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FRONTIERS IN CARDIOVASCULAR CARE:

2008 and Beyond

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Fall 2008

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What Factors Will Impact Future Care?

- Globalization of information / communication
- Explosion of scientific knowledge / technology
- Global economy
- Genetic typing

GENERAL CARDIAC CARE

- 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

PREVENTIVE CARDIOLOGY

- 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

VASCULAR DISEASES

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

Non Invasive Imaging

- 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

INVASIVE THERAPIES

- 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

Arrhythmia Therapies

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

SCIENTIFIC EMPHASIS

- 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

SPECIFIC DISEASE STATES

- 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

The Complexity of Genomics and Cardiovascular Medicine

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)

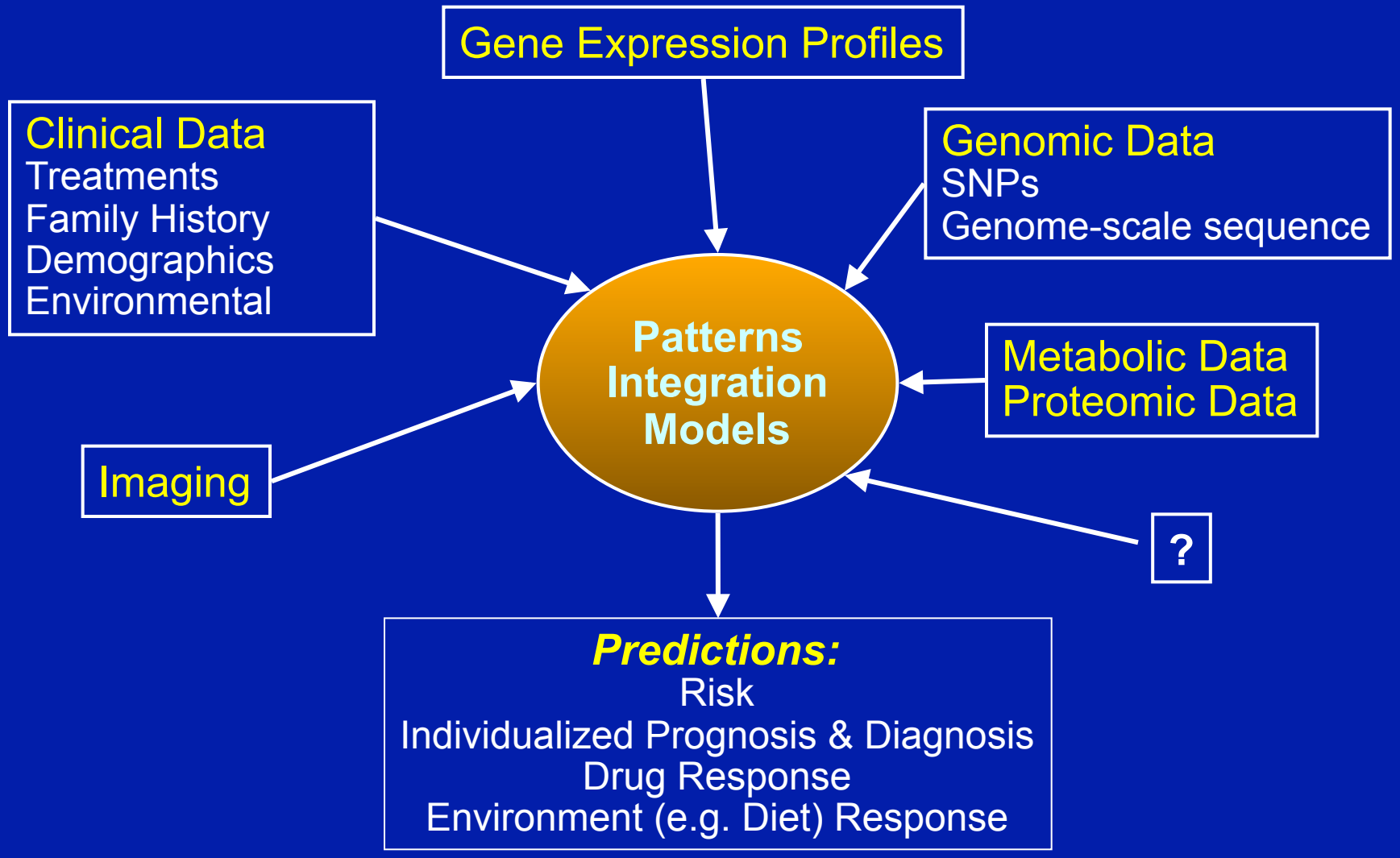
Examples of Candidate Genes: CAD or MI

- Apolipoprotein E
- Tetrahydrofolate Reductase
- Angiotensin Converting Enzyme
- Apolipoprotein B
- Plasminogen Activator Inhibitor
- Fibrinogen B-Chain
- Endothelial Nitric Oxide
- Connexin 37
- Factor VII
- Thrombopoetin
- 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

Clinical Area	Biomarker	Current Status	
		In Clinical Use	Emerging Clinical Use
Myocardial Necrosis			
	• Troponin I, T	X	
	• Creatinine Kinase-MB	X	
	• Myoglobin	X	
Hemodynamic Status			
	• B-type natriuretic peptide	X	
	• N-terminal pro-BNP	X	
Ischemia			
	• Unbound free fatty acids		X
	• Ischemia modified albumin		X
	• Whole blood choline		X
	• BNP	X	
Inflammation/ Plaque Stability			
	• HS-CRP	X	
	• IL-6, 10, 18		XXX
	• CD-40 Ligand		X
	• Myeloperoxidase		X
	• MMP's		X

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



What Genomics May Bring to Cardiovascular Medicine

- 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

- 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

- 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

CHALLENGES

- 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”

OPPORTUNITIES

- 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

EPILOGUE

"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."

“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

"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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