

# **FRONTIERS IN CARDIOVASCULAR CARE: 2008 and Beyond**

Kim A. Eagle, M.D.

Fall 2008



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# **FRONTIERS IN CARDIOVASCULAR CARE: 2008 and Beyond**

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# WHAT FACTORS WILL IMPACT FUTURE CARE?

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- Globalization of information / communication
  - Explosion of scientific knowledge / technology
  - Global economy
  - Genetic typing
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# GENERAL CARDIAC CARE

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- Increased emphasis on quality
  - Electronic medical records and communication
  - Less emphasis on episodic care / more on coordinated, cost-effective management
  - Clearer definition for end-of-line therapies
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# PREVENTIVE CARDIOLOGY

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- Identification of new risk factors, particularly genetic
  - Development of both lifestyle and pharmacologic treatment menus tailored to genetic “fingerprint”
  - Worsening burden of coronary disease world wide... “westernization” of fast foods and smoking
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# VASCULAR DISEASES

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- Computerized drug selection for hypertensive management
  - Expanded use of gene therapy
  - Expanded use of percutaneous stent therapies for occlusive disease in arterial beds
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# NON INVASIVE IMAGING

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- MRI and CT will reduce much of current-day angiography
  - Endothelial imaging will allow identification of “hot” areas... plaque, clot, etc.
  - Contrast echo in 3-D will emerge
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# INVASIVE THERAPIES

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- More coronary intervention for acute MI...  
genetic fingerprint will influence choice
  - Less coronary angiography for stable patients  
as medical / preventative therapies improve
  - Local drug delivery on stents
  - Smaller, slicker, safer catheters
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# ARRHYTHMIA THERAPIES

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- Expanded use of catheter based ablation
  - Expanded ability to map arrhythmic foci
  - Smaller, cheaper, more widely used defibrillators
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# SCIENTIFIC EMPHASIS

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- Genetic fingerprints - with ability to match best therapy with genetic substrate
  - Miniaturization of technology - defibrillators, catheters, robotic surgery, etc.
  - Vessel wall biology - why disease begins, how to stop it or treat it
  - Bioinformatics - the right information at the right time
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# SPECIFIC DISEASE STATES

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- Diabetes - keys to its' malignant vascular disease
  - Aging - better clarity of its' causes and optimal therapy
  - Women and heart disease - further definition of optimal choices
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# The Complexity of Genomics and Cardiovascular Medicine

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***Genes***

(3 Billion)



Single Nucleotide Polymorphisms (SNP's)

(10,000,000)



Gene Expression Profiles (Transcriptomics)

(20,000)



Protein Arrays of Specific Proteins (Proteomics)

(100,000)



Metabolic Profiles (Metabolomics)

(1,000 – 10,000)

# Examples of Candidate Genes: CAD or MI

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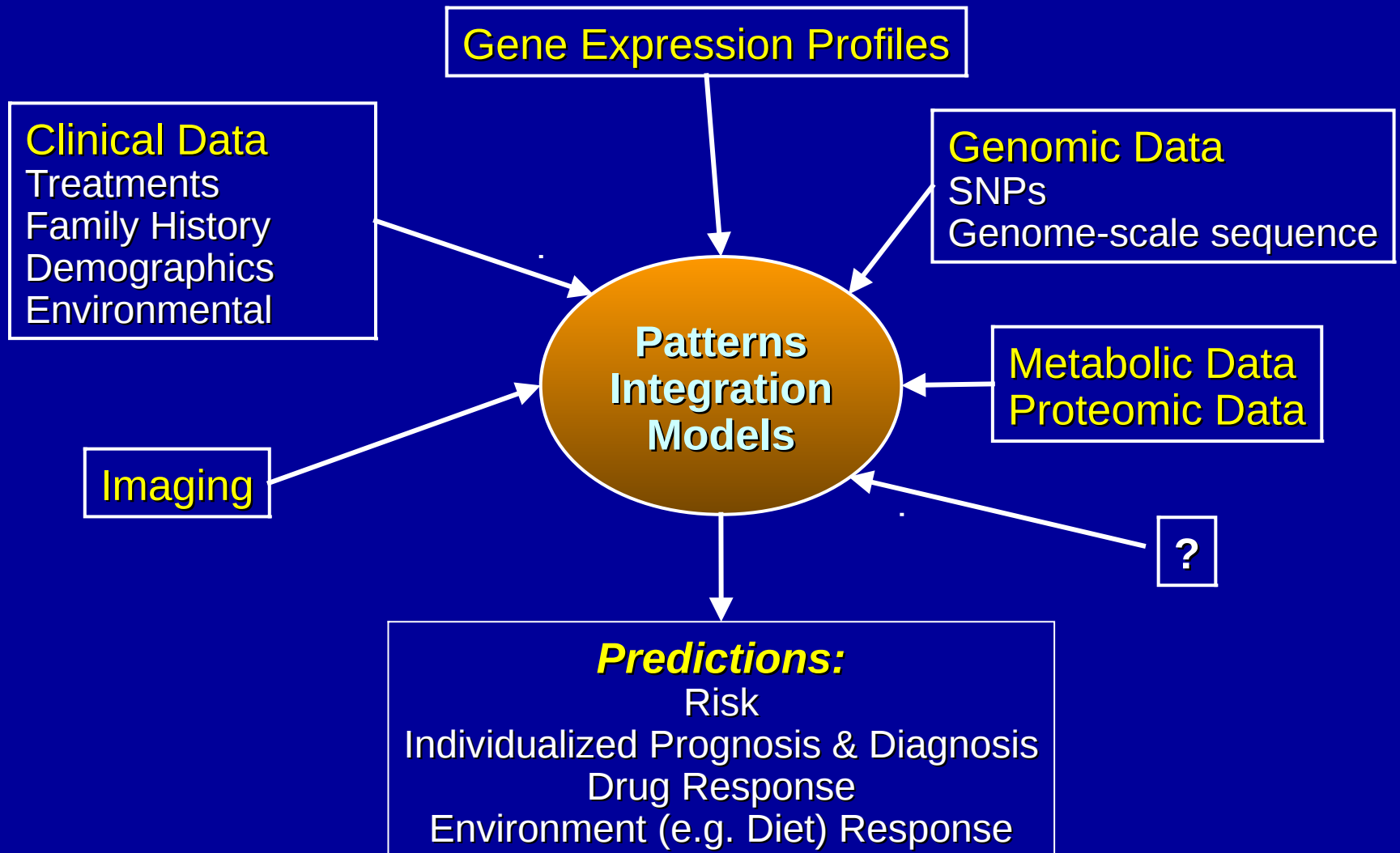
- Apolipoprotein E
- Tetrahydrofolate Reductase
- Angiotensin Converting Enzyme
- Apolipoprotein B
- Plasminogen Activator Inhibitor
- Fibrinogen B-Chain
- Endothelial Nitric Oxide
- Connexin 37
- Factor VII
- Thrombopoietin
- P-22
- Stromelysin
- Lymphotoxin-alpha
- Alpha-adducin
- Cholesterol Ester Transfer Protein
- Paraxonase 1,2
- Apolipoprotein C-III
- 5-Lipoxygenase activating protein (FLAP)
- Selectin-P
- Thrombospondin 2,4
- Fibrinogen B

