10793536	44842048	10q11	C	0,433	0,445	0,951	0,864	1,048	0,327
10	rs266076	44844381	10q11	G	0,435	0,446	0,959	0,871	1,055	0,397
10	rs1144480	44848921	10q11	A	0,463	0,456	1,029	0,935	1,134	0,579
10	rs266109	44850424	10q11	G	0,116	0,128	0,893	0,771	1,033	0,117
10	rs1144477	44851737	10q11	T	0,482	0,473	1,037	0,942	1,142	0,482
10	rs266105	44855663	10q11	A	0,137	0,140	0,974	0,849	1,118	0,681
10	rs11595588	44855740	10q11	C	0,395	0,399	0,984	0,892	1,085	0,716
10	rs17391002	44855927	10q11	G	0,203	0,196	1,048	0,928	1,183	0,464
10	rs266103	44856370	10q11	T	0,143	0,148	0,958	0,838	1,096	0,529
10	rs185545	44858840	10q11	C	0,185	0,181	1,032	0,910	1,170	0,620
10	rs7918568	44861220	10q11	T	0,175	0,166	1,066	0,940	1,209	0,342
10	rs7915848	44863434	10q11	C	0,176	0,168	1,061	0,936	1,203	0,366
10	rs266094	44864300	10q11	T	0,143	0,150	0,951	0,831	1,089	0,439
10	rs266093	44866208	10q11	C	0,362	0,359	1,014	0,918	1,120	0,786
10	rs1029153	44867146	10q11	G	0,274	0,279	0,976	0,878	1,086	0,660
10	rs1801157	44868257	10q11	T	0,245	0,247	0,989	0,885	1,106	0,855
10	rs266089	44869427	10q11	A	0,150	0,157	0,950	0,831	1,085	0,412
10	rs266088	44870015	10q11	T	0,150	0,144	1,050	0,918	1,201	0,448
10	rs266087	44871062	10q11	A	0,402	0,403	0,994	0,901	1,095	0,900
10	rs2297630	44871548	10q11	A	0,273	0,280	0,965	0,867	1,073	0,503
10	rs2839690	44875166	10q11	G	0,177	0,167	1,070	0,943	1,215	0,304
10	rs3780891	44878713	10q11	A	0,084	0,074	1,152	0,961	1,380	0,144

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CHR	**SNP**	**BP**	**Region**	**A1**	**F_A**	**F_U**	**OR**	**L95**	**U95**	**P**
1	rs4970833	109804646	1p13							
1	rs653635	109806313	1p13							
1	rs6657811	109807283	1p13	T	0,107	0,085	1,292	0,879	1,898	0,180
1	rs608196	109808117	1p13							
1	rs17035630	109810981	1p13							
1	rs17035665	109813719	1p13							
1	rs4970834	109814880	1p13	T	0,161	0,136	1,213	0,896	1,643	0,198
1	rs611917	109815252	1p13	G	0,277	0,252	1,160	0,888	1,516	0,256
1	rs12740374	109817590	1p13	T	0,203	0,185	1,129	0,855	1,491	0,359
1	rs629301	109818306	1p13	G	0,203	0,185	1,129	0,855	1,491	0,359
1	rs646776	109818530	1p13	C	0,203	0,185	1,129	0,855	1,491	0,359
1	rs17035949	109820919	1p13	G	0,053	0,054	1,002	0,612	1,640	0,997

1	rs583104	109821307	1p13	G	0,224	0,196	1,192	0,909	1,563	0,181
1	rs602633	109821511	1p13	T	0,223	0,191	1,213	0,925	1,591	0,151
1	rs599839	109822166	1p13	G	0,223	0,197	1,170	0,893	1,534	0,221
1	rs14000	109822509	1p13	C	0,123	0,114	1,098	0,771	1,564	0,609
1	rs672569	109827253	1p13	A	0,124	0,110	1,152	0,814	1,630	0,390
1	rs655246	109832283	1p13	A	0,369	0,382	0,941	0,730	1,211	0,620
1	rs17584208	109833187	1p13	A	0,058	0,046	1,311	0,787	2,185	0,285
1	rs17645031	109834938	1p13	T	0,058	0,046	1,311	0,787	2,185	0,285
1	rs17645143	109835757	1p13	C	0,207	0,233	0,842	0,636	1,114	0,216
1	rs629001	109838918	1p13	C	0,048	0,041	1,170	0,695	1,972	0,566
1	rs3850615	109839738	1p13	A	0,039	0,052	0,748	0,443	1,262	0,260
1	rs600806	109840629	1p13	G	0,257	0,222	1,217	0,933	1,589	0,147
1	rs680434	109842271	1p13	C	0,277	0,252	1,141	0,885	1,471	0,313
1	rs11583969	109843775	1p13	T	0,081	0,049	1,672	1,057	2,646	0,029
1	rs652651	109844532	1p13	A	0,276	0,260	1,087	0,842	1,403	0,511
1	rs407102	109846278	1p13	C	0,266	0,251	1,085	0,840	1,401	0,536
1	rs592107	109848726	1p13	A	0,266	0,251	1,085	0,840	1,401	0,536
1	rs444387	109851127	1p13	A	0,266	0,256	1,058	0,820	1,365	0,675
1	rs464218	109856306	1p13	G	0,452	0,459	0,969	0,770	1,218	0,781
1	rs17585355	109857815	1p13	C	0,031	0,039	0,786	0,440	1,403	0,410
1	rs370088	109858119	1p13	T	0,266	0,256	1,058	0,820	1,365	0,675
1	rs3853500	109864269	1p13	T	0,265	0,251	1,075	0,832	1,389	0,566
1	rs3768496	109866569	1p13	T	0,273	0,259	1,077	0,833	1,392	0,583
1	rs10745352	109871787	1p13	T	0,273	0,259	1,077	0,833	1,392	0,583
1	rs10745353	109877506	1p13	A	0,273	0,259	1,077	0,833	1,392	0,583
1	rs4603158	109879549	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs11102972	109880721	1p13	C	0,216	0,216	0,998	0,759	1,314	0,985
1	rs10858084	109882250	1p13	T	0,273	0,259	1,077	0,833	1,392	0,583
1	rs2228604	109884775	1p13	T	0,273	0,259	1,077	0,833	1,392	0,583
1	rs4970843	109887191	1p13	C	0,495	0,500	0,981	0,781	1,232	0,855
1	rs3879448	109891423	1p13	G	0,287	0,271	1,086	0,842	1,402	0,523
1	rs7536292	109894693	1p13	C	0,179	0,202	0,861	0,648	1,144	0,304
1	rs1030522	109900707	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs3879449	109904971	1p13	A	0,273	0,259	1,077	0,833	1,392	0,583
1	rs11581665	109910013	1p13	T	0,158	0,131	1,251	0,908	1,725	0,202
1	rs10858086	109915075	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs1149175	109922377	1p13	A	0,158	0,131	1,251	0,908	1,725	0,202
1	rs12037569	109923677	1p13	T	0,158	0,169	0,924	0,684	1,248	0,616
1	rs10858089	109926828	1p13	T	0,273	0,259	1,077	0,833	1,392	0,583
1	rs4970752	109930852	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs10745354	109931908	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs3768494	109935427	1p13	A	0,273	0,259	1,077	0,833	1,392	0,583
1	rs1880670	109941133	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs10858092	109943893	1p13	C	0,273	0,259	1,077	0,833	1,392	0,583
1	rs4120621	109949008	1p13	A	0,273	0,259	1,077	0,833	1,392	0,583

1	rs2936033	222751034	1q41	T	0,186	0,183	1,020	0,767	1,356	0,889
1	rs3008647	222759007	1q41	T	0,165	0,156	1,066	0,788	1,442	0,651
1	rs2270705	222761771	1q41							
1	rs2936027	222762316	1q41	T	0,142	0,125	1,166	0,837	1,624	0,377
1	rs17464857	222762709	1q41	G	0,165	0,156	1,066	0,788	1,442	0,651
1	rs2936041	222762773	1q41	T	0,165	0,156	1,066	0,788	1,442	0,651
1	rs4846767	222763026	1q41	C	0,229	0,233	0,973	0,736	1,288	0,890
1	rs3008650	222763215	1q41	G	0,147	0,136	1,100	0,796	1,520	0,572
1	rs2936040	222763661	1q41	A	0,142	0,125	1,166	0,837	1,624	0,377
1	rs3008653	222764791	1q41	G	0,166	0,156	1,078	0,798	1,455	0,604
1	rs3008654	222766609	1q41	A	0,155	0,145	1,089	0,787	1,508	0,573
1	rs1995152	222769593	1q41	C	0,142	0,125	1,166	0,837	1,624	0,377
1	rs1909194	222770703	1q41	G	0,166	0,156	1,078	0,798	1,455	0,604
1	rs3002130	222772139	1q41	C	0,165	0,156	1,065	0,789	1,439	0,643
1	rs3002142	222788062	1q41	C	0,095	0,145	0,619	0,436	0,879	0,006
1	rs904323	222790366	1q41	A	0,144	0,137	1,059	0,766	1,465	0,732
1	rs17163303	222795118	1q41	T	0,066	0,082	0,792	0,516	1,215	0,300
1	rs17011666	222798965	1q41	G	0,223	0,219	1,022	0,786	1,330	0,882
1	rs2936052	222802376	1q41	G	0,190	0,192	0,989	0,748	1,309	0,951
1	rs3008621	222804046	1q41	A	0,155	0,155	1,006	0,742	1,364	0,965
1	rs3002145	222807013	1q41	T	0,155	0,155	1,006	0,742	1,364	0,965
1	rs1391557	222809616	1q41	T	0,173	0,189	0,898	0,676	1,194	0,454
1	rs2133188	222813753	1q41	T	0,174	0,189	0,908	0,683	1,207	0,522
1	rs2133189	222814442	1q41	C	0,269	0,298	0,877	0,690	1,114	0,314
1	rs17163358	222820639	1q41	G	0,268	0,298	0,870	0,685	1,106	0,285
1	rs17531063	222821709	1q41	G	0,065	0,082	0,771	0,501	1,186	0,251
1	rs17465637	222823529	1q41	A	0,269	0,297	0,884	0,695	1,123	0,344
1	rs17011681	222825088	1q41	C	0,269	0,298	0,877	0,690	1,114	0,314
1	rs2291832	222826481	1q41	G	0,269	0,298	0,877	0,690	1,114	0,314
1	rs2088514	222831372	1q41	G	0,173	0,189	0,898	0,676	1,194	0,454
1	rs2291834	222832295	1q41	T	0,269	0,298	0,877	0,690	1,114	0,314
1	rs17163384	222835222	1q41	C	0,065	0,082	0,771	0,501	1,186	0,251
1	rs2270707	222837594	1q41	G	0,207	0,218	0,941	0,722	1,225	0,667
1	rs1053316	222839838	1q41	A	0,097	0,110	0,864	0,599	1,247	0,475
1	rs3008633	222844840	1q41	T	0,079	0,096	0,808	0,545	1,197	0,304
1	rs1391558	222848029	1q41	C	0,173	0,189	0,898	0,676	1,194	0,454
9	rs756641	21902354	9p21							
9	rs10811634	21905379	9p21							
9	rs16938590	21909979	9p21							
9	rs4977746	21920346	9p21	C	0,153	0,169	0,895	0,666	1,203	0,479
9	rs10811638	21923279	9p21	G	0,153	0,169	0,895	0,666	1,203	0,479
9	rs7852128	21925855	9p21	G	0,153	0,172	0,878	0,656	1,176	0,399
9	rs10965186	21927913	9p21	A	0,153	0,172	0,878	0,656	1,176	0,399
9	rs2518713	21929666	9p21	G	0,157	0,178	0,864	0,648	1,151	0,322
9	rs7864029	21930147	9p21	C	0,166	0,180	0,911	0,684	1,214	0,523

9	rs7869004	21931896	9p21	T	0,165	0,181	0,892	0,670	1,188	0,449
9	rs4977750	21944317	9p21	C	0,092	0,128	0,703	0,495	0,999	0,047
9	rs2811717	21946322	9p21	C	0,092	0,128	0,703	0,495	0,999	0,047
9	rs2811720	21947957	9p21	G	0,092	0,128	0,703	0,495	0,999	0,047
9	rs10965197	21948666	9p21	T	0,347	0,390	0,820	0,647	1,040	0,115
9	rs10757260	21953137	9p21	G	0,326	0,385	0,773	0,613	0,975	0,046
9	rs10757261	21954953	9p21	A	0,326	0,385	0,773	0,613	0,975	0,046
9	rs12335941	21955669	9p21	G	0,326	0,385	0,773	0,613	0,975	0,046
9	rs717326	21958524	9p21	C	0,056	0,080	0,678	0,434	1,061	0,095
9	rs7041637	21961866	9p21	A	0,407	0,323	1,495	1,168	1,914	0,004
9	rs3731257	21966221	9p21	A	0,350	0,289	1,407	1,081	1,830	0,011
9	rs2518719	21970427	9p21	G	0,153	0,159	0,954	0,699	1,302	0,799
9	rs2811708	21973422	9p21	T	0,279	0,309	0,861	0,673	1,102	0,260
9	rs3731239	21974218	9p21	G	0,289	0,300	0,949	0,740	1,217	0,694
9	rs3731222	21983914	9p21	C	0,153	0,161	0,942	0,689	1,288	0,732
9	rs3731213	21986218	9p21	T	0,010	0,008	1,229	0,371	4,070	0,699
9	rs3731211	21986847	9p21	T	0,271	0,309	0,824	0,642	1,058	0,158
9	rs3731204	21987584	9p21	C	0,153	0,161	0,942	0,689	1,288	0,732
9	rs3731201	21988896	9p21	C	0,119	0,148	0,779	0,562	1,080	0,136
9	rs7036656	21990457	9p21	C	0,273	0,317	0,802	0,626	1,027	0,100
9	rs2811710	21991923	9p21	T	0,326	0,383	0,782	0,622	0,984	0,045
9	rs2811711	21993964	9p21	C	0,158	0,172	0,900	0,662	1,225	0,526
9	rs3218020	21997872	9p21	A	0,484	0,409	1,374	1,091	1,729	0,005
9	rs3218002	22000841	9p21	A	0,082	0,106	0,770	0,531	1,117	0,200
9	rs3217992	22003223	9p21	T	0,507	0,439	1,339	1,063	1,688	0,009
9	rs3217986	22005330	9p21	G	0,052	0,065	0,779	0,483	1,258	0,312
9	rs974336	22006348	9p21	T	0,082	0,106	0,770	0,531	1,117	0,200
9	rs2069422	22008026	9p21	G	0,084	0,107	0,766	0,526	1,115	0,173
9	rs2069418	22009698	9p21	G	0,376	0,412	0,866	0,692	1,085	0,221
9	rs575427	22011477	9p21	G	0,100	0,112	0,883	0,613	1,271	0,509
9	rs10811640	22013411	9p21	G	0,457	0,517	0,781	0,623	0,979	0,035
9	rs643319	22017836	9p21	A	0,387	0,434	0,819	0,649	1,032	0,088
9	rs7044859	22018781	9p21	T	0,457	0,517	0,781	0,623	0,979	0,035
9	rs523096	22019129	9p21	G	0,373	0,402	0,888	0,708	1,113	0,313
9	rs518394	22019673	9p21	C	0,369	0,404	0,870	0,694	1,091	0,228
9	rs10757264	22019732	9p21	A	0,410	0,470	0,782	0,623	0,981	0,031
9	rs10965212	22023795	9p21	T	0,431	0,484	0,797	0,633	1,004	0,054
9	rs496892	22024351	9p21	C	0,382	0,432	0,805	0,637	1,017	0,065
9	rs10738604	22025493	9p21	A	0,495	0,421	1,366	1,085	1,719	0,005
9	rs1591136	22026834	9p21	G	0,431	0,484	0,797	0,633	1,004	0,054
9	rs598664	22027551	9p21	C	0,084	0,109	0,753	0,517	1,096	0,149
9	rs7049105	22028801	9p21	A	0,431	0,484	0,797	0,633	1,004	0,054
9	rs10965215	22029445	9p21	G	0,437	0,491	0,798	0,634	1,005	0,052
9	rs564398	22029547	9p21	C	0,347	0,372	0,897	0,711	1,132	0,367
9	rs662463	22030438	9p21	A	0,079	0,106	0,733	0,500	1,073	0,129

9	rs7865618	22031005	9p21	G	0,352	0,380	0,886	0,703	1,117	0,312
9	rs10115049	22032119	9p21	A	0,432	0,484	0,802	0,637	1,010	0,065
9	rs2157719	22033366	9p21	C	0,350	0,382	0,875	0,694	1,102	0,263
9	rs1008878	22036112	9p21	G	0,350	0,382	0,875	0,694	1,102	0,263
9	rs12376000	22039426	9p21	T	0,100	0,110	0,895	0,620	1,294	0,567
9	rs17694493	22041998	9p21	G	0,118	0,136	0,853	0,612	1,189	0,357
9	rs12352425	22042086	9p21	A	0,052	0,069	0,726	0,455	1,159	0,187
9	rs1412829	22043926	9p21	G	0,352	0,383	0,875	0,694	1,102	0,250
9	rs1360589	22045317	9p21	C	0,347	0,383	0,858	0,681	1,079	0,190
9	rs7028570	22048683	9p21	G	0,429	0,483	0,799	0,636	1,005	0,055
9	rs17756311	22053895	9p21	A	0,074	0,088	0,831	0,557	1,240	0,395
9	rs17694572	22054356	9p21	A	0,077	0,090	0,852	0,574	1,265	0,464
9	rs10120688	22056499	9p21	G	0,431	0,464	0,871	0,693	1,095	0,243
9	rs1537378	22061614	9p21	A	0,319	0,366	0,821	0,652	1,034	0,098
9	rs1011970	22062134	9p21	T	0,129	0,159	0,786	0,576	1,073	0,128
9	rs8181047	22064465	9p21	A	0,236	0,265	0,860	0,668	1,107	0,259
9	rs10811647	22065002	9p21	C	0,452	0,532	0,714	0,567	0,898	0,004
9	rs10965224	22067276	9p21	T	0,321	0,366	0,827	0,657	1,041	0,106
9	rs16905599	22069144	9p21	A	0,042	0,073	0,559	0,342	0,916	0,016
9	rs9632884	22072301	9p21	G	0,368	0,434	0,768	0,614	0,960	0,018
9	rs10757270	22072719	9p21	A	0,452	0,522	0,749	0,598	0,939	0,012
9	rs16923583	22073334	9p21	A	0,008	0,014	0,565	0,187	1,705	0,364
9	rs1412832	22077543	9p21	C	0,236	0,267	0,855	0,666	1,099	0,235
9	rs6475606	22081850	9p21	C	0,374	0,437	0,776	0,619	0,971	0,028
9	rs1547704	22082340	9p21	A	0,010	0,016	0,608	0,218	1,694	0,396
9	rs10965228	22082380	9p21	G	0,090	0,106	0,850	0,590	1,223	0,376
9	rs1333040	22083404	9p21	C	0,290	0,334	0,811	0,637	1,034	0,095
9	rs7857345	22087473	9p21	T	0,224	0,256	0,843	0,650	1,094	0,220
9	rs10757272	22088260	9p21	C	0,395	0,457	0,775	0,618	0,971	0,028
9	rs4977574	22098574	9p21	A	0,392	0,461	0,751	0,598	0,943	0,017
9	rs2891168	22098619	9p21	A	0,392	0,461	0,751	0,598	0,943	0,018
9	rs1537371	22099568	9p21	C	0,387	0,456	0,754	0,602	0,946	0,019
9	rs7859727	22102165	9p21	C	0,390	0,462	0,743	0,592	0,932	0,016
9	rs1333042	22103813	9p21	A	0,358	0,437	0,725	0,579	0,909	0,009
9	rs7859362	22105927	9p21	T	0,387	0,454	0,759	0,606	0,952	0,020
9	rs1333043	22106731	9p21	T	0,387	0,456	0,754	0,602	0,946	0,018
9	rs1412834	22110131	9p21	T	0,387	0,456	0,754	0,602	0,946	0,018
9	rs7341786	22112241	9p21	A	0,387	0,454	0,758	0,605	0,951	0,020
9	rs10733376	22114469	9p21	G	0,379	0,454	0,730	0,580	0,917	0,010
9	rs2383206	22115026	9p21	A	0,379	0,454	0,730	0,580	0,917	0,010
9	rs2383207	22115959	9p21	A	0,379	0,453	0,733	0,583	0,923	0,011
9	rs1333045	22119195	9p21	T	0,402	0,483	0,713	0,567	0,896	0,007
9	rs10738610	22123766	9p21	A	0,382	0,456	0,732	0,581	0,921	0,010
9	rs10757278	22124477	9p21	A	0,413	0,491	0,722	0,574	0,908	0,008
9	rs1333048	22125347	9p21	A	0,382	0,462	0,713	0,566	0,897	0,006

9	rs1333049	22125503	9p21	G	0,415	0,491	0,726	0,577	0,914	0,008
9	rs10757281	22127613	9p21	T	0,134	0,128	1,062	0,752	1,500	0,744
9	rs12347779	22128709	9p21	G	0,074	0,082	0,900	0,601	1,348	0,612
9	rs10965243	22130065	9p21	G	0,107	0,109	0,975	0,680	1,399	0,926
9	rs10965245	22130515	9p21	A	0,107	0,109	0,975	0,680	1,399	0,926
9	rs2891169	22131825	9p21	G	0,439	0,456	0,937	0,753	1,166	0,561
9	rs2383208	22132076	9p21	G	0,207	0,196	1,074	0,811	1,423	0,638
9	rs7045889	22133251	9p21	G	0,357	0,355	1,006	0,803	1,261	0,973
9	rs10811659	22133716	9p21	C	0,232	0,216	1,104	0,840	1,452	0,480
9	rs10757282	22133984	9p21	C	0,474	0,483	0,968	0,775	1,209	0,787
9	rs10811661	22134094	9p21	C	0,198	0,188	1,074	0,807	1,429	0,634
9	rs10757283	22134172	9p21	T	0,469	0,480	0,962	0,770	1,201	0,731
9	rs1333051	22136489	9p21	T	0,166	0,148	1,153	0,843	1,577	0,376
9	rs7018475	22137685	9p21	G	0,286	0,300	0,937	0,733	1,196	0,609
9	rs11791416	22138105	9p21	G	0,289	0,260	1,160	0,899	1,498	0,288
9	rs4977761	22138762	9p21	T	0,298	0,311	0,943	0,743	1,195	0,650
9	rs2065501	22140224	9p21							
9	rs4977577	22141875	9p21	C	0,310	0,322	0,936	0,719	1,219	0,618
9	rs7849199	22143293	9p21	A	0,297	0,270	1,141	0,893	1,457	0,302
9	rs2065500	22145694	9p21	G	0,213	0,235	0,877	0,672	1,145	0,325
9	rs7022662	22147715	9p21	G	0,215	0,238	0,870	0,667	1,135	0,308
9	rs12341394	22148055	9p21	T	0,298	0,271	1,141	0,893	1,457	0,302
9	rs7856219	22150261	9p21	C	0,302	0,278	1,123	0,880	1,434	0,333
9	rs10965256	22151465	9p21	A	0,065	0,074	0,863	0,557	1,337	0,544
9	rs7853123	22153360	9p21	A	0,424	0,424	1,002	0,797	1,260	0,990
9	rs944802	22155709	9p21	T	0,210	0,224	0,924	0,715	1,193	0,540
9	rs7028213	22157360	9p21	G	0,298	0,271	1,140	0,893	1,457	0,299
9	rs12238587	22158168	9p21	A	0,219	0,243	0,883	0,686	1,136	0,326
9	rs10757288	22159416	9p21	C	0,431	0,429	1,010	0,803	1,271	0,922
9	rs7864275	22161212	9p21	T	0,350	0,330	1,093	0,866	1,381	0,447
9	rs10965266	22161494	9p21	G	0,218	0,235	0,911	0,707	1,173	0,476
9	rs10965267	22161828	9p21	G	0,058	0,060	0,966	0,607	1,537	0,860
9	rs10811668	22164991	9p21	A	0,247	0,252	0,971	0,758	1,244	0,811
9	rs2779748	22166769	9p21	T	0,447	0,448	1,000	0,796	1,255	0,998
9	rs7863846	22168128	9p21	T	0,284	0,268	1,081	0,843	1,388	0,549
9	rs828580	22168464	9p21	T	0,048	0,054	0,899	0,549	1,472	0,662
9	rs1537377	22169700	9p21	C	0,332	0,320	1,055	0,832	1,337	0,660
9	rs954399	22170983	9p21	A	0,279	0,263	1,081	0,842	1,389	0,552
9	rs828582	22172259	9p21	A	0,339	0,325	1,062	0,839	1,346	0,604
9	rs10965278	22174712	9p21	A	0,271	0,263	1,038	0,811	1,329	0,758
9	rs10965279	22175188	9p21	C	0,069	0,066	1,049	0,672	1,637	0,849
9	rs10757292	22176961	9p21							
9	rs866666	22183781	9p21	C	0,366	0,377	0,950	0,741	1,218	0,687
9	rs2767409	22184997	9p21	A	0,300	0,304	0,975	0,754	1,260	0,840
9	rs1095904	22187074	9p21							

9	rs828576	22191189	9p21	T	0,358	0,371	0,940	0,730	1,210	0,607
9	rs2219849	22195820	9p21							
9	rs1751449	22196863	9p21	G	0,324	0,338	0,929	0,720	1,199	0,546
9	rs12375458	22198149	9p21							
10	rs1482472	44682973	10q11	C	0,389	0,377	1,052	0,838	1,320	0,648
10	rs12415866	44686664	10q11	G	0,107	0,107	0,996	0,686	1,445	0,989
10	rs7917089	44688587	10q11	A	0,098	0,103	0,957	0,654	1,400	0,829
10	rs1623851	44691241	10q11	G	0,158	0,170	0,911	0,669	1,239	0,560
10	rs1627329	44691633	10q11	C	0,158	0,170	0,911	0,669	1,239	0,560
10	rs10508883	44693544	10q11	C	0,018	0,021	0,857	0,378	1,944	0,768
10	rs7900182	44693742	10q11	G	0,207	0,181	1,162	0,885	1,525	0,305
10	rs11597731	44694201	10q11	T	0,210	0,191	1,119	0,854	1,464	0,447
10	rs7902040	44695308	10q11	G	0,089	0,079	1,148	0,764	1,724	0,497
10	rs11238911	44695862	10q11	A	0,089	0,077	1,174	0,780	1,766	0,431
10	rs11238913	44695973	10q11	C	0,350	0,328	1,099	0,874	1,383	0,428
10	rs2802477	44696034	10q11	G	0,416	0,424	0,963	0,762	1,218	0,739
10	rs11594522	44696352	10q11	A	0,205	0,181	1,153	0,877	1,516	0,338
10	rs2054620	44698075	10q11	C	0,350	0,328	1,099	0,874	1,383	0,428
10	rs11238921	44699910	10q11	T	0,350	0,328	1,099	0,874	1,383	0,428
10	rs768676	44702681	10q11	A	0,056	0,063	0,880	0,547	1,418	0,585
10	rs3865770	44705969	10q11	A	0,205	0,181	1,153	0,877	1,516	0,338
10	rs1482473	44707598	10q11	C	0,137	0,139	0,987	0,711	1,369	0,952
10	rs3851257	44709171	10q11	T	0,347	0,330	1,077	0,857	1,354	0,530
10	rs12573558	44712128	10q11	A	0,210	0,191	1,119	0,854	1,467	0,442
10	rs11238935	44714402	10q11	T	0,087	0,077	1,150	0,763	1,732	0,487
10	rs2209067	44716469	10q11	A	0,211	0,191	1,130	0,862	1,481	0,406
10	rs1704219	44729958	10q11	C	0,336	0,314	1,100	0,872	1,388	0,443
10	rs7907961	44730995	10q11	C	0,248	0,237	1,062	0,824	1,369	0,632
10	rs1746043	44732825	10q11	C	0,336	0,312	1,108	0,878	1,398	0,421
10	rs647419	44734995	10q11	A	0,373	0,350	1,101	0,875	1,384	0,430
10	rs88796	44737036	10q11	C	0,284	0,249	1,193	0,930	1,530	0,200
10	rs617019	44737246	10q11	A	0,084	0,076	1,127	0,745	1,705	0,560
10	rs17155733	44737433	10q11	G	0,197	0,170	1,188	0,894	1,578	0,263
10	rs583489	44738688	10q11	G	0,090	0,084	1,099	0,736	1,641	0,648
10	rs676966	44739594	10q11	T	0,087	0,076	1,175	0,779	1,773	0,437
10	rs494207	44741256	10q11	A	0,092	0,084	1,121	0,752	1,672	0,570
10	rs541483	44746395	10q11	G	0,139	0,134	1,049	0,751	1,465	0,766
10	rs535176	44747059	10q11	T	0,139	0,134	1,049	0,751	1,465	0,766
10	rs622472	44749211	10q11	C	0,139	0,134	1,049	0,751	1,465	0,766
10	rs513391	44749708	10q11	C	0,139	0,134	1,049	0,751	1,465	0,766
10	rs11238956	44749854	10q11	C	0,311	0,345	0,860	0,681	1,085	0,226
10	rs687175	44751910	10q11	C	0,134	0,133	1,018	0,727	1,426	0,918
10	rs559580	44752078	10q11	C	0,129	0,128	1,017	0,722	1,432	0,931
10	rs559469	44752118	10q11	C	0,134	0,133	1,018	0,727	1,426	0,918
10	rs2437935	44752268	10q11	G	0,387	0,368	1,091	0,866	1,375	0,478

10	rs535949	44752330	10q11	T	0,134	0,133	1,018	0,727	1,426	0,918
10	rs671765	44752976	10q11	G	0,134	0,133	1,018	0,727	1,426	0,918
10	rs501120	44753867	10q11	C	0,134	0,133	1,018	0,727	1,426	0,918
10	rs579058	44755104	10q11	G	0,134	0,133	1,018	0,727	1,426	0,918
10	rs604674	44756894	10q11	T	0,134	0,133	1,018	0,727	1,426	0,918
10	rs487465	44758197	10q11	C	0,134	0,133	1,018	0,727	1,426	0,918
10	rs475926	44760887	10q11	G	0,329	0,303	1,128	0,892	1,427	0,338
10	rs1632484	44773984	10q11	T	0,131	0,126	1,048	0,744	1,476	0,801
10	rs1746048	44775824	10q11	T	0,132	0,133	1,003	0,716	1,406	0,985
10	rs1746049	44776310	10q11	T	0,132	0,131	1,018	0,727	1,427	0,923
10	rs1746052	44778546	10q11	C	0,131	0,128	1,034	0,736	1,452	0,861
10	rs800314	44786364	10q11	G	0,073	0,066	1,114	0,712	1,743	0,652
10	rs11598523	44791433	10q11	A	0,208	0,174	1,247	0,942	1,650	0,135
10	rs2505734	44793299	10q11	C	0,358	0,334	1,110	0,882	1,398	0,381
10	rs754713	44797087	10q11	T	0,284	0,267	1,089	0,854	1,388	0,492
10	rs800320	44798482	10q11	T	0,032	0,033	0,969	0,514	1,826	0,916
10	rs800323	44801673	10q11	G	0,287	0,267	1,106	0,867	1,411	0,405
10	rs2437934	44803925	10q11	G	0,360	0,334	1,117	0,888	1,406	0,347
10	rs11238983	44810205	10q11	A	0,119	0,151	0,764	0,553	1,056	0,099
10	rs2146807	44813738	10q11	C	0,119	0,158	0,717	0,516	0,996	0,043
10	rs2146808	44813777	10q11	C	0,031	0,030	1,019	0,529	1,965	0,958
10	rs7082209	44814336	10q11	G	0,116	0,153	0,729	0,526	1,012	0,047
10	rs800310	44815048	10q11	A	0,155	0,204	0,707	0,524	0,955	0,017
10	rs2505735	44815709	10q11	A	0,150	0,181	0,793	0,585	1,075	0,132
10	rs977754	44817419	10q11	G	0,134	0,172	0,736	0,535	1,012	0,064
10	rs812889	44818563	10q11	G	0,053	0,074	0,709	0,448	1,122	0,130
10	rs2476351	44820157	10q11	C	0,129	0,161	0,768	0,557	1,060	0,123
10	rs11238987	44821220	10q11	A	0,034	0,030	1,139	0,600	2,163	0,724
10	rs10508884	44821387	10q11	T	0,303	0,276	1,141	0,895	1,454	0,289
10	rs1111259	44821772	10q11	T	0,079	0,091	0,844	0,563	1,265	0,436
10	rs2505741	44823136	10q11	G	0,453	0,443	1,043	0,837	1,299	0,704
10	rs2028100	44826376	10q11	A	0,290	0,254	1,198	0,936	1,532	0,162
10	rs1836982	44827164	10q11	G	0,144	0,175	0,777	0,567	1,066	0,125
10	rs982097	44828234	10q11	G	0,436	0,432	1,015	0,815	1,264	0,882
10	rs7918046	44830727	10q11	T	0,284	0,279	1,023	0,806	1,298	0,852
10	rs11815919	44831379	10q11	T	0,203	0,186	1,111	0,847	1,458	0,448
10	rs928565	44832884	10q11	G	0,466	0,476	0,963	0,773	1,200	0,727
10	rs11599561	44833031	10q11	C	0,113	0,110	1,025	0,718	1,465	0,918
10	rs266080	44833894	10q11	G	0,013	0,021	0,624	0,255	1,527	0,325
10	rs1144482	44835963	10q11	C	0,482	0,487	0,983	0,789	1,224	0,876
10	rs1360724	44837267	10q11	G	0,307	0,300	1,033	0,817	1,306	0,796
10	rs10900025	44838019	10q11	G	0,407	0,390	1,070	0,858	1,334	0,581
10	rs7069891	44838464	10q11	T	0,113	0,110	1,025	0,718	1,465	0,918
10	rs77839	44838530	10q11	G	0,419	0,410	1,038	0,834	1,293	0,742
10	rs17390084	44839865	10q11	A	0,040	0,028	1,436	0,777	2,653	0,248

10	rs10793536	44842048	10q11	C	0,426	0,413	1,051	0,844	1,308	0,683
10	rs266076	44844381	10q11	G	0,426	0,415	1,044	0,839	1,299	0,718
10	rs1144480	44848921	10q11	T	0,497	0,503	0,978	0,787	1,215	0,841
10	rs266109	44850424	10q11	G	0,097	0,104	0,920	0,640	1,324	0,665
10	rs1144477	44851737	10q11	C	0,489	0,489	1,001	0,806	1,245	0,993
10	rs266105	44855663	10q11	A	0,113	0,110	1,026	0,726	1,450	0,881
10	rs11595588	44855740	10q11	C	0,390	0,386	1,015	0,817	1,262	0,862
10	rs17391002	44855927	10q11	G	0,239	0,229	1,050	0,819	1,346	0,710
10	rs266103	44856370	10q11	T	0,111	0,110	1,010	0,716	1,424	0,957
10	rs185545	44858840	10q11	C	0,168	0,194	0,849	0,643	1,121	0,225
10	rs7918568	44861220	10q11	T	0,186	0,186	0,996	0,751	1,322	0,974
10	rs7915848	44863434	10q11	C	0,184	0,183	1,005	0,755	1,338	0,973
10	rs266094	44864300	10q11	T	0,124	0,126	0,984	0,709	1,364	0,902
10	rs266093	44866208	10q11	C	0,339	0,344	0,979	0,775	1,237	0,874
10	rs1029153	44867146	10q11	G	0,284	0,273	1,059	0,825	1,361	0,637
10	rs1801157	44868257	10q11	T	0,216	0,216	0,999	0,760	1,312	0,985
10	rs266089	44869427	10q11	A	0,132	0,148	0,879	0,641	1,206	0,426
10	rs266088	44870015	10q11	T	0,187	0,185	1,017	0,764	1,353	0,923
10	rs266087	44871062	10q11	A	0,413	0,410	1,010	0,802	1,274	0,930
10	rs2297630	44871548	10q11	A	0,282	0,273	1,050	0,818	1,350	0,693
10	rs2839690	44875166	10q11	G	0,181	0,186	0,964	0,723	1,285	0,786
10	rs3780891	44878713	10q11	A	0,105	0,109	0,959	0,672	1,369	0,821

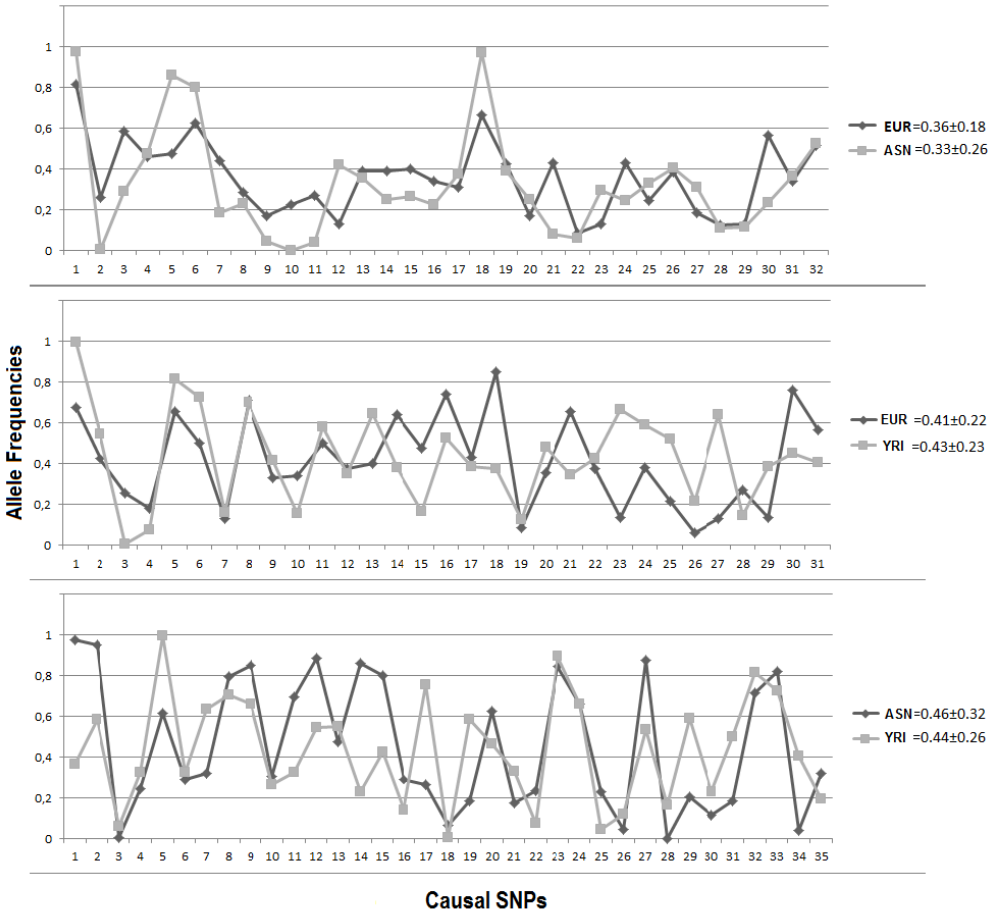
- **Table S3. Genomic location of the 6 North African SNPs used to calculate the risk score in the case-control samples.**

Region	Position	SNP
9p21	22136489	rs1333051
9p21	22191189	rs828576
10q11	44730995	rs7907961
10q11	44786364	rs800314
10q11	44856370	rs266103
10q11	44861220	rs7918568

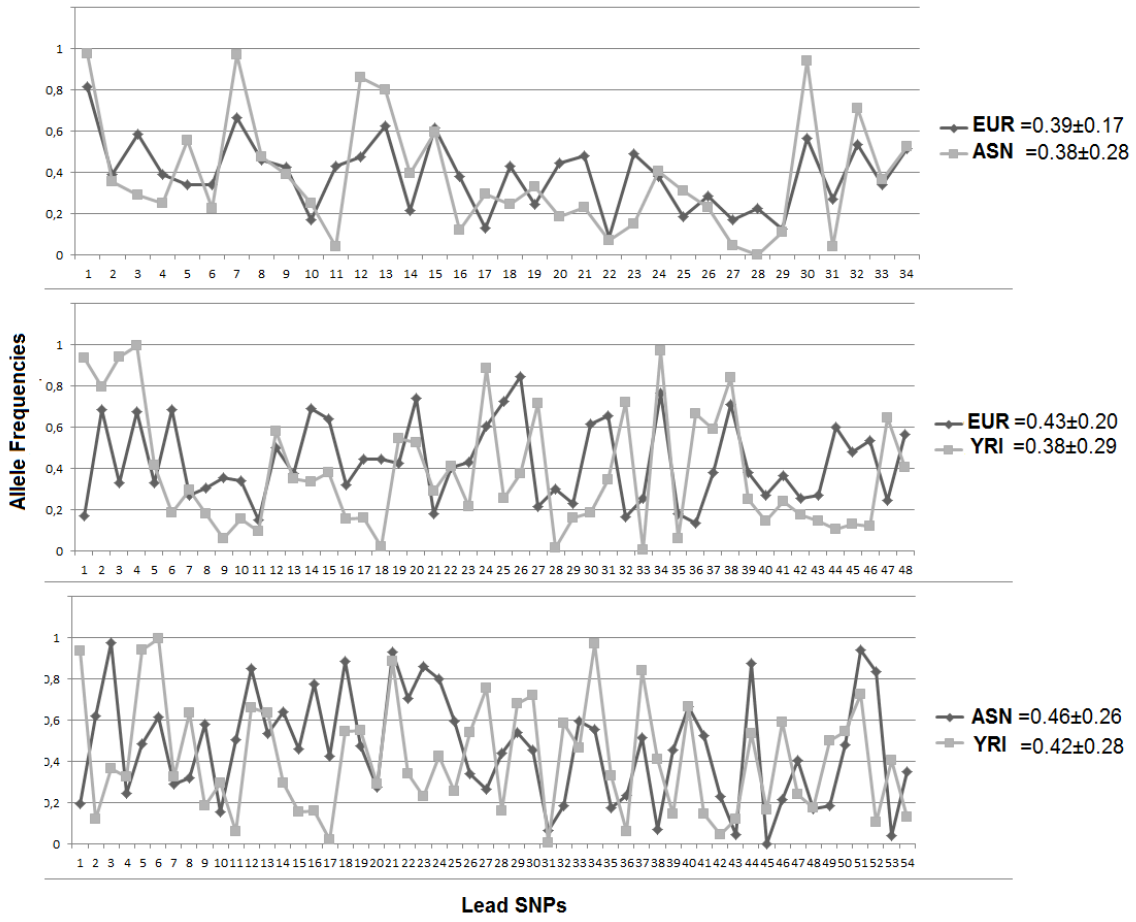
Appendix 3:

Additional files to the article: "Trans-ethnic differences in GWAS signals: a simulation study".

