## Personalized Health Care

### An Overview

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### Personalized Health Care

#### The Patient Perspective

- Compassionate and competent care that recognizes the patient as an individual with their own principles, values and cultural beliefs
Personalized Health Care
The Care-Giver Perspective

- Provision of health advice and disease therapy that recognizes the biologic, environmental, behavioral and cultural uniqueness of each patient.

- Interaction one of compassion and competence that incorporates patient values and beliefs.

The Classic Pillars of Health Care

Public Health
Personalized health care will combine the basic scientific breakthroughs of the human genome with computer-age ability to exchange and manage data.

HHS Secretary Leavitt
March, 2007

"Personalized health care will give us the ability to deliver the right treatment to the right patient at the right time …"

HHS Secretary Leavitt
March, 2007
Personalized Health Care
The Scientific Perspective

- Individualized care based upon the use of genetic information to understand a person’s risk of disease and response to therapy
- The use of biomarkers to understand a person’s health status, predilection for disease, disease state, and response to therapy.

✓ Biomarkers range from individual physical to behavioral characteristics, but often focus on compounds present in the blood or in solid tissues.

The Spectrum of Personalized Health Care

<table>
<thead>
<tr>
<th>Values</th>
<th>Culture</th>
<th>Environment</th>
<th>Phenotype</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personalized Care Delivery</td>
<td>Integrative Medicine</td>
<td>Behavioral Medicine</td>
<td>Palliative Medicine</td>
<td>Personalized Medicine</td>
</tr>
</tbody>
</table>

Personalized Health Care

May also include ...

Individual Environment, Behavior, Culture, Values

Personalized Medicine
Why Now?

- New knowledge
- New laboratory methods
- New advances in computer hardware and biomedical informatics software
The Human Genome Project

- The Human Genome Project, a 13-year project coordinated by the U.S. Department of Energy and the National Institutes of Health
- Draft genome 2003, sequence completed 2006
- The total gene # estimated at 30,000
- Functions unknown for over 50% of discovered genes.

Genetic Variation Between Individuals

Single Nucleotide Polymorphisms

- Single nucleotide polymorphisms (SNPs) are alterations in the DNA sequence that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered.
- To be called a SNP, the variations must occur in at least 1% of the population.
- SNPs make up about 90% of all human genetic variation
- Two of every three SNPs involve the replacement of cytosine (C) with thymine (T).
- SNPs can occur in both coding (gene) and noncoding regions of the genome.

The Human Genome

- 99.9 percent of the DNA bases are the same between any two people.
- The variation in 0.1 percent of the genome makes a person unique.

Genetic Variation Between Individuals

- DNA variations can affect protein structure and function as well as regulate gene expression.
- DNA regulatory polymorphisms are many time more frequent than those affecting protein structure and function.
- The most common outcome of regulatory polymorphisms is differences in the levels of mRNA
- These regulatory polymorphisms account for the majority of phenotypic variability
Pharmacogenomics

- The relationship between inter-individual genetic variability and its influence on drug disposition and effect.

Genetics and Drug Therapy

- Differences in drug response can be secondary to differences in drug metabolism
  - Greater than 50% of all drugs metabolized by the cytochrome P450 family of enzymes
  - Greater than 30 different P450 forms, each with its own gene
  - Patients can have variants that lead to increased drug metabolism or decreased drug metabolism.

Personalized Medicine Optimizing Therapy

- Patients respond differently to the same medicine
  - 10%-30% do not respond to ACE inhibitors
  - 20%-50% do not respond to antidepressants
  - 40%-70% do not respond to Beta-2 agonists

Genetics and Drug Therapy C450 Metabolized Drugs

- Antidepressants
- Antipsychotics
- Beta-blockers
- Proton-pump inhibitors
- Anti-epileptics
Optimizing Drug Therapy

Genetic Testing

• The AmpliChip® CYP450 Test
• Determines a patient's CYP2D6 and CYP2C19 genotype from genomic DNA extracted from a whole blood sample.
• The test identifies a patient's metabolic phenotype: poor, intermediate, extensive, or ultrarapid metabolizer.

