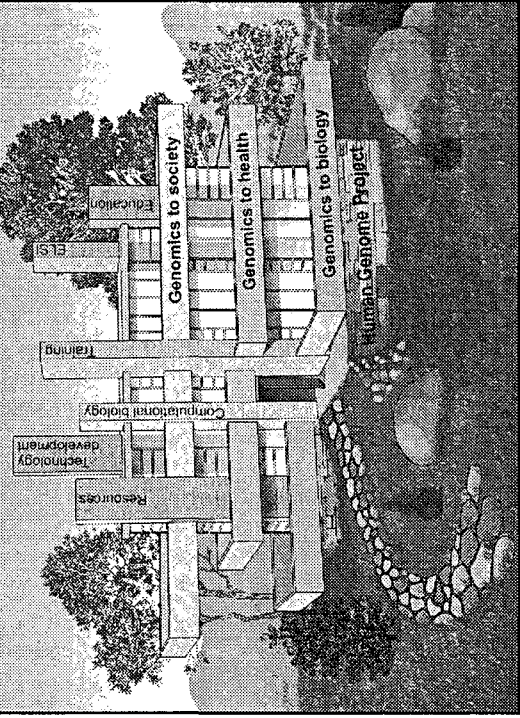
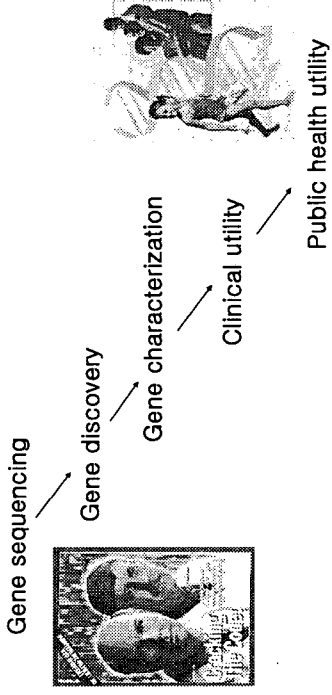


# Genome Epidemiology: Application to Public Health

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“The Genome is Mapped: Now What?”  
(M.D. Lemonick, Time Magazine 7/3/2000 p24)



## Genomics

■ Study of gene **structure** and their **functions**

## Functional Genomics?

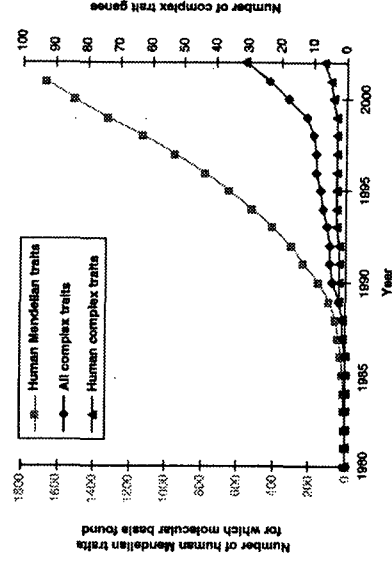
■ A comprehensive approach to study the dynamic network of genes that ultimately determines the physiology of an individual organism

## Genomics to Biology

- Define the structure of human variation: the human haplotype map
- Sequence lots of additional genomes
- Develop new technologies for sequencing, genotyping, expression analysis, and proteomics
- Identify all functional elements of the genome
- Identify all the proteins of the cell, and their interactions
- Develop a computational model of the cell

Finding genes for Mendelian phenotypes has made tremendous progress over the last 10 years

Finding genes for complex (polygenic) disorders and traits has moved much more slowly



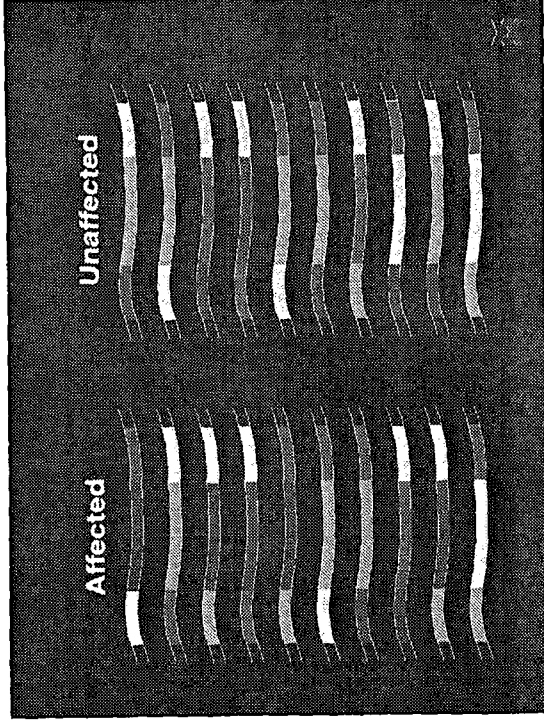
Whole Genome Association Approach to Common Disease and Pharmacogenomics