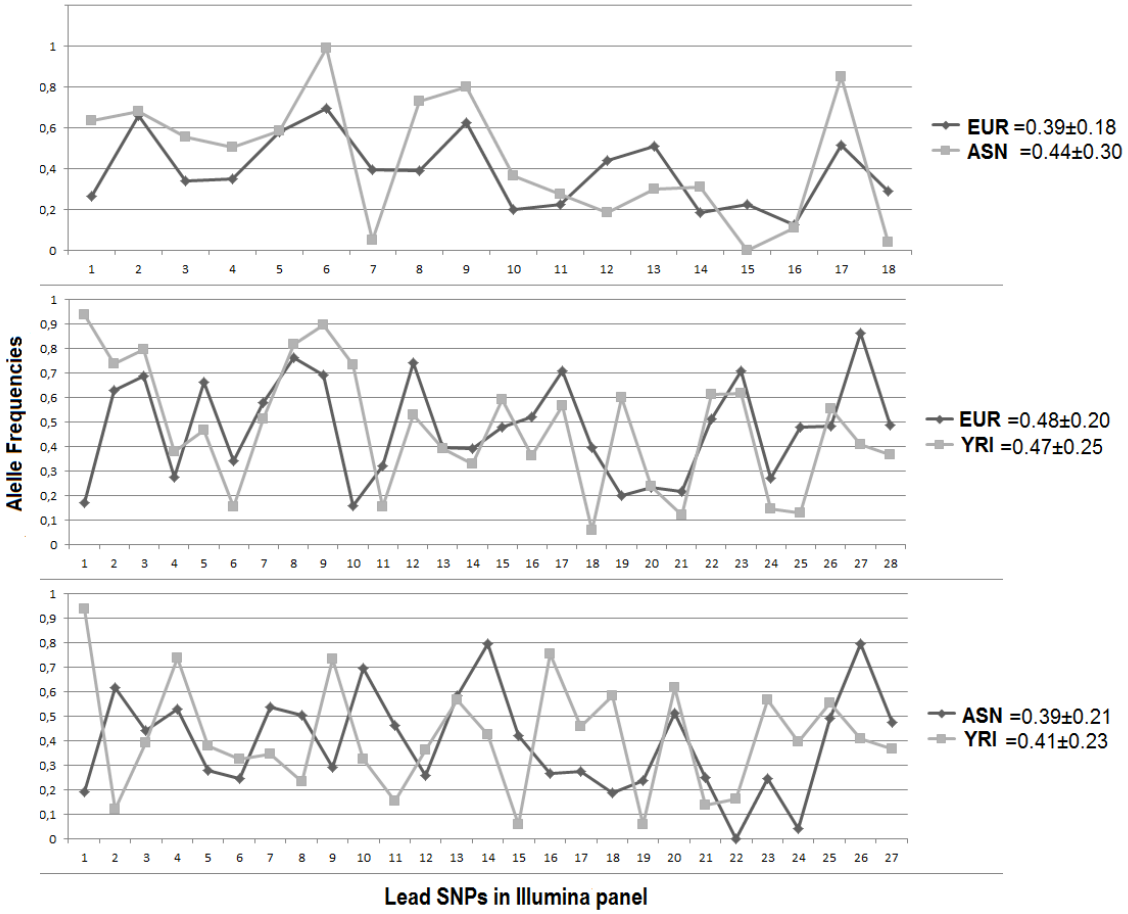
- **Supplementary Figure 1.** Allele frequency patterns of SNPS showing significant different effect size across populations, and their averages using "casual SNPs".



- **Supplementary Figure 2.** Allele frequency patterns of SNPs showing significant different effect size across populations, and their averages using "lead SNPs".



- **Supplementary Figure 3.** Allele frequency patterns of SNPs showing significant different effect size across populations, and their averages using "Lead SNPs included in the Illumina Panel".



- **Supplementary Tables 1-3. Observed discrepancies for ancestral effect size for the different reference SNPs: the causal SNP (Supplementary Table1); the lead SNP, with the lowest p-value in Europe and with MAF>1% (Supplementary Table2); the lead SNP, with the lowest p-value in Europe and also in the Human Omni Express Bead Chip array (Supplementary Table3).** stdbeta: standard deviation of beta values; P: p-value of the logistic association; EUR= Europeans; ASN= Asians; YRI= Sub-Saharan Africans. Different Z-score: 1 grey; No different Z-score: 0 white. Opposite direction: 0 grey; same direction: 1 white. Two fold difference: 1 grey. nGWAS_SNPs: number of SNPs included in the Illumina panel in each simulation.

Supplementary Table 1

DisChr	rsID_refSNP	pos_refSNP	Allele Frequency EUR	Allele Frequency ASN	Allele Frequency YRI	beta EUR	stdbeta EUR	P EUR
4	rs2333328	176852836	0,54	0,60	0,28	0,26	0,04	4E-09
9	rs10869238	75803635	0,18	0,46	0,50	0,35	0,06	2E-08
22	rs136571	45767696	0,49	0,67	0,99	0,39	0,05	4E-18
6	rs579329	47822681	0,48	0,73	0,41	0,22	0,05	1E-06
10	rs11591368	53523322	0,42	0,06	0,41	0,30	0,05	6E-11
6	rs2504907	12603401	0,17	0,19	0,85	0,37	0,06	3E-09
19	rs11083699	43755489	0,31	0,85	0,69	0,24	0,05	2E-06
8	rs73351724	114787818	0,20	0,65	0,28	0,23	0,06	8E-05
3	rs1387701	193147894	0,77	0,63	0,63	0,31	0,05	2E-09
4	rs6854328	119683492	0,71	0,62	0,27	0,27	0,05	2E-08
15	rs1604170	98040887	0,36	0,52	0,60	0,30	0,05	3E-10
15	rs1470901	69097765	0,53	0,52	0,23	0,28	0,04	4E-10
1	rs6696248	111404291	0,28	0,14	0,09	0,30	0,05	4E-09
7	rs9692258	69049578	0,73	0,80	0,84	0,35	0,05	3E-12
12	rs4761380	77829418	0,51	0,53	0,38	0,26	0,05	1E-08
14	rs1959523	52312746	0,82	0,98	0,36	0,28	0,06	7E-07
17	rs7213597	12053126	0,11	0,45	0,45	0,39	0,08	4E-07
22	rs6007526	45648224	0,29	0,20	0,15	0,32	0,05	3E-10
22	rs535842	27621151	0,80	0,33	0,67	0,31	0,05	2E-08
2	rs10190763	20573168	0,29	0,76	0,32	0,32	0,05	7E-10
11	rs76472587	47881487	0,15	0,32	0,26	0,17	0,07	1E-02
13	rs9549507	112996118	0,30	0,60	0,39	0,22	0,05	1E-05
11	rs10834146	23595982	0,13	0,42	0,16	0,11	0,07	1E-01
9	rs16925789	109495368	0,19	0,10	0,76	0,35	0,06	5E-09
5	rs76671135	144312509	0,13	0,22	0,24	0,23	0,07	1E-03
17	rs175382	49388390	0,56	0,61	0,84	0,29	0,04	2E-10
4	rs10716645	165101675	0,07	0,16	0,34	0,33	0,09	4E-04
4	rs7659549	103006301	0,35	0,37	0,23	0,33	0,05	8E-12
13	rs278034	30416637	0,64	0,55	0,32	0,33	0,05	1E-12
22	rs2530667	30044151	0,48	0,33	0,11	0,24	0,05	9E-08
8	rs9773025	6674458	0,47	0,95	0,76	0,26	0,05	2E-08
7	rs10277114	12013649	0,42	0,54	0,71	0,24	0,05	2E-07
7	rs686550	54728518	0,92	0,95	0,59	0,09	0,08	2E-01
2	rs7587455	240990568	0,08	0,00	0,60	0,20	0,08	2E-02
15	rs1191196	77646504	0,27	0,59	0,48	0,35	0,05	3E-11
7	rs28369400	132913071	0,20	0,06	0,38	0,16	0,06	6E-03
14	rs1950660	94774300	0,42	0,91	0,34	0,21	0,05	4E-06
6	rs9452207	93744485	0,21	0,12	0,63	0,32	0,06	3E-08
4	rs2045774	82822003	0,57	0,37	0,08	0,22	0,05	1E-06
7	rs7787377	89996777	0,44	0,38	0,71	0,31	0,05	3E-11
9	rs12686218	114601575	0,12	0,36	0,23	0,31	0,07	2E-05

3	**rs12330317**	**100836183**	0,11	0,00	0,50	0,20	0,08	9E-03
13	**rs2781311**	**87626740**	0,31	0,63	0,67	0,31	0,05	6E-10
5	**rs1422932**	**167397039**	0,39	0,36	0,31	0,37	0,05	8E-15
9	**rs10115645**	**107369931**	0,22	0,33	0,04	0,24	0,06	2E-05
7	**rs10952493**	**154253759**	0,69	0,47	0,53	0,30	0,05	2E-10
14	**rs28501387**	**81772667**	0,79	0,65	0,74	0,35	0,05	2E-10
7	**rs6947649**	**83415942**	0,79	0,55	0,86	0,32	0,05	2E-09
5	**rs35733634**	**12879768**	0,29	0,44	0,75	0,21	0,05	5E-05
4	**rs201086800**	**66370079**	0,37	0,36	0,14	0,34	0,05	4E-12
6	**rs6938226**	**118852561**	0,53	0,26	0,38	0,27	0,05	2E-09
1	**rs201832280**	**151339950**	0,68	0,24	0,45	0,23	0,05	1E-06
14	**rs875799**	**103618276**	0,12	0,20	0,31	0,19	0,07	1E-02
8	**rs465**	**90816058**	0,58	0,52	0,97	0,25	0,05	6E-08
2	**rs13409781**	**66203352**	0,13	0,25	0,27	0,31	0,07	1E-05
4	**rs150411487**	**9061499**	0,09	0,06	0,43	0,25	0,08	3E-03
10	**rs17663446**	**86272696**	0,13	0,17	0,11	0,28	0,07	7E-05
12	**rs10845348**	**11539880**	0,66	0,44	0,31	0,25	0,05	1E-07
9	**rs490491**	**108416462**	0,52	0,70	0,69	0,31	0,05	7E-12
17	**rs56256681**	**9712092**	0,45	0,52	0,62	0,26	0,05	1E-08
1	**rs3767246**	**21227086**	0,12	0,30	0,05	0,19	0,07	8E-03
14	**rs10782420**	**52681605**	0,42	0,84	0,25	0,31	0,05	4E-11
17	**rs1875558**	**7040018**	0,19	0,38	0,29	0,20	0,06	1E-03
6	**rs1321473**	**137158764**	0,63	0,53	0,73	0,33	0,05	5E-13
2	**rs10804341**	**229429905**	0,72	0,92	0,34	0,36	0,05	2E-13
15	**rs4778048**	**93401485**	0,61	0,40	0,81	0,34	0,05	1E-13
2	**rs6743294**	**229370567**	0,42	0,64	0,97	0,23	0,05	1E-06
12	**rs2428387**	**47379311**	0,17	0,05	0,14	0,35	0,06	3E-08
11	**rs11212624**	**108298019**	0,45	0,42	0,40	0,20	0,05	1E-05
20	**rs6054547**	**6828677**	0,52	0,52	0,80	0,24	0,04	9E-08
6	**rs1028483**	**65003887**	0,71	0,51	0,70	0,17	0,05	3E-04
3	**rs2242023**	**13670481**	0,68	0,78	0,55	0,30	0,05	2E-10
6	**rs6912599**	**9828518**	0,34	0,03	0,24	0,30	0,05	7E-10
5	**rs10065424**	**75841888**	0,47	0,70	0,73	0,27	0,05	5E-09
11	**rs523750**	**107705009**	0,44	0,48	0,76	0,26	0,05	7E-09
10	**rs10900234**	**46200866**	0,55	0,68	0,55	0,26	0,04	4E-09
2	**rs13425141**	**210322212**	0,26	0,00	0,06	0,30	0,05	2E-08
6	**rs114364056**	**28634891**	0,22	0,16	0,41	0,31	0,06	9E-08
8	**rs12540991**	**13079235**	0,28	0,66	0,52	0,27	0,05	1E-07
3	**rs73033920**	**164120039**	0,34	0,35	0,63	0,28	0,05	6E-09
10	**rs10763143**	**56521303**	0,74	0,81	0,51	0,13	0,05	1E-02
9	**rs7036260**	**122911053**	0,29	0,28	0,40	0,30	0,05	2E-09
8	**rs4273853**	**22698106**	0,39	0,34	0,30	0,34	0,05	1E-12
16	**rs3104790**	**52638663**	0,43	0,81	0,44	0,31	0,05	9E-12
1	**rs12564270**	**245571653**	0,12	0,26	0,55	0,28	0,07	1E-04
1	**rs10911095**	**182518264**	0,55	0,45	0,43	0,27	0,04	2E-09

6	**rs76902944**	**164074426**	0,53	0,95	0,28	0,24	0,04	4E-08
4	**rs7691160**	**26457487**	0,80	0,84	0,41	0,28	0,05	2E-07
20	**rs6035865**	**21368932**	0,72	0,83	0,46	0,29	0,05	3E-09
9	**rs72766254**	**130090926**	0,17	0,22	0,04	0,19	0,06	2E-03
9	**rs7847784**	**110001752**	0,41	0,24	0,32	0,29	0,05	9E-10
1	**rs7548054**	**39302020**	0,65	0,34	0,10	0,33	0,05	2E-12
3	**rs199797915**	**39051874**	0,33	0,48	0,94	0,33	0,05	8E-12
10	**rs773948**	**34716034**	0,68	0,62	0,99	0,21	0,05	5E-06
5	**rs56777318**	**87825189**	0,10	0,47	0,26	0,17	0,08	3E-02
1	**rs200576863**	**154798550**	0,26	0,74	0,38	0,26	0,05	5E-07
12	**rs7138235**	**133313237**	0,52	0,33	0,20	0,25	0,04	3E-08
20	**rs2983304**	**23508573**	0,58	0,43	0,19	0,30	0,04	4E-11
7	**rs10950822**	**20647108**	0,26	0,50	0,53	0,20	0,05	1E-04
6	**rs115700812**	**32511774**	0,35	0,36	0,63	0,29	0,05	4E-09
16	**rs7187576**	**25070579**	0,59	0,29	0,32	0,37	0,05	8E-16
3	**rs1388705**	**161584027**	0,24	0,39	0,01	0,18	0,05	1E-03
8	**rs10955282**	**103176946**	0,46	0,45	0,55	0,27	0,05	2E-09
1	**rs2256913**	**72402880**	0,12	0,11	0,51	0,22	0,07	2E-03
11	**rs12277881**	**6729061**	0,33	0,47	0,51	0,24	0,05	1E-06
14	**rs7156971**	**54854783**	0,33	0,41	0,39	0,23	0,05	2E-06
8	**rs28439245**	**3077166**	0,24	0,35	0,33	0,28	0,06	2E-07
3	**rs13085132**	**106837810**	0,47	0,58	0,48	0,24	0,05	2E-07
1	**rs6665839**	**49043877**	0,17	0,26	0,40	0,24	0,06	2E-04
6	**rs4236138**	**56151384**	0,13	0,59	0,03	0,37	0,07	2E-07
2	**rs35463898**	**71704005**	0,33	0,64	0,85	0,29	0,05	5E-09
6	**rs9688927**	**92701926**	0,09	0,37	0,04	0,34	0,08	2E-05
1	**rs150016402**	**94601236**	0,39	0,25	0,23	0,37	0,05	9E-15
6	**rs13199418**	**79874045**	0,42	0,15	0,35	0,26	0,05	1E-08
10	**rs507098**	**116062510**	0,16	0,32	0,52	0,32	0,06	6E-07
18	**rs9961465**	**8569882**	0,35	0,39	0,54	0,29	0,05	1E-09
21	**rs2236478**	**46917782**	0,36	0,32	0,64	0,27	0,05	2E-08
16	**rs10153134**	**90091099**	0,38	0,31	0,40	0,26	0,05	3E-08
11	**rs201202588**	**72258622**	0,33	0,31	0,41	0,36	0,05	3E-13
14	**rs77306894**	**88960851**	0,24	0,34	0,16	0,24	0,05	7E-06
20	**rs7264816**	**22955608**	0,35	0,51	0,23	0,30	0,05	7E-10
20	**rs6056189**	**8811896**	0,34	0,16	0,28	0,20	0,05	3E-05
2	**rs11899581**	**122712643**	0,27	0,16	0,36	0,33	0,05	3E-10
10	**rs7095313**	**17399051**	0,20	0,10	0,34	0,32	0,06	2E-08
5	**rs2904945**	**8777960**	0,82	0,89	0,35	0,28	0,06	1E-06
11	**rs7119996**	**93389932**	0,50	0,77	0,68	0,25	0,04	4E-08
3	**rs34638579**	**137385728**	0,32	0,25	0,49	0,32	0,05	3E-10
13	**rs9593302**	**78829464**	0,69	0,80	0,70	0,24	0,05	5E-07
8	**rs62509924**	**87103432**	0,35	0,51	0,15	0,28	0,05	1E-08
1	**rs1977125**	**63772373**	0,58	0,51	0,22	0,22	0,05	7E-07
10	**rs1926801**	**4433288**	0,34	0,01	0,15	0,31	0,05	4E-10

2	**rs1597944**	**234504098**	0,50	0,53	0,16	0,29	0,05	2E-10
10	**rs7902931**	**6141942**	0,50	0,25	0,58	0,16	0,05	4E-04
4	**rs200356168**	**7864140**	0,73	0,71	0,55	0,30	0,05	1E-09
2	**rs11126341**	**71916661**	0,52	0,60	0,47	0,23	0,05	3E-07
4	**rs147440574**	**128598143**	0,52	0,22	0,22	0,31	0,05	8E-12
7	**rs10276126**	**131306210**	0,82	0,67	0,25	0,31	0,06	8E-08
6	**rs366920**	**160737950**	0,52	0,26	0,30	0,28	0,05	1E-09
7	**rs28491038**	**104366640**	0,37	0,12	0,35	0,34	0,05	1E-12
8	**rs7836279**	**13775292**	0,45	0,48	0,19	0,23	0,04	5E-07
17	**rs2411041**	**74913863**	0,13	0,38	0,35	0,24	0,07	8E-04
20	**rs6092006**	**36809169**	0,30	0,17	0,27	0,26	0,05	4E-07
20	**rs72620874**	**1895889**	0,36	0,65	0,32	0,25	0,05	9E-08
2	**rs76136841**	**206820159**	0,13	0,46	0,01	0,29	0,07	4E-05
20	**rs138273314**	**19935337**	0,36	0,64	0,41	0,28	0,05	1E-08
4	**rs4862032**	**183071431**	0,54	0,71	0,77	0,23	0,05	4E-07
2	**rs13003505**	**159156020**	0,41	0,60	0,27	0,29	0,05	4E-10
9	**rs2017392**	**112820620**	0,31	0,41	0,06	0,32	0,05	2E-10
3	**rs729942**	**87066095**	0,75	0,50	0,07	0,30	0,05	1E-09
8	**rs59026256**	**66912273**	0,25	0,06	0,34	0,29	0,05	6E-08
5	**rs433211**	**151324761**	0,69	0,37	0,68	0,33	0,05	3E-12
12	**rs7132347**	**55714876**	0,76	0,88	0,81	0,31	0,05	2E-09
9	**rs9775725**	**27244202**	0,40	0,26	0,65	0,11	0,05	1E-02
17	**rs4605213**	**49244747**	0,34	0,22	0,97	0,36	0,05	2E-13
4	**rs12696692**	**6735941**	0,08	0,37	0,10	0,38	0,09	2E-05
1	**rs1014977**	**168457111**	0,12	0,28	0,39	0,24	0,07	8E-04
8	**rs1392143**	**3357940**	0,79	0,85	0,66	0,26	0,05	1E-06
9	**rs60795901**	**78895500**	0,07	0,08	0,31	0,24	0,09	1E-02
1	**rs17407657**	**66171667**	0,29	0,02	0,19	0,30	0,05	6E-09
7	**rs854074**	**95298272**	0,64	0,50	0,38	0,33	0,05	1E-12
9	**rs10980731**	**113838859**	0,23	0,27	0,05	0,29	0,06	1E-07
11	**rs1426926**	**87903141**	0,42	0,29	0,45	0,27	0,05	3E-09
2	**rs374954**	**176084790**	0,25	0,40	0,36	0,24	0,05	1E-05
6	**rs2327037**	**8228490**	0,31	0,38	0,49	0,14	0,05	6E-03
4	**rs62325107**	**154675105**	0,89	0,88	0,66	0,30	0,07	4E-06
12	**rs11532381**	**79936694**	0,12	0,31	0,95	0,29	0,07	4E-05
22	**rs136482**	**32590036**	0,49	0,13	0,94	0,25	0,04	2E-08
1	**rs17021956**	**119082264**	0,13	0,30	0,27	0,20	0,07	4E-03
14	**rs10141742**	**59406089**	0,67	0,97	0,93	0,26	0,05	4E-08
7	**rs2005764**	**105778633**	0,29	0,40	0,88	0,25	0,05	8E-07
3	**rs9816837**	**178705604**	0,68	0,53	0,72	0,25	0,05	1E-07
4	**rs631179**	**130411127**	0,63	0,58	0,57	0,30	0,05	8E-11
3	**rs66861711**	**162227359**	0,13	0,30	0,11	0,29	0,07	3E-05
4	**rs6824500**	**35487085**	0,30	0,33	0,33	0,21	0,05	3E-05
5	**rs76141132**	**24604993**	0,59	0,53	0,10	0,31	0,05	8E-12
6	**rs6912680**	**90300010**	0,80	0,70	0,32	0,22	0,05	4E-05

15	**rs17554431**	**95618191**	0,16	0,20	0,16	0,29	0,06	6E-06
10	**rs2802365**	**81038883**	0,32	0,47	0,14	0,30	0,05	2E-09
2	**rs72775986**	**12602098**	0,47	0,79	0,16	0,31	0,05	1E-11
4	**rs1545788**	**5715069**	0,60	0,59	0,91	0,31	0,05	9E-12
9	**rs1836460**	**110966650**	0,44	0,42	0,02	0,23	0,05	7E-07
1	**rs6656494**	**154839799**	0,43	0,89	0,55	0,22	0,05	2E-06
9	**rs2378675**	**87619462**	0,66	0,35	0,87	0,23	0,05	6E-07
17	**rs2729348**	**31015228**	0,65	0,72	0,46	0,30	0,05	7E-11
4	**rs11930919**	**92818352**	0,11	0,17	0,47	0,29	0,07	6E-05
3	**rs7629387**	**95193439**	0,46	0,48	0,55	0,25	0,04	2E-08
13	**rs2993574**	**96067494**	0,50	0,38	0,06	0,27	0,04	2E-09
7	**rs1179608**	**75245398**	0,20	0,27	0,62	0,26	0,06	1E-05
12	**rs12230050**	**93990553**	0,26	0,41	0,57	0,25	0,05	1E-06
21	**rs35265519**	**36683674**	0,71	0,59	0,22	0,24	0,05	5E-07
11	**rs12798276**	**32583375**	0,14	0,61	0,09	0,25	0,07	2E-04
5	**rs34446169**	**13261448**	0,82	0,57	0,49	0,32	0,06	2E-08
10	**rs2505398**	**32633516**	0,69	0,74	0,49	0,22	0,05	4E-06
5	**rs2918443**	**85213684**	0,42	0,39	0,07	0,19	0,05	3E-05
5	**rs244408**	**110021869**	0,80	0,77	0,35	0,25	0,05	6E-06
10	**rs2986035**	**105233110**	0,74	0,80	0,53	0,19	0,05	2E-04
7	**rs2390472**	**21156006**	0,17	0,25	0,23	0,44	0,06	1E-11
6	**rs1933989**	**103065057**	0,29	0,26	0,36	0,23	0,05	9E-06
14	**rs1147446**	**66461978**	0,18	0,25	0,57	0,35	0,06	2E-08
15	**rs4356443**	**88200417**	0,61	0,67	0,82	0,29	0,05	2E-10
6	**rs9484232**	**139365330**	0,37	0,05	0,44	0,28	0,05	3E-09
6	**rs3778021**	**36948805**	0,37	0,13	0,63	0,22	0,05	2E-06
1	**rs1568133**	**189822612**	0,20	0,36	0,57	0,24	0,06	2E-05
10	**rs10906446**	**13712074**	0,43	0,08	0,39	0,35	0,05	3E-14
4	**rs4395470**	**73055791**	0,31	0,80	0,61	0,36	0,05	7E-13
20	**rs2207889**	**34224898**	0,19	0,11	0,41	0,26	0,06	1E-05
5	**rs146990484**	**168728193**	0,72	0,79	0,95	0,28	0,05	1E-08
5	**rs70957010**	**20984328**	0,61	0,93	0,78	0,27	0,05	4E-09
3	**rs7614041**	**102578156**	0,66	0,73	0,33	0,24	0,05	2E-07
5	**rs55753822**	**55753822**	0,24	0,36	0,10	0,24	0,05	9E-06
18	**rs9950923**	**65714987**	0,25	0,42	0,10	0,24	0,05	1E-05
15	**rs79173965**	**74170559**	0,34	0,05	0,04	0,37	0,05	1E-13
15	**rs12439879**	**47179681**	0,30	0,72	0,37	0,33	0,05	6E-11
8	**rs984990**	**114368635**	0,68	0,74	0,43	0,27	0,05	1E-08
6	**rs9399242**	**138827658**	0,26	0,47	0,02	0,26	0,05	9E-07
12	**rs10748463**	**47580270**	0,63	0,65	0,57	0,29	0,05	5E-10
18	**rs12104083**	**13739269**	0,47	0,86	0,23	0,20	0,04	5E-06
4	**rs13135410**	**42565734**	0,21	0,40	0,07	0,31	0,06	7E-08
15	**rs7174210**	**58809493**	0,13	0,04	0,43	0,13	0,07	6E-02
20	**rs399698**	**15368919**	0,30	0,17	0,08	0,29	0,05	1E-08
2	**rs17006895**	**71575470**	0,22	0,00	0,57	0,26	0,06	7E-06

19	**rs55661666**	**15069191**	0,10	0,11	0,30	0,41	0,08	3E-07
11	**rs7941643**	**59460632**	0,07	0,05	0,40	0,35	0,10	4E-04
2	**rs1384781**	**145601057**	0,63	0,80	0,43	0,24	0,05	2E-07
13	**rs6492290**	**111254995**	0,32	0,39	0,57	0,23	0,05	4E-06
8	**rs684904**	**109199417**	0,47	0,49	0,68	0,25	0,05	6E-08
4	**rs17006215**	**123775433**	0,09	0,08	0,49	0,25	0,08	2E-03
22	**rs2156927**	**47288807**	0,73	0,59	0,18	0,34	0,05	9E-12
12	**rs10774768**	**115193194**	0,47	0,28	0,63	0,29	0,05	1E-10
1	**rs2232809**	**171750181**	0,62	0,67	0,85	0,28	0,05	7E-10
3	**rs36196715**	**66271617**	0,10	0,29	0,14	0,24	0,08	3E-03
11	**rs8186211**	**50542195**	0,09	0,25	0,23	0,33	0,08	9E-05
14	**rs9671906**	**84465538**	0,25	0,34	0,52	0,35	0,05	1E-10
14	**rs2753634**	**86144162**	0,39	0,42	0,16	0,32	0,05	3E-11
14	**rs7155200**	**86177170**	0,58	0,56	0,87	0,26	0,04	7E-09
5	**rs13187871**	**60554657**	0,85	0,92	0,38	0,41	0,06	3E-11
13	**rs4551930**	**62709282**	0,17	0,05	0,35	0,24	0,06	1E-04
2	**rs7578058**	**168040115**	0,08	0,06	0,13	0,51	0,09	1E-08
7	**rs6942816**	**107715658**	0,11	0,01	0,72	0,15	0,08	6E-02
9	**rs201898723**	**16603886**	0,92	0,98	0,47	0,14	0,08	8E-02
17	**rs9747201**	**80177852**	0,72	0,93	0,90	0,31	0,05	3E-10
3	**rs7640053**	**79531271**	0,64	0,51	0,97	0,25	0,05	4E-08
2	**rs12694291**	**213884452**	0,85	0,81	0,44	0,15	0,06	2E-02
2	**rs11675147**	**134327168**	0,34	0,40	0,14	0,19	0,05	9E-05
12	**rs10784065**	**40191778**	0,82	0,72	0,64	0,14	0,06	1E-02
16	**rs3759986**	**21225224**	0,34	0,16	0,23	0,28	0,05	8E-09
3	**rs6805084**	**111984736**	0,57	0,76	0,44	0,29	0,05	4E-10
5	**rs34181334**	**32893742**	0,37	0,49	0,51	0,29	0,05	7E-10
2	**rs10171098**	**235598521**	0,24	0,59	0,20	0,20	0,05	2E-04
17	**rs7501427**	**77726549**	0,56	0,56	0,32	0,21	0,04	3E-06
6	**rs12211701**	**133119757**	0,15	0,06	0,69	0,21	0,07	2E-03
7	**rs10951091**	**25734558**	0,32	0,94	0,41	0,28	0,05	1E-08
3	**rs62253006**	**53979904**	0,32	0,51	0,08	0,32	0,05	2E-10
7	**rs11979033**	**67224293**	0,24	0,20	0,37	0,34	0,06	1E-09
5	**rs4134393**	**30190699**	0,66	0,27	0,76	0,28	0,05	1E-09
4	**rs199541723**	**106416147**	0,85	0,49	0,74	0,21	0,06	4E-04
22	**rs9624286**	**24023203**	0,11	0,28	0,15	0,24	0,08	2E-03
6	**rs139304043**	**142387979**	0,13	0,15	0,11	0,39	0,07	4E-08
1	**rs7549723**	**150541812**	0,66	0,67	0,45	0,26	0,05	1E-08
12	**rs11179617**	**41446008**	0,16	0,07	0,02	0,41	0,06	4E-10
13	**rs9512696**	**28012527**	0,67	0,38	0,31	0,32	0,05	8E-12
16	**rs12446304**	**81046335**	0,23	0,44	0,16	0,36	0,06	1E-10
14	**rs726041**	**60073482**	0,53	0,85	0,12	0,27	0,04	1E-09
3	**rs2194607**	**21523342**	0,33	0,68	0,53	0,30	0,05	2E-09
7	**rs2374296**	**151626130**	0,60	0,25	0,77	0,29	0,05	3E-10
15	**rs16962490**	**49743628**	0,22	0,47	0,23	0,30	0,06	2E-07

4	**rs10710521**	**176988797**	0,65	0,57	0,37	0,26	0,05	3E-08
3	**rs13433983**	**161660646**	0,33	0,46	0,25	0,27	0,05	3E-08
5	**rs6555854**	**168712514**	0,76	0,77	0,89	0,31	0,05	2E-09
2	**rs12466544**	**49446174**	0,44	0,55	0,32	0,29	0,05	3E-10
3	**rs1563980**	**28800886**	0,68	0,92	0,72	0,30	0,05	1E-10
4	**rs28408137**	**100298982**	0,19	0,70	0,35	0,26	0,06	6E-06
8	**rs10089687**	**6795851**	0,15	0,21	0,44	0,31	0,07	2E-06
12	**rs34500073**	**81311382**	0,15	0,29	0,66	0,27	0,07	7E-05
7	**rs28483805**	**97269619**	0,28	0,52	0,76	0,31	0,05	2E-09
7	**rs7786334**	**76915253**	0,18	0,11	0,48	0,27	0,06	2E-05
8	**rs201435673**	**119729864**	0,35	0,05	0,48	0,13	0,05	8E-03
8	**rs11784720**	**23319898**	0,27	0,42	0,27	0,28	0,05	2E-07
6	**rs384323**	**9020424**	0,52	0,35	0,12	0,27	0,04	3E-09
10	**rs6585241**	**115486610**	0,80	0,86	0,95	0,31	0,05	1E-08
4	**rs7665844**	**40035613**	0,72	0,70	0,41	0,31	0,05	1E-10
11	**rs7114635**	**90344354**	0,42	0,65	0,52	0,28	0,05	3E-09
4	**rs7673951**	**102671279**	0,56	0,41	0,26	0,20	0,04	8E-06
3	**rs17012429**	**74409330**	0,06	0,26	0,02	0,32	0,10	8E-04
2	**rs35502315**	**13801678**	0,17	0,08	0,34	0,34	0,06	5E-08
4	**rs1584541**	**27690366**	0,67	0,56	0,53	0,24	0,05	3E-07
6	**rs9399030**	**132837049**	0,41	0,24	0,17	0,29	0,05	8E-10
17	**rs78373931**	**57755743**	0,10	0,49	0,10	0,28	0,08	4E-04
1	**rs66483747**	**237615284**	0,53	0,64	0,24	0,25	0,05	4E-08
6	**rs115768825**	**29868185**	0,71	0,54	0,68	0,37	0,05	2E-14
2	**rs1179683**	**217751546**	0,66	0,38	0,60	0,30	0,05	6E-10
8	**rs1866700**	**137519028**	0,75	0,67	0,69	0,29	0,05	1E-08
6	**rs199607379**	**152661834**	0,16	0,04	0,10	0,37	0,06	8E-09
18	**rs11663656**	**57567638**	0,19	0,42	0,18	0,26	0,06	1E-05
7	**rs10261050**	**114337652**	0,44	0,50	0,44	0,27	0,05	3E-09
3	**rs61690667**	**186926347**	0,13	0,30	0,15	0,47	0,07	5E-11
5	**rs5870400**	**109481424**	0,66	0,76	0,35	0,21	0,05	4E-06
4	**rs4691362**	**157527761**	0,19	0,38	0,11	0,25	0,06	2E-05
10	**rs146229701**	**88344342**	0,09	0,32	0,09	0,27	0,08	1E-03
15	**rs12050490**	**28540706**	0,07	0,38	0,36	0,30	0,10	2E-03
1	**rs1530490**	**67055392**	0,13	0,15	0,40	0,20	0,07	4E-03
4	**rs12507474**	**96576002**	0,58	0,46	0,32	0,23	0,05	5E-07
1	**rs12071218**	**81787875**	0,06	0,03	0,28	0,30	0,10	3E-03
17	**rs9674631**	**80096525**	0,48	0,86	0,49	0,29	0,05	2E-10
8	**rs7823203**	**77663181**	0,16	0,46	0,65	0,27	0,06	2E-05
1	**rs111772533**	**26523404**	0,19	0,02	0,21	0,31	0,06	2E-07
20	**rs1338412**	**4328047**	0,23	0,14	0,27	0,30	0,06	3E-08
5	**rs13167124**	**1223940**	0,43	0,25	0,66	0,32	0,05	3E-12
14	**rs2099860**	**85729632**	0,59	0,07	0,51	0,21	0,04	2E-06
4	**rs75874971**	**107457067**	0,46	0,65	0,59	0,27	0,04	1E-09
9	**rs7039175**	**6348355**	0,57	0,70	0,31	0,29	0,05	2E-10

