Addressing Health Disparities through Researching the Human Genome

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Founding Director, National Human Genome Center
Founder, President, and CEO
Whole Genome Science Foundation, Inc.

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Clayton Hall Conference Center
University of Delaware
OBJECTIVES

• Define the relationship of Human Genome Research to Health Disparities.

• Relate the science of the human genome to the science of health disparities.

• Describe how addressing health disparities through researching the human genome is relevant to achieving the USA Public Health Service goals of “Healthy People 2020”.
Y2K Signs of the Times

MILLENNIUM
of the mind

CENTURY
of consciousness

DECADE
of discovery/destiny

DAY
of decision on

Human Identity and Purpose
Genome Knowledge Revolution
Big Data to Knowledge (BD2K)

The beginning of a new cycle of KNOWLEDGE on the earth about LIFE and the SCIENCE of Human Identity and Population Diversity.
The Human Genome
The human genome forces us to become aware of how we define ourselves, and how ‘who we say we are’ governs our behavior, which is related to the health of our body, the integrity of our communities, and the stability of our world.
3rd Millennial Public Health Service (PHS) Initiatives

PHS ‘Healthy People 2010’
2. International Haplotype Mapping Project (2005)

PHS ‘Healthy People 2020’
3. BRAIN Initiative (2013)
5. 21st Century Cures Act (2016)
Healthy People 2020
Overarching Goals

1. Attain high-quality, longer lives free of preventable disease, disability, injury, and premature death.

2. Achieve health equity, eliminate disparities, and improve the health of all groups.

3. Create social and physical environments that promote good health for all.

4. Promote quality of life, healthy development, and healthy behaviors across all life stages.
A Living Information and Communication System for LIFE in the 3rd Millennial

With completion of the human genome project, comes a new KNOWLEDGE System for biology, biomedical and the LIFE sciences—KNOWLEDGE as old as the origins of humanity itself, and as new as the most recent genome and ‘omic’ discoveries.

Timeless Knowledge, Whose Time Has Come.
The Human Genome

It’s all about Life

Genome

DNA Sequence Variation

Biology

Identity

We use genome variation for gene and self discovery.
A Finished Human Genome Sequence from DNA to Life

http://www.ornl.gov/TechResources/Human_Genome/primer_pic.htm
The genome story of human origins, migrations, adaptations, transformation, and liberation, now unfolded in research on DNA sequence variation.

At the end of all our exploring, we shall arrive where we began and know the place for the first time.

T.S. Eliot
Genetic Variation in Diverse Populations

### P gene haplotype frequencies

**HAPLOTYPED**

- **R305W**
  - C/T
- **A355A**
  - G/A
- **A686A**
  - A/C
- **A776A**
  - C/T

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- **African American**
- **Nigerian**
- **Hispanic**
- **European American**
- **Asian**

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**3.4 kb**

- ~100 kb
- **10 kb**
In 2007 researchers came to appreciate the extent to which our genomes differ from person to person and the implications of this variation for deciphering the genetics of complex diseases and personal traits.
Published Genome-Wide Associations through 12/2012
Published GWA at $p \leq 5 \times 10^{-8}$ for 17 trait categories

NHGRI GWA Catalog
www.genome.gov/GWASTudies
www.ebi.ac.uk/fgpt/gwas/
Human Genome Variation in Health Disparities

- Climate
- Parasites
- Pollutants
- Smoking
- Alcohol
- Drugs

Clinical Phenotype

Environmental Factors

Cultural Factors

Family History
- Biology
- Disease
- Gender
- Age

Attitudes Beliefs
# Health Disparities

Age-adjusted Death Rates by Race and Sex, United States, 1998

<table>
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<tr>
<th>Diseases</th>
<th>Male (Per/100,000)</th>
<th>Female (Per/100,000)</th>
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<tr>
<td></td>
<td>White</td>
<td>Black</td>
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<tr>
<td>Heart Disease</td>
<td>162</td>
<td>232</td>
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<tr>
<td>Cancer</td>
<td>144</td>
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<tr>
<td>Stroke</td>
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<tr>
<td>Diabetes Mellitus</td>
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<td>Hypertension</td>
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1Source: Nat’l Vital Stat Rep. 2000:48(11);63-64)
# Chances of developing breast cancer for African American women

<table>
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<th>African American</th>
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<td>236.4</td>
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<td>184.3</td>
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<td>80-84</td>
<td>362.5</td>
<td>304.1</td>
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*Rates are per 100,000*
Chances of dying from breast cancer for African American women

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<th>Caucasian</th>
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*Rates are per 100,000

**The above information was taken from SEER data and can be found on the Internet (www.seer.ims.nci.nih.gov/).
Social Determinants of Health

• The social determinants of health are the conditions in which people are born, grow, live, work and age. These circumstances are shaped by the distribution of money, power and resources at global, national and local levels.

• The social determinants of health are mostly responsible for health inequities - the unfair and avoidable differences in health status seen within and between countries.

http://www.who.int/social_determinants/sdh_definition/en/
Can Social Determinants of Health Be Mapped to the Human Genome?