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Personalized Health Care Research

Biomarker Discovery

✓ Discovery of genetic linkages and polymorphisms
✓ Radiographic imaging refinement
✓ RNA, protein, lipid and carbohydrate markers in liquid and solid tissues

Personalized Health Care -- Under Construction

Research Advancement of Research Tools

• Bioinformatics: ability to communicate between divergent data sets and to analyze complex data sets for patterns
• Information Warehouses (IWs): ability to collect and collate diverse data sets on patients
• Biorepositories: storage of normal and diseased tissues, including fluids. Reference these in IWs
• DNA sequencing: speed, accuracy and price
Personalized Health Care

- Personalized
- Predictive
- Preemptive

Systems Biology in Medicine

Clay Marsh, MD
Director, Center for Critical Care
Center for Personalized Health Care

Go Bucks!

Patient Phenotype
What Determines Patient Phenotype?

Human Genome

- On average, each human differs from another by less than one percent of their genetic makeup.
  - These genetic differences give rise to our physical differences, including our potential predisposition to various diseases.
  - The ability to examine each individual’s unique genetic makeup and thereby customize our approaches to medical treatment is at the heart of this new era of predictive, preventive, personalized medicine.

From Genes to Proteins

From the Gene to the Protein

- Cells: Fundamental working units of every living system
- DNA: Building block of life – all organisms have the same chemical and physical DNA structure
  - Made up of subunits called nucleotides
- Genome: Complete set of DNA
- Chromosome: Largest ordered array of DNA, 24 in number, composed of 50-250 million base pairs
## From the Gene to the Protein

<table>
<thead>
<tr>
<th>Gene: Smallest functional units of heredity. 25-30,000 genes in humans.</th>
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<tbody>
<tr>
<td>Only 1.5% of the genome</td>
</tr>
<tr>
<td>Protein: Perform most life functions and make up the majority of cell structures.</td>
</tr>
<tr>
<td>Made up of subunits called amino acids.</td>
</tr>
<tr>
<td>Proteome: Constellation of all proteins in the cell.</td>
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## Are There Currently Genetic Tests for Human Disease?

<table>
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<tr>
<th>Chronic Myelogenous Leukemia</th>
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<tbody>
<tr>
<td>Bcr-Abl gene (9-22 chromosomal translocation)</td>
</tr>
<tr>
<td>High Cholesterol</td>
</tr>
<tr>
<td>LDL receptor mutation</td>
</tr>
<tr>
<td>Sickle Cell Anemia</td>
</tr>
<tr>
<td>β-globin gene mutation</td>
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</tbody>
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## Are There Currently Genetic Tests for Human Disease?

- Yes
  - Breast cancer
    - BCRA-1 or BCRA-2 mutation
  - Cystic Fibrosis
    - Cystic Fibrosis Transmembrane conductance Regulator mutation

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## Are Genetic Differences Enough to Explain Complex Disease?

- Yes
Complex Human Phenotypes

- Diabetes
- Lung Cancer
- Cardiomyopathies
- Emphysema
- Asthma
- Infectious Disease
- Rheumatologic Disease
- Renal failure

How Do We Study Complex Disease?

Complex diseases are conditions that are influenced by the actions of multiple genes, their interactions with each other and with the environment.
Systems Biology

- Emergent field that aims at systems-level understanding of biological systems.
  - System view differentiates this from normal research approach and focuses at understanding:
    - The structure of the system
    - The dynamics of the system
    - The control methods of the system
    - The design methods of the system

Systems Biology in Clinical Medicine

- Phenotyping patients
  - Connecting outcomes to networks whose functional properties emerge as definable phenotypes.
    - Technology development
    - Advances in biology
    - Predictive and preventive medicine

How Do We Apply Systems Biology to Patient Care?
How Do We Plan to Accomplish Personalized, Preventive and Predictive Medicine?

Scheme for Systems Biology

Examples of Systems Biology Approaches in Respiratory Medicine

Examples of Systems Biology Approaches in Critical Care Medicine
Systems Biology in Medicine

How Personalized Health Care will Change Practice

• Diagnostic testing at home
• Doctor on demand through software interfaces with patients
• Personalized health care and prevention on the desktop computer and internet
• Individualized prescriptions for health

How Personalized Health Care will Change Practice

• Definition of genetic profiles for all people
• Understanding of adaptations that promote health
• Understanding subtle disease classification based on molecular abnormalities
• Individualized prediction, treatment and ultimately prevention of disease