11	**rs12362603**	**22566023**	0,60	0,37	0,02	0,28	0,05	1E-09
17	**rs684690**	**6577803**	0,17	0,31	0,38	0,25	0,06	1E-04
2	**rs7599471**	**20904018**	0,28	0,35	0,42	0,29	0,05	2E-08
7	**rs12669900**	**135702344**	0,25	0,33	0,29	0,22	0,05	3E-05
4	**rs201189120**	**163298951**	0,25	0,06	0,01	0,31	0,05	7E-09
16	**rs8062033**	**25509426**	0,44	0,19	0,59	0,24	0,05	2E-07
12	**rs11065695**	**109595386**	0,84	0,49	0,22	0,22	0,06	1E-04
11	**rs77626887**	**69861644**	0,08	0,42	0,24	0,31	0,09	2E-04
4	**rs62329002**	**104178267**	0,23	0,20	0,05	0,33	0,05	2E-09
6	**rs4336469**	**104281391**	0,62	0,64	0,64	0,26	0,05	2E-08
4	**rs10017933**	**190427804**	0,37	0,21	0,43	0,15	0,05	2E-03
6	**rs200957116**	**13738918**	0,24	0,15	0,38	0,35	0,06	4E-10
3	**rs34746516**	**63459254**	0,25	0,39	0,31	0,29	0,05	3E-08
3	**rs68015175**	**5497135**	0,43	0,32	0,31	0,26	0,05	1E-08
4	**rs28475791**	**85074939**	0,38	0,57	0,66	0,27	0,05	1E-08
13	**rs7994720**	**64583323**	0,69	0,54	0,45	0,27	0,05	2E-08
9	**rs4272463**	**20999770**	0,34	0,53	0,32	0,29	0,05	5E-09
3	**rs950336**	**118586272**	0,41	0,52	0,14	0,28	0,05	3E-09
12	**rs1857736**	**98568477**	0,37	0,11	0,64	0,27	0,05	9E-09
2	**rs1448291**	**224021256**	0,65	0,63	0,47	0,29	0,05	2E-10
20	**rs856964**	**61412098**	0,78	0,58	0,95	0,27	0,05	4E-07
15	**rs12592571**	**59707163**	0,73	0,52	0,11	0,30	0,05	8E-10
4	**rs4691702**	**161736289**	0,66	0,86	0,85	0,33	0,05	2E-12
18	**rs4581807**	**68874816**	0,74	0,90	0,45	0,23	0,05	3E-06
17	**rs806874**	**51427558**	0,51	0,30	0,51	0,28	0,05	4E-10
22	**rs4821661**	**37782256**	0,80	0,81	0,93	0,32	0,05	1E-09
4	**rs201017255**	**106205194**	0,45	0,38	0,51	0,24	0,05	1E-07
5	**rs6871530**	**111175425**	0,68	0,40	0,66	0,29	0,05	8E-10
6	**rs34059065**	**140301421**	0,30	0,05	0,07	0,33	0,05	2E-10
3	**rs9852128**	**12635623**	0,24	0,03	0,43	0,32	0,05	3E-09
4	**rs35553952**	**187742898**	0,29	0,23	0,34	0,33	0,05	1E-10
5	**rs1058310**	**14509903**	0,32	0,12	0,39	0,29	0,05	6E-09
9	**rs913182**	**97478309**	0,11	0,24	0,65	0,33	0,08	9E-06
1	**rs4653183**	**33984987**	0,18	0,34	0,31	0,32	0,06	2E-07
14	**rs12879605**	**27295802**	0,51	0,18	0,33	0,29	0,05	5E-10
1	**rs403657**	**83157293**	0,61	0,49	0,57	0,25	0,05	6E-08
16	**rs4534832**	**85273356**	0,18	0,24	0,07	0,28	0,06	3E-06
5	**rs76120834**	**125372245**	0,62	0,65	0,68	0,32	0,05	5E-12
15	**rs79988905**	**42677731**	0,14	0,14	0,66	0,38	0,07	4E-08
9	**rs34977776**	**12887247**	0,07	0,07	0,23	0,21	0,09	3E-02
2	**rs35679012**	**211873996**	0,34	0,24	0,06	0,28	0,05	7E-09
12	**rs7958081**	**23093846**	0,47	0,39	0,76	0,21	0,04	2E-06
6	**rs116647600**	**32828248**	0,41	0,35	0,39	0,17	0,05	2E-04
6	**rs35434813**	**74802323**	0,16	0,02	0,44	0,27	0,06	4E-05
8	**rs3808462**	**116606177**	0,45	0,53	0,90	0,30	0,05	4E-11

14	**rs4020134**	**78420741**	0,63	0,76	0,47	0,28	0,05	7E-10
21	**rs396969**	**27281177**	0,91	0,84	0,90	0,25	0,08	1E-03
22	**rs28702070**	**50344912**	0,29	0,40	0,93	0,27	0,05	5E-08
8	**rs4366044**	**135516280**	0,07	0,30	0,40	0,37	0,10	1E-04
8	**rs34479083**	**57752240**	0,20	0,53	0,12	0,34	0,06	8E-09
6	**rs9377003**	**146861189**	0,67	0,22	0,07	0,29	0,05	6E-10
5	**rs12520117**	**163522236**	0,37	0,50	0,49	0,23	0,05	1E-06
2	**rs147741771**	**132742123**	0,38	0,18	0,59	0,35	0,05	2E-13
14	**rs1959120**	**101568230**	0,44	0,72	0,46	0,19	0,05	4E-05
6	**rs1922970**	**65028748**	0,71	0,51	0,70	0,37	0,05	5E-14
14	**rs10131950**	**60382997**	0,09	0,14	0,41	0,26	0,08	1E-03
10	**rs201533606**	**124511268**	0,58	0,70	0,27	0,25	0,05	3E-08
10	**rs11819372**	**116594934**	0,49	0,29	0,63	0,23	0,04	2E-07
3	**rs298756**	**164199329**	0,30	0,36	0,68	0,23	0,05	5E-06
9	**rs611335**	**116384750**	0,77	1,00	0,78	0,27	0,05	2E-07
5	**rs6877686**	**172231762**	0,09	0,09	0,29	0,17	0,08	5E-02
4	**rs34881324**	**15217750**	0,20	0,53	0,31	0,28	0,06	3E-06
11	**rs4923447**	**27495259**	0,94	0,85	0,66	0,19	0,09	3E-02
1	**rs6663889**	**194388586**	0,63	0,68	0,54	0,27	0,05	7E-09
8	**rs12176618**	**16067292**	0,85	0,44	0,35	0,16	0,06	5E-03
12	**rs201055230**	**49143466**	0,40	0,00	0,19	0,27	0,05	4E-09
2	**rs4663158**	**235598952**	0,50	0,30	0,22	0,30	0,05	3E-11
3	**rs9828959**	**48091207**	0,69	0,77	0,88	0,25	0,05	2E-07
14	**rs7148239**	**104785526**	0,22	0,30	0,52	0,16	0,06	4E-03
5	**rs6883952**	**171961443**	0,24	0,14	0,13	0,27	0,05	7E-07
12	**rs11047649**	**7418257**	0,28	0,46	0,15	0,20	0,05	1E-04
5	**rs11241748**	**123846498**	0,37	0,37	0,15	0,27	0,05	2E-08
1	**rs10586162**	**227176164**	0,49	0,19	0,27	0,28	0,05	5E-10
20	**rs34448893**	**43771407**	0,16	0,03	0,06	0,41	0,07	7E-10
1	**rs2236539**	**182096856**	0,57	0,56	0,63	0,25	0,05	2E-08
9	**rs9406772**	**20014075**	0,77	0,66	0,66	0,23	0,05	7E-06
7	**rs152651505**	**152651505**	0,38	0,41	0,52	0,38	0,05	3E-15
1	**rs1501568**	**211087439**	0,61	0,81	0,70	0,27	0,05	8E-09
17	**rs2005132**	**62008232**	0,65	0,45	0,84	0,21	0,05	6E-06
7	**rs28424095**	**158616163**	0,06	0,57	0,28	0,32	0,10	1E-03
14	**rs9918**	**51722690**	0,10	0,31	0,04	0,34	0,08	1E-05
5	**rs7718109**	**61145102**	0,18	0,31	0,31	0,36	0,06	3E-09
1	**rs12064174**	**194086050**	0,32	0,42	0,77	0,23	0,05	4E-06
12	**rs5744844**	**133238076**	0,43	0,69	0,64	0,26	0,05	2E-08
9	**rs12685848**	**5477766**	0,27	0,53	0,02	0,30	0,05	1E-08
7	**rs34636358**	**146422279**	0,11	0,10	0,44	0,21	0,08	6E-03
1	**rs10857817**	**110803755**	0,38	0,42	0,60	0,31	0,05	4E-11
10	**rs66623103**	**90825658**	0,06	0,08	0,22	0,03	0,10	7E-01
6	**rs28397995**	**91209527**	0,27	0,03	0,55	0,24	0,05	4E-06
4	**rs1479768**	**37472597**	0,36	0,59	0,47	0,21	0,05	9E-06

5	**rs12516866**	**35851261**	0,42	0,44	0,36	0,27	0,05	3E-09
1	**rs1289014**	**163625114**	0,59	0,28	0,81	0,28	0,05	7E-10
7	**rs10232533**	**64875899**	0,64	1,00	0,94	0,27	0,05	2E-09
13	**rs12184575**	**23793343**	0,28	0,23	0,05	0,37	0,05	1E-12
10	**rs1670816**	**56694920**	0,13	0,24	0,05	0,35	0,07	8E-07
13	**rs7989061**	**63466449**	0,46	0,81	0,78	0,25	0,04	4E-08
5	**rs765177**	**41336784**	0,05	0,37	0,03	0,33	0,11	4E-03
10	**rs2815650**	**12558035**	0,54	0,46	0,62	0,22	0,04	1E-06
2	**rs13400029**	**3582069**	0,22	0,14	0,14	0,35	0,06	6E-10
3	**rs9819550**	**176058604**	0,18	0,19	0,57	0,38	0,06	4E-10
15	**rs8034321**	**63248945**	0,46	0,73	0,46	0,20	0,05	2E-05
2	**rs4663439**	**235497621**	0,72	0,84	0,80	0,28	0,05	1E-08
14	**rs12892887**	**100055023**	0,39	0,51	0,67	0,28	0,05	1E-09
11	**rs7128459**	**58179291**	0,22	0,17	0,27	0,31	0,06	4E-08
7	**rs35308546**	**119209501**	0,17	0,05	0,12	0,42	0,06	2E-11
12	**rs79193410**	**41029850**	0,23	0,43	0,07	0,31	0,06	3E-08
18	**rs9945362**	**59908482**	0,10	0,14	0,28	0,14	0,08	6E-02
7	**rs12699522**	**13580422**	0,28	0,00	0,05	0,29	0,05	2E-08
5	**rs35098163**	**4779714**	0,84	0,45	0,67	0,16	0,06	6E-03
10	**rs7895030**	**132941656**	0,93	0,87	0,53	0,35	0,08	2E-05
3	**rs2713647**	**124292021**	0,30	0,35	0,39	0,32	0,05	4E-10
11	**rs202080484**	**98078985**	0,42	0,35	0,37	0,25	0,05	5E-08
13	**rs17370031**	**84977254**	0,30	0,12	0,07	0,34	0,05	2E-11
22	**rs133181**	**25741258**	0,76	0,83	0,99	0,28	0,05	5E-08
19	**rs1468773**	**57106401**	0,23	0,00	0,16	0,35	0,06	2E-10
13	**rs7984909**	**19401097**	0,23	0,21	0,59	0,26	0,06	3E-06
19	**rs11669449**	**15890517**	0,60	0,22	0,41	0,23	0,05	6E-07
20	**rs6091025**	**48297561**	0,54	0,36	0,34	0,26	0,05	8E-09
9	**rs10813570**	**31392327**	0,49	0,80	0,54	0,29	0,04	1E-10
2	**rs10197142**	**13623160**	0,43	0,65	0,92	0,22	0,05	2E-06
6	**rs201328726**	**145185032**	0,36	0,93	0,80	0,23	0,05	1E-06
12	**rs7315657**	**44111950**	0,48	0,57	0,52	0,28	0,05	8E-10
10	**rs12356466**	**31142344**	0,36	0,40	0,30	0,28	0,05	2E-09
8	**rs8180941**	**90336707**	0,35	0,36	0,21	0,31	0,05	1E-10
14	**rs113204453**	**44482023**	0,24	0,03	0,14	0,33	0,05	2E-09
5	**rs2910299**	**160790065**	0,79	0,78	0,52	0,29	0,05	4E-08
15	**rs11854693**	**58712965**	0,79	0,58	0,45	0,30	0,05	2E-08
2	**rs334068**	**179005438**	0,49	0,63	0,14	0,31	0,05	3E-11
13	**rs7317830**	**57274268**	0,38	0,29	0,05	0,26	0,05	5E-08
9	**rs10984992**	**123473416**	0,70	0,56	0,23	0,28	0,05	8E-09
9	**rs55695858**	**138440554**	0,26	0,15	0,12	0,30	0,05	1E-08
1	**rs59048447**	**2766314**	0,38	0,39	0,02	0,29	0,05	7E-10
4	**rs432164**	**177391093**	0,82	0,81	0,82	0,28	0,06	6E-07
3	**rs4339124**	**82316577**	0,80	0,76	0,79	0,26	0,05	3E-06
11	**rs7952283**	**103837145**	0,12	0,11	0,19	0,40	0,07	2E-08

11	**rs11213382**	**97836453**	0,46	0,12	0,23	0,33	0,05	1E-12
1	**rs10604003**	**237788262**	0,11	0,14	0,45	0,26	0,07	4E-04
4	**rs1383567**	**34531200**	0,15	0,19	0,50	0,23	0,06	4E-04
12	**rs12313074**	**117206787**	0,89	0,70	0,36	0,30	0,07	1E-05
7	**rs11772033**	**48527011**	0,16	0,26	0,24	0,24	0,07	2E-04
4	**rs1129304**	**158092422**	0,29	0,44	0,73	0,29	0,05	2E-08
3	**rs12629621**	**66883699**	0,13	0,43	0,29	0,37	0,07	2E-07
7	**rs6948652**	**157225138**	0,53	0,40	0,77	0,28	0,04	3E-10
14	**rs6573543**	**64499805**	0,87	0,81	0,58	0,21	0,06	1E-03
5	**rs154668**	**57598572**	0,05	0,17	0,17	0,16	0,11	1E-01
2	**rs10207163**	**69014280**	0,50	0,50	0,62	0,31	0,05	1E-11
15	**rs1564688**	**93761742**	0,71	0,61	0,88	0,22	0,05	4E-06
1	**rs4255374**	**237561785**	0,34	0,42	0,13	0,27	0,05	2E-08
16	**rs441832**	**83881337**	0,78	0,67	0,88	0,25	0,05	1E-06
7	**rs12537292**	**201060**	0,66	0,72	0,82	0,23	0,05	8E-07
1	**rs4287207**	**107714954**	0,85	0,78	0,61	0,33	0,06	6E-08
8	**rs671655**	**60875824**	0,46	0,52	0,72	0,27	0,05	5E-09
12	**rs11169127**	**50120901**	0,11	0,34	0,55	0,27	0,07	4E-04
11	**rs11217793**	**120161886**	0,18	0,18	0,14	0,38	0,06	4E-10
18	**rs9946168**	**34634176**	0,13	0,12	0,64	0,10	0,07	2E-01
9	**rs11789058**	**119826169**	0,42	0,30	0,60	0,32	0,05	7E-12
13	**rs75297616**	**53308128**	0,07	0,11	0,02	0,22	0,10	3E-02
2	**rs6749895**	**172875442**	0,26	0,03	0,13	0,31	0,05	9E-09
10	**rs668014**	**55320664**	0,50	0,82	0,73	0,28	0,05	5E-10
14	**rs9323205**	**51586467**	0,24	0,01	0,20	0,34	0,05	5E-10
5	**rs2434352**	**68333094**	0,42	0,15	0,17	0,22	0,05	9E-07
1	**rs10453833**	**111909959**	0,27	0,15	0,15	0,29	0,05	4E-08
7	**rs2709956**	**83039231**	0,40	0,16	0,89	0,29	0,05	4E-10
16	**rs149766632**	**78638797**	0,21	0,03	0,14	0,36	0,06	2E-10
6	**rs28869479**	**120471593**	0,06	0,28	0,49	0,25	0,10	1E-02
1	**rs598031**	**5333479**	0,70	0,59	0,99	0,27	0,05	2E-08
22	**rs28755**	**29685711**	0,63	0,70	0,78	0,22	0,05	1E-06
8	**rs12676126**	**24960158**	0,17	0,06	0,53	0,33	0,06	2E-07
15	**rs12324446**	**94721997**	0,27	0,04	0,40	0,21	0,05	4E-05
18	**rs34623028**	**1312629**	0,48	0,35	0,38	0,27	0,05	2E-09
6	**rs6908931**	**144735877**	0,77	0,83	0,84	0,29	0,05	5E-08
10	**rs10900190**	**45733045**	0,57	0,24	0,64	0,17	0,04	1E-04
3	**rs12054033**	**132531654**	0,27	0,54	0,22	0,25	0,05	3E-06
15	**rs58193517**	**49834494**	0,23	0,42	0,57	0,39	0,06	2E-12
6	**rs2798364**	**107161116**	0,78	0,77	0,73	0,30	0,05	2E-08
14	**rs11490385**	**31718057**	0,60	0,85	0,79	0,27	0,05	2E-09
6	**rs515144**	**81659184**	0,27	0,59	0,29	0,22	0,05	2E-05
9	**rs7467510**	**140181362**	0,70	0,61	0,61	0,23	0,05	2E-06
1	**rs12070530**	**12138629**	0,14	0,06	0,39	0,20	0,07	3E-03
4	**rs7440026**	**116326266**	0,62	0,77	0,51	0,30	0,05	1E-10

6	**rs116440502**	**32637135**	0,16	0,32	0,19	0,24	0,07	2E-04
5	**rs165188330**	**165188330**	0,24	0,13	0,14	0,32	0,05	5E-09
12	**rs12315134**	**38419857**	0,49	0,09	0,11	0,25	0,04	4E-08
16	**rs4783251**	**82698974**	0,50	0,04	0,29	0,32	0,04	1E-12
10	**rs12780864**	**22421961**	0,22	0,06	0,14	0,33	0,06	6E-09
6	**rs12192993**	**12380922**	0,41	0,30	0,05	0,35	0,05	4E-14
4	**rs11735893**	**142896936**	0,22	0,01	0,05	0,32	0,06	1E-08
14	**rs1761003**	**46912966**	0,54	0,60	0,12	0,26	0,04	9E-09
12	**rs142837217**	**86002875**	0,34	0,37	0,03	0,24	0,05	1E-06
2	**rs6739828**	**43616008**	0,45	0,08	0,57	0,24	0,05	2E-07
8	**rs2891977**	**122180353**	0,37	0,72	0,67	0,31	0,05	1E-10
9	**rs7874886**	**18865265**	0,23	0,19	0,57	0,27	0,06	7E-07
15	**rs7170241**	**62810138**	0,41	0,60	0,66	0,27	0,05	6E-09
6	**rs7775711**	**112161786**	0,13	0,27	0,84	0,33	0,07	4E-06
10	**rs928578**	**99846671**	0,36	0,37	0,14	0,26	0,05	4E-08
18	**rs59713847**	**12330337**	0,76	0,63	0,45	0,16	0,05	2E-03
3	**rs6438092**	**95479393**	0,38	0,51	0,61	0,27	0,05	1E-08
17	**rs4796450**	**6139713**	0,33	0,22	0,01	0,31	0,05	5E-10
1	**rs11102013**	**110376463**	0,54	0,23	0,26	0,24	0,04	4E-08
4	**rs3967098**	**144195781**	0,57	0,85	0,40	0,26	0,05	2E-08
10	**rs11599612**	**86422743**	0,45	0,40	0,36	0,27	0,05	6E-09
11	**rs1784430**	**102474813**	0,56	0,54	0,45	0,32	0,04	1E-12
19	**rs454904**	**44511589**	0,12	0,47	0,01	0,33	0,07	5E-06
1	**rs289686**	**76608491**	0,30	0,12	0,08	0,29	0,05	1E-08
3	**rs1875732**	**192313035**	0,45	0,43	0,55	0,24	0,04	1E-07
3	**rs7610236**	**197083393**	0,08	0,04	0,30	0,28	0,09	1E-03
6	**rs2048695**	**163338231**	0,52	0,52	0,19	0,35	0,04	2E-15
11	**rs10838609**	**5780716**	0,34	0,28	0,03	0,19	0,05	6E-05
19	**rs3826798**	**5785113**	0,17	0,49	0,33	0,23	0,06	3E-04
1	**rs609125**	**22915030**	0,39	0,28	0,75	0,26	0,05	3E-08
2	**rs200778275**	**162693103**	0,64	0,97	0,44	0,30	0,05	6E-11
9	**rs116941153**	**112797749**	0,13	0,30	0,01	0,19	0,07	6E-03
14	**rs202227171**	**87861177**	0,50	0,42	0,53	0,28	0,04	3E-10
13	**rs3832886**	**76419421**	0,74	0,50	0,60	0,28	0,05	4E-08
7	**rs12669437**	**95253404**	0,41	0,96	0,51	0,33	0,05	1E-12
6	**rs4706299**	**88491110**	0,47	0,56	0,06	0,20	0,04	7E-06
5	**rs78479231**	**21293851**	0,23	0,44	0,20	0,30	0,06	9E-08
2	**rs12993670**	**215491816**	0,86	0,80	0,41	0,27	0,06	2E-05
4	**rs12108436**	**77910959**	0,62	0,35	0,38	0,25	0,05	6E-08
19	**rs11084579**	**31802723**	0,29	0,46	0,22	0,23	0,05	5E-06

DisChr	rsID_refSNP	pos_refSNP	beta ASN	stdbeta ASN	P ASN	beta YRI	stdbeta YRI	P YRI
4	**rs2333328**	**176852836**	0,27	0,05	2E-09	0,25	0,05	1E-06
9	**rs10869238**	**75803635**	0,24	0,05	6E-08	0,30	0,04	1E-11

22	**rs136571**	**45767696**	0,27	0,05	5E-09	0,16	0,29	6E-01
6	**rs579329**	**47822681**	0,31	0,05	1E-10	0,26	0,05	3E-08
10	**rs11591368**	**53523322**	0,21	0,11	5E-02	0,23	0,05	5E-07
6	**rs2504907**	**12603401**	0,31	0,06	3E-07	0,27	0,06	8E-06
19	**rs11083699**	**43755489**	0,37	0,06	8E-10	0,23	0,05	2E-06
8	**rs73351724**	**114787818**	0,28	0,05	2E-09	0,31	0,05	2E-09
3	**rs1387701**	**193147894**	0,25	0,05	7E-08	0,18	0,05	6E-05
4	**rs6854328**	**119683492**	0,34	0,05	2E-13	0,31	0,05	6E-09
15	**rs1604170**	**98040887**	0,29	0,05	2E-10	0,36	0,05	1E-14
15	**rs1470901**	**69097765**	0,20	0,05	9E-06	0,19	0,06	5E-04
1	**rs6696248**	**111404291**	0,29	0,07	3E-05	0,37	0,08	7E-06
7	**rs9692258**	**69049578**	0,26	0,05	2E-06	0,25	0,06	1E-05
12	**rs4761380**	**77829418**	0,27	0,04	2E-09	0,30	0,05	2E-10
14	**rs1959523**	**52312746**	-0,02	0,14	9E-01	0,38	0,05	4E-15
17	**rs7213597**	**12053126**	0,31	0,05	4E-11	0,28	0,05	2E-09
22	**rs6007526**	**45648224**	0,25	0,06	1E-05	0,23	0,07	6E-04
22	**rs535842**	**27621151**	0,40	0,05	8E-16	0,31	0,05	6E-11
2	**rs10190763**	**20573168**	0,24	0,05	3E-06	0,33	0,05	1E-10
11	**rs76472587**	**47881487**	0,28	0,05	1E-08	0,25	0,05	2E-06
13	**rs9549507**	**112996118**	0,31	0,05	2E-11	0,34	0,05	1E-12
11	**rs10834146**	**23595982**	0,29	0,05	3E-10	0,37	0,06	7E-09
9	**rs16925789**	**109495368**	0,16	0,08	5E-02	0,33	0,05	1E-10
5	**rs76671135**	**144312509**	0,24	0,06	3E-05	0,31	0,05	1E-08
17	**rs175382**	**49388390**	0,27	0,05	4E-09	0,28	0,06	2E-06
4	**rs10716645**	**165101675**	0,27	0,06	2E-05	0,31	0,05	3E-10
4	**rs7659549**	**103006301**	0,36	0,05	5E-14	0,27	0,05	1E-06
13	**rs278034**	**30416637**	0,31	0,04	2E-12	0,28	0,05	2E-08
22	**rs2530667**	**30044151**	0,27	0,05	5E-08	0,30	0,08	8E-05
8	**rs9773025**	**6674458**	0,22	0,10	2E-02	0,20	0,05	5E-05
7	**rs10277114**	**12013649**	0,33	0,05	4E-13	0,26	0,05	8E-08
7	**rs686550**	**54728518**	0,01	0,09	9E-01	0,25	0,05	4E-08
2	**rs7587455**	**240990568**	0,56	0,63	4E-01	0,27	0,05	2E-09
15	**rs1191196**	**77646504**	0,26	0,05	8E-09	0,25	0,04	2E-08
7	**rs28369400**	**132913071**	0,32	0,10	2E-03	0,27	0,05	2E-08
14	**rs1950660**	**94774300**	0,27	0,08	4E-04	0,28	0,05	1E-08
6	**rs9452207**	**93744485**	0,22	0,07	2E-03	0,23	0,05	4E-07
4	**rs2045774**	**82822003**	0,27	0,05	5E-09	0,20	0,09	2E-02
7	**rs7787377**	**89996777**	0,34	0,05	5E-13	0,25	0,05	2E-07
9	**rs12686218**	**114601575**	0,35	0,05	2E-13	0,30	0,06	5E-08
3	**rs12330317**	**100836183**	1,10	0,82	2E-01	0,28	0,05	5E-10
13	**rs2781311**	**87626740**	0,30	0,05	1E-10	0,32	0,05	1E-11
5	**rs1422932**	**167397039**	0,23	0,05	2E-06	0,27	0,05	3E-08
9	**rs10115645**	**107369931**	0,29	0,05	6E-09	0,42	0,12	6E-04
7	**rs10952493**	**154253759**	0,31	0,05	7E-12	0,29	0,05	1E-10
14	**rs28501387**	**81772667**	0,28	0,05	1E-09	0,29	0,05	6E-09

7	**rs6947649**	**83415942**	0,24	0,05	7E-08	0,36	0,06	3E-09
5	**rs35733634**	**12879768**	0,34	0,05	2E-13	0,30	0,05	4E-09
4	**rs201086800**	**66370079**	0,22	0,05	6E-06	0,28	0,07	8E-05
6	**rs6938226**	**118852561**	0,16	0,05	2E-03	0,18	0,05	2E-04
1	**rs201832280**	**151339950**	0,26	0,06	3E-06	0,25	0,05	5E-08
14	**rs875799**	**103618276**	0,28	0,06	2E-06	0,31	0,05	2E-09
8	**rs465**	**90816058**	0,33	0,05	5E-13	0,18	0,11	1E-01
2	**rs13409781**	**66203352**	0,32	0,05	2E-09	0,30	0,05	2E-08
4	**rs150411487**	**9061499**	0,30	0,10	2E-03	0,31	0,05	2E-11
10	**rs17663446**	**86272696**	0,37	0,06	5E-09	0,31	0,08	8E-05
12	**rs10845348**	**11539880**	0,23	0,05	3E-07	0,30	0,05	2E-09
9	**rs490491**	**108416462**	0,30	0,05	2E-10	0,29	0,05	3E-09
17	**rs56256681**	**9712092**	0,29	0,05	9E-11	0,28	0,05	7E-10
1	**rs3767246**	**21227086**	0,34	0,05	1E-11	0,33	0,11	3E-03
14	**rs10782420**	**52681605**	0,29	0,06	9E-07	0,28	0,05	3E-07
17	**rs1875558**	**7040018**	0,27	0,05	1E-08	0,29	0,05	2E-08
6	**rs1321473**	**137158764**	0,28	0,05	8E-10	0,22	0,05	6E-06
2	**rs10804341**	**229429905**	0,21	0,08	7E-03	0,25	0,05	4E-07
15	**rs4778048**	**93401485**	0,28	0,05	2E-09	0,28	0,06	8E-07
2	**rs6743294**	**229370567**	0,34	0,05	2E-13	0,25	0,13	5E-02
12	**rs2428387**	**47379311**	0,29	0,11	1E-02	0,28	0,07	4E-05
11	**rs11212624**	**108298019**	0,30	0,05	1E-10	0,27	0,05	5E-09
20	**rs6054547**	**6828677**	0,26	0,04	4E-09	0,24	0,05	1E-05
6	**rs1028483**	**65003887**	0,23	0,04	1E-07	0,32	0,05	5E-11
3	**rs2242023**	**13670481**	0,29	0,05	5E-08	0,25	0,05	6E-08
6	**rs6912599**	**9828518**	0,13	0,14	3E-01	0,24	0,05	8E-06
5	**rs10065424**	**75841888**	0,32	0,05	3E-11	0,28	0,05	8E-09
11	**rs523750**	**107705009**	0,26	0,05	1E-08	0,19	0,05	2E-04
10	**rs10900234**	**46200866**	0,28	0,05	2E-09	0,23	0,05	5E-07
2	**rs13425141**	**210322212**	0,00	0,00	1E+00	0,21	0,10	3E-02
6	**rs114364056**	**28634891**	0,26	0,06	4E-05	0,29	0,05	2E-10
8	**rs12540991**	**13079235**	0,30	0,05	2E-10	0,22	0,05	7E-07
3	**rs73033920**	**164120039**	0,29	0,05	2E-09	0,24	0,04	1E-07
10	**rs10763143**	**56521303**	0,20	0,06	3E-04	0,26	0,05	9E-09
9	**rs7036260**	**122911053**	0,28	0,05	7E-08	0,33	0,05	1E-12
8	**rs4273853**	**22698106**	0,25	0,05	2E-07	0,29	0,05	2E-08
16	**rs3104790**	**52638663**	0,24	0,05	2E-05	0,29	0,05	3E-10
1	**rs12564270**	**245571653**	0,33	0,05	9E-10	0,29	0,05	1E-10
1	**rs10911095**	**182518264**	0,25	0,05	4E-08	0,28	0,05	2E-09
6	**rs76902944**	**164074426**	0,27	0,10	6E-03	0,29	0,05	2E-08
4	**rs7691160**	**26457487**	0,34	0,06	7E-09	0,35	0,05	1E-13
20	**rs6035865**	**21368932**	0,18	0,06	1E-03	0,30	0,05	5E-11
9	**rs72766254**	**130090926**	0,31	0,06	4E-08	0,20	0,12	9E-02
9	**rs7847784**	**110001752**	0,17	0,05	1E-03	0,32	0,05	5E-11
1	**rs7548054**	**39302020**	0,28	0,05	1E-08	0,32	0,08	3E-05

3	**rs199797915**	**39051874**	0,33	0,05	4E-13	0,28	0,09	1E-03
10	**rs773948**	**34716034**	0,28	0,05	2E-09	-0,35	0,27	2E-01
5	**rs56777318**	**87825189**	0,27	0,05	9E-09	0,20	0,05	1E-04
1	**rs200576863**	**154798550**	0,28	0,05	3E-08	0,21	0,05	1E-05
12	**rs7138235**	**133313237**	0,27	0,05	4E-08	0,32	0,06	4E-08
20	**rs2983304**	**23508573**	0,29	0,05	1E-10	0,34	0,06	1E-08
7	**rs10950822**	**20647108**	0,25	0,05	5E-08	0,31	0,05	1E-11
6	**rs115700812**	**32511774**	0,25	0,05	2E-07	0,24	0,05	2E-07
16	**rs7187576**	**25070579**	0,19	0,05	2E-04	0,35	0,05	9E-13
3	**rs1388705**	**161584027**	0,29	0,05	1E-09	-0,14	0,30	7E-01
8	**rs10955282**	**103176946**	0,26	0,05	7E-09	0,23	0,04	3E-07
1	**rs2256913**	**72402880**	0,21	0,08	6E-03	0,29	0,04	6E-11
11	**rs12277881**	**6729061**	0,35	0,05	4E-14	0,30	0,05	6E-11
14	**rs7156971**	**54854783**	0,26	0,05	2E-08	0,25	0,05	6E-08
8	**rs28439245**	**3077166**	0,29	0,05	3E-09	0,16	0,05	9E-04
3	**rs13085132**	**106837810**	0,32	0,05	9E-13	0,26	0,05	1E-08
1	**rs6665839**	**49043877**	0,21	0,05	7E-05	0,31	0,05	7E-11
6	**rs4236138**	**56151384**	0,31	0,05	9E-12	0,30	0,14	3E-02
2	**rs35463898**	**71704005**	0,38	0,05	2E-16	0,30	0,06	5E-07
6	**rs9688927**	**92701926**	0,26	0,05	2E-08	0,38	0,12	2E-03
1	**rs150016402**	**94601236**	0,19	0,05	5E-04	0,32	0,06	1E-08
6	**rs13199418**	**79874045**	0,32	0,07	7E-07	0,26	0,05	4E-08
10	**rs507098**	**116062510**	0,32	0,05	1E-10	0,29	0,05	2E-10
18	**rs9961465**	**8569882**	0,27	0,05	1E-08	0,27	0,05	3E-09
21	**rs2236478**	**46917782**	0,33	0,05	4E-11	0,17	0,05	2E-04
16	**rs10153134**	**90091099**	0,29	0,05	9E-09	0,23	0,05	4E-07
11	**rs201202588**	**72258622**	0,26	0,05	2E-07	0,22	0,05	3E-06
14	**rs77306894**	**88960851**	0,30	0,05	1E-09	0,36	0,07	3E-08
20	**rs7264816**	**22955608**	0,21	0,05	4E-06	0,29	0,06	2E-07
20	**rs6056189**	**8811896**	0,23	0,06	2E-04	0,30	0,05	7E-09
2	**rs11899581**	**122712643**	0,34	0,07	2E-07	0,19	0,05	5E-05
10	**rs7095313**	**17399051**	0,26	0,08	2E-03	0,23	0,05	2E-06
5	**rs2904945**	**8777960**	0,22	0,07	1E-03	0,31	0,05	1E-10
11	**rs7119996**	**93389932**	0,27	0,05	1E-07	0,23	0,05	7E-07
3	**rs34638579**	**137385728**	0,24	0,05	7E-06	0,29	0,05	1E-10
13	**rs9593302**	**78829464**	0,16	0,05	2E-03	0,31	0,05	2E-10
8	**rs62509924**	**87103432**	0,32	0,04	1E-12	0,23	0,07	6E-04
1	**rs1977125**	**63772373**	0,27	0,04	1E-09	0,27	0,06	2E-06
10	**rs1926801**	**4433288**	0,28	0,21	2E-01	0,11	0,07	1E-01
2	**rs1597944**	**234504098**	0,25	0,04	2E-08	0,38	0,07	5E-09
10	**rs7902931**	**6141942**	0,23	0,05	1E-05	0,32	0,05	1E-12
4	**rs200356168**	**7864140**	0,34	0,05	3E-12	0,29	0,05	2E-10
2	**rs11126341**	**71916661**	0,25	0,05	5E-08	0,23	0,05	4E-07
4	**rs147440574**	**128598143**	0,29	0,06	3E-07	0,19	0,06	6E-04
7	**rs10276126**	**131306210**	0,28	0,05	2E-09	0,28	0,05	2E-07

6	**rs366920**	**160737950**	0,22	0,05	2E-05	0,32	0,05	2E-10
7	**rs28491038**	**104366640**	0,32	0,07	9E-06	0,18	0,05	2E-04
8	**rs7836279**	**13775292**	0,30	0,05	2E-11	0,26	0,06	2E-05
17	**rs2411041**	**74913863**	0,28	0,05	5E-09	0,25	0,05	2E-07
20	**rs6092006**	**36809169**	0,29	0,06	5E-06	0,29	0,05	4E-08
20	**rs72620874**	**1895889**	0,34	0,05	3E-13	0,24	0,05	8E-07
2	**rs76136841**	**206820159**	0,33	0,05	7E-13	0,34	0,22	1E-01
20	**rs138273314**	**19935337**	0,29	0,05	3E-10	0,30	0,05	4E-10
4	**rs4862032**	**183071431**	0,27	0,05	3E-08	0,26	0,05	4E-07
2	**rs13003505**	**159156020**	0,26	0,05	8E-09	0,20	0,05	1E-04
9	**rs2017392**	**112820620**	0,28	0,05	2E-09	0,11	0,10	3E-01
3	**rs729942**	**87066095**	0,25	0,05	3E-08	0,22	0,09	2E-02
8	**rs59026256**	**66912273**	0,34	0,10	5E-04	0,31	0,05	6E-10
5	**rs433211**	**151324761**	0,31	0,05	1E-10	0,23	0,05	1E-06
12	**rs7132347**	**55714876**	0,21	0,07	2E-03	0,20	0,06	3E-04
9	**rs9775725**	**27244202**	0,29	0,05	3E-08	0,29	0,05	1E-10
17	**rs4605213**	**49244747**	0,17	0,06	3E-03	0,24	0,13	6E-02
4	**rs12696692**	**6735941**	0,29	0,05	1E-09	0,34	0,08	3E-05
1	**rs1014977**	**168457111**	0,24	0,05	2E-06	0,28	0,05	3E-09
8	**rs1392143**	**3357940**	0,21	0,06	6E-04	0,39	0,05	4E-17
9	**rs60795901**	**78895500**	0,28	0,09	1E-03	0,29	0,05	9E-09
1	**rs17407657**	**66171667**	0,16	0,17	3E-01	0,26	0,06	2E-05
7	**rs854074**	**95298272**	0,29	0,04	1E-10	0,18	0,05	1E-04
9	**rs10980731**	**113838859**	0,33	0,05	8E-10	0,51	0,12	2E-05
11	**rs1426926**	**87903141**	0,28	0,05	4E-08	0,33	0,05	9E-13
2	**rs374954**	**176084790**	0,27	0,05	5E-09	0,22	0,05	5E-06
6	**rs2327037**	**8228490**	0,32	0,05	2E-11	0,21	0,05	5E-06
4	**rs62325107**	**154675105**	0,27	0,07	4E-05	0,28	0,05	2E-09
12	**rs11532381**	**79936694**	0,28	0,05	4E-08	0,28	0,09	3E-03
22	**rs136482**	**32590036**	0,25	0,07	6E-04	0,24	0,09	9E-03
1	**rs17021956**	**119082264**	0,16	0,05	1E-03	0,34	0,05	9E-11
14	**rs10141742**	**59406089**	-0,03	0,13	8E-01	0,17	0,08	5E-02
7	**rs2005764**	**105778633**	0,34	0,05	4E-13	0,27	0,07	4E-05
3	**rs9816837**	**178705604**	0,27	0,05	3E-09	0,18	0,05	1E-04
4	**rs631179**	**130411127**	0,21	0,05	3E-06	0,29	0,05	3E-10
3	**rs66861711**	**162227359**	0,32	0,05	1E-10	0,38	0,08	1E-06
4	**rs6824500**	**35487085**	0,26	0,05	1E-07	0,32	0,05	2E-10
5	**rs76141132**	**24604993**	0,35	0,05	1E-14	0,25	0,08	1E-03
6	**rs6912680**	**90300010**	0,30	0,05	4E-10	0,15	0,05	2E-03
15	**rs17554431**	**95618191**	0,34	0,06	1E-08	0,27	0,06	2E-05
10	**rs2802365**	**81038883**	0,30	0,05	6E-11	0,24	0,07	3E-04
2	**rs72775986**	**12602098**	0,25	0,05	2E-06	0,11	0,06	8E-02
4	**rs1545788**	**5715069**	0,31	0,05	2E-11	0,32	0,08	4E-05
9	**rs1836460**	**110966650**	0,28	0,05	3E-09	0,36	0,17	3E-02
1	**rs6656494**	**154839799**	0,20	0,07	4E-03	0,37	0,05	2E-16