VALUES
- Income & Social Status
- Employment & Working Conditions
- Biology & Genetic Endowment
- Culture

ASSUMPTIONS
- Health Services
- Social Support Networks
- Social Environments
- Personal Health
- Practice and Coping Skills

BELIEFS
- Education
- Physical Environments
- Healthy Child Development
- Gender
A Major Determinant in Health Disparities is BEHAVIOR

• What is the link between genes and behavior?
• How does our genotype interact with our environment to produce behavior?
• What methods are available to investigate these questions?
• What are the societal (social) and philosophical (ethical) implications of discovering such links?
Clinical Genome Sequencing

- The application of genomic information in individual health care is inevitable.
- Examples of how whole-exome or whole-genome information may be used in clinical diagnosis and decision making are no longer rare.
- Commercial and academic molecular laboratories all over the world are beginning to offer whole-exome or whole genome as a clinical genome service.
The BRAIN Initiative extends beyond the mapping of the brain and bridges scales that span from atoms to thoughts and **behavior**, linking what is known about single cells and subcellular activities in the brain to whole brain function leading to complex behavior.
After decades of research, we are poised to enter a new era of medical practice where detailed genetic and other molecular information about a patient's disease is routinely used to deploy effective, patient-specific remedies to treat it. We are about to enter the era of precision medicine.
Precision Medicine and Pharmacogenomics

Precision Medicine (PM) is customized healthcare, practices, medical decisions, and products tailored to the individual patient. Until now, most medical treatments used a “one-size-fits-all” approach. But PM focuses on the individual differences of one’s genes, social environment, and lifestyle.

Pharmacogenomics (PGx) is the study of how genes affect a person’s response to medication. This relatively new field combines pharmacology, the science of drugs, and genomics, the study of genes and their functions, to develop effective, safe medications that will be tailored to a person’s genomic makeup. PGx testing dramatically improves clinical judgment and helps physicians form a more accurate, comprehensive, and effective treatment procedure for their patients.
To fulfill the promise of targeted interventions, clinical trials and observational epidemiologic studies are needed to assess:

• prevalence of relevant genotypes in the population,

• how drug response varies among individuals with different genotypes,

• whether and to what degree environmental factors interact with genetic factors to influence drug response.
Reward Circuitry of the Brain

Dopamine Pathways

- Frontal cortex

- Functions
  - Reward (motivation)
  - Pleasure, euphoria
  - Motor function (fine-tuning)
  - Compulsion
  - Perseveration

Serotonin Pathways

- Striatum
- Substantia nigra

- Functions
  - Mood
  - Memory processing
  - Sleep
  - Cognition

NIDA

Delaware Health Sciences Alliance
Polymorphic Reward Gene Variants

Epigenetic Expression

Hypodopaminergic State or Trait

Associated Behavioral Outcome

Reward Deficiency Syndrome

Disruptive Anti-social
Conduct

Spectrum Autism
ADHD

Borderline Narcissistic
Avoidant Paranoid

Substance Alcoholism
Polysubstance
Non-substance
Gambling
Sexual S&M
Thrill seeking

Hoardings,
Non-suicidal
Self-Injury

Opioid Use Disorder
Genome Variation

African-Americans and Hispanics express the dopamine receptor DRD2A1 allele at double the frequency of European-Americans.

In preliminary pharmacogenomics testing in a cohort of African American heroin users reveal a significant 85% frequency of the CYP3A4 *1B allele, the variant which confers higher metabolism of the treatment drug, buprenorphine, but only a frequency of 13% in European Americans.


To explore the biophysical underpinnings of common variation in the genome to better understand the functional aspects of natural variation (i.e. polymorphisms using first principles of thermodynamics and statistical physics (genodynamics).

Research focus on genome variation expressed in human identity and through population diversity—a natural probe for interrogating the biology and science of health and disease.
E=MC\(^2\)

Like everything in the universe, the human genome, and the biology it encodes, is made of energy.

The significant problems we have cannot be solved at the same level of thinking with which we created them.

*Albert Einstein*
Happy New Year

The Human Genome is a dynamic information and communication system that encodes both systematic and creative aspects of being.

From the Biophysics Research and Interdisciplinary Development Group (BRIDG)

“Truth is the ultimate theoretical construct for all science.”
Georgina M. Dunston, PhD

“Quantum biology has driven scientists to re-examine long-held assumptions of origins, purpose, and identity.”
Philip Kurian, PhD

“As it turns out, the human genome is an interface between the known, knowable and unknowable aspects of the science of life.”
James Lindsay, PhD

The (Re)union of SCIENCE and SPIRITUALITY in Human Identity and Population Diversity in Health and Disease

Towards Healthy People 2020
**Genomics-Driven Paradigm Shift in Reality**

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<td>and dying</td>
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Summary

ADVANCES IN HUMAN GENOME SCIENCE

Offer Unprecedented

Medical opportunity
Commercial promise
Ethical danger
Social challenge
Future Directions
COMMUNITY-ACADEMIC PARTNERSHIPS IN TRANSLATIONAL RESEARCH

For conducting research at the interface of genetics, neuroscience, drug abuse, and behavior---

• How can academic research centers, community health service providers, and communities collaborate in using translational research to eliminate health disparities and optimize health equity for ‘All of Us’?
The 21st Century Cures Act

The bill contains $4.8 billion in spending over 10 years for new research at the National Institutes of Health, including:

- **$1.8 billion for the cancer research “moonshot”** championed by Vice President Joe Biden.

- **$1.56 billion for the BRAIN Initiative**, a project to create new technologies that will allow for comprehensive mapping of the human brain.

- **$1.4 billion for the Precision Medicine Initiative**, a project supported by Obama to collect genetic data on one million American volunteers that will be used to help develop new treatments.

- States will receive grants worth **$1 billion** over the next two years for drug abuse prevention and treatment programs.