- Identify all 10 million common SNPs
- Collect 1000 cases and 1000 controls
- Genotype all DNAs for all SNPs

2000 DNAs x 10,000,000

SNPs = 20,000,000,000

genotypes



### A Haplotype Map of Human Variation

- Goal is to define all common haplotypes in the human genome
- Genome-wide association studies can then be done with 30 – 50 times less work
- Project is international (9 labs in 5 countries); was initiated in October 2002, using samples of African, Asian, and European origin

### From Genes to the Genome

- The genome-level study may actually reduce the complexity of the tasks for identifying the mechanism of complex traits. *At least we hope so.*
- Because the structure of the genome limits the possibilities that the genes can be interconnected.

## Emerging “Genomic” Methods in Epidemiology

- Susceptibility → DNA sequence variations (SNPs & hap structure)
- Exposure → RNA Studies (Toxicogenomics)
- Outcomes → Disease characterization (Proteomics)

## Dissecting Human Disease in the PostGenome Era: The Importance of Epidemiology

- “Although experimental species are of great value for the initial identification and functional analysis of complex disease genes, **final evidence** for the involvement of these genes in human diseases **must come from extensive epidemiological studies, preferably in different populations**”  
– Peltonen and McKusick, Science 2002;291:1224

## Human Genome Epidemiology (Khoury, 2003)

- Applications of epidemiologic methods and approaches in evaluating the **impact of human genome variation** on health and disease in various populations (e.g. genomic determinants)
- HuGE involves a continuum from discovery to applications



## Public Health

- Efforts organized by society to **protect, promote, and restore people’s health** (Last, Dic Epi, 2001)
- The process of mobilizing and engaging local, state, national, and international resources to **assure the conditions in which people can be healthy** (Detels & Breslow, Oxford Textbook of Public Health, 2002)

### Public Health in Brief (Detels & Breslow, 2002)

- Prevention of disease
- Promotion of health

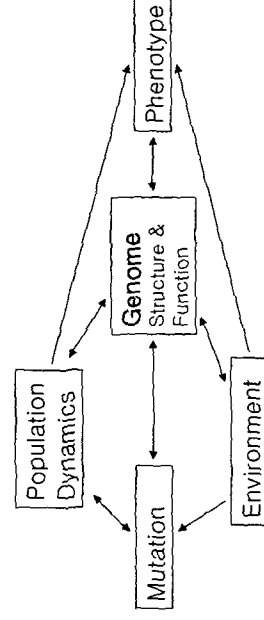
### Epidemiology is a Part of Public Health

- The study of the **distribution and determinants** of health-related states or events in specified populations, and the **application of this study to control** of health problems.  
(Last JM, 2001)
- “Control” means prevention (primary, secondary, and tertiary)

### Genomic (Genome) Epidemiology

- The study of the **distribution and (genomic) determinants** of health-related states or events in specified populations, and the **application of this study to control** of health problems.

### Scope of Genomic Epidemiology (Modified from Khoury, 1993)



## Strategies of Genome Epidemiology

(Modified from Khoury, 1993)

Approach	Population Studies	Family Studies
Descriptive	Distribution of genetic traits and disease	Distribution of genetic traits and disease
Analytic	Risk factors for genetic traits	Risk factors for familial aggregation
	Role of <b>genome structure and function</b> in disease etiology	Specific <b>genomic mechanisms</b> in families

## Human Genome Epidemiology: From Gene Discovery to Public Action

- Gene Discovery (classical genetic epidemiology)
  - Family Studies
  - Association Studies
- Gene Characterization (molecular epidemiology)
- Assessing Genetic Tests (applied epidemiology)