9	**rs2378675**	**87619462**	0,31	0,05	1E-10	0,31	0,06	2E-06
17	**rs2729348**	**31015228**	0,29	0,05	4E-09	0,17	0,05	2E-04
4	**rs11930919**	**92818352**	0,30	0,06	2E-06	0,26	0,05	1E-08
3	**rs7629387**	**95193439**	0,11	0,05	2E-02	0,26	0,05	7E-09
13	**rs2993574**	**96067494**	0,27	0,05	1E-08	0,30	0,10	3E-03
7	**rs1179608**	**75245398**	0,34	0,05	6E-11	0,24	0,05	3E-07
12	**rs12230050**	**93990553**	0,22	0,05	3E-06	0,33	0,04	8E-14
21	**rs35265519**	**36683674**	0,28	0,05	5E-10	0,34	0,06	2E-09
11	**rs12798276**	**32583375**	0,33	0,05	1E-12	0,33	0,08	8E-05
5	**rs34446169**	**13261448**	0,22	0,04	1E-06	0,24	0,05	7E-08
10	**rs2505398**	**32633516**	0,23	0,05	3E-06	0,25	0,04	4E-08
5	**rs2918443**	**85213684**	0,34	0,05	9E-13	0,38	0,10	6E-05
5	**rs244408**	**110021869**	0,23	0,05	6E-06	0,32	0,05	7E-11
10	**rs2986035**	**105233110**	0,25	0,05	3E-06	0,35	0,05	1E-14
7	**rs2390472**	**21156006**	0,22	0,05	5E-05	0,31	0,05	2E-08
6	**rs1933989**	**103065057**	0,24	0,05	7E-06	0,32	0,05	5E-11
14	**rs1147446**	**66461978**	0,28	0,05	3E-07	0,24	0,04	8E-08
15	**rs4356443**	**88200417**	0,23	0,05	1E-06	0,19	0,06	7E-04
6	**rs9484232**	**139365330**	0,32	0,11	4E-03	0,25	0,05	2E-08
6	**rs3778021**	**36948805**	0,27	0,07	6E-05	0,30	0,05	8E-11
1	**rs1568133**	**189822612**	0,28	0,05	4E-09	0,21	0,04	3E-06
10	**rs10906446**	**13712074**	0,15	0,09	9E-02	0,19	0,05	5E-05
4	**rs4395470**	**73055791**	0,37	0,05	2E-11	0,29	0,05	1E-10
20	**rs2207889**	**34224898**	0,21	0,08	4E-03	0,32	0,05	2E-12
5	**rs146990484**	**168728193**	0,29	0,05	4E-08	0,30	0,11	6E-03
5	**rs70957010**	**20984328**	0,33	0,09	1E-04	0,32	0,05	2E-09
3	**rs7614041**	**102578156**	0,34	0,05	5E-12	0,27	0,05	1E-07
5	**rs55753822**	**55753822**	0,31	0,05	1E-10	0,34	0,08	1E-05
18	**rs9950923**	**65714987**	0,28	0,05	1E-09	0,13	0,08	9E-02
15	**rs79173965**	**74170559**	0,26	0,11	2E-02	0,35	0,13	5E-03
15	**rs12439879**	**47179681**	0,26	0,05	2E-07	0,22	0,05	3E-06
8	**rs984990**	**114368635**	0,33	0,05	3E-11	0,26	0,05	7E-09
6	**rs9399242**	**138827658**	0,25	0,05	4E-08	0,05	0,16	7E-01
12	**rs10748463**	**47580270**	0,26	0,05	2E-08	0,34	0,04	8E-14
18	**rs12104083**	**13739269**	0,41	0,06	3E-11	0,24	0,06	1E-05
4	**rs13135410**	**42565734**	0,29	0,05	1E-09	0,21	0,09	3E-02
15	**rs7174210**	**58809493**	0,23	0,11	3E-02	0,26	0,05	1E-08
20	**rs399698**	**15368919**	0,35	0,06	3E-08	0,19	0,09	3E-02
2	**rs17006895**	**71575470**	0,92	0,59	1E-01	0,35	0,05	2E-14
19	**rs55661666**	**15069191**	0,27	0,08	5E-04	0,34	0,05	2E-11
11	**rs7941643**	**59460632**	0,20	0,11	7E-02	0,27	0,05	1E-08
2	**rs1384781**	**145601057**	0,41	0,05	7E-14	0,24	0,05	1E-07
13	**rs6492290**	**111254995**	0,24	0,05	3E-07	0,29	0,04	2E-10
8	**rs684904**	**109199417**	0,29	0,04	1E-10	0,34	0,05	1E-12
4	**rs17006215**	**123775433**	0,30	0,09	4E-04	0,29	0,05	1E-10

22	**rs2156927**	**47288807**	0,24	0,05	2E-07	0,26	0,06	2E-05
12	**rs10774768**	**115193194**	0,33	0,05	2E-10	0,25	0,05	4E-08
1	**rs2232809**	**171750181**	0,29	0,05	1E-09	0,31	0,06	3E-07
3	**rs36196715**	**66271617**	0,20	0,05	7E-05	0,37	0,07	5E-08
11	**rs8186211**	**50542195**	0,38	0,05	3E-12	0,25	0,06	8E-06
14	**rs9671906**	**84465538**	0,36	0,05	6E-14	0,25	0,05	3E-08
14	**rs2753634**	**86144162**	0,19	0,05	4E-05	0,25	0,06	9E-05
14	**rs7155200**	**86177170**	0,21	0,04	4E-06	0,24	0,06	1E-04
5	**rs13187871**	**60554657**	0,31	0,08	1E-04	0,22	0,05	5E-06
13	**rs4551930**	**62709282**	0,40	0,12	8E-04	0,28	0,05	1E-08
2	**rs7578058**	**168040115**	0,04	0,10	7E-01	0,22	0,07	2E-03
7	**rs6942816**	**107715658**	0,37	0,23	1E-01	0,30	0,05	6E-10
9	**rs201898723**	**16603886**	0,32	0,13	2E-02	0,27	0,04	2E-09
17	**rs9747201**	**80177852**	0,25	0,08	3E-03	0,26	0,07	3E-04
3	**rs7640053**	**79531271**	0,23	0,04	3E-07	0,42	0,13	1E-03
2	**rs12694291**	**213884452**	0,18	0,06	1E-03	0,26	0,05	3E-08
2	**rs11675147**	**134327168**	0,28	0,05	2E-09	0,30	0,07	2E-05
12	**rs10784065**	**40191778**	0,28	0,05	9E-09	0,27	0,05	2E-09
16	**rs3759986**	**21225224**	0,20	0,07	2E-03	0,29	0,06	1E-07
3	**rs6805084**	**111984736**	0,32	0,05	3E-10	0,29	0,05	2E-10
5	**rs34181334**	**32893742**	0,30	0,05	3E-11	0,24	0,05	1E-07
2	**rs10171098**	**235598521**	0,30	0,05	6E-11	0,30	0,06	4E-07
17	**rs7501427**	**77726549**	0,27	0,05	2E-09	0,26	0,05	2E-07
6	**rs12211701**	**133119757**	0,23	0,10	2E-02	0,34	0,05	6E-13
7	**rs10951091**	**25734558**	0,29	0,09	2E-03	0,32	0,05	9E-12
3	**rs62253006**	**53979904**	0,19	0,05	2E-05	0,38	0,09	3E-05
7	**rs11979033**	**67224293**	0,25	0,06	3E-05	0,24	0,05	4E-07
5	**rs4134393**	**30190699**	0,20	0,05	2E-04	0,36	0,05	8E-12
4	**rs199541723**	**106416147**	0,26	0,05	1E-08	0,33	0,05	5E-11
22	**rs9624286**	**24023203**	0,30	0,05	3E-09	0,26	0,07	9E-05
6	**rs139304043**	**142387979**	0,22	0,06	6E-04	0,25	0,08	1E-03
1	**rs7549723**	**150541812**	0,27	0,05	1E-08	0,27	0,04	2E-09
12	**rs11179617**	**41446008**	0,26	0,09	5E-03	0,25	0,16	1E-01
13	**rs9512696**	**28012527**	0,29	0,05	1E-09	0,28	0,05	3E-08
16	**rs12446304**	**81046335**	0,24	0,05	2E-07	0,27	0,06	2E-05
14	**rs726041**	**60073482**	0,19	0,06	1E-03	0,33	0,07	5E-06
3	**rs2194607**	**21523342**	0,31	0,05	3E-11	0,24	0,05	8E-08
7	**rs2374296**	**151626130**	0,26	0,05	1E-06	0,22	0,05	1E-05
15	**rs16962490**	**49743628**	0,30	0,04	1E-11	0,26	0,05	3E-06
4	**rs10710521**	**176988797**	0,26	0,05	9E-09	0,34	0,05	2E-12
3	**rs13433983**	**161660646**	0,22	0,04	1E-06	0,28	0,05	2E-07
5	**rs6555854**	**168712514**	0,20	0,05	1E-04	0,29	0,07	2E-05
2	**rs12466544**	**49446174**	0,25	0,04	1E-08	0,24	0,05	1E-06
3	**rs1563980**	**28800886**	0,26	0,08	1E-03	0,27	0,05	5E-08
4	**rs28408137**	**100298982**	0,40	0,05	6E-17	0,28	0,05	5E-09

8	**rs10089687**	**6795851**	0,19	0,06	8E-04	0,27	0,05	6E-09
12	**rs34500073**	**81311382**	0,23	0,05	5E-06	0,28	0,05	2E-09
7	**rs28483805**	**97269619**	0,29	0,04	8E-11	0,30	0,05	3E-09
7	**rs7786334**	**76915253**	0,17	0,07	3E-02	0,26	0,05	6E-09
8	**rs201435673**	**119729864**	0,28	0,11	9E-03	0,31	0,05	8E-12
8	**rs11784720**	**23319898**	0,22	0,05	2E-06	0,30	0,05	2E-08
6	**rs384323**	**9020424**	0,25	0,05	3E-07	0,27	0,07	3E-04
10	**rs6585241**	**115486610**	0,28	0,06	5E-06	0,15	0,10	1E-01
4	**rs7665844**	**40035613**	0,24	0,05	6E-07	0,22	0,05	9E-07
11	**rs7114635**	**90344354**	0,22	0,05	2E-06	0,22	0,05	1E-06
4	**rs7673951**	**102671279**	0,28	0,05	3E-09	0,26	0,05	1E-06
3	**rs17012429**	**74409330**	0,29	0,05	4E-08	0,29	0,19	1E-01
2	**rs35502315**	**13801678**	0,35	0,09	6E-05	0,36	0,05	4E-14
4	**rs1584541**	**27690366**	0,30	0,05	2E-11	0,25	0,04	5E-08
6	**rs9399030**	**132837049**	0,26	0,05	1E-06	0,36	0,06	1E-08
17	**rs78373931**	**57755743**	0,30	0,05	4E-11	0,37	0,08	2E-06
1	**rs66483747**	**237615284**	0,32	0,05	3E-12	0,30	0,05	4E-08
6	**rs115768825**	**29868185**	0,30	0,04	3E-11	0,43	0,05	7E-19
2	**rs1179683**	**217751546**	0,33	0,05	1E-12	0,31	0,05	3E-11
8	**rs1866700**	**137519028**	0,23	0,05	8E-07	0,26	0,05	6E-08
6	**rs199607379**	**152661834**	0,31	0,12	1E-02	0,20	0,08	1E-02
18	**rs11663656**	**57567638**	0,33	0,05	1E-12	0,34	0,06	9E-08
7	**rs10261050**	**114337652**	0,20	0,04	4E-06	0,28	0,05	8E-10
3	**rs61690667**	**186926347**	0,26	0,05	6E-07	0,37	0,07	4E-08
5	**rs5870400**	**109481424**	0,32	0,05	1E-10	0,35	0,05	7E-13
4	**rs4691362**	**157527761**	0,26	0,05	4E-08	0,17	0,08	2E-02
10	**rs146229701**	**88344342**	0,27	0,05	3E-08	0,22	0,08	9E-03
15	**rs12050490**	**28540706**	0,27	0,05	1E-08	0,22	0,05	6E-06
1	**rs1530490**	**67055392**	0,28	0,07	2E-05	0,33	0,05	4E-12
4	**rs12507474**	**96576002**	0,26	0,05	1E-08	0,31	0,05	2E-10
1	**rs12071218**	**81787875**	0,01	0,15	9E-01	0,30	0,05	1E-08
17	**rs9674631**	**80096525**	0,28	0,06	7E-06	0,32	0,05	2E-12
8	**rs7823203**	**77663181**	0,28	0,05	3E-10	0,24	0,05	2E-07
1	**rs111772533**	**26523404**	0,31	0,19	1E-01	0,33	0,06	8E-09
20	**rs1338412**	**4328047**	0,20	0,07	2E-03	0,34	0,05	6E-11
5	**rs13167124**	**1223940**	0,16	0,05	4E-03	0,20	0,05	2E-05
14	**rs2099860**	**85729632**	0,14	0,10	1E-01	0,25	0,04	2E-08
4	**rs75874971**	**107457067**	0,27	0,05	9E-09	0,28	0,05	7E-10
9	**rs7039175**	**6348355**	0,22	0,05	7E-06	0,24	0,05	7E-07
11	**rs12362603**	**22566023**	0,29	0,05	1E-09	0,19	0,19	3E-01
17	**rs684690**	**6577803**	0,21	0,05	4E-05	0,28	0,05	2E-09
2	**rs7599471**	**20904018**	0,32	0,05	1E-11	0,24	0,05	3E-07
7	**rs12669900**	**135702344**	0,37	0,05	1E-13	0,29	0,05	7E-09
4	**rs201189120**	**163298951**	0,36	0,10	3E-04	-0,33	0,31	3E-01
16	**rs8062033**	**25509426**	0,40	0,06	5E-11	0,25	0,05	6E-08

12	**rs11065695**	**109595386**	0,28	0,04	1E-10	0,36	0,06	2E-10
11	**rs77626887**	**69861644**	0,30	0,05	8E-11	0,32	0,06	2E-08
4	**rs62329002**	**104178267**	0,26	0,06	2E-05	0,33	0,12	4E-03
6	**rs4336469**	**104281391**	0,28	0,05	8E-10	0,26	0,05	2E-08
4	**rs10017933**	**190427804**	0,21	0,06	4E-04	0,30	0,05	2E-10
6	**rs200957116**	**13738918**	0,28	0,06	1E-05	0,31	0,05	9E-11
3	**rs34746516**	**63459254**	0,32	0,05	1E-11	0,24	0,05	2E-06
3	**rs68015175**	**5497135**	0,26	0,05	1E-07	0,24	0,05	2E-06
4	**rs28475791**	**85074939**	0,21	0,05	6E-06	0,24	0,05	2E-07
13	**rs7994720**	**64583323**	0,17	0,04	1E-04	0,28	0,05	7E-10
9	**rs4272463**	**20999770**	0,30	0,04	1E-11	0,29	0,05	1E-08
3	**rs950336**	**118586272**	0,29	0,05	1E-10	0,30	0,07	8E-06
12	**rs1857736**	**98568477**	0,27	0,08	4E-04	0,17	0,05	3E-04
2	**rs1448291**	**224021256**	0,22	0,05	1E-06	0,36	0,05	2E-15
20	**rs856964**	**61412098**	0,33	0,05	3E-13	0,26	0,10	8E-03
15	**rs12592571**	**59707163**	0,30	0,05	3E-11	0,36	0,08	1E-06
4	**rs4691702**	**161736289**	0,31	0,06	8E-07	0,31	0,06	1E-07
18	**rs4581807**	**68874816**	0,33	0,07	9E-06	0,28	0,05	9E-10
17	**rs806874**	**51427558**	0,24	0,05	2E-06	0,25	0,04	1E-08
22	**rs4821661**	**37782256**	0,36	0,06	2E-10	0,32	0,08	2E-04
4	**rs201017255**	**106205194**	0,27	0,05	2E-08	0,27	0,05	5E-09
5	**rs6871530**	**111175425**	0,23	0,05	5E-07	0,24	0,05	2E-07
6	**rs34059065**	**140301421**	0,20	0,11	7E-02	0,23	0,09	1E-02
3	**rs9852128**	**12635623**	0,35	0,13	8E-03	0,19	0,05	4E-05
4	**rs35553952**	**187742898**	0,24	0,06	2E-05	0,27	0,05	2E-08
5	**rs1058310**	**14509903**	0,22	0,07	2E-03	0,29	0,05	6E-10
9	**rs913182**	**97478309**	0,26	0,06	3E-06	0,31	0,05	4E-11
1	**rs4653183**	**33984987**	0,32	0,05	4E-11	0,26	0,05	2E-07
14	**rs12879605**	**27295802**	0,16	0,06	1E-02	0,31	0,05	1E-10
1	**rs403657**	**83157293**	0,26	0,05	1E-08	0,33	0,05	1E-13
16	**rs4534832**	**85273356**	0,30	0,05	3E-08	0,07	0,09	5E-01
5	**rs76120834**	**125372245**	0,26	0,05	4E-08	0,25	0,05	2E-07
15	**rs79988905**	**42677731**	0,24	0,07	4E-04	0,19	0,05	5E-05
9	**rs34977776**	**12887247**	0,31	0,09	8E-04	0,31	0,06	2E-08
2	**rs35679012**	**211873996**	0,29	0,06	1E-07	0,50	0,10	2E-06
12	**rs7958081**	**23093846**	0,28	0,05	2E-09	0,19	0,05	2E-04
6	**rs116647600**	**32828248**	0,26	0,05	4E-08	0,24	0,05	4E-07
6	**rs35434813**	**74802323**	0,36	0,17	3E-02	0,26	0,05	7E-09
8	**rs3808462**	**116606177**	0,25	0,05	4E-08	0,18	0,07	1E-02
14	**rs4020134**	**78420741**	0,29	0,05	1E-08	0,25	0,05	5E-08
21	**rs396969**	**27281177**	0,20	0,06	6E-04	0,41	0,07	6E-09
22	**rs28702070**	**50344912**	0,27	0,05	6E-09	0,27	0,08	1E-03
8	**rs4366044**	**135516280**	0,34	0,05	1E-11	0,22	0,05	3E-06
8	**rs34479083**	**57752240**	0,30	0,04	1E-11	0,34	0,07	3E-06
6	**rs9377003**	**146861189**	0,23	0,06	5E-05	0,17	0,09	7E-02

5	**rs12520117**	**163522236**	0,25	0,05	4E-08	0,36	0,05	2E-14
2	**rs147741771**	**132742123**	0,25	0,06	6E-05	0,18	0,05	9E-05
14	**rs1959120**	**101568230**	0,21	0,05	1E-05	0,27	0,05	2E-09
6	**rs1922970**	**65028748**	0,33	0,05	1E-13	0,27	0,05	2E-08
14	**rs10131950**	**60382997**	0,26	0,07	9E-05	0,32	0,05	1E-11
10	**rs201533606**	**124511268**	0,34	0,05	9E-13	0,28	0,05	9E-08
10	**rs11819372**	**116594934**	0,31	0,05	3E-09	0,25	0,05	3E-08
3	**rs298756**	**164199329**	0,28	0,05	5E-09	0,30	0,05	5E-10
9	**rs611335**	**116384750**	0,25	0,50	6E-01	0,31	0,05	9E-09
5	**rs6877686**	**172231762**	0,19	0,09	3E-02	0,32	0,05	2E-10
4	**rs34881324**	**15217750**	0,31	0,04	6E-12	0,25	0,05	3E-07
11	**rs4923447**	**27495259**	0,25	0,06	4E-05	0,33	0,05	2E-12
1	**rs6663889**	**194388586**	0,34	0,05	2E-12	0,24	0,05	3E-07
8	**rs12176618**	**16067292**	0,25	0,05	8E-08	0,30	0,05	7E-10
12	**rs201055230**	**49143466**	1,10	0,58	6E-02	0,29	0,06	1E-06
2	**rs4663158**	**235598952**	0,22	0,05	2E-05	0,33	0,06	2E-08
3	**rs9828959**	**48091207**	0,33	0,05	1E-10	0,25	0,06	1E-04
14	**rs7148239**	**104785526**	0,28	0,05	9E-08	0,36	0,05	3E-15
5	**rs6883952**	**171961443**	0,40	0,07	8E-09	0,22	0,07	2E-03
12	**rs11047649**	**7418257**	0,28	0,05	6E-10	0,36	0,07	1E-07
5	**rs11241748**	**123846498**	0,32	0,05	2E-11	0,21	0,07	1E-03
1	**rs10586162**	**227176164**	0,30	0,06	5E-07	0,23	0,05	1E-05
20	**rs34448893**	**43771407**	0,28	0,14	5E-02	0,21	0,10	3E-02
1	**rs2236539**	**182096856**	0,27	0,05	3E-09	0,27	0,05	5E-09
9	**rs9406772**	**20014075**	0,10	0,05	4E-02	0,32	0,05	9E-12
7	**rs152651505**	**152651505**	0,19	0,05	4E-05	0,29	0,04	6E-11
1	**rs1501568**	**211087439**	0,26	0,06	2E-06	0,34	0,05	3E-12
17	**rs2005132**	**62008232**	0,29	0,05	3E-10	0,31	0,06	9E-08
7	**rs28424095**	**158616163**	0,27	0,05	4E-09	0,22	0,05	2E-05
14	**rs9918**	**51722690**	0,36	0,05	3E-13	0,25	0,12	3E-02
5	**rs7718109**	**61145102**	0,20	0,05	5E-05	0,27	0,05	6E-08
1	**rs12064174**	**194086050**	0,34	0,05	1E-13	0,34	0,05	1E-10
12	**rs5744844**	**133238076**	0,20	0,05	4E-05	0,29	0,05	3E-10
9	**rs12685848**	**5477766**	0,29	0,05	8E-11	0,40	0,19	4E-02
7	**rs34636358**	**146422279**	0,40	0,08	3E-07	0,27	0,05	4E-09
1	**rs10857817**	**110803755**	0,30	0,05	5E-11	0,31	0,05	8E-12
10	**rs66623103**	**90825658**	0,19	0,08	2E-02	0,32	0,06	1E-08
6	**rs28397995**	**91209527**	0,46	0,15	2E-03	0,35	0,05	6E-15
4	**rs1479768**	**37472597**	0,18	0,05	7E-05	0,28	0,05	1E-09
5	**rs12516866**	**35851261**	0,32	0,05	2E-12	0,29	0,05	1E-09
1	**rs1289014**	**163625114**	0,32	0,05	4E-10	0,24	0,06	9E-06
7	**rs10232533**	**64875899**	0,88	0,53	1E-01	0,20	0,09	3E-02
13	**rs12184575**	**23793343**	0,21	0,05	2E-04	0,48	0,11	2E-05
10	**rs1670816**	**56694920**	0,32	0,06	8E-09	0,32	0,11	5E-03
13	**rs7989061**	**63466449**	0,22	0,05	6E-05	0,29	0,05	4E-08

5	**rs765177**	**41336784**	0,33	0,05	3E-12	0,39	0,14	5E-03
10	**rs2815650**	**12558035**	0,31	0,04	2E-12	0,27	0,05	6E-09
2	**rs13400029**	**3582069**	0,19	0,07	6E-03	0,27	0,07	5E-05
3	**rs9819550**	**176058604**	0,31	0,06	2E-07	0,30	0,05	6E-11
15	**rs8034321**	**63248945**	0,30	0,05	1E-09	0,28	0,04	5E-10
2	**rs4663439**	**235497621**	0,27	0,06	1E-06	0,29	0,05	6E-08
14	**rs12892887**	**100055023**	0,28	0,04	7E-10	0,24	0,05	2E-07
11	**rs7128459**	**58179291**	0,24	0,06	1E-04	0,26	0,05	7E-07
7	**rs35308546**	**119209501**	0,05	0,12	7E-01	0,36	0,07	1E-06
12	**rs79193410**	**41029850**	0,30	0,05	2E-10	0,30	0,09	1E-03
18	**rs9945362**	**59908482**	0,29	0,07	2E-05	0,32	0,05	8E-10
7	**rs12699522**	**13580422**	0,47	0,57	4E-01	0,27	0,12	2E-02
5	**rs35098163**	**4779714**	0,27	0,05	4E-09	0,19	0,05	7E-05
10	**rs7895030**	**132941656**	0,50	0,07	6E-14	0,30	0,05	1E-11
3	**rs2713647**	**124292021**	0,30	0,05	6E-10	0,21	0,05	8E-06
11	**rs202080484**	**98078985**	0,30	0,05	2E-09	0,24	0,05	3E-07
13	**rs17370031**	**84977254**	0,23	0,07	2E-03	0,38	0,09	7E-05
22	**rs133181**	**25741258**	0,38	0,06	7E-11	0,38	0,20	6E-02
19	**rs1468773**	**57106401**	0,00	0,00	1E+00	0,20	0,06	2E-03
13	**rs7984909**	**19401097**	0,14	0,06	1E-02	0,30	0,05	8E-11
19	**rs11669449**	**15890517**	0,31	0,06	3E-08	0,27	0,05	1E-08
20	**rs6091025**	**48297561**	0,21	0,05	2E-05	0,21	0,05	1E-05
9	**rs10813570**	**31392327**	0,31	0,06	2E-08	0,35	0,04	9E-15
2	**rs10197142**	**13623160**	0,35	0,05	2E-13	0,25	0,08	1E-03
6	**rs201328726**	**145185032**	0,22	0,08	9E-03	0,32	0,06	1E-08
12	**rs7315657**	**44111950**	0,38	0,05	1E-16	0,26	0,05	6E-09
10	**rs12356466**	**31142344**	0,28	0,05	6E-09	0,30	0,05	5E-09
8	**rs8180941**	**90336707**	0,29	0,05	1E-09	0,39	0,06	8E-12
14	**rs113204453**	**44482023**	0,14	0,14	3E-01	0,34	0,07	5E-07
5	**rs2910299**	**160790065**	0,35	0,05	3E-11	0,26	0,05	1E-08
15	**rs11854693**	**58712965**	0,26	0,05	6E-09	0,33	0,05	8E-13
2	**rs334068**	**179005438**	0,25	0,05	3E-08	0,23	0,07	7E-04
13	**rs7317830**	**57274268**	0,25	0,05	2E-06	0,17	0,12	1E-01
9	**rs10984992**	**123473416**	0,21	0,04	2E-06	0,27	0,06	2E-06
9	**rs55695858**	**138440554**	0,27	0,07	5E-05	0,37	0,07	4E-07
1	**rs59048447**	**2766314**	0,32	0,05	5E-12	0,31	0,17	8E-02
4	**rs432164**	**177391093**	0,32	0,06	2E-08	0,35	0,06	6E-10
3	**rs4339124**	**82316577**	0,29	0,05	2E-08	0,31	0,05	8E-09
11	**rs7952283**	**103837145**	0,18	0,07	1E-02	0,27	0,06	9E-06
11	**rs11213382**	**97836453**	0,41	0,07	6E-08	0,20	0,05	2E-04
1	**rs10604003**	**237788262**	0,27	0,07	1E-04	0,33	0,05	8E-13
4	**rs1383567**	**34531200**	0,10	0,06	9E-02	0,31	0,05	2E-11
12	**rs12313074**	**117206787**	0,29	0,05	1E-09	0,29	0,05	1E-09
7	**rs11772033**	**48527011**	0,31	0,05	6E-09	0,21	0,06	1E-04
4	**rs1129304**	**158092422**	0,28	0,05	9E-10	0,24	0,05	7E-07

3	**rs12629621**	**66883699**	0,25	0,05	9E-08	0,29	0,05	1E-08
7	**rs6948652**	**157225138**	0,31	0,05	2E-11	0,25	0,05	1E-06
14	**rs6573543**	**64499805**	0,34	0,06	2E-09	0,24	0,05	9E-08
5	**rs154668**	**57598572**	0,25	0,06	9E-05	0,37	0,06	5E-09
2	**rs10207163**	**69014280**	0,28	0,05	1E-09	0,27	0,05	4E-09
15	**rs1564688**	**93761742**	0,26	0,05	6E-09	0,25	0,07	1E-04
1	**rs4255374**	**237561785**	0,23	0,05	1E-06	0,29	0,07	3E-05
16	**rs441832**	**83881337**	0,33	0,05	3E-12	0,39	0,07	4E-09
7	**rs12537292**	**201060**	0,14	0,05	4E-03	0,40	0,06	6E-13
1	**rs4287207**	**107714954**	0,21	0,05	4E-05	0,28	0,05	6E-10
8	**rs671655**	**60875824**	0,23	0,05	5E-07	0,35	0,05	1E-12
12	**rs11169127**	**50120901**	0,26	0,05	2E-07	0,27	0,04	2E-09
11	**rs11217793**	**120161886**	0,23	0,06	1E-04	0,31	0,07	4E-06
18	**rs9946168**	**34634176**	0,31	0,07	3E-05	0,29	0,05	6E-10
9	**rs11789058**	**119826169**	0,29	0,05	1E-08	0,29	0,05	3E-10
13	**rs75297616**	**53308128**	0,45	0,08	4E-09	0,54	0,18	3E-03
2	**rs6749895**	**172875442**	0,49	0,14	4E-04	0,18	0,07	1E-02
10	**rs668014**	**55320664**	0,17	0,06	4E-03	0,42	0,05	2E-16
14	**rs9323205**	**51586467**	0,20	0,21	3E-01	0,37	0,06	7E-10
5	**rs2434352**	**68333094**	0,26	0,07	8E-05	0,36	0,06	3E-08
1	**rs10453833**	**111909959**	0,25	0,07	1E-04	0,12	0,07	6E-02
7	**rs2709956**	**83039231**	0,23	0,06	3E-04	0,29	0,07	2E-05
16	**rs149766632**	**78638797**	0,39	0,15	9E-03	0,27	0,07	1E-04
6	**rs28869479**	**120471593**	0,26	0,05	6E-07	0,28	0,05	6E-10
1	**rs598031**	**5333479**	0,32	0,05	1E-12	-0,22	0,30	5E-01
22	**rs28755**	**29685711**	0,26	0,05	5E-08	0,19	0,05	3E-04
8	**rs12676126**	**24960158**	0,36	0,10	4E-04	0,27	0,05	3E-09
15	**rs12324446**	**94721997**	0,57	0,12	2E-06	0,26	0,05	9E-09
18	**rs34623028**	**1312629**	0,25	0,05	2E-07	0,28	0,05	3E-09
6	**rs6908931**	**144735877**	0,22	0,06	9E-05	0,21	0,06	3E-04
10	**rs10900190**	**45733045**	0,34	0,06	5E-10	0,24	0,05	1E-07
3	**rs12054033**	**132531654**	0,26	0,05	8E-09	0,29	0,06	3E-07
15	**rs58193517**	**49834494**	0,31	0,05	4E-11	0,27	0,05	5E-09
6	**rs2798364**	**107161116**	0,31	0,05	3E-09	0,26	0,05	8E-08
14	**rs11490385**	**31718057**	0,36	0,06	3E-09	0,32	0,05	2E-09
6	**rs515144**	**81659184**	0,26	0,05	1E-08	0,25	0,05	8E-07
9	**rs7467510**	**140181362**	0,32	0,05	1E-12	0,24	0,05	1E-07
1	**rs12070530**	**12138629**	0,28	0,10	5E-03	0,38	0,05	8E-16
4	**rs7440026**	**116326266**	0,30	0,05	7E-09	0,30	0,04	2E-11
6	**rs116440502**	**32637135**	0,33	0,05	3E-11	0,18	0,06	2E-03
5	**rs165188330**	**165188330**	0,34	0,07	1E-06	0,26	0,07	1E-04
12	**rs12315134**	**38419857**	0,27	0,08	1E-03	0,16	0,08	3E-02
16	**rs4783251**	**82698974**	0,18	0,13	2E-01	0,31	0,05	1E-09
10	**rs12780864**	**22421961**	0,33	0,10	1E-03	0,27	0,07	5E-05
6	**rs12192993**	**12380922**	0,26	0,05	5E-07	0,27	0,11	1E-02

4	**rs11735893**	**142896936**	-0,11	0,27	7E-01	0,11	0,11	3E-01
14	**rs1761003**	**46912966**	0,30	0,05	5E-11	0,19	0,07	8E-03
12	**rs142837217**	**86002875**	0,37	0,05	8E-15	0,43	0,14	2E-03
2	**rs6739828**	**43616008**	0,41	0,09	4E-06	0,33	0,05	3E-13
8	**rs2891977**	**122180353**	0,25	0,05	3E-07	0,23	0,05	1E-06
9	**rs7874886**	**18865265**	0,26	0,06	2E-05	0,33	0,05	2E-13
15	**rs7170241**	**62810138**	0,29	0,04	2E-10	0,27	0,05	1E-08
6	**rs7775711**	**112161786**	0,30	0,05	1E-08	0,21	0,06	3E-04
10	**rs928578**	**99846671**	0,23	0,05	1E-06	0,20	0,07	2E-03
18	**rs59713847**	**12330337**	0,28	0,05	1E-09	0,35	0,05	8E-14
3	**rs6438092**	**95479393**	0,28	0,05	5E-10	0,36	0,05	8E-15
17	**rs4796450**	**6139713**	0,19	0,06	5E-04	-0,13	0,29	7E-01
1	**rs11102013**	**110376463**	0,28	0,06	3E-07	0,26	0,05	1E-06
4	**rs3967098**	**144195781**	0,25	0,06	3E-05	0,39	0,05	3E-17
10	**rs11599612**	**86422743**	0,24	0,05	8E-08	0,31	0,05	2E-10
11	**rs1784430**	**102474813**	0,24	0,05	8E-08	0,27	0,04	2E-09
19	**rs454904**	**44511589**	0,27	0,05	6E-09	0,08	0,23	7E-01
1	**rs289686**	**76608491**	0,25	0,07	7E-04	0,30	0,09	5E-04
3	**rs1875732**	**192313035**	0,30	0,05	7E-11	0,31	0,05	9E-12
3	**rs7610236**	**197083393**	0,05	0,12	7E-01	0,31	0,05	9E-10
6	**rs2048695**	**163338231**	0,22	0,05	2E-06	0,30	0,06	9E-07
11	**rs10838609**	**5780716**	0,30	0,05	6E-09	0,39	0,13	3E-03
19	**rs3826798**	**5785113**	0,25	0,05	2E-08	0,30	0,05	1E-09
1	**rs609125**	**22915030**	0,22	0,05	1E-05	0,28	0,05	3E-08
2	**rs200778275**	**162693103**	0,27	0,12	2E-02	0,22	0,05	8E-07
9	**rs116941153**	**112797749**	0,31	0,05	2E-09	0,81	0,34	2E-02
14	**rs202227171**	**87861177**	0,31	0,05	5E-11	0,30	0,05	2E-11
13	**rs3832886**	**76419421**	0,22	0,05	8E-07	0,16	0,05	5E-04
7	**rs12669437**	**95253404**	0,30	0,11	4E-03	0,27	0,05	4E-09
6	**rs4706299**	**88491110**	0,26	0,04	3E-09	0,38	0,10	2E-04
5	**rs78479231**	**21293851**	0,32	0,05	8E-12	0,22	0,06	2E-04
2	**rs12993670**	**215491816**	0,31	0,05	1E-08	0,17	0,05	1E-04
4	**rs12108436**	**77910959**	0,33	0,05	2E-11	0,33	0,05	8E-12
19	**rs11084579**	**31802723**	0,25	0,05	2E-08	0,27	0,06	2E-06

DisChr	rsID_refSNP	pos_refSNP	Zhit_ eurasn	Zhit_ euryri	Zhit_ asnyri	Same_ eurasn	Same_ euryri	Same_ asnyri
4	**rs2333328**	**176852836**	0	0	0	1	1	1
9	**rs10869238**	**75803635**	0	0	0	1	1	1
22	**rs136571**	**45767696**	0	0	0	1	1	1
6	**rs579329**	**47822681**	0	0	0	1	1	1
10	**rs11591368**	**53523322**	0	0	0	1	1	1
6	**rs2504907**	**12603401**	0	0	0	1	1	1
19	**rs11083699**	**43755489**	0	0	0	1	1	1
8	**rs73351724**	**114787818**	0	0	0	1	1	1

3	rs1387701	193147894	0	0	0	1	1	1
4	rs6854328	119683492	0	0	0	1	1	1
15	rs1604170	98040887	0	0	0	1	1	1
15	rs1470901	69097765	0	0	0	1	1	1
1	rs6696248	111404291	0	0	0	1	1	1
7	rs9692258	69049578	0	0	0	1	1	1
12	rs4761380	77829418	0	0	0	1	1	1
14	rs1959523	52312746	1	0	1	0	1	0
17	rs7213597	12053126	0	0	0	1	1	1
22	rs6007526	45648224	0	0	0	1	1	1
22	rs535842	27621151	0	0	0	1	1	1
2	rs10190763	20573168	0	0	0	1	1	1
11	rs76472587	47881487	0	0	0	1	1	1
13	rs9549507	112996118	0	0	0	1	1	1
11	rs10834146	23595982	1	1	0	1	1	1
9	rs16925789	109495368	0	0	0	1	1	1
5	rs76671135	144312509	0	0	0	1	1	1
17	rs175382	49388390	0	0	0	1	1	1
4	rs10716645	165101675	0	0	0	1	1	1
4	rs7659549	103006301	0	0	0	1	1	1
13	rs278034	30416637	0	0	0	1	1	1
22	rs2530667	30044151	0	0	0	1	1	1
8	rs9773025	6674458	0	0	0	1	1	1
7	rs10277114	12013649	0	0	0	1	1	1
7	rs686550	54728518	0	0	1	1	1	1
2	rs7587455	240990568	0	0	0	1	1	1
15	rs1191196	77646504	0	0	0	1	1	1
7	rs28369400	132913071	0	0	0	1	1	1
14	rs1950660	94774300	0	0	0	1	1	1
6	rs9452207	93744485	0	0	0	1	1	1
4	rs2045774	82822003	0	0	0	1	1	1
7	rs7787377	89996777	0	0	0	1	1	1
9	rs12686218	114601575	0	0	0	1	1	1
3	rs12330317	100836183	0	0	0	1	1	1
13	rs2781311	87626740	0	0	0	1	1	1
5	rs1422932	167397039	1	0	0	1	1	1
9	rs10115645	107369931	0	0	0	1	1	1
7	rs10952493	154253759	0	0	0	1	1	1
14	rs28501387	81772667	0	0	0	1	1	1
7	rs6947649	83415942	0	0	0	1	1	1
5	rs35733634	12879768	0	0	0	1	1	1
4	rs201086800	66370079	0	0	0	1	1	1
6	rs6938226	118852561	0	0	0	1	1	1
1	rs201832280	151339950	0	0	0	1	1	1
14	rs875799	103618276	0	0	0	1	1	1

8	**rs465**	**90816058**	0	0	0	1	1	1
2	**rs13409781**	**66203352**	0	0	0	1	1	1
4	**rs150411487**	**9061499**	0	0	0	1	1	1
10	**rs17663446**	**86272696**	0	0	0	1	1	1
12	**rs10845348**	**11539880**	0	0	0	1	1	1
9	**rs490491**	**108416462**	0	0	0	1	1	1
17	**rs56256681**	**9712092**	0	0	0	1	1	1
1	**rs3767246**	**21227086**	0	0	0	1	1	1
14	**rs10782420**	**52681605**	0	0	0	1	1	1
17	**rs1875558**	**7040018**	0	0	0	1	1	1
6	**rs1321473**	**137158764**	0	0	0	1	1	1
2	**rs10804341**	**229429905**	0	0	0	1	1	1
15	**rs4778048**	**93401485**	0	0	0	1	1	1
2	**rs6743294**	**229370567**	0	0	0	1	1	1
12	**rs2428387**	**47379311**	0	0	0	1	1	1
11	**rs11212624**	**108298019**	0	0	0	1	1	1
20	**rs6054547**	**6828677**	0	0	0	1	1	1
6	**rs1028483**	**65003887**	0	1	0	1	1	1
3	**rs2242023**	**13670481**	0	0	0	1	1	1
6	**rs6912599**	**9828518**	0	0	0	1	1	1
5	**rs10065424**	**75841888**	0	0	0	1	1	1
11	**rs523750**	**107705009**	0	0	0	1	1	1
10	**rs10900234**	**46200866**	0	0	0	1	1	1
2	**rs13425141**	**210322212**	1	0	1	0	1	0
6	**rs114364056**	**28634891**	0	0	0	1	1	1
8	**rs12540991**	**13079235**	0	0	0	1	1	1
3	**rs73033920**	**164120039**	0	0	0	1	1	1
10	**rs10763143**	**56521303**	0	0	0	1	1	1
9	**rs7036260**	**122911053**	0	0	0	1	1	1
8	**rs4273853**	**22698106**	0	0	0	1	1	1
16	**rs3104790**	**52638663**	0	0	0	1	1	1
1	**rs12564270**	**245571653**	0	0	0	1	1	1
1	**rs10911095**	**182518264**	0	0	0	1	1	1
6	**rs76902944**	**164074426**	0	0	0	1	1	1
4	**rs7691160**	**26457487**	0	0	0	1	1	1
20	**rs6035865**	**21368932**	0	0	0	1	1	1
9	**rs72766254**	**130090926**	0	0	0	1	1	1
9	**rs7847784**	**110001752**	0	0	1	1	1	1
1	**rs7548054**	**39302020**	0	0	0	1	1	1
3	**rs199797915**	**39051874**	0	0	0	1	1	1
10	**rs773948**	**34716034**	0	1	1	1	0	0
5	**rs56777318**	**87825189**	0	0	0	1	1	1
1	**rs200576863**	**154798550**	0	0	0	1	1	1
12	**rs7138235**	**133313237**	0	0	0	1	1	1
20	**rs2983304**	**23508573**	0	0	0	1	1	1