# Protein Biomarkers in CV Disease

<u>Clinical Area</u>	<u>Biomarker</u>	<u>Current Status</u>	
		<u>In Clinical Use</u>	<u>Emerging Clinical Use</u>
<u>Myocardial Necrosis</u>	<ul style="list-style-type: none"> <li>• Troponin I, T</li> <li>• Creatinine Kinase-MB</li> <li>• Myoglobin</li> </ul>	X X X	
<u>Hemodynamic Status</u>	<ul style="list-style-type: none"> <li>• B-type natriuretic peptide</li> <li>• N-terminal pro-BNP</li> </ul>	X X	
<u>Ischemia</u>	<ul style="list-style-type: none"> <li>• Unbound free fatty acids</li> <li>• Ischemia modified albumin</li> <li>• Whole blood choline</li> <li>• BNP</li> </ul>		X X X
<u>Inflammation/ Plaque Stability</u>	<ul style="list-style-type: none"> <li>• HS-CRP</li> <li>• IL-6, 10, 18</li> <li>• CD-40 Ligand</li> <li>• Myeloperoxidase</li> <li>• MMP's</li> </ul>	X	XXX X X X



# Clinico-genomic Biosignatures to Predict Health, Disease and Environmental Drug Response



# What Genomics May Bring to Cardiovascular Medicine

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- Clinical use of genomic variation to predict health and disease in individuals, communities, and whole populations
- Incorporation of the complex interplay of genes and the environment vis-à-vis patient care, whether that environment be cellular, industrial or socioeconomic
- Integration of precise phenotypic data with equally precise genotypic data in a comprehensive computationally robust clinical framework

# What Genomics May Bring to Cardiovascular Medicine

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- Development of state-of-the-art technologies that assess the activity of large portions of the genome, transcriptome, proteome, and metabolome
- Utilization of genomic information to streamline drug development and improve our understanding of drug safety, tolerance and efficacy
- Discussion of the ethical, legal and policy issues raised by the integration of the genome sciences into the practice of medicine
- Fundamentally alter the way in which health care is delivered and practiced in order to optimize care and reduce costs overall

# CHALLENGES YOU'LL FACE

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- Ethics - genetic hair color... “bad person, good person”
  - End - of - life medical spending
  - 2 - class health system
  - Cost - widening gap between what we can afford to give all citizens vs. what's available to give one (wealthy) citizen
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# CHALLENGES

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- Human cloning
  - Organ cloning
  - Disease identification years before its development
  - Defining the degree of environmental influence on disease
  - “Shaping human behavior: the cardiology - general has determined that *french fries* are bad for your health”
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# OPPORTUNITIES

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- No generation has had more opportunity to change health care than yours will
  - The new science, genomics, will allow “diagnostics and therapeutics of mind-boggling proportion”
  - Globalization of science creates an opportunity for a kinder, more gentle world
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# EPILOGUE

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*“The faculty consider it a great honor to participate in your education. Best wishes for your continued success. You will carry the work that we have started.”*

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*“There are those who just wander about the wards and those who do the doctoring. The difference is having (and using) the data.”*

*Eugene Stead, 1960's*

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*“Never doubt that a small group of thoughtful, committed people can change the world. Indeed, it is the only thing that ever has.”*

*Mead*

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