7	rs10950822	20647108	0	0	0	1	1	1
6	rs115700812	32511774	0	0	0	1	1	1
16	rs7187576	25070579	1	0	1	1	1	1
3	rs1388705	161584027	0	0	0	1	0	0
8	rs10955282	103176946	0	0	0	1	1	1
1	rs2256913	72402880	0	0	0	1	1	1
11	rs12277881	6729061	0	0	0	1	1	1
14	rs7156971	54854783	0	0	0	1	1	1
8	rs28439245	3077166	0	0	0	1	1	1
3	rs13085132	106837810	0	0	0	1	1	1
1	rs6665839	49043877	0	0	0	1	1	1
6	rs4236138	56151384	0	0	0	1	1	1
2	rs35463898	71704005	0	0	0	1	1	1
6	rs9688927	92701926	0	0	0	1	1	1
1	rs150016402	94601236	1	0	0	1	1	1
6	rs13199418	79874045	0	0	0	1	1	1
10	rs507098	116062510	0	0	0	1	1	1
18	rs9961465	8569882	0	0	0	1	1	1
21	rs2236478	46917782	0	0	1	1	1	1
16	rs10153134	90091099	0	0	0	1	1	1
11	rs201202588	72258622	0	1	0	1	1	1
14	rs77306894	88960851	0	0	0	1	1	1
20	rs7264816	22955608	0	0	0	1	1	1
20	rs6056189	8811896	0	0	0	1	1	1
2	rs11899581	122712643	0	0	0	1	1	1
10	rs7095313	17399051	0	0	0	1	1	1
5	rs2904945	8777960	0	0	0	1	1	1
11	rs7119996	93389932	0	0	0	1	1	1
3	rs34638579	137385728	0	0	0	1	1	1
13	rs9593302	78829464	0	0	1	1	1	1
8	rs62509924	87103432	0	0	0	1	1	1
1	rs1977125	63772373	0	0	0	1	1	1
10	rs1926801	4433288	0	1	0	1	1	1
2	rs1597944	234504098	0	0	0	1	1	1
10	rs7902931	6141942	0	1	0	1	1	1
4	rs200356168	7864140	0	0	0	1	1	1
2	rs11126341	71916661	0	0	0	1	1	1
4	rs147440574	128598143	0	0	0	1	1	1
7	rs10276126	131306210	0	0	0	1	1	1
6	rs366920	160737950	0	0	0	1	1	1
7	rs28491038	104366640	0	1	0	1	1	1
8	rs7836279	13775292	0	0	0	1	1	1
17	rs2411041	74913863	0	0	0	1	1	1
20	rs6092006	36809169	0	0	0	1	1	1
20	rs72620874	1895889	0	0	0	1	1	1

2	**rs76136841**	**206820159**	0	0	0	1	1	1
20	**rs138273314**	**19935337**	0	0	0	1	1	1
4	**rs4862032**	**183071431**	0	0	0	1	1	1
2	**rs13003505**	**159156020**	0	0	0	1	1	1
9	**rs2017392**	**112820620**	0	0	0	1	1	1
3	**rs729942**	**87066095**	0	0	0	1	1	1
8	**rs59026256**	**66912273**	0	0	0	1	1	1
5	**rs433211**	**151324761**	0	0	0	1	1	1
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9	**rs9775725**	**27244202**	1	1	0	1	1	1
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4	**rs12696692**	**6735941**	0	0	0	1	1	1
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9	**rs60795901**	**78895500**	0	0	0	1	1	1
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7	**rs854074**	**95298272**	0	1	0	1	1	1
9	**rs10980731**	**113838859**	0	0	0	1	1	1
11	**rs1426926**	**87903141**	0	0	0	1	1	1
2	**rs374954**	**176084790**	0	0	0	1	1	1
6	**rs2327037**	**8228490**	1	0	0	1	1	1
4	**rs62325107**	**154675105**	0	0	0	1	1	1
12	**rs11532381**	**79936694**	0	0	0	1	1	1
22	**rs136482**	**32590036**	0	0	0	1	1	1
1	**rs17021956**	**119082264**	0	0	1	1	1	1
14	**rs10141742**	**59406089**	1	0	0	0	1	0
7	**rs2005764**	**105778633**	0	0	0	1	1	1
3	**rs9816837**	**178705604**	0	0	0	1	1	1
4	**rs631179**	**130411127**	0	0	0	1	1	1
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4	**rs6824500**	**35487085**	0	0	0	1	1	1
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2	**rs72775986**	**12602098**	0	1	0	1	1	1
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9	**rs1836460**	**110966650**	0	0	0	1	1	1
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9	**rs2378675**	**87619462**	0	0	0	1	1	1
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4	**rs11930919**	**92818352**	0	0	0	1	1	1
3	**rs7629387**	**95193439**	1	0	1	1	1	1
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12	rs12230050	93990553	0	0	0	1	1	1
21	rs35265519	36683674	0	0	0	1	1	1
11	rs12798276	32583375	0	0	0	1	1	1
5	rs34446169	13261448	0	0	0	1	1	1
10	rs2505398	32633516	0	0	0	1	1	1
5	rs2918443	85213684	1	0	0	1	1	1
5	rs244408	110021869	0	0	0	1	1	1
10	rs2986035	105233110	0	1	0	1	1	1
7	rs2390472	21156006	1	0	0	1	1	1
6	rs1933989	103065057	0	0	0	1	1	1
14	rs1147446	66461978	0	0	0	1	1	1
15	rs4356443	88200417	0	0	0	1	1	1
6	rs9484232	139365330	0	0	0	1	1	1
6	rs3778021	36948805	0	0	0	1	1	1
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10	rs10906446	13712074	1	1	0	1	1	1
4	rs4395470	73055791	0	0	0	1	1	1
20	rs2207889	34224898	0	0	0	1	1	1
5	rs146990484	168728193	0	0	0	1	1	1
5	rs70957010	20984328	0	0	0	1	1	1
3	rs7614041	102578156	0	0	0	1	1	1
5	rs55753822	55753822	0	0	0	1	1	1
18	rs9950923	65714987	0	0	0	1	1	1
15	rs79173965	74170559	0	0	0	1	1	1
15	rs12439879	47179681	0	0	0	1	1	1
8	rs984990	114368635	0	0	0	1	1	1
6	rs9399242	138827658	0	0	0	1	1	1
12	rs10748463	47580270	0	0	0	1	1	1
18	rs12104083	13739269	1	0	1	1	1	1
4	rs13135410	42565734	0	0	0	1	1	1
15	rs7174210	58809493	0	0	0	1	1	1
20	rs399698	15368919	0	0	0	1	1	1
2	rs17006895	71575470	0	0	0	1	1	1
19	rs55661666	15069191	0	0	0	1	1	1
11	rs7941643	59460632	0	0	0	1	1	1
2	rs1384781	145601057	1	0	1	1	1	1
13	rs6492290	111254995	0	0	0	1	1	1
8	rs684904	109199417	0	0	0	1	1	1
4	rs17006215	123775433	0	0	0	1	1	1
22	rs2156927	47288807	0	0	0	1	1	1
12	rs10774768	115193194	0	0	0	1	1	1
1	rs2232809	171750181	0	0	0	1	1	1
3	rs36196715	66271617	0	0	1	1	1	1
11	rs8186211	50542195	0	0	0	1	1	1
14	rs9671906	84465538	0	0	0	1	1	1

14	**rs2753634**	**86144162**	0	0	0	1	1	1
14	**rs7155200**	**86177170**	0	0	0	1	1	1
5	**rs13187871**	**60554657**	0	1	0	1	1	1
13	**rs4551930**	**62709282**	0	0	0	1	1	1
2	**rs7578058**	**168040115**	1	1	0	1	1	1
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12	rs7315657	44111950	0	0	0
10	rs12356466	31142344	0	0	0
8	rs8180941	90336707	0	0	0
14	rs113204453	44482023	0	0	0
5	rs2910299	160790065	0	0	0
15	rs11854693	58712965	0	0	0
2	rs334068	179005438	0	0	0
13	rs7317830	57274268	0	0	0
9	rs10984992	123473416	0	0	0
9	rs55695858	138440554	0	0	0
1	rs59048447	2766314	0	0	0
4	rs432164	177391093	0	0	0
3	rs4339124	82316577	0	0	0
11	rs7952283	103837145	0	0	0
11	rs11213382	97836453	0	0	0
1	rs10604003	237788262	0	0	0
4	rs1383567	34531200	0	0	0
12	rs12313074	117206787	0	0	0
7	rs11772033	48527011	0	0	0
4	rs1129304	158092422	0	0	0
3	rs12629621	66883699	0	0	0
7	rs6948652	157225138	0	0	0
14	rs6573543	64499805	0	0	0
5	rs154668	57598572	0	0	0
2	rs10207163	69014280	0	0	0
15	rs1564688	93761742	0	0	0
1	rs4255374	237561785	0	0	0
16	rs441832	83881337	0	0	0
7	rs12537292	201060	0	0	0
1	rs4287207	107714954	0	0	0
8	rs671655	60875824	0	0	0
12	rs11169127	50120901	0	0	0

11	rs11217793	120161886	0	0	0
18	rs9946168	34634176	0	0	0
9	rs11789058	119826169	0	0	0
13	rs75297616	53308128	0	0	0
2	rs6749895	172875442	0	0	0
10	rs668014	55320664	0	0	0
14	rs9323205	51586467	0	0	0
5	rs2434352	68333094	0	0	0
1	rs10453833	111909959	0	0	0
7	rs2709956	83039231	0	0	0
16	rs149766632	78638797	0	0	0
6	rs28869479	120471593	0	0	0
1	rs598031	5333479	0	1	1
22	rs28755	29685711	0	0	0
8	rs12676126	24960158	0	0	0
15	rs12324446	94721997	0	0	0
18	rs34623028	1312629	0	0	0
6	rs6908931	144735877	0	0	0
10	rs10900190	45733045	0	0	0
3	rs12054033	132531654	0	0	0
15	rs58193517	49834494	0	0	0
6	rs2798364	107161116	0	0	0
14	rs11490385	31718057	0	0	0
6	rs515144	81659184	0	0	0
9	rs7467510	140181362	0	0	0
1	rs12070530	12138629	0	0	0
4	rs7440026	116326266	0	0	0
6	rs116440502	32637135	0	0	0
5	rs165188330	165188330	0	0	0
12	rs12315134	38419857	0	0	0
16	rs4783251	82698974	0	0	0
10	rs12780864	22421961	0	0	0
6	rs12192993	12380922	0	0	0
4	rs11735893	142896936	1	0	1
14	rs1761003	46912966	0	0	0
12	rs142837217	86002875	0	0	0
2	rs6739828	43616008	0	0	0
8	rs2891977	122180353	0	0	0
9	rs7874886	18865265	0	0	0
15	rs7170241	62810138	0	0	0
6	rs7775711	112161786	0	0	0
10	rs928578	99846671	0	0	0
18	rs59713847	12330337	0	0	0
3	rs6438092	95479393	0	0	0
17	rs4796450	6139713	0	1	1

1	**rs11102013**	**110376463**	0	0	0
4	**rs3967098**	**144195781**	0	0	0
10	**rs11599612**	**86422743**	0	0	0
11	**rs1784430**	**102474813**	0	0	0
19	**rs454904**	**44511589**	0	0	0
1	**rs289686**	**76608491**	0	0	0
3	**rs1875732**	**192313035**	0	0	0
3	**rs7610236**	**197083393**	0	0	0
6	**rs2048695**	**163338231**	0	0	0
11	**rs10838609**	**5780716**	0	0	0
19	**rs3826798**	**5785113**	0	0	0
1	**rs609125**	**22915030**	0	0	0
2	**rs200778275**	**162693103**	0	0	0
9	**rs116941153**	**112797749**	0	0	0
14	**rs202227171**	**87861177**	0	0	0
13	**rs3832886**	**76419421**	0	0	0
7	**rs12669437**	**95253404**	0	0	0
6	**rs4706299**	**88491110**	0	0	0
5	**rs78479231**	**21293851**	0	0	0
2	**rs12993670**	**215491816**	0	0	0
4	**rs12108436**	**77910959**	0	0	0
19	**rs11084579**	**31802723**	0	0	0

Supplementary Table 2

DisChr	rsID_refSNP	pos_refSNP	Allele Frequency EUR	Allele Frequency ASN	Allele Frequency YRI	beta EUR	stdbeta EUR	P EUR
4	**rs2333328**	**176852836**	0,54	0,60	0,28	0,26	0,04	4E-09
9	**rs10869238**	**75803635**	0,18	0,46	0,50	0,35	0,06	2E-08
22	**rs136575**	**45769245**	0,49	0,67	0,99	0,40	0,05	1E-18
6	**rs579329**	**47822681**	0,48	0,73	0,41	0,22	0,05	1E-06
10	**rs10999327**	**53522817**	0,42	0,06	0,48	0,30	0,05	5E-11
6	**rs2516226**	**12604062**	0,17	0,19	0,94	0,38	0,06	2E-09
8	**rs73351724**	**114787818**	0,20	0,65	0,28	0,23	0,06	8E-05
3	**rs1387701**	**193147894**	0,77	0,63	0,63	0,31	0,05	2E-09
4	**rs4340779**	**119678580**	0,71	0,62	0,12	0,28	0,05	7E-09
15	**rs1604172**	**98040555**	0,36	0,53	0,51	0,31	0,05	1E-10
15	**rs1470901**	**69097765**	0,53	0,52	0,23	0,28	0,04	4E-10
1	**rs7556147**	**111407322**	0,28	0,14	0,09	0,31	0,05	4E-09
7	**rs9692258**	**69049578**	0,73	0,80	0,84	0,35	0,05	3E-12
12	**rs4761380**	**77829418**	0,51	0,53	0,38	0,26	0,05	1E-08
14	**rs1959524**	**52312705**	0,82	0,98	0,36	0,28	0,06	7E-07
17	**rs55969697**	**15264671**	0,27	0,22	0,41	0,26	0,05	3E-08

17	**rs7213597**	**12053126**	0,11	0,45	0,45	0,39	0,08	4E-07
22	**rs6007521**	**45647534**	0,29	0,21	0,15	0,32	0,05	3E-10
22	**rs535842**	**27621151**	0,80	0,33	0,67	0,31	0,05	2E-08
2	**rs6754782**	**20573530**	0,32	0,76	0,56	0,32	0,05	4E-10
13	**rs9549507**	**112996118**	0,30	0,60	0,39	0,22	0,05	1E-05
9	**rs16925789**	**109495368**	0,19	0,10	0,76	0,35	0,06	5E-09
17	**rs175381**	**49387207**	0,56	0,61	0,85	0,29	0,04	2E-10
4	**rs7659549**	**103006301**	0,35	0,37	0,23	0,33	0,05	8E-12
13	**rs278034**	**30416637**	0,64	0,55	0,32	0,33	0,05	1E-12
22	**rs2531850**	**30043563**	0,48	0,33	0,11	0,24	0,05	9E-08
8	**rs9773025**	**6674458**	0,47	0,95	0,76	0,26	0,05	2E-08
7	**rs10228515**	**12013256**	0,42	0,54	0,71	0,24	0,05	2E-07
15	**rs1191196**	**77646504**	0,27	0,59	0,48	0,35	0,05	3E-11
14	**rs8023023**	**94773876**	0,42	0,91	0,34	0,21	0,05	4E-06
6	**rs9452207**	**93744485**	0,21	0,12	0,63	0,32	0,06	3E-08
4	**rs2045774**	**82822003**	0,57	0,37	0,08	0,22	0,05	1E-06
7	**rs7787377**	**89996777**	0,44	0,38	0,71	0,31	0,05	3E-11
9	**rs12686218**	**114601575**	0,12	0,36	0,23	0,31	0,07	2E-05
13	**rs2781311**	**87626740**	0,31	0,63	0,67	0,31	0,05	6E-10
5	**rs1422932**	**167397039**	0,39	0,36	0,31	0,37	0,05	8E-15
9	**rs10115645**	**107369931**	0,22	0,33	0,04	0,24	0,06	2E-05
7	**rs10952494**	**154253804**	0,68	0,47	0,53	0,30	0,05	1E-10
14	**rs6574639**	**81771541**	0,79	0,65	0,74	0,35	0,05	2E-10
7	**rs6947649**	**83415942**	0,79	0,55	0,86	0,32	0,05	2E-09
5	**rs35733634**	**12879768**	0,29	0,44	0,75	0,21	0,05	5E-05
4	**rs201086800**	**66370079**	0,37	0,36	0,14	0,34	0,05	4E-12
6	**rs6938041**	**118852468**	0,53	0,26	0,38	0,27	0,05	2E-09
1	**rs201832280**	**151339950**	0,68	0,24	0,45	0,23	0,05	1E-06
8	**rs465**	**90816058**	0,58	0,52	0,97	0,25	0,05	6E-08
12	**rs10845348**	**11539880**	0,66	0,44	0,31	0,25	0,05	1E-07
9	**rs490491**	**108416462**	0,52	0,70	0,69	0,31	0,05	7E-12
17	**rs9914518**	**9709946**	0,45	0,57	0,68	0,26	0,05	1E-08
14	**rs10782420**	**52681605**	0,42	0,84	0,25	0,31	0,05	4E-11
6	**rs1321473**	**137158764**	0,63	0,53	0,73	0,33	0,05	5E-13
2	**rs10804341**	**229429905**	0,72	0,92	0,34	0,36	0,05	2E-13
15	**rs4778048**	**93401485**	0,61	0,40	0,81	0,34	0,05	1E-13
2	**rs6743294**	**229370567**	0,42	0,64	0,97	0,23	0,05	1E-06
12	**rs2428387**	**47379311**	0,17	0,05	0,14	0,35	0,06	3E-08
11	**rs7952492**	**108296680**	0,45	0,42	0,43	0,20	0,05	1E-05
3	**rs9843344**	**13670536**	0,69	0,99	0,80	0,30	0,05	1E-10
6	**rs4373367**	**9830006**	0,34	0,03	0,24	0,30	0,05	5E-10
5	**rs10065424**	**75841888**	0,47	0,70	0,73	0,27	0,05	5E-09
11	**rs28758793**	**107707070**	0,42	0,46	0,75	0,26	0,04	4E-09
10	**rs10900234**	**46200866**	0,55	0,68	0,55	0,26	0,04	4E-09
2	**rs13425141**	**210322212**	0,26	0,00	0,06	0,30	0,05	2E-08

6	**rs114364056**	**28634891**	0,22	0,16	0,41	0,31	0,06	9E-08
8	**rs2697748**	**13079233**	0,28	0,66	0,39	0,27	0,05	1E-07
3	**rs9873142**	**164119265**	0,33	0,35	0,59	0,29	0,05	1E-09
9	**rs7036260**	**122911053**	0,29	0,28	0,40	0,30	0,05	2E-09
8	**rs4273853**	**22698106**	0,39	0,34	0,30	0,34	0,05	1E-12
16	**rs3104790**	**52638663**	0,43	0,81	0,44	0,31	0,05	9E-12
1	**rs10911089**	**182514852**	0,54	0,45	0,41	0,27	0,04	9E-10
6	**rs9364697**	**164074139**	0,53	0,95	0,28	0,24	0,04	4E-08
4	**rs3109848**	**26457168**	0,81	0,84	0,66	0,31	0,05	8E-09
20	**rs6035865**	**21368932**	0,72	0,83	0,46	0,29	0,05	3E-09
9	**rs10816472**	**110001457**	0,41	0,24	0,32	0,29	0,05	9E-10
1	**rs7548054**	**39302020**	0,65	0,34	0,10	0,33	0,05	2E-12
3	**rs4645092**	**39051718**	0,33	0,49	0,94	0,33	0,05	6E-12
10	**rs773948**	**34716034**	0,68	0,62	0,99	0,21	0,05	5E-06
1	**rs200576863**	**154798550**	0,26	0,74	0,38	0,26	0,05	5E-07
12	**rs7138235**	**133313237**	0,52	0,33	0,20	0,25	0,04	3E-08
20	**rs2983304**	**23508573**	0,58	0,43	0,19	0,30	0,04	4E-11
7	**rs10950821**	**20647015**	0,26	0,50	0,53	0,20	0,05	1E-04
6	**rs115645489**	**32511977**	0,36	0,36	0,63	0,29	0,05	4E-09
16	**rs7187576**	**25070579**	0,59	0,29	0,32	0,37	0,05	8E-16
3	**rs1388705**	**161584027**	0,24	0,39	0,01	0,18	0,05	1E-03
8	**rs10955282**	**103176946**	0,46	0,45	0,55	0,27	0,05	2E-09
11	**rs1395558**	**6727468**	0,67	0,53	0,31	-0,24	0,05	1E-06
14	**rs1955463**	**54854386**	0,33	0,41	0,41	0,23	0,05	2E-06
8	**rs17079639**	**3077005**	0,24	0,36	0,30	0,28	0,06	2E-07
3	**rs13085132**	**106837810**	0,47	0,58	0,48	0,24	0,05	2E-07
1	**rs6665839**	**49043877**	0,17	0,26	0,40	0,24	0,06	2E-04
6	**rs4236138**	**56151384**	0,13	0,59	0,03	0,37	0,07	2E-07
2	**rs35463898**	**71704005**	0,33	0,64	0,85	0,29	0,05	5E-09
1	**rs150016402**	**94601236**	0,39	0,25	0,23	0,37	0,05	9E-15
6	**rs13199418**	**79874045**	0,42	0,15	0,35	0,26	0,05	1E-08
10	**rs507098**	**116062510**	0,16	0,32	0,52	0,32	0,06	6E-07
18	**rs9961465**	**8569882**	0,35	0,39	0,54	0,29	0,05	1E-09
21	**rs2236478**	**46917782**	0,36	0,32	0,64	0,27	0,05	2E-08
16	**rs10153134**	**90091099**	0,38	0,31	0,40	0,26	0,05	3E-08
11	**rs201202588**	**72258622**	0,33	0,31	0,41	0,36	0,05	3E-13
14	**rs1152376**	**88961465**	0,68	0,58	0,19	-0,26	0,06	5E-06
20	**rs6113869**	**22953698**	0,34	0,55	0,45	0,29	0,05	5E-10
2	**rs61227128**	**122705170**	0,27	0,16	0,30	0,33	0,05	3E-10
10	**rs7095313**	**17399051**	0,20	0,10	0,34	0,32	0,06	2E-08
11	**rs7119996**	**93389932**	0,50	0,77	0,68	0,25	0,04	4E-08
3	**rs34638579**	**137385728**	0,32	0,25	0,49	0,32	0,05	3E-10
13	**rs11282754**	**78829394**	0,31	0,21	0,18	-0,27	0,05	1E-08
8	**rs61629815**	**87104916**	0,35	0,51	0,06	0,28	0,05	9E-09
1	**rs1977125**	**63772373**	0,58	0,51	0,22	0,22	0,05	7E-07

10	**rs12770204**	**4432617**	0,34	0,01	0,15	0,31	0,05	4E-10
2	**rs1597944**	**234504098**	0,50	0,53	0,16	0,29	0,05	2E-10
4	**rs35659552**	**37709539**	0,15	0,01	0,10	0,36	0,07	3E-08
10	**rs7902931**	**6141942**	0,50	0,25	0,58	0,16	0,05	4E-04
4	**rs59283470**	**7863978**	0,73	0,71	0,52	0,30	0,05	1E-09
4	**rs147440574**	**128598143**	0,52	0,22	0,22	0,31	0,05	8E-12
6	**rs378479**	**160737140**	0,52	0,26	0,30	0,28	0,05	1E-09
7	**rs28491038**	**104366640**	0,37	0,12	0,35	0,34	0,05	1E-12
8	**rs7836279**	**13775292**	0,45	0,48	0,19	0,23	0,04	5E-07
20	**rs6092006**	**36809169**	0,30	0,17	0,27	0,26	0,05	4E-07
20	**rs6136376**	**1896244**	0,37	0,66	0,32	0,26	0,05	5E-08
2	**rs76136841**	**206820159**	0,13	0,46	0,01	0,29	0,07	4E-05
20	**rs138273314**	**19935337**	0,36	0,64	0,41	0,28	0,05	1E-08
4	**rs4862032**	**183071431**	0,54	0,71	0,77	0,23	0,05	4E-07
2	**rs13003505**	**159156020**	0,41	0,60	0,27	0,29	0,05	4E-10
3	**rs11708814**	**87063964**	0,75	0,50	0,07	0,30	0,05	1E-09
8	**rs59026256**	**66912273**	0,25	0,06	0,34	0,29	0,05	6E-08
5	**rs302396**	**151324533**	0,69	0,36	0,34	0,34	0,05	2E-12
12	**rs7132347**	**55714876**	0,76	0,88	0,81	0,31	0,05	2E-09
17	**rs4605213**	**49244747**	0,34	0,22	0,97	0,36	0,05	2E-13
8	**rs1392143**	**3357940**	0,79	0,85	0,66	0,26	0,05	1E-06
1	**rs17407657**	**66171667**	0,29	0,02	0,19	0,30	0,05	6E-09
7	**rs321282**	**95297614**	0,64	0,50	0,38	0,33	0,05	1E-12
2	**rs202028570**	**41482288**	0,39	0,22	0,32	0,26	0,04	7E-09
9	**rs10980731**	**113838859**	0,23	0,27	0,05	0,29	0,06	1E-07
11	**rs1426926**	**87903141**	0,42	0,29	0,45	0,27	0,05	3E-09
2	**rs374954**	**176084790**	0,25	0,40	0,36	0,24	0,05	1E-05
6	**rs148601969**	**8226853**	0,41	0,54	0,64	0,20	0,05	1E-04
4	**rs62325107**	**154675105**	0,89	0,88	0,66	0,30	0,07	4E-06
12	**rs11532381**	**79936694**	0,12	0,31	0,95	0,29	0,07	4E-05
22	**rs136483**	**32590069**	0,49	0,12	0,91	0,25	0,04	2E-08
14	**rs10141742**	**59406089**	0,67	0,97	0,93	0,26	0,05	4E-08
7	**rs10234007**	**105778435**	0,29	0,40	0,88	0,25	0,05	8E-07
3	**rs9815772**	**178704926**	0,68	0,53	0,72	0,25	0,05	1E-07
4	**rs631179**	**130411127**	0,63	0,58	0,57	0,30	0,05	8E-11
3	**rs66861711**	**162227359**	0,13	0,30	0,11	0,29	0,07	3E-05
5	**rs75923162**	**24604987**	0,59	0,53	0,10	0,31	0,05	8E-12
6	**rs4707552**	**90300841**	0,73	0,64	0,30	0,23	0,05	3E-05
15	**rs56200331**	**95617954**	0,16	0,20	0,19	0,29	0,06	6E-06
10	**rs1250538**	**81037800**	0,32	0,46	0,15	0,30	0,05	2E-09
2	**rs72775988**	**12602099**	0,44	0,78	0,16	0,33	0,05	7E-13
4	**rs1545788**	**5715069**	0,60	0,59	0,91	0,31	0,05	9E-12
9	**rs519980**	**110961597**	0,45	0,42	0,02	0,23	0,05	7E-07
1	**rs6656494**	**154839799**	0,43	0,89	0,55	0,22	0,05	2E-06
9	**rs200533218**	**87619460**	0,66	0,35	0,87	0,23	0,05	6E-07

17	**rs2640842**	**31014803**	0,65	0,72	0,46	0,30	0,05	7E-11
4	**rs991346**	**92817071**	0,11	0,17	0,47	0,29	0,07	6E-05
3	**rs13093484**	**95191114**	0,46	0,48	0,55	0,26	0,04	7E-09
13	**rs2993574**	**96067494**	0,50	0,38	0,06	0,27	0,04	2E-09
7	**rs1179608**	**75245398**	0,20	0,27	0,62	0,26	0,06	1E-05
12	**rs12230050**	**93990553**	0,26	0,41	0,57	0,25	0,05	1E-06
21	**rs57592847**	**36682910**	0,71	0,58	0,22	0,24	0,05	5E-07
11	**rs12798276**	**32583375**	0,14	0,61	0,09	0,25	0,07	2E-04
5	**rs34446169**	**13261448**	0,82	0,57	0,49	0,32	0,06	2E-08
10	**rs2505398**	**32633516**	0,69	0,74	0,49	0,22	0,05	4E-06
5	**rs2918443**	**85213684**	0,42	0,39	0,07	0,19	0,05	3E-05
5	**rs244408**	**110021869**	0,80	0,77	0,35	0,25	0,05	6E-06
10	**rs2986034**	**105232580**	0,74	0,80	0,53	0,19	0,05	2E-04
7	**rs2390472**	**21156006**	0,17	0,25	0,23	0,44	0,06	1E-11
14	**rs1147445**	**66463384**	0,18	0,28	0,29	0,34	0,06	7E-09
15	**rs4356443**	**88200417**	0,61	0,67	0,82	0,29	0,05	2E-10
6	**rs11453102**	**139363410**	0,40	0,05	0,41	0,29	0,05	5E-10
6	**rs3778021**	**36948805**	0,37	0,13	0,63	0,22	0,05	2E-06
1	**rs1568134**	**189822309**	0,20	0,36	0,57	0,24	0,06	2E-05
10	**rs10906445**	**13712038**	0,43	0,04	0,22	0,35	0,05	3E-14
4	**rs11727317**	**73054448**	0,32	0,80	0,62	0,36	0,05	5E-13
5	**rs146990484**	**168728193**	0,72	0,79	0,95	0,28	0,05	1E-08
5	**rs67533941**	**20984272**	0,61	0,93	0,89	0,28	0,05	2E-09
3	**rs35931086**	**102579206**	0,64	0,71	0,34	0,26	0,05	4E-08
5	**rs55753822**	**55753822**	0,24	0,36	0,10	0,24	0,05	9E-06
18	**rs9950923**	**65714987**	0,25	0,42	0,10	0,24	0,05	1E-05
15	**rs79173965**	**74170559**	0,34	0,05	0,04	0,37	0,05	1E-13
15	**rs7166592**	**47179916**	0,31	0,74	0,49	0,33	0,05	6E-11
8	**rs984990**	**114368635**	0,68	0,74	0,43	0,27	0,05	1E-08
6	**rs9399242**	**138827658**	0,26	0,47	0,02	0,26	0,05	9E-07
12	**rs10748463**	**47580270**	0,63	0,65	0,57	0,29	0,05	5E-10
18	**rs12104083**	**13739269**	0,47	0,86	0,23	0,20	0,04	5E-06
4	**rs13135410**	**42565734**	0,21	0,40	0,07	0,31	0,06	7E-08
20	**rs399698**	**15368919**	0,30	0,17	0,08	0,29	0,05	1E-08
2	**rs17006895**	**71575470**	0,22	0,00	0,57	0,26	0,06	7E-06
19	**rs55661666**	**15069191**	0,10	0,11	0,30	0,41	0,08	3E-07
11	**rs7941643**	**59460632**	0,07	0,05	0,40	0,35	0,10	4E-04
2	**rs1384781**	**145601057**	0,63	0,80	0,43	0,24	0,05	2E-07
13	**rs6492292**	**111255057**	0,36	0,41	0,59	0,24	0,05	2E-06
8	**rs36070162**	**109199296**	0,47	0,49	0,68	0,25	0,05	4E-08
22	**rs1981438**	**47288122**	0,73	0,59	0,26	0,34	0,05	4E-12
12	**rs10774768**	**115193194**	0,47	0,28	0,63	0,29	0,05	1E-10
1	**rs2232809**	**171750181**	0,62	0,67	0,85	0,28	0,05	7E-10
11	**rs8186211**	**50542195**	0,09	0,25	0,23	0,33	0,08	9E-05
14	**rs9671901**	**84465529**	0,27	0,34	0,54	0,35	0,05	1E-10

14	**rs2638802**	**86145123**	0,39	0,42	0,16	0,32	0,05	2E-11
14	**rs10145617**	**86176395**	0,58	0,56	0,87	0,26	0,04	7E-09
5	**rs13167246**	**60554383**	0,85	0,92	0,38	0,41	0,06	3E-11
13	**rs111538000**	**62708839**	0,17	0,05	0,35	0,24	0,06	1E-04
2	**rs4000962**	**168031396**	0,22	0,40	0,72	0,58	0,10	2E-09
17	**rs11651738**	**80178691**	0,72	0,93	0,90	0,31	0,05	2E-10
3	**rs7640053**	**79531271**	0,64	0,51	0,97	0,25	0,05	4E-08
16	**rs3759986**	**21225224**	0,34	0,16	0,23	0,28	0,05	8E-09
3	**rs6805084**	**111984736**	0,57	0,76	0,44	0,29	0,05	4E-10
5	**rs4867482**	**32893465**	0,36	0,49	0,51	0,30	0,05	4E-10
2	**rs10196874**	**235599018**	0,26	0,60	0,22	0,22	0,05	3E-05
17	**rs7501427**	**77726549**	0,56	0,56	0,32	0,21	0,04	3E-06
7	**rs9639516**	**25729418**	0,32	0,94	0,40	0,28	0,05	1E-08
3	**rs62253005**	**53978529**	0,30	0,42	0,02	0,32	0,05	6E-11
7	**rs4419707**	**67223257**	0,24	0,20	0,37	0,34	0,06	1E-09
5	**rs4134393**	**30190699**	0,66	0,27	0,76	0,28	0,05	1E-09
4	**rs199541723**	**106416147**	0,85	0,49	0,74	0,21	0,06	4E-04
6	**rs139304043**	**142387979**	0,13	0,15	0,11	0,39	0,07	4E-08
1	**rs7549723**	**150541812**	0,66	0,67	0,45	0,26	0,05	1E-08
12	**rs11179617**	**41446008**	0,16	0,07	0,02	0,41	0,06	4E-10
13	**rs9512696**	**28012527**	0,67	0,38	0,31	0,32	0,05	8E-12
16	**rs9938541**	**81045228**	0,23	0,44	0,16	0,36	0,06	1E-10
14	**rs1950787**	**60071972**	0,53	0,85	0,11	0,27	0,04	1E-09
3	**rs2194607**	**21523342**	0,33	0,68	0,53	0,30	0,05	2E-09
7	**rs2374296**	**151626130**	0,60	0,25	0,77	0,29	0,05	3E-10
15	**rs16962490**	**49743628**	0,22	0,47	0,23	0,30	0,06	2E-07
4	**rs10710521**	**176988797**	0,65	0,57	0,37	0,26	0,05	3E-08
3	**rs35910618**	**161660914**	0,33	0,46	0,41	0,27	0,05	3E-08
5	**rs888777**	**168712456**	0,76	0,77	0,89	0,31	0,05	2E-09
2	**rs12465480**	**49445554**	0,44	0,55	0,44	0,29	0,05	3E-10
3	**rs1563980**	**28800886**	0,68	0,92	0,72	0,30	0,05	1E-10
8	**rs10089687**	**6795851**	0,15	0,21	0,44	0,31	0,07	2E-06
12	**rs7974884**	**81309283**	0,15	0,29	0,65	0,27	0,07	7E-05
7	**rs200586366**	**97269518**	0,30	0,52	0,78	0,33	0,05	2E-10
7	**rs76190866**	**76915613**	0,18	0,11	0,48	0,27	0,06	7E-06
8	**rs35066759**	**23318892**	0,27	0,42	0,28	0,28	0,05	2E-07
6	**rs384323**	**9020424**	0,52	0,35	0,12	0,27	0,04	3E-09
10	**rs6585241**	**115486610**	0,80	0,86	0,95	0,31	0,05	1E-08
4	**rs2667714**	**40038395**	0,61	0,60	0,19	0,34	0,05	4E-11
11	**rs7114635**	**90344354**	0,42	0,65	0,52	0,28	0,05	3E-09
3	**rs17012429**	**74409330**	0,06	0,26	0,02	0,32	0,10	8E-04
2	**rs72775667**	**13800460**	0,17	0,08	0,34	0,34	0,06	5E-08
4	**rs1449763**	**27688976**	0,67	0,56	0,44	0,25	0,05	1E-07
6	**rs9399030**	**132837049**	0,41	0,24	0,17	0,29	0,05	8E-10
17	**rs200905171**	**57755742**	0,10	0,49	0,10	0,28	0,08	4E-04

1	**rs7521183**	**237615068**	0,61	0,73	0,25	0,27	0,05	6E-09
6	**rs35911690**	**29867954**	0,71	0,54	0,68	0,37	0,05	1E-14
2	**rs1179683**	**217751546**	0,66	0,38	0,60	0,30	0,05	6E-10
8	**rs1866700**	**137519028**	0,75	0,67	0,69	0,29	0,05	1E-08
6	**rs199607379**	**152661834**	0,16	0,04	0,10	0,37	0,06	8E-09
18	**rs11663656**	**57567638**	0,19	0,42	0,18	0,26	0,06	1E-05
7	**rs12705985**	**114337975**	0,38	0,12	0,09	0,28	0,05	7E-10
3	**rs61690667**	**186926347**	0,13	0,30	0,15	0,47	0,07	5E-11
5	**rs5870400**	**109481424**	0,66	0,76	0,35	0,21	0,05	4E-06
4	**rs4691362**	**157527761**	0,19	0,38	0,11	0,25	0,06	2E-05
4	**rs12507474**	**96576002**	0,58	0,46	0,32	0,23	0,05	5E-07
17	**rs58875634**	**80091726**	0,46	0,86	0,48	0,30	0,05	2E-11
8	**rs7817489**	**77661560**	0,16	0,46	0,72	0,27	0,06	2E-05
1	**rs111772533**	**26523404**	0,19	0,02	0,21	0,31	0,06	2E-07
20	**rs8115705**	**4327451**	0,23	0,14	0,27	0,30	0,06	3E-08
5	**rs13167124**	**1223940**	0,43	0,25	0,66	0,32	0,05	3E-12
4	**rs75874971**	**107457067**	0,46	0,65	0,59	0,27	0,04	1E-09
9	**rs7039175**	**6348355**	0,57	0,70	0,31	0,29	0,05	2E-10
11	**rs11026630**	**22565466**	0,60	0,37	0,02	0,28	0,05	1E-09
17	**rs684690**	**6577803**	0,17	0,31	0,38	0,25	0,06	1E-04
2	**rs7599471**	**20904018**	0,28	0,35	0,42	0,29	0,05	2E-08
7	**rs12669900**	**135702344**	0,25	0,33	0,29	0,22	0,05	3E-05
4	**rs201189120**	**163298951**	0,25	0,06	0,01	0,31	0,05	7E-09
16	**rs12448127**	**25510655**	0,45	0,19	0,59	0,24	0,05	1E-07
12	**rs11065695**	**109595386**	0,84	0,49	0,22	0,22	0,06	1E-04
11	**rs77626887**	**69861644**	0,08	0,42	0,24	0,31	0,09	2E-04
4	**rs62329001**	**104178265**	0,23	0,20	0,05	0,33	0,05	2E-09
6	**rs34932157**	**104281272**	0,62	0,64	0,65	0,26	0,05	2E-08
6	**rs10456703**	**13739490**	0,24	0,17	0,38	0,35	0,06	3E-10
3	**rs13088837**	**63459125**	0,25	0,39	0,31	0,29	0,05	3E-08
3	**rs68015175**	**5497135**	0,43	0,32	0,31	0,26	0,05	1E-08
4	**rs1316866**	**85074129**	0,39	0,58	0,85	0,28	0,05	4E-09
13	**rs7994720**	**64583323**	0,69	0,54	0,45	0,27	0,05	2E-08
9	**rs4272463**	**20999770**	0,34	0,53	0,32	0,29	0,05	5E-09
3	**rs1589439**	**118586026**	0,41	0,52	0,14	0,28	0,05	3E-09
12	**rs1504558**	**98568966**	0,31	0,10	0,64	0,28	0,05	7E-10
2	**rs2053804**	**224020406**	0,65	0,60	0,47	0,30	0,05	9E-11
20	**rs856959**	**61411432**	0,77	0,56	0,97	0,28	0,05	1E-07
15	**rs12592571**	**59707163**	0,73	0,52	0,11	0,30	0,05	8E-10
4	**rs7675641**	**161737304**	0,65	0,86	0,85	0,33	0,05	1E-12
18	**rs4581807**	**68874816**	0,74	0,90	0,45	0,23	0,05	3E-06
17	**rs9897027**	**51422273**	0,48	0,23	0,35	0,29	0,05	3E-10
22	**rs4821661**	**37782256**	0,80	0,81	0,93	0,32	0,05	1E-09
4	**rs201017255**	**106205194**	0,45	0,38	0,51	0,24	0,05	1E-07
5	**rs4296844**	**111175320**	0,32	0,60	0,33	-0,29	0,05	8E-10

6	**rs34059065**	**140301421**	0,30	0,05	0,07	0,33	0,05	2E-10
3	**rs9852128**	**12635623**	0,24	0,03	0,43	0,32	0,05	3E-09
4	**rs35553952**	**187742898**	0,29	0,23	0,34	0,33	0,05	1E-10
5	**rs1058312**	**14509966**	0,31	0,12	0,31	0,29	0,05	5E-09
9	**rs913182**	**97478309**	0,11	0,24	0,65	0,33	0,08	9E-06
1	**rs4653183**	**33984987**	0,18	0,34	0,31	0,32	0,06	2E-07
14	**rs12879605**	**27295802**	0,51	0,18	0,33	0,29	0,05	5E-10
1	**rs386012**	**83155380**	0,61	0,49	0,57	0,25	0,05	6E-08
16	**rs58675609**	**85273226**	0,18	0,24	0,06	0,28	0,06	3E-06
5	**rs76120834**	**125372245**	0,62	0,65	0,68	0,32	0,05	5E-12
15	**rs79988905**	**42677731**	0,14	0,14	0,66	0,38	0,07	4E-08
2	**rs920211**	**211874991**	0,34	0,24	0,22	0,28	0,05	6E-09
12	**rs7958081**	**23093846**	0,47	0,39	0,76	0,21	0,04	2E-06
6	**rs35434813**	**74802323**	0,16	0,02	0,44	0,27	0,06	4E-05
8	**rs3808462**	**116606177**	0,45	0,53	0,90	0,30	0,05	4E-11
14	**rs4020134**	**78420741**	0,63	0,76	0,47	0,28	0,05	7E-10
22	**rs28702070**	**50344912**	0,29	0,40	0,93	0,27	0,05	5E-08
8	**rs4366044**	**135516280**	0,07	0,30	0,40	0,37	0,10	1E-04
8	**rs1834197**	**57755644**	0,20	0,53	0,12	0,35	0,06	6E-09
6	**rs9377003**	**146861189**	0,67	0,22	0,07	0,29	0,05	6E-10
5	**rs12520117**	**163522236**	0,37	0,50	0,49	0,23	0,05	1E-06
2	**rs77847962**	**132742098**	0,38	0,18	0,59	0,35	0,05	2E-13
14	**rs1959120**	**101568230**	0,44	0,72	0,46	0,19	0,05	4E-05
6	**rs6914523**	**65027043**	0,71	0,51	0,84	0,38	0,05	5E-15
14	**rs8009305**	**60383685**	0,09	0,07	0,41	0,26	0,08	7E-04
10	**rs201533606**	**124511268**	0,58	0,70	0,27	0,25	0,05	3E-08
10	**rs11819372**	**116594934**	0,49	0,29	0,63	0,23	0,04	2E-07
3	**rs298756**	**164199329**	0,30	0,36	0,68	0,23	0,05	5E-06
9	**rs551960**	**116384661**	0,78	1,00	0,78	0,28	0,05	4E-08
4	**rs34881324**	**15217750**	0,20	0,53	0,31	0,28	0,06	3E-06
1	**rs10921568**	**194387825**	0,63	0,68	0,54	0,27	0,05	7E-09
12	**rs201055230**	**49143466**	0,40	0,00	0,19	0,27	0,05	4E-09
2	**rs12987457**	**235599023**	0,50	0,30	0,29	0,30	0,05	2E-11
3	**rs34197745**	**48090946**	0,69	0,75	0,35	0,25	0,05	1E-07
13	**rs7339096**	**20711140**	0,35	0,21	0,12	0,27	0,05	4E-08
5	**rs6883952**	**171961443**	0,24	0,14	0,13	0,27	0,05	7E-07
12	**rs12426677**	**7414864**	0,28	0,46	0,15	0,20	0,05	1E-04
5	**rs11241748**	**123846498**	0,37	0,37	0,15	0,27	0,05	2E-08
1	**rs10586161**	**227175967**	0,49	0,15	0,27	0,28	0,05	5E-10
20	**rs34973476**	**43770291**	0,16	0,03	0,06	0,41	0,07	7E-10
1	**rs2236539**	**182096856**	0,57	0,56	0,63	0,25	0,05	2E-08
9	**rs7048995**	**20012984**	0,77	0,66	0,66	0,23	0,05	6E-06
7	**rs72077057**	**152651502**	0,38	0,41	0,25	0,38	0,05	8E-16
1	**rs1501568**	**211087439**	0,61	0,81	0,70	0,27	0,05	8E-09
17	**rs3815358**	**62010270**	0,64	0,45	0,07	0,21	0,05	5E-06

14	**rs13156**	**51722349**	0,10	0,31	0,09	0,34	0,08	1E-05
5	**rs7718109**	**61145102**	0,18	0,31	0,31	0,36	0,06	3E-09
1	**rs12064174**	**194086050**	0,32	0,42	0,77	0,23	0,05	4E-06
12	**rs5744884**	**133234389**	0,43	0,69	0,66	0,26	0,05	2E-08
9	**rs140533307**	**5474598**	0,27	0,53	0,15	0,30	0,05	1E-08
1	**rs10857817**	**110803755**	0,38	0,42	0,60	0,31	0,05	4E-11
6	**rs28397995**	**91209527**	0,27	0,03	0,55	0,24	0,05	4E-06
5	**rs12516866**	**35851261**	0,42	0,44	0,36	0,27	0,05	3E-09
1	**rs1289014**	**163625114**	0,59	0,28	0,81	0,28	0,05	7E-10
7	**rs10232533**	**64875899**	0,64	1,00	0,94	0,27	0,05	2E-09
13	**rs12184575**	**23793343**	0,28	0,23	0,05	0,37	0,05	1E-12
10	**rs1670819**	**56695937**	0,45	0,34	0,44	0,43	0,08	3E-07
13	**rs7989061**	**63466449**	0,46	0,81	0,78	0,25	0,04	4E-08
10	**rs7909637**	**12557574**	0,52	0,38	0,56	0,23	0,04	4E-07
2	**rs13400029**	**3582069**	0,22	0,14	0,14	0,35	0,06	6E-10
3	**rs34643186**	**176058319**	0,18	0,19	0,57	0,38	0,06	4E-10
15	**rs7167940**	**63247935**	0,45	0,73	0,49	0,21	0,05	3E-06
2	**rs4663439**	**235497621**	0,72	0,84	0,80	0,28	0,05	1E-08
14	**rs12892887**	**100055023**	0,39	0,51	0,67	0,28	0,05	1E-09
11	**rs7128459**	**58179291**	0,22	0,17	0,27	0,31	0,06	4E-08
7	**rs35308546**	**119209501**	0,17	0,05	0,12	0,42	0,06	2E-11
12	**rs79193410**	**41029850**	0,23	0,43	0,07	0,31	0,06	3E-08
7	**rs12699522**	**13580422**	0,28	0,00	0,05	0,29	0,05	2E-08
10	**rs7895030**	**132941656**	0,93	0,87	0,53	0,35	0,08	2E-05
3	**rs12695439**	**124291245**	0,30	0,35	0,39	0,32	0,05	4E-10
11	**rs10891454**	**98080130**	0,43	0,37	0,37	0,26	0,05	1E-08
13	**rs17370031**	**84977254**	0,30	0,12	0,07	0,34	0,05	2E-11
22	**rs133181**	**25741258**	0,76	0,83	0,99	0,28	0,05	5E-08
19	**rs1468773**	**57106401**	0,23	0,00	0,16	0,35	0,06	2E-10
13	**rs200371919**	**19400990**	0,23	0,21	0,59	0,26	0,06	3E-06
19	**rs11669449**	**15890517**	0,60	0,22	0,41	0,23	0,05	6E-07
20	**rs6012712**	**48297253**	0,54	0,36	0,34	0,26	0,05	8E-09
9	**rs10813569**	**31392324**	0,49	0,80	0,54	0,29	0,04	1E-10
2	**rs10197142**	**13623160**	0,43	0,65	0,92	0,22	0,05	2E-06
12	**rs7315639**	**44111933**	0,48	0,57	0,60	0,28	0,05	8E-10
10	**rs138034016**	**31136540**	0,37	0,41	0,24	0,28	0,05	2E-09
8	**rs8180941**	**90336707**	0,35	0,36	0,21	0,31	0,05	1E-10
14	**rs113204453**	**44482023**	0,24	0,03	0,14	0,33	0,05	2E-09
5	**rs2910300**	**160788827**	0,67	0,58	0,25	0,31	0,06	2E-08
15	**rs11854693**	**58712965**	0,79	0,58	0,45	0,30	0,05	2E-08
2	**rs334068**	**179005438**	0,49	0,63	0,14	0,31	0,05	3E-11
13	**rs7317830**	**57274268**	0,38	0,29	0,05	0,26	0,05	5E-08
9	**rs10984992**	**123473416**	0,70	0,56	0,23	0,28	0,05	8E-09
9	**rs79288453**	**138440834**	0,26	0,17	0,18	0,29	0,05	1E-08
1	**rs34133714**	**2765089**	0,38	0,39	0,02	0,29	0,05	7E-10

4	**rs432164**	**177391093**	0,82	0,81	0,82	0,28	0,06	6E-07
3	**rs4524298**	**82315953**	0,80	0,76	0,79	0,26	0,05	3E-06
11	**rs6591063**	**103836968**	0,12	0,11	0,22	0,40	0,07	2E-08
11	**rs11821564**	**97836250**	0,48	0,19	0,24	0,33	0,05	7E-13
1	**rs10604003**	**237788262**	0,11	0,14	0,45	0,26	0,07	4E-04
4	**rs1383567**	**34531200**	0,15	0,19	0,50	0,23	0,06	4E-04
12	**rs12313074**	**117206787**	0,89	0,70	0,36	0,30	0,07	1E-05
4	**rs1129304**	**158092422**	0,29	0,44	0,73	0,29	0,05	2E-08
3	**rs12632694**	**66883694**	0,13	0,43	0,29	0,37	0,07	2E-07
7	**rs6948652**	**157225138**	0,53	0,40	0,77	0,28	0,04	3E-10
2	**rs10207163**	**69014280**	0,50	0,50	0,62	0,31	0,05	1E-11
15	**rs1564688**	**93761742**	0,71	0,61	0,88	0,22	0,05	4E-06
1	**rs4255374**	**237561785**	0,34	0,42	0,13	0,27	0,05	2E-08
16	**rs395111**	**83881146**	0,78	0,67	0,40	0,25	0,05	1E-06
8	**rs589933**	**60876977**	0,42	0,48	0,55	0,27	0,05	2E-09
11	**rs11217793**	**120161886**	0,18	0,18	0,14	0,38	0,06	4E-10
9	**rs11789058**	**119826169**	0,42	0,30	0,60	0,32	0,05	7E-12
2	**rs6749895**	**172875442**	0,26	0,03	0,13	0,31	0,05	9E-09
10	**rs632005**	**55320515**	0,57	0,94	0,73	0,29	0,05	2E-10
14	**rs9323205**	**51586467**	0,24	0,01	0,20	0,34	0,05	5E-10
5	**rs2434352**	**68333094**	0,42	0,15	0,17	0,22	0,05	9E-07
1	**rs10453833**	**111909959**	0,27	0,15	0,15	0,29	0,05	4E-08
7	**rs2709931**	**83033278**	0,60	0,84	0,11	-0,30	0,05	6E-11
16	**rs149766632**	**78638797**	0,21	0,03	0,14	0,36	0,06	2E-10
1	**rs598031**	**5333479**	0,70	0,59	0,99	0,27	0,05	2E-08
22	**rs28755**	**29685711**	0,63	0,70	0,78	0,22	0,05	1E-06
15	**rs12324446**	**94721997**	0,27	0,04	0,40	0,21	0,05	4E-05
18	**rs12965056**	**1324114**	0,48	0,35	0,13	0,27	0,05	2E-09
6	**rs6908931**	**144735877**	0,77	0,83	0,84	0,29	0,05	5E-08
3	**rs12054033**	**132531654**	0,27	0,54	0,22	0,25	0,05	3E-06
15	**rs57843897**	**49833641**	0,23	0,42	0,57	0,39	0,06	2E-12
6	**rs2798364**	**107161116**	0,78	0,77	0,73	0,30	0,05	2E-08
14	**rs11490385**	**31718057**	0,60	0,85	0,79	0,27	0,05	2E-09
9	**rs13283039**	**140181667**	0,70	0,61	0,61	0,23	0,05	2E-06
4	**rs4833477**	**116324508**	0,62	0,77	0,51	0,30	0,05	1E-10
5	**rs165188330**	**165188330**	0,24	0,13	0,14	0,32	0,05	5E-09
12	**rs12309369**	**38419683**	0,49	0,09	0,11	0,25	0,04	4E-08
16	**rs4783251**	**82698974**	0,50	0,04	0,29	0,32	0,04	1E-12
10	**rs12780864**	**22421961**	0,22	0,06	0,14	0,33	0,06	6E-09
6	**rs12192993**	**12380922**	0,41	0,30	0,05	0,35	0,05	4E-14
4	**rs11735893**	**142896936**	0,22	0,01	0,05	0,32	0,06	1E-08
14	**rs1761004**	**46912023**	0,54	0,71	0,12	0,27	0,05	4E-09
12	**rs142837217**	**86002875**	0,34	0,37	0,03	0,24	0,05	1E-06
2	**rs6739828**	**43616008**	0,45	0,08	0,57	0,24	0,05	2E-07
8	**rs2891977**	**122180353**	0,37	0,72	0,67	0,31	0,05	1E-10

2	**rs2199883**	**185565463**	0,25	0,04	0,65	0,43	0,08	2E-08
9	**rs7874886**	**18865265**	0,23	0,19	0,57	0,27	0,06	7E-07
15	**rs7170241**	**62810138**	0,41	0,60	0,66	0,27	0,05	6E-09
6	**rs7775711**	**112161786**	0,13	0,27	0,84	0,33	0,07	4E-06
10	**rs10883034**	**99845389**	0,36	0,37	0,14	0,26	0,05	4E-08
3	**rs6438092**	**95479393**	0,38	0,51	0,61	0,27	0,05	1E-08
17	**rs4796450**	**6139713**	0,33	0,22	0,01	0,31	0,05	5E-10
1	**rs2884855**	**110376651**	0,54	0,23	0,26	0,25	0,04	3E-08
4	**rs11100785**	**144195557**	0,57	0,85	0,40	0,26	0,05	1E-08
10	**rs11599612**	**86422743**	0,45	0,40	0,36	0,27	0,05	6E-09
11	**rs1784430**	**102474813**	0,56	0,54	0,45	0,32	0,04	1E-12
19	**rs454904**	**44511589**	0,12	0,47	0,01	0,33	0,07	5E-06
1	**rs289686**	**76608491**	0,30	0,12	0,08	0,29	0,05	1E-08
3	**rs2654695**	**192311851**	0,46	0,43	0,51	0,25	0,05	4E-08
6	**rs2048696**	**163337823**	0,52	0,53	0,19	0,35	0,04	2E-15
11	**rs10838609**	**5780716**	0,34	0,28	0,03	0,19	0,05	6E-05
19	**rs3826798**	**5785113**	0,17	0,49	0,33	0,23	0,06	3E-04
1	**rs609125**	**22915030**	0,39	0,28	0,75	0,26	0,05	3E-08
2	**rs201400225**	**162693099**	0,65	0,96	0,45	0,31	0,05	2E-11
14	**rs202227171**	**87861177**	0,50	0,42	0,53	0,28	0,04	3E-10
13	**rs3832886**	**76419421**	0,74	0,50	0,60	0,28	0,05	4E-08
7	**rs12669437**	**95253404**	0,41	0,96	0,51	0,33	0,05	1E-12
6	**rs9344725**	**88493376**	0,52	0,44	0,20	-0,21	0,04	3E-06
5	**rs78479231**	**21293851**	0,23	0,44	0,20	0,30	0,06	9E-08
4	**rs1078566**	**77914535**	0,62	0,35	0,38	0,25	0,05	6E-08
19	**rs11084579**	**31802723**	0,29	0,46	0,22	0,23	0,05	5E-06

DisChr	rsID_refSNP	pos_refSNP	beta ASN	stdbeta ASN	P ASN	beta YRI	stdbeta YRI	P YRI
4	**rs2333328**	**176852836**	0,27	0,05	2E-09	0,25	0,05	1E-06
9	**rs10869238**	**75803635**	0,24	0,05	6E-08	0,30	0,04	1E-11
22	**rs136575**	**45769245**	0,27	0,05	5E-09	0,16	0,29	6E-01
6	**rs579329**	**47822681**	0,31	0,05	1E-10	0,26	0,05	3E-08
10	**rs10999327**	**53522817**	0,21	0,11	5E-02	0,22	0,05	3E-06
6	**rs2516226**	**12604062**	0,31	0,06	2E-07	0,08	0,05	7E-02
8	**rs73351724**	**114787818**	0,28	0,05	2E-09	0,31	0,05	2E-09
3	**rs1387701**	**193147894**	0,25	0,05	7E-08	0,18	0,05	6E-05
4	**rs4340779**	**119678580**	0,33	0,05	5E-13	0,16	0,05	1E-03
15	**rs1604172**	**98040555**	0,28	0,05	1E-09	0,27	0,05	3E-09
15	**rs1470901**	**69097765**	0,20	0,05	9E-06	0,19	0,06	5E-04
1	**rs7556147**	**111407322**	0,29	0,07	3E-05	0,37	0,08	7E-06
7	**rs9692258**	**69049578**	0,26	0,05	2E-06	0,25	0,06	1E-05
12	**rs4761380**	**77829418**	0,27	0,04	2E-09	0,30	0,05	2E-10
14	**rs1959524**	**52312705**	-0,02	0,14	9E-01	0,38	0,05	4E-15
17	**rs55969697**	**15264671**	0,17	0,05	1E-03	0,17	0,04	2E-04

17	**rs7213597**	**12053126**	0,31	0,05	4E-11	0,28	0,05	2E-09
22	**rs6007521**	**45647534**	0,26	0,06	6E-06	0,23	0,07	6E-04
22	**rs535842**	**27621151**	0,40	0,05	8E-16	0,31	0,05	6E-11
2	**rs6754782**	**20573530**	0,23	0,05	4E-06	0,31	0,06	2E-07
13	**rs9549507**	**112996118**	0,31	0,05	2E-11	0,34	0,05	1E-12
9	**rs16925789**	**109495368**	0,16	0,08	5E-02	0,33	0,05	1E-10
17	**rs175381**	**49387207**	0,27	0,05	4E-09	0,23	0,05	2E-05
4	**rs7659549**	**103006301**	0,36	0,05	5E-14	0,27	0,05	1E-06
13	**rs278034**	**30416637**	0,31	0,04	2E-12	0,28	0,05	2E-08
22	**rs2531850**	**30043563**	0,27	0,05	4E-08	0,30	0,08	8E-05
8	**rs9773025**	**6674458**	0,22	0,10	2E-02	0,20	0,05	5E-05
7	**rs10228515**	**12013256**	0,33	0,05	4E-13	0,26	0,05	8E-08
15	**rs1191196**	**77646504**	0,26	0,05	8E-09	0,25	0,04	2E-08
14	**rs8023023**	**94773876**	0,27	0,08	4E-04	0,28	0,05	1E-08
6	**rs9452207**	**93744485**	0,22	0,07	2E-03	0,23	0,05	4E-07
4	**rs2045774**	**82822003**	0,27	0,05	5E-09	0,20	0,09	2E-02
7	**rs7787377**	**89996777**	0,34	0,05	5E-13	0,25	0,05	2E-07
9	**rs12686218**	**114601575**	0,35	0,05	2E-13	0,30	0,06	5E-08
13	**rs2781311**	**87626740**	0,30	0,05	1E-10	0,32	0,05	1E-11
5	**rs1422932**	**167397039**	0,23	0,05	2E-06	0,27	0,05	3E-08
9	**rs10115645**	**107369931**	0,29	0,05	6E-09	0,42	0,12	6E-04
7	**rs10952494**	**154253804**	0,31	0,05	6E-12	0,29	0,05	1E-10
14	**rs6574639**	**81771541**	0,28	0,05	1E-09	0,29	0,05	6E-09
7	**rs6947649**	**83415942**	0,24	0,05	7E-08	0,36	0,06	3E-09
5	**rs35733634**	**12879768**	0,34	0,05	2E-13	0,30	0,05	4E-09
4	**rs201086800**	**66370079**	0,22	0,05	6E-06	0,28	0,07	8E-05
6	**rs6938041**	**118852468**	0,16	0,05	2E-03	0,18	0,05	2E-04
1	**rs201832280**	**151339950**	0,26	0,06	3E-06	0,25	0,05	5E-08
8	**rs465**	**90816058**	0,33	0,05	5E-13	0,18	0,11	1E-01
12	**rs10845348**	**11539880**	0,23	0,05	3E-07	0,30	0,05	2E-09
9	**rs490491**	**108416462**	0,30	0,05	2E-10	0,29	0,05	3E-09
17	**rs9914518**	**9709946**	0,28	0,05	9E-10	0,18	0,04	6E-05
14	**rs10782420**	**52681605**	0,29	0,06	9E-07	0,28	0,05	3E-07
6	**rs1321473**	**137158764**	0,28	0,05	8E-10	0,22	0,05	6E-06
2	**rs10804341**	**229429905**	0,21	0,08	7E-03	0,25	0,05	4E-07
15	**rs4778048**	**93401485**	0,28	0,05	2E-09	0,28	0,06	8E-07
2	**rs6743294**	**229370567**	0,34	0,05	2E-13	0,25	0,13	5E-02
12	**rs2428387**	**47379311**	0,29	0,11	1E-02	0,28	0,07	4E-05
11	**rs7952492**	**108296680**	0,30	0,05	1E-10	0,26	0,05	3E-08
3	**rs9843344**	**13670536**	0,39	0,14	5E-03	0,12	0,05	3E-02
6	**rs4373367**	**9830006**	0,13	0,14	3E-01	0,24	0,05	6E-06
5	**rs10065424**	**75841888**	0,32	0,05	3E-11	0,28	0,05	8E-09
11	**rs28758793**	**107707070**	0,24	0,04	4E-08	0,19	0,05	2E-04
10	**rs10900234**	**46200866**	0,28	0,05	2E-09	0,23	0,05	5E-07
2	**rs13425141**	**210322212**	0,00	0,00	1E+00	0,21	0,10	3E-02

6	**rs114364056**	**28634891**	0,26	0,06	4E-05	0,29	0,05	2E-10
8	**rs2697748**	**13079233**	0,30	0,05	2E-10	0,18	0,05	1E-04
3	**rs9873142**	**164119265**	0,29	0,05	2E-09	0,26	0,05	1E-08
9	**rs7036260**	**122911053**	0,28	0,05	7E-08	0,33	0,05	1E-12
8	**rs4273853**	**22698106**	0,25	0,05	2E-07	0,29	0,05	2E-08
16	**rs3104790**	**52638663**	0,24	0,05	2E-05	0,29	0,05	3E-10
1	**rs10911089**	**182514852**	0,25	0,05	5E-08	0,28	0,05	2E-09
6	**rs9364697**	**164074139**	0,27	0,10	6E-03	0,29	0,05	2E-08
4	**rs3109848**	**26457168**	0,34	0,06	7E-09	0,37	0,05	1E-11
20	**rs6035865**	**21368932**	0,18	0,06	1E-03	0,30	0,05	5E-11
9	**rs10816472**	**110001457**	0,17	0,05	1E-03	0,32	0,05	5E-11
1	**rs7548054**	**39302020**	0,28	0,05	1E-08	0,32	0,08	3E-05
3	**rs4645092**	**39051718**	0,33	0,05	7E-13	0,14	0,06	3E-02
10	**rs773948**	**34716034**	0,28	0,05	2E-09	-0,35	0,27	2E-01
1	**rs200576863**	**154798550**	0,28	0,05	3E-08	0,21	0,05	1E-05
12	**rs7138235**	**133313237**	0,27	0,05	4E-08	0,32	0,06	4E-08
20	**rs2983304**	**23508573**	0,29	0,05	1E-10	0,34	0,06	1E-08
7	**rs10950821**	**20647015**	0,25	0,05	5E-08	0,30	0,05	2E-11
6	**rs115645489**	**32511977**	0,25	0,05	2E-07	0,24	0,05	2E-07
16	**rs7187576**	**25070579**	0,19	0,05	2E-04	0,35	0,05	9E-13
3	**rs1388705**	**161584027**	0,29	0,05	1E-09	-0,14	0,30	7E-01
8	**rs10955282**	**103176946**	0,26	0,05	7E-09	0,23	0,04	3E-07
11	**rs1395558**	**6727468**	-0,34	0,05	1E-13	-0,21	0,05	2E-05
14	**rs1955463**	**54854386**	0,26	0,05	2E-08	0,26	0,05	5E-08
8	**rs17079639**	**3077005**	0,28	0,05	6E-09	0,17	0,05	3E-04
3	**rs13085132**	**106837810**	0,32	0,05	9E-13	0,26	0,05	1E-08
1	**rs6665839**	**49043877**	0,21	0,05	7E-05	0,31	0,05	7E-11
6	**rs4236138**	**56151384**	0,31	0,05	9E-12	0,30	0,14	3E-02
2	**rs35463898**	**71704005**	0,38	0,05	2E-16	0,30	0,06	5E-07
1	**rs150016402**	**94601236**	0,19	0,05	5E-04	0,32	0,06	1E-08
6	**rs13199418**	**79874045**	0,32	0,07	7E-07	0,26	0,05	4E-08
10	**rs507098**	**116062510**	0,32	0,05	1E-10	0,29	0,05	2E-10
18	**rs9961465**	**8569882**	0,27	0,05	1E-08	0,27	0,05	3E-09
21	**rs2236478**	**46917782**	0,33	0,05	4E-11	0,17	0,05	2E-04
16	**rs10153134**	**90091099**	0,29	0,05	9E-09	0,23	0,05	4E-07
11	**rs201202588**	**72258622**	0,26	0,05	2E-07	0,22	0,05	3E-06
14	**rs1152376**	**88961465**	-0,29	0,05	2E-08	0,03	0,08	7E-01
20	**rs6113869**	**22953698**	0,13	0,05	4E-03	0,19	0,05	1E-04
2	**rs61227128**	**122705170**	0,34	0,07	2E-07	0,08	0,05	9E-02
10	**rs7095313**	**17399051**	0,26	0,08	2E-03	0,23	0,05	2E-06
11	**rs7119996**	**93389932**	0,27	0,05	1E-07	0,23	0,05	7E-07
3	**rs34638579**	**137385728**	0,24	0,05	7E-06	0,29	0,05	1E-10
13	**rs11282754**	**78829394**	-0,16	0,05	3E-03	-0,14	0,05	3E-03
8	**rs61629815**	**87104916**	0,31	0,04	7E-12	0,05	0,08	5E-01
1	**rs1977125**	**63772373**	0,27	0,04	1E-09	0,27	0,06	2E-06

10	**rs12770204**	**4432617**	0,28	0,21	2E-01	0,11	0,07	1E-01
2	**rs1597944**	**234504098**	0,25	0,04	2E-08	0,38	0,07	5E-09
4	**rs35659552**	**37709539**	0,38	0,24	1E-01	0,04	0,05	4E-01
10	**rs7902931**	**6141942**	0,23	0,05	1E-05	0,32	0,05	1E-12
4	**rs59283470**	**7863978**	0,34	0,05	3E-12	0,22	0,05	2E-06
4	**rs147440574**	**128598143**	0,29	0,06	3E-07	0,19	0,06	6E-04
6	**rs378479**	**160737140**	0,22	0,05	2E-05	0,32	0,05	4E-10
7	**rs28491038**	**104366640**	0,32	0,07	9E-06	0,18	0,05	2E-04
8	**rs7836279**	**13775292**	0,30	0,05	2E-11	0,26	0,06	2E-05
20	**rs6092006**	**36809169**	0,29	0,06	5E-06	0,29	0,05	4E-08
20	**rs6136376**	**1896244**	0,32	0,05	4E-12	0,24	0,05	8E-07
2	**rs76136841**	**206820159**	0,33	0,05	7E-13	0,34	0,22	1E-01
20	**rs138273314**	**19935337**	0,29	0,05	3E-10	0,30	0,05	4E-10
4	**rs4862032**	**183071431**	0,27	0,05	3E-08	0,26	0,05	4E-07
2	**rs13003505**	**159156020**	0,26	0,05	8E-09	0,20	0,05	1E-04
3	**rs11708814**	**87063964**	0,25	0,05	3E-08	0,22	0,09	2E-02
8	**rs59026256**	**66912273**	0,34	0,10	5E-04	0,31	0,05	6E-10
5	**rs302396**	**151324533**	0,29	0,05	4E-10	0,19	0,06	2E-03
12	**rs7132347**	**55714876**	0,21	0,07	2E-03	0,20	0,06	3E-04
17	**rs4605213**	**49244747**	0,17	0,06	3E-03	0,24	0,13	6E-02
8	**rs1392143**	**3357940**	0,21	0,06	6E-04	0,39	0,05	4E-17
1	**rs17407657**	**66171667**	0,16	0,17	3E-01	0,26	0,06	2E-05
7	**rs321282**	**95297614**	0,29	0,04	1E-10	0,18	0,05	1E-04
2	**rs202028570**	**41482288**	0,18	0,05	1E-04	0,18	0,04	7E-05
9	**rs10980731**	**113838859**	0,33	0,05	8E-10	0,51	0,12	2E-05
11	**rs1426926**	**87903141**	0,28	0,05	4E-08	0,33	0,05	9E-13
2	**rs374954**	**176084790**	0,27	0,05	5E-09	0,22	0,05	5E-06
6	**rs148601969**	**8226853**	0,33	0,05	5E-10	0,15	0,05	2E-03
4	**rs62325107**	**154675105**	0,27	0,07	4E-05	0,28	0,05	2E-09
12	**rs11532381**	**79936694**	0,28	0,05	4E-08	0,28	0,09	3E-03
22	**rs136483**	**32590069**	0,21	0,06	8E-04	0,23	0,09	1E-02
14	**rs10141742**	**59406089**	-0,03	0,13	8E-01	0,17	0,08	5E-02
7	**rs10234007**	**105778435**	0,34	0,05	4E-13	0,27	0,07	4E-05
3	**rs9815772**	**178704926**	0,27	0,05	3E-09	0,18	0,05	1E-04
4	**rs631179**	**130411127**	0,21	0,05	3E-06	0,29	0,05	3E-10
3	**rs66861711**	**162227359**	0,32	0,05	1E-10	0,38	0,08	1E-06
5	**rs75923162**	**24604987**	0,35	0,05	1E-14	0,25	0,08	1E-03
6	**rs4707552**	**90300841**	0,28	0,05	1E-08	0,11	0,05	2E-02
15	**rs56200331**	**95617954**	0,34	0,06	1E-08	0,25	0,07	1E-04
10	**rs1250538**	**81037800**	0,28	0,05	8E-10	0,12	0,06	4E-02
2	**rs72775988**	**12602099**	0,26	0,05	2E-06	0,05	0,06	4E-01
4	**rs1545788**	**5715069**	0,31	0,05	2E-11	0,32	0,08	4E-05
9	**rs519980**	**110961597**	0,28	0,05	1E-09	0,04	0,05	4E-01
1	**rs6656494**	**154839799**	0,20	0,07	4E-03	0,37	0,05	2E-16
9	**rs200533218**	**87619460**	0,31	0,05	1E-10	0,31	0,06	2E-06

17	**rs2640842**	**31014803**	0,29	0,05	4E-09	0,17	0,05	2E-04
4	**rs991346**	**92817071**	0,30	0,06	2E-06	0,26	0,05	1E-08
3	**rs13093484**	**95191114**	0,11	0,05	2E-02	0,26	0,05	7E-09
13	**rs2993574**	**96067494**	0,27	0,05	1E-08	0,30	0,10	3E-03
7	**rs1179608**	**75245398**	0,34	0,05	6E-11	0,24	0,05	3E-07
12	**rs12230050**	**93990553**	0,22	0,05	3E-06	0,33	0,04	8E-14
21	**rs57592847**	**36682910**	0,28	0,05	6E-10	0,34	0,06	2E-09
11	**rs12798276**	**32583375**	0,33	0,05	1E-12	0,33	0,08	8E-05
5	**rs34446169**	**13261448**	0,22	0,04	1E-06	0,24	0,05	7E-08
10	**rs2505398**	**32633516**	0,23	0,05	3E-06	0,25	0,04	4E-08
5	**rs2918443**	**85213684**	0,34	0,05	9E-13	0,38	0,10	6E-05
5	**rs244408**	**110021869**	0,23	0,05	6E-06	0,32	0,05	7E-11
10	**rs2986034**	**105232580**	0,25	0,05	3E-06	0,35	0,05	1E-14
7	**rs2390472**	**21156006**	0,22	0,05	5E-05	0,31	0,05	2E-08
14	**rs1147445**	**66463384**	0,28	0,05	2E-07	0,08	0,05	1E-01
15	**rs4356443**	**88200417**	0,23	0,05	1E-06	0,19	0,06	7E-04
6	**rs11453102**	**139363410**	0,16	0,09	6E-02	0,11	0,04	2E-02
6	**rs3778021**	**36948805**	0,27	0,07	6E-05	0,30	0,05	8E-11
1	**rs1568134**	**189822309**	0,28	0,05	4E-09	0,21	0,04	3E-06
10	**rs10906445**	**13712038**	0,08	0,04	8E-02	0,14	0,05	2E-03
4	**rs11727317**	**73054448**	0,37	0,05	2E-11	0,28	0,05	7E-10
5	**rs146990484**	**168728193**	0,29	0,05	4E-08	0,30	0,11	6E-03
5	**rs67533941**	**20984272**	0,33	0,09	1E-04	0,12	0,05	2E-02
3	**rs35931086**	**102579206**	0,34	0,05	6E-12	0,14	0,05	3E-03
5	**rs55753822**	**55753822**	0,31	0,05	1E-10	0,34	0,08	1E-05
18	**rs9950923**	**65714987**	0,28	0,05	1E-09	0,13	0,08	9E-02
15	**rs79173965**	**74170559**	0,26	0,11	2E-02	0,35	0,13	5E-03
15	**rs7166592**	**47179916**	0,25	0,05	2E-07	0,20	0,05	6E-05
8	**rs984990**	**114368635**	0,33	0,05	3E-11	0,26	0,05	7E-09
6	**rs9399242**	**138827658**	0,25	0,05	4E-08	0,05	0,16	7E-01
12	**rs10748463**	**47580270**	0,26	0,05	2E-08	0,34	0,04	8E-14
18	**rs12104083**	**13739269**	0,41	0,06	3E-11	0,24	0,06	1E-05
4	**rs13135410**	**42565734**	0,29	0,05	1E-09	0,21	0,09	3E-02
20	**rs399698**	**15368919**	0,35	0,06	3E-08	0,19	0,09	3E-02
2	**rs17006895**	**71575470**	0,92	0,59	1E-01	0,35	0,05	2E-14
19	**rs55661666**	**15069191**	0,27	0,08	5E-04	0,34	0,05	2E-11
11	**rs7941643**	**59460632**	0,20	0,11	7E-02	0,27	0,05	1E-08
2	**rs1384781**	**145601057**	0,41	0,05	7E-14	0,24	0,05	1E-07
13	**rs6492292**	**111255057**	0,24	0,05	3E-07	0,27	0,04	2E-09
8	**rs36070162**	**109199296**	0,29	0,04	1E-10	0,34	0,05	1E-12
22	**rs1981438**	**47288122**	0,24	0,05	1E-07	0,01	0,04	7E-01
12	**rs10774768**	**115193194**	0,33	0,05	2E-10	0,25	0,05	4E-08
1	**rs2232809**	**171750181**	0,29	0,05	1E-09	0,31	0,06	3E-07
11	**rs8186211**	**50542195**	0,38	0,05	3E-12	0,25	0,06	8E-06
14	**rs9671901**	**84465529**	0,36	0,05	6E-14	0,22	0,05	7E-07

14	**rs2638802**	**86145123**	0,19	0,05	2E-05	0,25	0,06	9E-05
14	**rs10145617**	**86176395**	0,21	0,04	4E-06	0,24	0,06	1E-04
5	**rs13167246**	**60554383**	0,31	0,08	1E-04	0,22	0,05	5E-06
13	**rs111538000**	**62708839**	0,40	0,12	8E-04	0,28	0,05	1E-08
2	**rs4000962**	**168031396**	-0,08	0,12	5E-01	0,07	0,11	5E-01
17	**rs11651738**	**80178691**	0,25	0,08	3E-03	0,26	0,07	3E-04
3	**rs7640053**	**79531271**	0,23	0,04	3E-07	0,42	0,13	1E-03
16	**rs3759986**	**21225224**	0,20	0,07	2E-03	0,29	0,06	1E-07
3	**rs6805084**	**111984736**	0,32	0,05	3E-10	0,29	0,05	2E-10
5	**rs4867482**	**32893465**	0,30	0,05	3E-11	0,24	0,05	1E-07
2	**rs10196874**	**235599018**	0,27	0,05	2E-09	0,28	0,06	2E-06
17	**rs7501427**	**77726549**	0,27	0,05	2E-09	0,26	0,05	2E-07
7	**rs9639516**	**25729418**	0,29	0,09	2E-03	0,21	0,05	5E-06
3	**rs62253005**	**53978529**	0,19	0,05	3E-05	0,07	0,06	2E-01
7	**rs4419707**	**67223257**	0,25	0,06	3E-05	0,24	0,05	4E-07
5	**rs4134393**	**30190699**	0,20	0,05	2E-04	0,36	0,05	8E-12
4	**rs199541723**	**106416147**	0,26	0,05	1E-08	0,33	0,05	5E-11
6	**rs139304043**	**142387979**	0,22	0,06	6E-04	0,25	0,08	1E-03
1	**rs7549723**	**150541812**	0,27	0,05	1E-08	0,27	0,04	2E-09
12	**rs11179617**	**41446008**	0,26	0,09	5E-03	0,25	0,16	1E-01
13	**rs9512696**	**28012527**	0,29	0,05	1E-09	0,28	0,05	3E-08
16	**rs9938541**	**81045228**	0,24	0,05	1E-07	0,10	0,05	4E-02
14	**rs1950787**	**60071972**	0,19	0,06	1E-03	0,19	0,06	1E-03
3	**rs2194607**	**21523342**	0,31	0,05	3E-11	0,24	0,05	8E-08
7	**rs2374296**	**151626130**	0,26	0,05	1E-06	0,22	0,05	1E-05
15	**rs16962490**	**49743628**	0,30	0,04	1E-11	0,26	0,05	3E-06
4	**rs10710521**	**176988797**	0,26	0,05	9E-09	0,34	0,05	2E-12
3	**rs35910618**	**161660914**	0,22	0,04	2E-06	0,26	0,06	7E-06
5	**rs888777**	**168712456**	0,20	0,05	1E-04	0,29	0,07	2E-05
2	**rs12465480**	**49445554**	0,25	0,04	1E-08	0,22	0,05	2E-05
3	**rs1563980**	**28800886**	0,26	0,08	1E-03	0,27	0,05	5E-08
8	**rs10089687**	**6795851**	0,19	0,06	8E-04	0,27	0,05	6E-09
12	**rs7974884**	**81309283**	0,22	0,05	1E-05	0,27	0,05	8E-09
7	**rs200586366**	**97269518**	0,29	0,04	8E-11	0,23	0,05	8E-07
7	**rs76190866**	**76915613**	0,17	0,07	3E-02	0,26	0,05	6E-09
8	**rs35066759**	**23318892**	0,22	0,05	2E-06	0,29	0,05	5E-08
6	**rs384323**	**9020424**	0,25	0,05	3E-07	0,27	0,07	3E-04
10	**rs6585241**	**115486610**	0,28	0,06	5E-06	0,15	0,10	1E-01
4	**rs2667714**	**40038395**	0,16	0,05	5E-04	0,14	0,05	6E-03
11	**rs7114635**	**90344354**	0,22	0,05	2E-06	0,22	0,05	1E-06
3	**rs17012429**	**74409330**	0,29	0,05	4E-08	0,29	0,19	1E-01
2	**rs72775667**	**13800460**	0,35	0,09	6E-05	0,19	0,05	2E-05
4	**rs1449763**	**27688976**	0,30	0,05	2E-11	0,19	0,04	3E-05
6	**rs9399030**	**132837049**	0,26	0,05	1E-06	0,36	0,06	1E-08
17	**rs200905171**	**57755742**	0,30	0,05	4E-11	0,37	0,08	2E-06

1	**rs7521183**	**237615068**	0,28	0,04	9E-10	0,30	0,05	4E-08
6	**rs35911690**	**29867954**	0,29	0,04	7E-11	0,43	0,05	7E-19
2	**rs1179683**	**217751546**	0,33	0,05	1E-12	0,31	0,05	3E-11
8	**rs1866700**	**137519028**	0,23	0,05	8E-07	0,26	0,05	6E-08
6	**rs199607379**	**152661834**	0,31	0,12	1E-02	0,20	0,08	1E-02
18	**rs11663656**	**57567638**	0,33	0,05	1E-12	0,34	0,06	9E-08
7	**rs12705985**	**114337975**	-0,03	0,07	7E-01	0,15	0,07	4E-02
3	**rs61690667**	**186926347**	0,26	0,05	6E-07	0,37	0,07	4E-08
5	**rs5870400**	**109481424**	0,32	0,05	1E-10	0,35	0,05	7E-13
4	**rs4691362**	**157527761**	0,26	0,05	4E-08	0,17	0,08	2E-02
4	**rs12507474**	**96576002**	0,26	0,05	1E-08	0,31	0,05	2E-10
17	**rs58875634**	**80091726**	0,28	0,06	1E-05	0,33	0,05	4E-13
8	**rs7817489**	**77661560**	0,28	0,05	3E-10	0,07	0,04	1E-01
1	**rs111772533**	**26523404**	0,31	0,19	1E-01	0,33	0,06	8E-09
20	**rs8115705**	**4327451**	0,20	0,07	2E-03	0,34	0,05	6E-11
5	**rs13167124**	**1223940**	0,16	0,05	4E-03	0,20	0,05	2E-05
4	**rs75874971**	**107457067**	0,27	0,05	9E-09	0,28	0,05	7E-10
9	**rs7039175**	**6348355**	0,22	0,05	7E-06	0,24	0,05	7E-07
11	**rs11026630**	**22565466**	0,29	0,05	1E-09	0,19	0,19	3E-01
17	**rs684690**	**6577803**	0,21	0,05	4E-05	0,28	0,05	2E-09
2	**rs7599471**	**20904018**	0,32	0,05	1E-11	0,24	0,05	3E-07
7	**rs12669900**	**135702344**	0,37	0,05	1E-13	0,29	0,05	7E-09
4	**rs201189120**	**163298951**	0,36	0,10	3E-04	-0,33	0,31	3E-01
16	**rs12448127**	**25510655**	0,40	0,06	5E-11	0,15	0,04	1E-03
12	**rs11065695**	**109595386**	0,28	0,04	1E-10	0,36	0,06	2E-10
11	**rs77626887**	**69861644**	0,30	0,05	8E-11	0,32	0,06	2E-08
4	**rs62329001**	**104178265**	0,26	0,06	2E-05	0,33	0,12	4E-03
6	**rs34932157**	**104281272**	0,28	0,05	8E-10	0,23	0,05	6E-07
6	**rs10456703**	**13739490**	0,28	0,07	2E-05	0,27	0,05	1E-08
3	**rs13088837**	**63459125**	0,32	0,05	1E-11	0,24	0,05	2E-06
3	**rs68015175**	**5497135**	0,26	0,05	1E-07	0,24	0,05	2E-06
4	**rs1316866**	**85074129**	0,22	0,05	2E-06	0,20	0,05	8E-05
13	**rs7994720**	**64583323**	0,17	0,04	1E-04	0,28	0,05	7E-10
9	**rs4272463**	**20999770**	0,30	0,04	1E-11	0,29	0,05	1E-08
3	**rs1589439**	**118586026**	0,29	0,05	2E-10	0,30	0,07	8E-06
12	**rs1504558**	**98568966**	0,24	0,07	2E-04	0,17	0,05	3E-04
2	**rs2053804**	**224020406**	0,23	0,05	6E-07	0,36	0,05	2E-15
20	**rs856959**	**61411432**	0,32	0,05	2E-12	-0,01	0,04	8E-01
15	**rs12592571**	**59707163**	0,30	0,05	3E-11	0,36	0,08	1E-06
4	**rs7675641**	**161737304**	0,31	0,06	6E-07	0,31	0,06	1E-07
18	**rs4581807**	**68874816**	0,33	0,07	9E-06	0,28	0,05	9E-10
17	**rs9897027**	**51422273**	0,12	0,05	1E-02	0,19	0,05	5E-05
22	**rs4821661**	**37782256**	0,36	0,06	2E-10	0,32	0,08	2E-04
4	**rs201017255**	**106205194**	0,27	0,05	2E-08	0,27	0,05	5E-09
5	**rs4296844**	**111175320**	-0,23	0,05	5E-07	-0,21	0,05	8E-06

6	**rs34059065**	**140301421**	0,20	0,11	7E-02	0,23	0,09	1E-02
3	**rs9852128**	**12635623**	0,35	0,13	8E-03	0,19	0,05	4E-05
4	**rs35553952**	**187742898**	0,24	0,06	2E-05	0,27	0,05	2E-08
5	**rs1058312**	**14509966**	0,22	0,07	1E-03	0,23	0,05	2E-07
9	**rs913182**	**97478309**	0,26	0,06	3E-06	0,31	0,05	4E-11
1	**rs4653183**	**33984987**	0,32	0,05	4E-11	0,26	0,05	2E-07
14	**rs12879605**	**27295802**	0,16	0,06	1E-02	0,31	0,05	1E-10
1	**rs386012**	**83155380**	0,26	0,05	1E-08	0,33	0,05	1E-13
16	**rs58675609**	**85273226**	0,30	0,05	2E-08	-0,02	0,05	7E-01
5	**rs76120834**	**125372245**	0,26	0,05	4E-08	0,25	0,05	2E-07
15	**rs79988905**	**42677731**	0,24	0,07	4E-04	0,19	0,05	5E-05
2	**rs920211**	**211874991**	0,29	0,06	2E-07	0,48	0,12	3E-05
12	**rs7958081**	**23093846**	0,28	0,05	2E-09	0,19	0,05	2E-04
6	**rs35434813**	**74802323**	0,36	0,17	3E-02	0,26	0,05	7E-09
8	**rs3808462**	**116606177**	0,25	0,05	4E-08	0,18	0,07	1E-02
14	**rs4020134**	**78420741**	0,29	0,05	1E-08	0,25	0,05	5E-08
22	**rs28702070**	**50344912**	0,27	0,05	6E-09	0,27	0,08	1E-03
8	**rs4366044**	**135516280**	0,34	0,05	1E-11	0,22	0,05	3E-06
8	**rs1834197**	**57755644**	0,28	0,04	4E-10	0,34	0,07	3E-06
6	**rs9377003**	**146861189**	0,23	0,06	5E-05	0,17	0,09	7E-02
5	**rs12520117**	**163522236**	0,25	0,05	4E-08	0,36	0,05	2E-14
2	**rs77847962**	**132742098**	0,22	0,06	2E-04	0,18	0,05	9E-05
14	**rs1959120**	**101568230**	0,21	0,05	1E-05	0,27	0,05	2E-09
6	**rs6914523**	**65027043**	0,33	0,05	1E-13	0,19	0,05	1E-04
14	**rs8009305**	**60383685**	0,03	0,05	6E-01	0,32	0,05	1E-11
10	**rs201533606**	**124511268**	0,34	0,05	9E-13	0,28	0,05	9E-08
10	**rs11819372**	**116594934**	0,31	0,05	3E-09	0,25	0,05	3E-08
3	**rs298756**	**164199329**	0,28	0,05	5E-09	0,30	0,05	5E-10
9	**rs551960**	**116384661**	0,25	0,50	6E-01	0,31	0,05	9E-09
4	**rs34881324**	**15217750**	0,31	0,04	6E-12	0,25	0,05	3E-07
1	**rs10921568**	**194387825**	0,34	0,05	2E-12	0,24	0,05	3E-07
12	**rs201055230**	**49143466**	1,10	0,58	6E-02	0,29	0,06	1E-06
2	**rs12987457**	**235599023**	0,22	0,05	1E-05	0,31	0,06	2E-07
3	**rs34197745**	**48090946**	0,31	0,05	2E-09	0,22	0,10	2E-02
13	**rs7339096**	**20711140**	0,25	0,06	1E-05	0,31	0,08	2E-04
5	**rs6883952**	**171961443**	0,40	0,07	8E-09	0,22	0,07	2E-03
12	**rs12426677**	**7414864**	0,28	0,05	4E-10	0,07	0,05	2E-01
5	**rs11241748**	**123846498**	0,32	0,05	2E-11	0,21	0,07	1E-03
1	**rs10586161**	**227175967**	0,15	0,05	2E-03	0,23	0,05	1E-05
20	**rs34973476**	**43770291**	0,28	0,14	5E-02	0,20	0,10	4E-02
1	**rs2236539**	**182096856**	0,27	0,05	3E-09	0,27	0,05	5E-09
9	**rs7048995**	**20012984**	0,10	0,05	3E-02	0,31	0,05	1E-11
7	**rs72077057**	**152651502**	0,19	0,05	4E-05	0,19	0,05	3E-04
1	**rs1501568**	**211087439**	0,26	0,06	2E-06	0,34	0,05	3E-12
17	**rs3815358**	**62010270**	0,28	0,05	1E-09	0,32	0,18	8E-02

14	**rs13156**	**51722349**	0,36	0,05	3E-13	0,21	0,12	8E-02
5	**rs7718109**	**61145102**	0,20	0,05	5E-05	0,27	0,05	6E-08
1	**rs12064174**	**194086050**	0,34	0,05	1E-13	0,34	0,05	1E-10
12	**rs5744884**	**133234389**	0,20	0,05	4E-05	0,18	0,05	6E-05
9	**rs140533307**	**5474598**	0,29	0,05	8E-11	0,00	0,04	1E+00
1	**rs10857817**	**110803755**	0,30	0,05	5E-11	0,31	0,05	8E-12
6	**rs28397995**	**91209527**	0,46	0,15	2E-03	0,35	0,05	6E-15
5	**rs12516866**	**35851261**	0,32	0,05	2E-12	0,29	0,05	1E-09
1	**rs1289014**	**163625114**	0,32	0,05	4E-10	0,24	0,06	9E-06
7	**rs10232533**	**64875899**	0,88	0,53	1E-01	0,20	0,09	3E-02
13	**rs12184575**	**23793343**	0,21	0,05	2E-04	0,48	0,11	2E-05
10	**rs1670819**	**56695937**	0,35	0,06	3E-09	0,27	0,14	6E-02
13	**rs7989061**	**63466449**	0,22	0,05	6E-05	0,29	0,05	4E-08
10	**rs7909637**	**12557574**	0,25	0,04	2E-08	0,25	0,05	2E-07
2	**rs13400029**	**3582069**	0,19	0,07	6E-03	0,27	0,07	5E-05
3	**rs34643186**	**176058319**	0,31	0,06	2E-07	0,30	0,05	6E-11
15	**rs7167940**	**63247935**	0,30	0,05	2E-09	0,24	0,05	9E-08
2	**rs4663439**	**235497621**	0,27	0,06	1E-06	0,29	0,05	6E-08
14	**rs12892887**	**100055023**	0,28	0,04	7E-10	0,24	0,05	2E-07
11	**rs7128459**	**58179291**	0,24	0,06	1E-04	0,26	0,05	7E-07
7	**rs35308546**	**119209501**	0,05	0,12	7E-01	0,36	0,07	1E-06
12	**rs79193410**	**41029850**	0,30	0,05	2E-10	0,30	0,09	1E-03
7	**rs12699522**	**13580422**	0,47	0,57	4E-01	0,27	0,12	2E-02
10	**rs7895030**	**132941656**	0,50	0,07	6E-14	0,30	0,05	1E-11
3	**rs12695439**	**124291245**	0,30	0,05	6E-10	0,21	0,05	8E-06
11	**rs10891454**	**98080130**	0,28	0,05	7E-09	0,24	0,05	3E-07
13	**rs17370031**	**84977254**	0,23	0,07	2E-03	0,38	0,09	7E-05
22	**rs133181**	**25741258**	0,38	0,06	7E-11	0,38	0,20	6E-02
19	**rs1468773**	**57106401**	0,00	0,00	1E+00	0,20	0,06	2E-03
13	**rs200371919**	**19400990**	0,14	0,06	2E-02	0,30	0,05	8E-11
19	**rs11669449**	**15890517**	0,31	0,06	3E-08	0,27	0,05	1E-08
20	**rs6012712**	**48297253**	0,21	0,05	2E-05	0,21	0,05	1E-05
9	**rs10813569**	**31392324**	0,31	0,06	2E-08	0,35	0,04	9E-15
2	**rs10197142**	**13623160**	0,35	0,05	2E-13	0,25	0,08	1E-03
12	**rs7315639**	**44111933**	0,38	0,05	1E-16	0,26	0,05	2E-08
10	**rs138034016**	**31136540**	0,27	0,05	1E-08	0,14	0,05	2E-03
8	**rs8180941**	**90336707**	0,29	0,05	1E-09	0,39	0,06	8E-12
14	**rs113204453**	**44482023**	0,14	0,14	3E-01	0,34	0,07	5E-07
5	**rs2910300**	**160788827**	0,28	0,06	7E-07	0,17	0,05	1E-03
15	**rs11854693**	**58712965**	0,26	0,05	6E-09	0,33	0,05	8E-13
2	**rs334068**	**179005438**	0,25	0,05	3E-08	0,23	0,07	7E-04
13	**rs7317830**	**57274268**	0,25	0,05	2E-06	0,17	0,12	1E-01
9	**rs10984992**	**123473416**	0,21	0,04	2E-06	0,27	0,06	2E-06
9	**rs79288453**	**138440834**	0,19	0,06	2E-03	0,01	0,05	8E-01
1	**rs34133714**	**2765089**	0,32	0,05	5E-12	0,31	0,17	8E-02

4	**rs432164**	**177391093**	0,32	0,06	2E-08	0,35	0,06	6E-10
3	**rs4524298**	**82315953**	0,29	0,05	2E-08	0,31	0,05	8E-09
11	**rs6591063**	**103836968**	0,18	0,07	1E-02	0,26	0,06	2E-05
11	**rs11821564**	**97836250**	0,38	0,08	1E-06	0,19	0,05	3E-04
1	**rs10604003**	**237788262**	0,27	0,07	1E-04	0,33	0,05	8E-13
4	**rs1383567**	**34531200**	0,10	0,06	9E-02	0,31	0,05	2E-11
12	**rs12313074**	**117206787**	0,29	0,05	1E-09	0,29	0,05	1E-09
4	**rs1129304**	**158092422**	0,28	0,05	9E-10	0,24	0,05	7E-07
3	**rs12632694**	**66883694**	0,25	0,05	9E-08	0,29	0,05	1E-08
7	**rs6948652**	**157225138**	0,31	0,05	2E-11	0,25	0,05	1E-06
2	**rs10207163**	**69014280**	0,28	0,05	1E-09	0,27	0,05	4E-09
15	**rs1564688**	**93761742**	0,26	0,05	6E-09	0,25	0,07	1E-04
1	**rs4255374**	**237561785**	0,23	0,05	1E-06	0,29	0,07	3E-05
16	**rs395111**	**83881146**	0,32	0,05	6E-12	0,36	0,09	1E-04
8	**rs589933**	**60876977**	0,21	0,05	4E-06	0,35	0,05	3E-11
11	**rs11217793**	**120161886**	0,23	0,06	1E-04	0,31	0,07	4E-06
9	**rs11789058**	**119826169**	0,29	0,05	1E-08	0,29	0,05	3E-10
2	**rs6749895**	**172875442**	0,49	0,14	4E-04	0,18	0,07	1E-02
10	**rs632005**	**55320515**	0,04	0,05	4E-01	0,42	0,05	2E-16
14	**rs9323205**	**51586467**	0,20	0,21	3E-01	0,37	0,06	7E-10
5	**rs2434352**	**68333094**	0,26	0,07	8E-05	0,36	0,06	3E-08
1	**rs10453833**	**111909959**	0,25	0,07	1E-04	0,12	0,07	6E-02
7	**rs2709931**	**83033278**	-0,22	0,06	3E-04	0,01	0,06	8E-01
16	**rs149766632**	**78638797**	0,39	0,15	9E-03	0,27	0,07	1E-04
1	**rs598031**	**5333479**	0,32	0,05	1E-12	-0,22	0,30	5E-01
22	**rs28755**	**29685711**	0,26	0,05	5E-08	0,19	0,05	3E-04
15	**rs12324446**	**94721997**	0,57	0,12	2E-06	0,26	0,05	9E-09
18	**rs12965056**	**1324114**	0,24	0,05	4E-07	0,05	0,06	4E-01
6	**rs6908931**	**144735877**	0,22	0,06	9E-05	0,21	0,06	3E-04
3	**rs12054033**	**132531654**	0,26	0,05	8E-09	0,29	0,06	3E-07
15	**rs57843897**	**49833641**	0,31	0,05	4E-11	0,27	0,05	5E-09
6	**rs2798364**	**107161116**	0,31	0,05	3E-09	0,26	0,05	8E-08
14	**rs11490385**	**31718057**	0,36	0,06	3E-09	0,32	0,05	2E-09
9	**rs13283039**	**140181667**	0,32	0,05	3E-12	0,24	0,05	1E-07
4	**rs4833477**	**116324508**	0,29	0,05	1E-08	0,20	0,04	6E-06
5	**rs165188330**	**165188330**	0,34	0,07	1E-06	0,26	0,07	1E-04
12	**rs12309369**	**38419683**	0,27	0,08	1E-03	0,16	0,08	3E-02
16	**rs4783251**	**82698974**	0,18	0,13	2E-01	0,31	0,05	1E-09
10	**rs12780864**	**22421961**	0,33	0,10	1E-03	0,27	0,07	5E-05
6	**rs12192993**	**12380922**	0,26	0,05	5E-07	0,27	0,11	1E-02
4	**rs11735893**	**142896936**	-0,11	0,27	7E-01	0,11	0,11	3E-01
14	**rs1761004**	**46912023**	0,05	0,05	3E-01	0,02	0,04	6E-01
12	**rs142837217**	**86002875**	0,37	0,05	8E-15	0,43	0,14	2E-03
2	**rs6739828**	**43616008**	0,41	0,09	4E-06	0,33	0,05	3E-13
8	**rs2891977**	**122180353**	0,25	0,05	3E-07	0,23	0,05	1E-06

2	**rs2199883**	**185565463**	0,25	0,16	1E-01	-0,14	0,27	6E-01
9	**rs7874886**	**18865265**	0,26	0,06	2E-05	0,33	0,05	2E-13
15	**rs7170241**	**62810138**	0,29	0,04	2E-10	0,27	0,05	1E-08
6	**rs7775711**	**112161786**	0,30	0,05	1E-08	0,21	0,06	3E-04
10	**rs10883034**	**99845389**	0,23	0,05	9E-07	0,20	0,07	2E-03
3	**rs6438092**	**95479393**	0,28	0,05	5E-10	0,36	0,05	8E-15
17	**rs4796450**	**6139713**	0,19	0,06	5E-04	-0,13	0,29	7E-01
1	**rs2884855**	**110376651**	0,28	0,06	3E-07	0,26	0,05	1E-06
4	**rs11100785**	**144195557**	0,25	0,06	3E-05	0,39	0,05	3E-17
10	**rs11599612**	**86422743**	0,24	0,05	8E-08	0,31	0,05	2E-10
11	**rs1784430**	**102474813**	0,24	0,05	8E-08	0,27	0,04	2E-09
19	**rs454904**	**44511589**	0,27	0,05	6E-09	0,08	0,23	7E-01
1	**rs289686**	**76608491**	0,25	0,07	7E-04	0,30	0,09	5E-04
3	**rs2654695**	**192311851**	0,31	0,05	3E-11	0,28	0,05	1E-09
6	**rs2048696**	**163337823**	0,22	0,05	2E-06	0,30	0,06	9E-07
11	**rs10838609**	**5780716**	0,30	0,05	6E-09	0,39	0,13	3E-03
19	**rs3826798**	**5785113**	0,25	0,05	2E-08	0,30	0,05	1E-09
1	**rs609125**	**22915030**	0,22	0,05	1E-05	0,28	0,05	3E-08
2	**rs201400225**	**162693099**	0,28	0,12	2E-02	0,22	0,05	1E-06
14	**rs202227171**	**87861177**	0,31	0,05	5E-11	0,30	0,05	2E-11
13	**rs3832886**	**76419421**	0,22	0,05	8E-07	0,16	0,05	5E-04
7	**rs12669437**	**95253404**	0,30	0,11	4E-03	0,27	0,05	4E-09
6	**rs9344725**	**88493376**	-0,26	0,04	3E-09	-0,23	0,21	3E-01
5	**rs78479231**	**21293851**	0,32	0,05	8E-12	0,22	0,06	2E-04
4	**rs1078566**	**77914535**	0,33	0,05	2E-11	0,32	0,05	1E-11
19	**rs11084579**	**31802723**	0,25	0,05	2E-08	0,27	0,06	2E-06

DisChr	rsID_refSNP	pos_refSNP	Zhit_ eurasn	Zhit_ euryri	Zhit_ asnyri	Same_ eurasn	Same_ euryri	Same_ asnyri
4	**rs2333328**	**176852836**	0	0	0	1	1	1
9	**rs10869238**	**75803635**	0	0	0	1	1	1
22	**rs136575**	**45769245**	0	0	0	1	1	1
6	**rs579329**	**47822681**	0	0	0	1	1	1
10	**rs10999327**	**53522817**	0	0	0	1	1	1
6	**rs2516226**	**12604062**	0	1	1	1	1	1
8	**rs73351724**	**114787818**	0	0	0	1	1	1
3	**rs1387701**	**193147894**	0	0	0	1	1	1
4	**rs4340779**	**119678580**	0	0	1	1	1	1
15	**rs1604172**	**98040555**	0	0	0	1	1	1
15	**rs1470901**	**69097765**	0	0	0	1	1	1
1	**rs7556147**	**111407322**	0	0	0	1	1	1
7	**rs9692258**	**69049578**	0	0	0	1	1	1
12	**rs4761380**	**77829418**	0	0	0	1	1	1
14	**rs1959524**	**52312705**	1	0	1	0	1	0
17	**rs55969697**	**15264671**	0	0	0	1	1	1

17	rs7213597	12053126	0	0	0	1	1	1
22	rs6007521	45647534	0	0	0	1	1	1
22	rs535842	27621151	0	0	0	1	1	1
2	rs6754782	20573530	0	0	0	1	1	1
13	rs9549507	112996118	0	0	0	1	1	1
9	rs16925789	109495368	0	0	0	1	1	1
17	rs175381	49387207	0	0	0	1	1	1
4	rs7659549	103006301	0	0	0	1	1	1
13	rs278034	30416637	0	0	0	1	1	1
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5	rs1058312	14509966	0	0	0
9	rs913182	97478309	0	0	0
1	rs4653183	33984987	0	0	0
14	rs12879605	27295802	0	0	0
1	rs386012	83155380	0	0	0
16	rs58675609	85273226	0	1	1
5	rs76120834	125372245	0	0	0
15	rs79988905	42677731	0	0	0
2	rs920211	211874991	0	0	0
12	rs7958081	23093846	0	0	0
6	rs35434813	74802323	0	0	0
8	rs3808462	116606177	0	0	0
14	rs4020134	78420741	0	0	0
22	rs28702070	50344912	0	0	0
8	rs4366044	135516280	0	0	0
8	rs1834197	57755644	0	0	0
6	rs9377003	146861189	0	0	0
5	rs12520117	163522236	0	0	0
2	rs77847962	132742098	0	0	0
14	rs1959120	101568230	0	0	0
6	rs6914523	65027043	0	0	0
14	rs8009305	60383685	0	0	0
10	rs201533606	124511268	0	0	0
10	rs11819372	116594934	0	0	0
3	rs298756	164199329	0	0	0
9	rs551960	116384661	0	0	0
4	rs34881324	15217750	0	0	0
1	rs10921568	194387825	0	0	0
12	rs201055230	49143466	1	0	1
2	rs12987457	235599023	0	0	0
3	rs34197745	48090946	0	0	0
13	rs7339096	20711140	0	0	0
5	rs6883952	171961443	0	0	0
12	rs12426677	7414864	0	0	0
5	rs11241748	123846498	0	0	0
1	rs10586161	227175967	0	0	0
20	rs34973476	43770291	0	0	0
1	rs2236539	182096856	0	0	0
9	rs7048995	20012984	0	0	0
7	rs72077057	152651502	0	0	0
1	rs1501568	211087439	0	0	0
17	rs3815358	62010270	0	0	0

14	rs13156	51722349	0	0	0
5	rs7718109	61145102	0	0	0
1	rs12064174	194086050	0	0	0
12	rs5744884	133234389	0	0	0
9	rs140533307	5474598	0	0	0
1	rs10857817	110803755	0	0	0
6	rs28397995	91209527	0	0	0
5	rs12516866	35851261	0	0	0
1	rs1289014	163625114	0	0	0
7	rs10232533	64875899	0	0	0
13	rs12184575	23793343	0	0	0
10	rs1670819	56695937	0	0	0
13	rs7989061	63466449	0	0	0
10	rs7909637	12557574	0	0	0
2	rs13400029	3582069	0	0	0
3	rs34643186	176058319	0	0	0
15	rs7167940	63247935	0	0	0
2	rs4663439	235497621	0	0	0
14	rs12892887	100055023	0	0	0
11	rs7128459	58179291	0	0	0
7	rs35308546	119209501	0	0	0
12	rs79193410	41029850	0	0	0
7	rs12699522	13580422	0	0	0
10	rs7895030	132941656	0	0	0
3	rs12695439	124291245	0	0	0
11	rs10891454	98080130	0	0	0
13	rs17370031	84977254	0	0	0
22	rs133181	25741258	0	0	0
19	rs1468773	57106401	0	0	0
13	rs200371919	19400990	0	0	0
19	rs11669449	15890517	0	0	0
20	rs6012712	48297253	0	0	0
9	rs10813569	31392324	0	0	0
2	rs10197142	13623160	0	0	0
12	rs7315639	44111933	0	0	0
10	rs138034016	31136540	0	0	0
8	rs8180941	90336707	0	0	0
14	rs113204453	44482023	0	0	0
5	rs2910300	160788827	0	0	0
15	rs11854693	58712965	0	0	0
2	rs334068	179005438	0	0	0
13	rs7317830	57274268	0	0	0
9	rs10984992	123473416	0	0	0
9	rs79288453	138440834	0	0	0
1	rs34133714	2765089	0	0	0

4	rs432164	177391093	0	0	0
3	rs4524298	82315953	0	0	0
11	rs6591063	103836968	0	0	0
11	rs11821564	97836250	0	0	0
1	rs10604003	237788262	0	0	0
4	rs1383567	34531200	0	0	0
12	rs12313074	117206787	0	0	0
4	rs1129304	158092422	0	0	0
3	rs12632694	66883694	0	0	0
7	rs6948652	157225138	0	0	0
2	rs10207163	69014280	0	0	0
15	rs1564688	93761742	0	0	0
1	rs4255374	237561785	0	0	0
16	rs395111	83881146	0	0	0
8	rs589933	60876977	0	0	0
11	rs11217793	120161886	0	0	0
9	rs11789058	119826169	0	0	0
2	rs6749895	172875442	0	0	0
10	rs632005	55320515	0	0	0
14	rs9323205	51586467	0	0	0
5	rs2434352	68333094	0	0	0
1	rs10453833	111909959	0	0	0
7	rs2709931	83033278	0	1	1
16	rs149766632	78638797	0	0	0
1	rs598031	5333479	0	1	1
22	rs28755	29685711	0	0	0
15	rs12324446	94721997	0	0	0
18	rs12965056	1324114	0	0	0
6	rs6908931	144735877	0	0	0
3	rs12054033	132531654	0	0	0
15	rs57843897	49833641	0	0	0
6	rs2798364	107161116	0	0	0
14	rs11490385	31718057	0	0	0
9	rs13283039	140181667	0	0	0
4	rs4833477	116324508	0	0	0
5	rs165188330	165188330	0	0	0
12	rs12309369	38419683	0	0	0
16	rs4783251	82698974	0	0	0
10	rs12780864	22421961	0	0	0
6	rs12192993	12380922	0	0	0
4	rs11735893	142896936	1	0	1
14	rs1761004	46912023	0	0	0
12	rs142837217	86002875	0	0	0
2	rs6739828	43616008	0	0	0
8	rs2891977	122180353	0	0	0

2	**rs2199883**	**185565463**	0	1	1
9	**rs7874886**	**18865265**	0	0	0
15	**rs7170241**	**62810138**	0	0	0
6	**rs7775711**	**112161786**	0	0	0
10	**rs10883034**	**99845389**	0	0	0
3	**rs6438092**	**95479393**	0	0	0
17	**rs4796450**	**6139713**	0	1	1
1	**rs2884855**	**110376651**	0	0	0
4	**rs11100785**	**144195557**	0	0	0
10	**rs11599612**	**86422743**	0	0	0
11	**rs1784430**	**102474813**	0	0	0
19	**rs454904**	**44511589**	0	0	0
1	**rs289686**	**76608491**	0	0	0
3	**rs2654695**	**192311851**	0	0	0
6	**rs2048696**	**163337823**	0	0	0
11	**rs10838609**	**5780716**	0	0	0
19	**rs3826798**	**5785113**	0	0	0
1	**rs609125**	**22915030**	0	0	0
2	**rs201400225**	**162693099**	0	0	0
14	**rs202227171**	**87861177**	0	0	0
13	**rs3832886**	**76419421**	0	0	0
7	**rs12669437**	**95253404**	0	0	0
6	**rs9344725**	**88493376**	0	0	0
5	**rs78479231**	**21293851**	0	0	0
4	**rs1078566**	**77914535**	0	0	0
19	**rs11084579**	**31802723**	0	0	0

Supplementary Table 3

DisChr	rsID_refSNP	pos_refSNP	Allele Frequency EUR	Allele Frequency ASN	Allele Frequency YRI	beta EUR	stdbeta EUR	P EUR
6	rs2516225	12604455	0,17	0,19	0,94	0,36	0,06	1E-08
4	rs4340779	119678580	0,71	0,62	0,12	0,28	0,05	7E-09
12	rs4761380	77829418	0,51	0,53	0,38	0,26	0,05	1E-08
17	rs12938468	12049697	0,06	0,44	0,39	0,17	0,05	2E-04
22	rs6006959	45648846	0,29	0,20	0,15	0,30	0,05	2E-09
22	rs535842	27621151	0,80	0,33	0,67	0,31	0,05	2E-08
8	rs9773025	6674458	0,47	0,95	0,76	0,26	0,05	2E-08
7	rs10228515	12013256	0,42	0,54	0,71	0,24	0,05	2E-07
14	rs10498639	94775526	0,42	0,91	0,34	0,21	0,05	4E-06
13	rs2265354	87628517	0,21	0,45	0,36	0,25	0,04	2E-08
7	rs6947649	83415942	0,79	0,55	0,86	0,32	0,05	2E-09
2	rs1385167	66200648	0,13	0,27	0,26	0,31	0,07	1E-05
17	rs9914518	9709946	0,45	0,57	0,68	0,26	0,05	1E-08
6	rs7740484	137161671	0,63	0,53	0,74	0,26	0,05	7E-09
3	rs9843344	13670536	0,69	0,99	0,80	0,30	0,05	1E-10
6	rs9296996	9825495	0,34	0,03	0,23	0,30	0,05	7E-10
5	rs10065424	75841888	0,47	0,70	0,73	0,27	0,05	5E-09
11	rs566238	107706832	0,44	0,48	0,76	0,26	0,05	6E-09
3	rs16848141	164123367	0,33	0,35	0,59	0,27	0,05	3E-08
9	rs4836804	122908894	0,27	0,28	0,38	0,26	0,05	6E-08
8	rs4273853	22698106	0,39	0,34	0,30	0,34	0,05	1E-12
6	rs9458878	164073368	0,53	0,95	0,27	0,24	0,04	5E-08
4	rs3109848	26457168	0,81	0,84	0,66	0,31	0,05	8E-09
9	rs10978764	110001533	0,41	0,25	0,32	0,29	0,05	9E-10
10	rs7079002	34714686	0,63	0,54	0,35	0,20	0,05	2E-05
8	rs10955282	103176946	0,46	0,45	0,55	0,27	0,05	2E-09
11	rs1395558	6727468	0,67	0,53	0,31	-0,24	0,05	1E-06
1	rs6665839	49043877	0,17	0,26	0,40	0,24	0,06	2E-04
2	rs10865385	71703945	0,26	0,64	0,49	0,21	0,05	3E-06
10	rs507098	116062510	0,16	0,32	0,52	0,32	0,06	6E-07
11	rs193170	72259140	0,66	0,68	0,47	-0,27	0,05	2E-08
20	rs6048470	22954330	0,34	0,55	0,49	0,29	0,05	6E-10
8	rs16883602	87106685	0,35	0,51	0,23	0,13	0,05	4E-03
10	rs12770204	4432617	0,34	0,01	0,15	0,31	0,05	4E-10
2	rs1597944	234504098	0,50	0,53	0,16	0,29	0,05	2E-10
4	rs13115041	37707375	0,58	0,58	0,51	-0,41	0,08	5E-08
17	rs730714	74913718	0,13	0,38	0,26	0,24	0,07	8E-04
9	rs2017392	112820620	0,31	0,41	0,06	0,32	0,05	2E-10
5	rs172545	151323268	0,39	0,34	0,07	0,25	0,06	2E-05
12	rs7132916	55715119	0,76	0,88	0,82	0,31	0,05	2E-09
1	rs11208722	66171001	0,69	0,99	0,90	-0,29	0,05	2E-08

9	**rs7873139**	**113838967**	0,58	0,73	0,57	-0,28	0,06	7E-06
2	**rs374954**	**176084790**	0,25	0,40	0,36	0,24	0,05	1E-05
7	**rs10277426**	**105776457**	0,16	0,29	0,73	0,19	0,05	4E-05
6	**rs6912680**	**90300010**	0,80	0,70	0,32	0,22	0,05	4E-05
10	**rs1250538**	**81037800**	0,32	0,46	0,15	0,30	0,05	2E-09
9	**rs923559**	**87616532**	0,70	0,35	0,88	0,22	0,04	1E-06
21	**rs2178817**	**36679830**	0,71	0,58	0,22	0,23	0,05	9E-07
5	**rs244408**	**110021869**	0,80	0,77	0,35	0,25	0,05	6E-06
10	**rs2986034**	**105232580**	0,74	0,80	0,53	0,19	0,05	2E-04
14	**rs1147446**	**66461978**	0,18	0,25	0,57	0,35	0,06	2E-08
6	**rs6906235**	**139363102**	0,40	0,05	0,39	0,29	0,05	8E-10
6	**rs3778021**	**36948805**	0,37	0,13	0,63	0,22	0,05	2E-06
10	**rs7093277**	**13710897**	0,39	0,73	0,33	-0,34	0,05	2E-11
5	**rs10473457**	**20991326**	0,48	0,82	0,59	0,27	0,05	3E-08
5	**rs16877004**	**55753652**	0,24	0,36	0,10	0,24	0,05	1E-05
15	**rs4445847**	**74172013**	0,52	0,26	0,36	0,33	0,05	1E-09
12	**rs10736031**	**47580227**	0,71	0,58	0,57	0,16	0,04	3E-04
20	**rs399698**	**15368919**	0,30	0,17	0,08	0,29	0,05	1E-08
2	**rs10928230**	**145599194**	0,63	0,80	0,43	0,24	0,05	2E-07
8	**rs624311**	**109204437**	0,45	0,46	0,68	0,22	0,04	1E-06
1	**rs2232809**	**171750181**	0,62	0,67	0,85	0,28	0,05	7E-10
14	**rs1742180**	**86176908**	0,40	0,42	0,06	-0,25	0,04	3E-08
2	**rs10451542**	**168046215**	0,20	0,37	0,60	0,54	0,10	2E-08
17	**rs4239020**	**80176641**	0,72	0,93	0,90	0,31	0,05	2E-10
3	**rs4264699**	**111985428**	0,61	0,80	0,46	0,27	0,05	2E-09
7	**rs4613871**	**67223669**	0,23	0,20	0,24	0,31	0,05	1E-08
5	**rs4134393**	**30190699**	0,66	0,27	0,76	0,28	0,05	1E-09
1	**rs6655975**	**150542128**	0,66	0,67	0,69	0,26	0,05	2E-08
16	**rs9925780**	**81045176**	0,22	0,37	0,12	0,33	0,05	4E-10
3	**rs2194607**	**21523342**	0,33	0,68	0,53	0,30	0,05	2E-09
12	**rs11114652**	**81310652**	0,15	0,30	0,66	0,27	0,07	7E-05
7	**rs17267335**	**97269909**	0,38	0,76	0,97	0,30	0,05	3E-08
7	**rs6953266**	**76916010**	0,18	0,11	0,48	0,20	0,06	4E-04
6	**rs384323**	**9020424**	0,52	0,35	0,12	0,27	0,04	3E-09
10	**rs6585241**	**115486610**	0,80	0,86	0,95	0,31	0,05	1E-08
4	**rs7665844**	**40035613**	0,72	0,70	0,41	0,31	0,05	1E-10
3	**rs17012429**	**74409330**	0,06	0,26	0,02	0,32	0,10	8E-04
1	**rs6429014**	**237614434**	0,61	0,64	0,24	0,27	0,05	1E-08
6	**rs9371587**	**152660837**	0,22	0,27	0,46	0,36	0,06	2E-08
7	**rs10261050**	**114337652**	0,44	0,50	0,44	0,27	0,05	3E-09
17	**rs11077969**	**80085633**	0,53	0,14	0,52	-0,30	0,05	6E-11
8	**rs7822914**	**77663038**	0,16	0,46	0,59	0,27	0,06	2E-05
17	**rs684690**	**6577803**	0,17	0,31	0,38	0,25	0,06	1E-04
16	**rs11642831**	**25510461**	0,44	0,19	0,59	0,23	0,05	3E-07
6	**rs10456703**	**13739490**	0,24	0,17	0,38	0,35	0,06	3E-10

3	**rs950336**	**118586272**	0,41	0,52	0,14	0,28	0,05	3E-09
12	**rs1480073**	**98568330**	0,37	0,11	0,64	0,27	0,05	9E-09
4	**rs4691702**	**161736289**	0,66	0,86	0,85	0,33	0,05	2E-12
17	**rs806884**	**51422163**	0,51	0,30	0,61	0,27	0,05	4E-09
10	**rs954488**	**62616883**	0,14	0,29	0,32	0,33	0,07	5E-06
22	**rs4821661**	**37782256**	0,80	0,81	0,93	0,32	0,05	1E-09
3	**rs1532533**	**12635706**	0,46	0,11	0,55	0,33	0,06	5E-08
5	**rs1058312**	**14509966**	0,31	0,12	0,31	0,29	0,05	5E-09
1	**rs393017**	**83158517**	0,61	0,49	0,57	0,25	0,05	6E-08
2	**rs11684145**	**211873461**	0,35	0,24	0,06	0,28	0,05	6E-09
8	**rs3808462**	**116606177**	0,45	0,53	0,90	0,30	0,05	4E-11
8	**rs4366044**	**135516280**	0,07	0,30	0,40	0,37	0,10	1E-04
8	**rs1834197**	**57755644**	0,20	0,53	0,12	0,35	0,06	6E-09
6	**rs7770439**	**65027989**	0,71	0,51	0,62	0,37	0,05	3E-14
10	**rs11248479**	**124511073**	0,28	0,25	0,14	-0,18	0,05	1E-04
10	**rs17095662**	**116596071**	0,48	0,27	0,39	0,22	0,04	1E-06
9	**rs611335**	**116384750**	0,77	1,00	0,78	0,27	0,05	2E-07
11	**rs4923447**	**27495259**	0,94	0,85	0,66	0,19	0,09	3E-02
5	**rs6883952**	**171961443**	0,24	0,14	0,13	0,27	0,05	7E-07
1	**rs2236539**	**182096856**	0,57	0,56	0,63	0,25	0,05	2E-08
17	**rs1051684**	**62006497**	0,65	0,46	0,78	0,21	0,05	6E-06
14	**rs9918**	**51722690**	0,10	0,31	0,04	0,34	0,08	1E-05
5	**rs7718109**	**61145102**	0,18	0,31	0,31	0,36	0,06	3E-09
12	**rs5744844**	**133238076**	0,43	0,69	0,64	0,26	0,05	2E-08
7	**rs10232533**	**64875899**	0,64	1,00	0,94	0,27	0,05	2E-09
10	**rs1733795**	**56691305**	0,13	0,24	0,05	0,35	0,07	8E-07
10	**rs7078672**	**12558701**	0,28	0,34	0,27	0,15	0,05	4E-03
15	**rs8034321**	**63248945**	0,46	0,73	0,46	0,20	0,05	2E-05
14	**rs8017842**	**100055722**	0,39	0,51	0,72	0,23	0,05	5E-07
3	**rs2713649**	**124292219**	0,30	0,35	0,39	0,32	0,05	4E-10
19	**rs1468773**	**57106401**	0,23	0,00	0,16	0,35	0,06	2E-10
2	**rs10197142**	**13623160**	0,43	0,65	0,92	0,22	0,05	2E-06
12	**rs11182226**	**44110656**	0,39	0,48	0,35	0,25	0,05	4E-08
10	**rs10160116**	**31138817**	0,36	0,40	0,30	0,28	0,05	2E-09
8	**rs1038160**	**90337941**	0,35	0,36	0,22	0,30	0,05	3E-10
4	**rs365051**	**177391167**	0,40	0,25	0,57	0,22	0,08	3E-03
11	**rs6591063**	**103836968**	0,12	0,11	0,22	0,40	0,07	2E-08
1	**rs6683048**	**237788786**	0,11	0,13	0,45	0,22	0,07	1E-03
7	**rs11762388**	**48527244**	0,16	0,26	0,24	0,24	0,07	2E-04
7	**rs6978435**	**157224794**	0,53	0,40	0,78	0,28	0,04	5E-10
1	**rs4287207**	**107714954**	0,85	0,78	0,61	0,33	0,06	6E-08
11	**rs11217793**	**120161886**	0,18	0,18	0,14	0,38	0,06	4E-10
9	**rs11789058**	**119826169**	0,42	0,30	0,60	0,32	0,05	7E-12
10	**rs689581**	**55318856**	0,51	0,85	0,79	0,25	0,05	2E-08
14	**rs9323205**	**51586467**	0,24	0,01	0,20	0,34	0,05	5E-10

1	**rs10453833**	**111909959**	0,27	0,15	0,15	0,29	0,05	4E-08
7	**rs2722985**	**83037751**	0,60	0,84	0,11	-0,29	0,05	4E-10
15	**rs7164241**	**94721532**	0,29	0,04	0,40	0,21	0,05	5E-05
18	**rs1115296**	**1320397**	0,48	0,35	0,13	0,27	0,05	2E-09
3	**rs1376952**	**132533009**	0,27	0,54	0,22	0,25	0,05	3E-06
6	**rs2642465**	**107161532**	0,78	0,77	0,65	0,30	0,05	2E-08
6	**rs9361688**	**81656521**	0,27	0,59	0,29	0,23	0,05	9E-06
2	**rs6739828**	**43616008**	0,45	0,08	0,57	0,24	0,05	2E-07
10	**rs928578**	**99846671**	0,36	0,37	0,14	0,26	0,05	4E-08
17	**rs4796449**	**6139595**	0,49	0,49	0,56	-0,31	0,05	1E-08
10	**rs11599612**	**86422743**	0,45	0,40	0,36	0,27	0,05	6E-09
11	**rs1784430**	**102474813**	0,56	0,54	0,45	0,32	0,04	1E-12
19	**rs454904**	**44511589**	0,12	0,47	0,01	0,33	0,07	5E-06
1	**rs289686**	**76608491**	0,30	0,12	0,08	0,29	0,05	1E-08
3	**rs2654694**	**192312270**	0,46	0,43	0,55	0,25	0,05	4E-08
19	**rs3826798**	**5785113**	0,17	0,49	0,33	0,23	0,06	3E-04
7	**rs12669414**	**95253449**	0,38	0,92	0,51	0,28	0,05	7E-10
2	**rs1400863**	**215485519**	0,86	0,80	0,41	0,27	0,06	2E-05
4	**rs6836567**	**77916705**	0,62	0,35	0,37	0,25	0,05	6E-08
19	**rs10412617**	**31802550**	0,49	0,48	0,37	0,18	0,06	1E-03

DisChr	rsID_refSNP	pos_refSNP	beta ASN	stdbeta ASN	P ASN	beta YRI	stdbeta YRI	P YRI
6	**rs2516225**	**12604455**	0,31	0,06	2E-07	0,08	0,05	7E-02
4	**rs4340779**	**119678580**	0,33	0,05	5E-13	0,16	0,05	1E-03
12	**rs4761380**	**77829418**	0,27	0,04	2E-09	0,30	0,05	2E-10
17	**rs12938468**	**12049697**	0,29	0,05	3E-10	0,13	0,05	4E-03
22	**rs6006959**	**45648846**	0,25	0,06	1E-05	0,23	0,07	6E-04
22	**rs535842**	**27621151**	0,40	0,05	8E-16	0,31	0,05	6E-11
8	**rs9773025**	**6674458**	0,22	0,10	2E-02	0,20	0,05	5E-05
7	**rs10228515**	**12013256**	0,33	0,05	4E-13	0,26	0,05	8E-08
14	**rs10498639**	**94775526**	0,27	0,08	4E-04	0,27	0,05	3E-08
13	**rs2265354**	**87628517**	0,22	0,05	5E-06	0,29	0,06	7E-07
7	**rs6947649**	**83415942**	0,24	0,05	7E-08	0,36	0,06	3E-09
2	**rs1385167**	**66200648**	0,32	0,05	7E-09	0,24	0,05	8E-07
17	**rs9914518**	**9709946**	0,28	0,05	9E-10	0,18	0,04	6E-05
6	**rs7740484**	**137161671**	0,25	0,05	2E-08	0,03	0,05	5E-01
3	**rs9843344**	**13670536**	0,39	0,14	5E-03	0,12	0,05	3E-02
6	**rs9296996**	**9825495**	0,13	0,14	3E-01	0,21	0,05	7E-05
5	**rs10065424**	**75841888**	0,32	0,05	3E-11	0,28	0,05	8E-09
11	**rs566238**	**107706832**	0,26	0,05	1E-08	0,19	0,05	2E-04
3	**rs16848141**	**164123367**	0,29	0,05	1E-09	0,24	0,05	8E-08
9	**rs4836804**	**122908894**	0,28	0,05	4E-08	0,00	0,00	1E+00
8	**rs4273853**	**22698106**	0,25	0,05	2E-07	0,29	0,05	2E-08
6	**rs9458878**	**164073368**	0,27	0,10	6E-03	0,23	0,05	3E-06

4	**rs3109848**	**26457168**	0,34	0,06	7E-09	0,37	0,05	1E-11
9	**rs10978764**	**110001533**	0,18	0,05	9E-04	0,32	0,05	5E-11
10	**rs7079002**	**34714686**	0,29	0,05	1E-09	-0,92	0,59	1E-01
8	**rs10955282**	**103176946**	0,26	0,05	7E-09	0,23	0,04	3E-07
11	**rs1395558**	**6727468**	-0,34	0,05	1E-13	-0,21	0,05	2E-05
1	**rs6665839**	**49043877**	0,21	0,05	7E-05	0,31	0,05	7E-11
2	**rs10865385**	**71703945**	0,37	0,05	1E-15	0,26	0,08	7E-04
10	**rs507098**	**116062510**	0,32	0,05	1E-10	0,29	0,05	2E-10
11	**rs193170**	**72259140**	-0,13	0,05	4E-03	-0,01	0,05	9E-01
20	**rs6048470**	**22954330**	0,15	0,05	1E-03	0,22	0,05	1E-05
8	**rs16883602**	**87106685**	0,32	0,05	9E-13	0,01	0,05	8E-01
10	**rs12770204**	**4432617**	0,28	0,21	2E-01	0,11	0,07	1E-01
2	**rs1597944**	**234504098**	0,25	0,04	2E-08	0,38	0,07	5E-09
4	**rs13115041**	**37707375**	0,00	0,05	9E-01	0,02	0,05	6E-01
17	**rs730714**	**74913718**	0,28	0,05	5E-09	0,16	0,04	4E-04
9	**rs2017392**	**112820620**	0,28	0,05	2E-09	0,11	0,10	3E-01
5	**rs172545**	**151323268**	0,25	0,05	3E-08	0,07	0,09	5E-01
12	**rs7132916**	**55715119**	0,21	0,07	1E-03	0,16	0,05	3E-03
1	**rs11208722**	**66171001**	0,24	0,25	3E-01	0,08	0,07	3E-01
9	**rs7873139**	**113838967**	-0,33	0,05	1E-09	-0,47	0,15	1E-03
2	**rs374954**	**176084790**	0,27	0,05	5E-09	0,22	0,05	5E-06
7	**rs10277426**	**105776457**	0,27	0,05	2E-09	0,06	0,05	2E-01
6	**rs6912680**	**90300010**	0,30	0,05	4E-10	0,15	0,05	2E-03
10	**rs1250538**	**81037800**	0,28	0,05	8E-10	0,12	0,06	4E-02
9	**rs923559**	**87616532**	0,30	0,05	6E-10	0,25	0,06	2E-05
21	**rs2178817**	**36679830**	0,28	0,05	1E-09	0,24	0,05	1E-06
5	**rs244408**	**110021869**	0,23	0,05	6E-06	0,32	0,05	7E-11
10	**rs2986034**	**105232580**	0,25	0,05	3E-06	0,35	0,05	1E-14
14	**rs1147446**	**66461978**	0,28	0,05	3E-07	0,24	0,04	8E-08
6	**rs6906235**	**139363102**	0,10	0,07	2E-01	0,11	0,05	2E-02
6	**rs3778021**	**36948805**	0,27	0,07	6E-05	0,30	0,05	8E-11
10	**rs7093277**	**13710897**	-0,13	0,06	3E-02	-0,02	0,05	6E-01
5	**rs10473457**	**20991326**	0,27	0,08	7E-04	0,11	0,05	1E-02
5	**rs16877004**	**55753652**	0,31	0,05	1E-10	0,34	0,08	1E-05
15	**rs4445847**	**74172013**	0,36	0,13	5E-03	-0,05	0,05	3E-01
12	**rs10736031**	**47580227**	0,14	0,05	2E-03	0,29	0,04	9E-11
20	**rs399698**	**15368919**	0,35	0,06	3E-08	0,19	0,09	3E-02
2	**rs10928230**	**145599194**	0,41	0,05	7E-14	0,24	0,05	1E-07
8	**rs624311**	**109204437**	0,29	0,04	1E-10	0,34	0,05	1E-12
1	**rs2232809**	**171750181**	0,29	0,05	1E-09	0,31	0,06	3E-07
14	**rs1742180**	**86176908**	-0,17	0,04	2E-04	-0,04	0,05	4E-01
2	**rs10451542**	**168046215**	0,11	0,12	4E-01	0,04	0,05	5E-01
17	**rs4239020**	**80176641**	0,25	0,08	3E-03	0,26	0,07	3E-04
3	**rs4264699**	**111985428**	0,24	0,05	2E-07	0,28	0,05	2E-09
7	**rs4613871**	**67223669**	0,25	0,06	3E-05	0,14	0,05	1E-03

5	**rs4134393**	**30190699**	0,20	0,05	2E-04	0,36	0,05	8E-12
1	**rs6655975**	**150542128**	0,27	0,05	1E-08	0,18	0,05	4E-04
16	**rs9925780**	**81045176**	0,23	0,05	5E-07	0,13	0,05	7E-03
3	**rs2194607**	**21523342**	0,31	0,05	3E-11	0,24	0,05	8E-08
12	**rs11114652**	**81310652**	0,23	0,05	4E-06	0,28	0,05	2E-09
7	**rs17267335**	**97269909**	0,20	0,05	1E-04	0,16	0,08	3E-02
7	**rs6953266**	**76916010**	0,11	0,07	1E-01	0,26	0,05	7E-09
6	**rs384323**	**9020424**	0,25	0,05	3E-07	0,27	0,07	3E-04
10	**rs6585241**	**115486610**	0,28	0,06	5E-06	0,15	0,10	1E-01
4	**rs7665844**	**40035613**	0,24	0,05	6E-07	0,22	0,05	9E-07
3	**rs17012429**	**74409330**	0,29	0,05	4E-08	0,29	0,19	1E-01
1	**rs6429014**	**237614434**	0,22	0,04	6E-07	0,26	0,05	9E-07
6	**rs9371587**	**152660837**	-0,08	0,05	7E-02	0,20	0,08	1E-02
7	**rs10261050**	**114337652**	0,20	0,04	4E-06	0,28	0,05	8E-10
17	**rs11077969**	**80085633**	-0,28	0,06	7E-06	-0,30	0,05	4E-11
8	**rs7822914**	**77663038**	0,28	0,05	3E-10	0,19	0,05	6E-05
17	**rs684690**	**6577803**	0,21	0,05	4E-05	0,28	0,05	2E-09
16	**rs11642831**	**25510461**	0,40	0,06	5E-11	0,15	0,04	1E-03
6	**rs10456703**	**13739490**	0,28	0,07	2E-05	0,27	0,05	1E-08
3	**rs950336**	**118586272**	0,29	0,05	1E-10	0,30	0,07	8E-06
12	**rs1480073**	**98568330**	0,28	0,08	3E-04	0,17	0,05	3E-04
4	**rs4691702**	**161736289**	0,31	0,06	8E-07	0,31	0,06	1E-07
17	**rs806884**	**51422163**	0,08	0,05	8E-02	0,11	0,05	2E-02
10	**rs954488**	**62616883**	0,30	0,06	4E-08	0,27	0,05	5E-07
22	**rs4821661**	**37782256**	0,36	0,06	2E-10	0,32	0,08	2E-04
3	**rs1532533**	**12635706**	0,38	0,14	8E-03	0,20	0,05	4E-05
5	**rs1058312**	**14509966**	0,22	0,07	1E-03	0,23	0,05	2E-07
1	**rs393017**	**83158517**	0,26	0,05	4E-09	0,33	0,05	1E-13
2	**rs11684145**	**211873461**	0,25	0,05	3E-06	0,50	0,10	2E-06
8	**rs3808462**	**116606177**	0,25	0,05	4E-08	0,18	0,07	1E-02
8	**rs4366044**	**135516280**	0,34	0,05	1E-11	0,22	0,05	3E-06
8	**rs1834197**	**57755644**	0,28	0,04	4E-10	0,34	0,07	3E-06
6	**rs7770439**	**65027989**	0,33	0,05	1E-13	0,19	0,05	3E-05
10	**rs11248479**	**124511073**	-0,25	0,05	4E-08	0,02	0,10	8E-01
10	**rs17095662**	**116596071**	0,29	0,05	1E-09	0,21	0,05	7E-05
9	**rs611335**	**116384750**	0,25	0,50	6E-01	0,31	0,05	9E-09
11	**rs4923447**	**27495259**	0,25	0,06	4E-05	0,33	0,05	2E-12
5	**rs6883952**	**171961443**	0,40	0,07	8E-09	0,22	0,07	2E-03
1	**rs2236539**	**182096856**	0,27	0,05	3E-09	0,27	0,05	5E-09
17	**rs1051684**	**62006497**	0,29	0,05	2E-10	0,30	0,06	4E-07
14	**rs9918**	**51722690**	0,36	0,05	3E-13	0,25	0,12	3E-02
5	**rs7718109**	**61145102**	0,20	0,05	5E-05	0,27	0,05	6E-08
12	**rs5744844**	**133238076**	0,20	0,05	4E-05	0,29	0,05	3E-10
7	**rs10232533**	**64875899**	0,88	0,53	1E-01	0,20	0,09	3E-02
10	**rs1733795**	**56691305**	0,32	0,06	8E-09	0,32	0,11	5E-03

10	**rs7078672**	**12558701**	0,26	0,05	1E-08	0,22	0,06	2E-04
15	**rs8034321**	**63248945**	0,30	0,05	1E-09	0,28	0,04	5E-10
14	**rs8017842**	**100055722**	0,27	0,04	1E-09	0,15	0,05	7E-04
3	**rs2713649**	**124292219**	0,30	0,05	6E-10	0,21	0,05	8E-06
19	**rs1468773**	**57106401**	0,00	0,00	1E+00	0,20	0,06	2E-03
2	**rs10197142**	**13623160**	0,35	0,05	2E-13	0,25	0,08	1E-03
12	**rs11182226**	**44110656**	0,34	0,05	6E-13	0,22	0,05	4E-06
10	**rs10160116**	**31138817**	0,27	0,05	1E-08	0,30	0,05	5E-09
8	**rs1038160**	**90337941**	0,28	0,05	6E-09	0,41	0,06	3E-12
4	**rs365051**	**177391167**	0,12	0,09	2E-01	0,37	0,06	1E-08
11	**rs6591063**	**103836968**	0,18	0,07	1E-02	0,26	0,06	2E-05
1	**rs6683048**	**237788786**	0,20	0,06	2E-03	0,31	0,05	9E-12
7	**rs11762388**	**48527244**	0,31	0,05	6E-09	0,21	0,06	1E-04
7	**rs6978435**	**157224794**	0,30	0,05	1E-10	0,17	0,05	3E-04
1	**rs4287207**	**107714954**	0,21	0,05	4E-05	0,28	0,05	6E-10
11	**rs11217793**	**120161886**	0,23	0,06	1E-04	0,31	0,07	4E-06
9	**rs11789058**	**119826169**	0,29	0,05	1E-08	0,29	0,05	3E-10
10	**rs689581**	**55318856**	0,09	0,05	5E-02	0,21	0,05	5E-06
14	**rs9323205**	**51586467**	0,20	0,21	3E-01	0,37	0,06	7E-10
1	**rs10453833**	**111909959**	0,25	0,07	1E-04	0,12	0,07	6E-02
7	**rs2722985**	**83037751**	-0,22	0,06	3E-04	-0,29	0,07	2E-05
15	**rs7164241**	**94721532**	0,57	0,12	2E-06	0,27	0,05	5E-09
18	**rs1115296**	**1320397**	0,25	0,05	3E-07	0,12	0,06	3E-02
3	**rs1376952**	**132533009**	0,26	0,05	9E-09	0,29	0,06	3E-07
6	**rs2642465**	**107161532**	0,30	0,05	5E-09	0,24	0,05	2E-06
6	**rs9361688**	**81656521**	0,25	0,05	3E-08	0,23	0,05	2E-06
2	**rs6739828**	**43616008**	0,41	0,09	4E-06	0,33	0,05	3E-13
10	**rs928578**	**99846671**	0,23	0,05	1E-06	0,20	0,07	2E-03
17	**rs4796449**	**6139595**	-0,21	0,07	2E-03	0,00	0,00	1E+00
10	**rs11599612**	**86422743**	0,24	0,05	8E-08	0,31	0,05	2E-10
11	**rs1784430**	**102474813**	0,24	0,05	8E-08	0,27	0,04	2E-09
19	**rs454904**	**44511589**	0,27	0,05	6E-09	0,08	0,23	7E-01
1	**rs289686**	**76608491**	0,25	0,07	7E-04	0,30	0,09	5E-04
3	**rs2654694**	**192312270**	0,30	0,05	7E-11	0,31	0,05	9E-12
19	**rs3826798**	**5785113**	0,25	0,05	2E-08	0,30	0,05	1E-09
7	**rs12669414**	**95253449**	0,31	0,11	4E-03	0,27	0,05	4E-09
2	**rs1400863**	**215485519**	0,31	0,05	1E-08	0,03	0,04	5E-01
4	**rs6836567**	**77916705**	0,33	0,05	2E-11	0,30	0,05	2E-10
19	**rs10412617**	**31802550**	0,26	0,05	1E-08	-0,27	0,08	3E-04

DisChr	rsID_refSNP	pos_refSNP	Zhit_ eurasn	Zhit_ euryri	Zhit_ asnyri	Same_ eurasn	Same_ euryri	Same_ asnyri
6	**rs2516225**	**12604455**	0	1	1	1	1	1

4	rs4340779	119678580	0	0	1	1	1	1
12	rs4761380	77829418	0	0	0	1	1	1
17	rs12938468	12049697	0	0	1	1	1	1
22	rs6006959	45648846	0	0	0	1	1	1
22	rs535842	27621151	0	0	0	1	1	1
8	rs9773025	6674458	0	0	0	1	1	1
7	rs10228515	12013256	0	0	0	1	1	1
14	rs10498639	94775526	0	0	0	1	1	1
13	rs2265354	87628517	0	0	0	1	1	1
7	rs6947649	83415942	0	0	0	1	1	1
2	rs1385167	66200648	0	0	0	1	1	1
17	rs9914518	9709946	0	0	0	1	1	1
6	rs7740484	137161671	0	1	1	1	1	1
3	rs9843344	13670536	0	1	0	1	1	1
6	rs9296996	9825495	0	0	0	1	1	1
5	rs10065424	75841888	0	0	0	1	1	1
11	rs566238	107706832	0	0	0	1	1	1
3	rs16848141	164123367	0	0	0	1	1	1
9	rs4836804	122908894	0	1	1	1	0	0
8	rs4273853	22698106	0	0	0	1	1	1
6	rs9458878	164073368	0	0	0	1	1	1
4	rs3109848	26457168	0	0	0	1	1	1
9	rs10978764	110001533	0	0	1	1	1	1
10	rs7079002	34714686	0	0	1	1	0	0
8	rs10955282	103176946	0	0	0	1	1	1
11	rs1395558	6727468	0	0	0	1	1	1
1	rs6665839	49043877	0	0	0	1	1	1
2	rs10865385	71703945	1	0	0	1	1	1
10	rs507098	116062510	0	0	0	1	1	1
11	rs193170	72259140	1	1	0	1	1	1
20	rs6048470	22954330	1	0	0	1	1	1
8	rs16883602	87106685	1	0	1	1	1	1
10	rs12770204	4432617	0	1	0	1	1	1
2	rs1597944	234504098	0	0	0	1	1	1
4	rs13115041	37707375	1	1	0	0	0	1
17	rs730714	74913718	0	0	0	1	1	1
9	rs2017392	112820620	0	0	0	1	1	1
5	rs172545	151323268	0	0	0	1	1	1
12	rs7132916	55715119	0	1	0	1	1	1
1	rs11208722	66171001	1	1	0	0	0	1
9	rs7873139	113838967	0	0	0	1	1	1
2	rs374954	176084790	0	0	0	1	1	1
7	rs10277426	105776457	0	1	1	1	1	1
6	rs6912680	90300010	0	0	1	1	1	1
10	rs1250538	81037800	0	1	1	1	1	1

9	rs923559	87616532	0	0	0	1	1	1
21	rs2178817	36679830	0	0	0	1	1	1
5	rs244408	110021869	0	0	0	1	1	1
10	rs2986034	105232580	0	1	0	1	1	1
14	rs1147446	66461978	0	0	0	1	1	1
6	rs6906235	139363102	1	1	0	1	1	1
6	rs3778021	36948805	0	0	0	1	1	1
10	rs7093277	13710897	1	1	0	1	1	1
5	rs10473457	20991326	0	1	0	1	1	1
5	rs16877004	55753652	0	0	0	1	1	1
15	rs4445847	74172013	0	1	1	1	0	0
12	rs10736031	47580227	0	1	1	1	1	1
20	rs399698	15368919	0	0	0	1	1	1
2	rs10928230	145599194	1	0	1	1	1	1
8	rs624311	109204437	0	0	0	1	1	1
1	rs2232809	171750181	0	0	0	1	1	1
14	rs1742180	86176908	0	1	1	1	1	1
2	rs10451542	168046215	1	1	0	1	1	1
17	rs4239020	80176641	0	0	0	1	1	1
3	rs4264699	111985428	0	0	0	1	1	1
7	rs4613871	67223669	0	1	0	1	1	1
5	rs4134393	30190699	0	0	1	1	1	1
1	rs6655975	150542128	0	0	0	1	1	1
16	rs9925780	81045176	0	1	0	1	1	1
3	rs2194607	21523342	0	0	0	1	1	1
12	rs11114652	81310652	0	0	0	1	1	1
7	rs17267335	97269909	0	0	0	1	1	1
7	rs6953266	76916010	0	0	0	1	1	1
6	rs384323	9020424	0	0	0	1	1	1
10	rs6585241	115486610	0	0	0	1	1	1
4	rs7665844	40035613	0	0	0	1	1	1
3	rs17012429	74409330	0	0	0	1	1	1
1	rs6429014	237614434	0	0	0	1	1	1
6	rs9371587	152660837	1	0	1	0	1	0
7	rs10261050	114337652	0	0	0	1	1	1
17	rs11077969	80085633	0	0	0	1	1	1
8	rs7822914	77663038	0	0	0	1	1	1
17	rs684690	6577803	0	0	0	1	1	1
16	rs11642831	25510461	1	0	1	1	1	1
6	rs10456703	13739490	0	0	0	1	1	1
3	rs950336	118586272	0	0	0	1	1	1
12	rs1480073	98568330	0	0	0	1	1	1
4	rs4691702	161736289	0	0	0	1	1	1
17	rs806884	51422163	1	1	0	1	1	1
10	rs954488	62616883	0	0	0	1	1	1

22	rs4821661	37782256	0	0	0	1	1	1
3	rs1532533	12635706	0	0	0	1	1	1
5	rs1058312	14509966	0	0	0	1	1	1
1	rs393017	83158517	0	0	0	1	1	1
2	rs11684145	211873461	0	0	1	1	1	1
8	rs3808462	116606177	0	0	0	1	1	1
8	rs4366044	135516280	0	0	0	1	1	1
8	rs1834197	57755644	0	0	0	1	1	1
6	rs7770439	65027989	0	1	1	1	1	1
10	rs11248479	124511073	0	0	1	1	0	0
10	rs17095662	116596071	0	0	0	1	1	1
9	rs611335	116384750	0	0	0	1	1	1
11	rs4923447	27495259	0	0	0	1	1	1
5	rs6883952	171961443	0	0	0	1	1	1
1	rs2236539	182096856	0	0	0	1	1	1
17	rs1051684	62006497	0	0	0	1	1	1
14	rs9918	51722690	0	0	0	1	1	1
5	rs7718109	61145102	1	0	0	1	1	1
12	rs5744844	133238076	0	0	0	1	1	1
7	rs10232533	64875899	0	0	0	1	1	1
10	rs1733795	56691305	0	0	0	1	1	1
10	rs7078672	12558701	0	0	0	1	1	1
15	rs8034321	63248945	0	0	0	1	1	1
14	rs8017842	100055722	0	0	0	1	1	1
3	rs2713649	124292219	0	0	0	1	1	1
19	rs1468773	57106401	1	0	1	0	1	0
2	rs10197142	13623160	0	0	0	1	1	1
12	rs11182226	44110656	0	0	0	1	1	1
10	rs10160116	31138817	0	0	0	1	1	1
8	rs1038160	90337941	0	0	0	1	1	1
4	rs365051	177391167	0	0	1	1	1	1
11	rs6591063	103836968	1	0	0	1	1	1
1	rs6683048	237788786	0	0	0	1	1	1
7	rs11762388	48527244	0	0	0	1	1	1
7	rs6978435	157224794	0	0	0	1	1	1
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11	rs11217793	120161886	0	0	0	1	1	1
9	rs11789058	119826169	0	0	0	1	1	1
10	rs689581	55318856	1	0	0	1	1	1
14	rs9323205	51586467	0	0	0	1	1	1
1	rs10453833	111909959	0	1	0	1	1	1
7	rs2722985	83037751	0	0	0	1	1	1
15	rs7164241	94721532	1	0	1	1	1	1
18	rs1115296	1320397	0	1	0	1	1	1
3	rs1376952	132533009	0	0	0	1	1	1

6	rs2642465	107161532	0	0	0	1	1	1
6	rs9361688	81656521	0	0	0	1	1	1
2	rs6739828	43616008	0	0	0	1	1	1
10	rs928578	99846671	0	0	0	1	1	1
17	rs4796449	6139595	0	1	1	1	0	0
10	rs11599612	86422743	0	0	0	1	1	1
11	rs1784430	102474813	0	0	0	1	1	1
19	rs454904	44511589	0	0	0	1	1	1
1	rs289686	76608491	0	0	0	1	1	1
3	rs2654694	192312270	0	0	0	1	1	1
19	rs3826798	5785113	0	0	0	1	1	1
7	rs12669414	95253449	0	0	0	1	1	1
2	rs1400863	215485519	0	1	1	1	1	1
4	rs6836567	77916705	0	0	0	1	1	1
19	rs10412617	31802550	0	1	1	1	0	0

DisChr	rsID_refSNP	pos_refSNP	twoF_eurasn	twoF_euryri	twoF_asnyri	nGWAS_SNPs
6	rs2516225	12604455	0	0	0	147
4	rs4340779	119678580	0	0	0	93
12	rs4761380	77829418	0	0	0	142
17	rs12938468	12049697	0	0	0	122
22	rs6006959	45648846	0	0	0	196
22	rs535842	27621151	0	0	0	341
8	rs9773025	6674458	0	0	0	268
7	rs10228515	12013256	0	0	0	214
14	rs10498639	94775526	0	0	0	202
13	rs2265354	87628517	0	0	0	47
7	rs6947649	83415942	0	0	0	145
2	rs1385167	66200648	0	0	0	159
17	rs9914518	9709946	0	0	0	187
6	rs7740484	137161671	0	0	0	96
3	rs9843344	13670536	0	0	0	185
6	rs9296996	9825495	0	0	0	128
5	rs10065424	75841888	0	0	0	176
11	rs566238	107706832	0	0	0	116
3	rs16848141	164123367	0	0	0	76
9	rs4836804	122908894	0	0	0	115
8	rs4273853	22698106	0	0	0	197
6	rs9458878	164073368	0	0	0	132
4	rs3109848	26457168	0	0	0	90
9	rs10978764	110001533	0	0	0	175
10	rs7079002	34714686	0	1	1	105
8	rs10955282	103176946	0	0	0	137
11	rs1395558	6727468	0	0	0	216

1	**rs6665839**	**49043877**	0	0	0	147
2	**rs10865385**	**71703945**	0	0	0	143
10	**rs507098**	**116062510**	0	0	0	138
11	**rs193170**	**72259140**	0	0	0	131
20	**rs6048470**	**22954330**	0	0	0	183
8	**rs16883602**	**87106685**	0	0	0	87
10	**rs12770204**	**4432617**	0	0	0	207
2	**rs1597944**	**234504098**	0	0	0	284
4	**rs13115041**	**37707375**	1	1	0	209
17	**rs730714**	**74913718**	0	0	0	185
9	**rs2017392**	**112820620**	0	0	0	198
5	**rs172545**	**151323268**	0	0	0	116
12	**rs7132916**	**55715119**	0	0	0	84
1	**rs11208722**	**66171001**	1	1	0	140
9	**rs7873139**	**113838967**	0	0	0	175
2	**rs374954**	**176084790**	0	0	0	64
7	**rs10277426**	**105776457**	0	0	0	162
6	**rs6912680**	**90300010**	0	0	0	101
10	**rs1250538**	**81037800**	0	0	0	215
9	**rs923559**	**87616532**	0	0	0	148
21	**rs2178817**	**36679830**	0	0	0	153
5	**rs244408**	**110021869**	0	0	0	72
10	**rs2986034**	**105232580**	0	0	0	113
14	**rs1147446**	**66461978**	0	0	0	133
6	**rs6906235**	**139363102**	0	0	0	120
6	**rs3778021**	**36948805**	0	0	0	202
10	**rs7093277**	**13710897**	0	0	0	216
5	**rs10473457**	**20991326**	0	0	0	64
5	**rs16877004**	**55753652**	0	0	0	206
15	**rs4445847**	**74172013**	0	1	1	138
12	**rs10736031**	**47580227**	0	0	0	162
20	**rs399698**	**15368919**	0	0	0	253
2	**rs10928230**	**145599194**	0	0	0	83
8	**rs624311**	**109204437**	0	0	0	66
1	**rs2232809**	**171750181**	0	0	0	133
14	**rs1742180**	**86176908**	0	0	0	166
2	**rs10451542**	**168046215**	0	0	0	87
17	**rs4239020**	**80176641**	0	0	0	102
3	**rs4264699**	**111985428**	0	0	0	130
7	**rs4613871**	**67223669**	0	0	0	132
5	**rs4134393**	**30190699**	0	0	0	91
1	**rs6655975**	**150542128**	0	0	0	80
16	**rs9925780**	**81045176**	0	0	0	237
3	**rs2194607**	**21523342**	0	0	0	209
12	**rs11114652**	**81310652**	0	0	0	135

7	**rs17267335**	**97269909**	0	0	0	134
7	**rs6953266**	**76916010**	0	0	0	119
6	**rs384323**	**9020424**	0	0	0	113
10	**rs6585241**	**115486610**	0	0	0	208
4	**rs7665844**	**40035613**	0	0	0	106
3	**rs17012429**	**74409330**	0	0	0	132
1	**rs6429014**	**237614434**	0	0	0	201
6	**rs9371587**	**152660837**	1	0	1	197
7	**rs10261050**	**114337652**	0	0	0	65
17	**rs11077969**	**80085633**	0	0	0	92
8	**rs7822914**	**77663038**	0	0	0	113
17	**rs684690**	**6577803**	0	0	0	187
16	**rs11642831**	**25510461**	0	0	0	123
6	**rs10456703**	**13739490**	0	0	0	104
3	**rs950336**	**118586272**	0	0	0	107
12	**rs1480073**	**98568330**	0	0	0	130
4	**rs4691702**	**161736289**	0	0	0	111
17	**rs806884**	**51422163**	0	0	0	118
10	**rs954488**	**62616883**	0	0	0	118
22	**rs4821661**	**37782256**	0	0	0	210
3	**rs1532533**	**12635706**	0	0	0	206
5	**rs1058312**	**14509966**	0	0	0	133
1	**rs393017**	**83158517**	0	0	0	149
2	**rs11684145**	**211873461**	0	0	0	124
8	**rs3808462**	**116606177**	0	0	0	70
8	**rs4366044**	**135516280**	0	0	0	186
8	**rs1834197**	**57755644**	0	0	0	156
6	**rs7770439**	**65027989**	0	0	0	56
10	**rs11248479**	**124511073**	0	1	1	124
10	**rs17095662**	**116596071**	0	0	0	114
9	**rs611335**	**116384750**	0	0	0	137
11	**rs4923447**	**27495259**	0	0	0	108
5	**rs6883952**	**171961443**	0	0	0	155
1	**rs2236539**	**182096856**	0	0	0	113
17	**rs1051684**	**62006497**	0	0	0	111
14	**rs9918**	**51722690**	0	0	0	174
5	**rs7718109**	**61145102**	0	0	0	121
12	**rs5744844**	**133238076**	0	0	0	130
7	**rs10232533**	**64875899**	0	0	0	46
10	**rs1733795**	**56691305**	0	0	0	135
10	**rs7078672**	**12558701**	0	0	0	233
15	**rs8034321**	**63248945**	0	0	0	193
14	**rs8017842**	**100055722**	0	0	0	128
3	**rs2713649**	**124292219**	0	0	0	197
19	**rs1468773**	**57106401**	0	0	0	165

2	**rs10197142**	**13623160**	0	0	0	103
12	**rs11182226**	**44110656**	0	0	0	99
10	**rs10160116**	**31138817**	0	0	0	146
8	**rs1038160**	**90337941**	0	0	0	94
4	**rs365051**	**177391167**	0	0	0	164
11	**rs6591063**	**103836968**	0	0	0	141
1	**rs6683048**	**237788786**	0	0	0	206
7	**rs11762388**	**48527244**	0	0	0	143
7	**rs6978435**	**157224794**	0	0	0	146
1	**rs4287207**	**107714954**	0	0	0	157
11	**rs11217793**	**120161886**	0	0	0	137
9	**rs11789058**	**119826169**	0	0	0	235
10	**rs689581**	**55318856**	0	0	0	162
14	**rs9323205**	**51586467**	0	0	0	176
1	**rs10453833**	**111909959**	0	0	0	239
7	**rs2722985**	**83037751**	0	0	0	131
15	**rs7164241**	**94721532**	0	0	0	234
18	**rs1115296**	**1320397**	0	0	0	100
3	**rs1376952**	**132533009**	0	0	0	108
6	**rs2642465**	**107161532**	0	0	0	198
6	**rs9361688**	**81656521**	0	0	0	97
2	**rs6739828**	**43616008**	0	0	0	99
10	**rs928578**	**99846671**	0	0	0	131
17	**rs4796449**	**6139595**	0	0	0	217
10	**rs11599612**	**86422743**	0	0	0	130
11	**rs1784430**	**102474813**	0	0	0	194
19	**rs454904**	**44511589**	0	0	0	146
1	**rs289686**	**76608491**	0	0	0	164
3	**rs2654694**	**192312270**	0	0	0	109
19	**rs3826798**	**5785113**	0	0	0	124
7	**rs12669414**	**95253449**	0	0	0	208
2	**rs1400863**	**215485519**	0	0	0	116
4	**rs6836567**	**77916705**	0	0	0	146
19	**rs10412617**	**31802550**	0	1	1	108