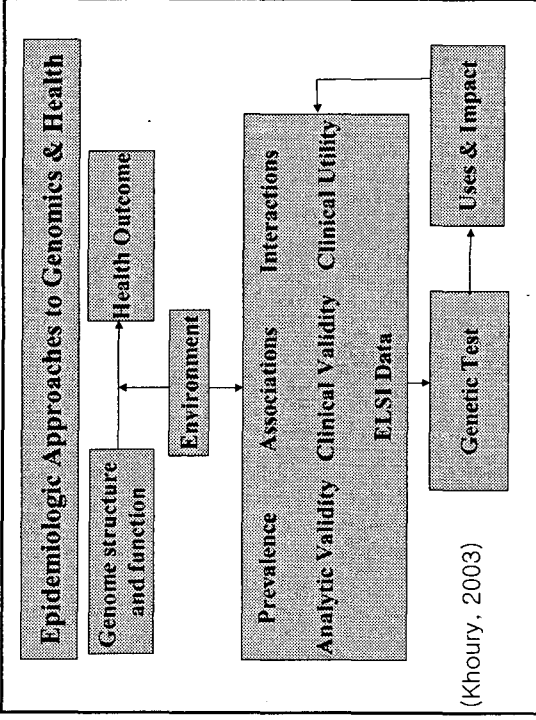
## Importance of the Epidemiologic Approach to Genetic Information

<b>Prevalence</b>	Most current data based on selected unrepresentative populations
<b>Associations</b>	Need for unbiased data on relative, absolute & attributable risks
<b>Interactions</b>	Enhances biologic plausibility and targeting interventions

Epidemiology borrow methods from genomics, but also contributes to the goal of genomics to improve (public) health

## Genome Epidemiology

- Is an application of genomic methods to epidemiology
- Is also an application of epidemiologic methods to genomics
- Epidemiology, as a field of public health science, promotes the social benefits of genomics



## Human Genome Epidemiologic Data

From Gene Discovery to Medical and Public Health Action

- Gene Discovery
  - Gene location, function, variants
- Gene Characterization
  - Genetic risk, and interaction with the environment e, associations, interactions
- Assessing Genetic Tests
  - Analytic validity
  - Clinical validity and utility
  - ELSI data
  - Population impact

## Purposes of Gene Characterization

- To assess genetic risk for health problems
- To assess genetic susceptibility to environmental exposures
- To identify environmental exposures that produce adverse gene function

## Intrinsic Contradiction in “Genome Epidemiology”

- Epidemiology aims at modifying health status
- Genome does not change in an individual
- Genome epidemiology contributes most by identifying environmental (modifiable) factors, rather than genetic factors.
- Fundamentally, genome epidemiology is about genome–environment interaction

## Genomic Epidemiology: Potential Contributions to Public Health

- Prevention
  - Primary prevention (gene-environment interaction)
  - Secondary prevention (screening)
  - Tertiary prevention (natural history, treatment)
- Health promotion
  - Physical health
  - Mental health
  - Social health: assuring fairness in benefits and risks

## Implications for Research

### Questions that must be asked:

- Which genes are important for human health?
- What variants in these genes are relevant to risk of human disease?
- How do these genes interact with other genes and the environment to affect human health?

## Opportunities for Disease Prevention & Control

- Identify genetically based disease susceptibility within populations
- Examine the roles of behavioral factors in susceptibility
- Investigate disease outbreak
- Detect and track the effects of environmental toxins and infectious diseases

## Genomics to Health

(Collins, 2003)

- Identify the genetic and environmental risk factors for all common disease
- Develop “sentinel systems” for early detection of disease and molecular taxonomy of illness
- Develop and deploy high-throughput robotic screening of small molecules for academic researchers
- Catalyze development of large human cohorts for genotype-phenotype correlations
- Elucidate the role that genomics can play in reducing health disparities
- Utilize genomics to improve health in the developing world



## Multidisciplinary Nature of Human Genome Epidemiology

- Genetics
- Clinical Medicine
- Laboratory Sciences
- Behavioral and Social Sciences
- Statistics



## Who Needs HuGE information?

- Policy makers
- Researchers
- Health care providers
- Consumers



## Genomics to Society

- Enhance genetic privacy and protection against genetic discrimination
- Oversee responsible introduction of genetic testing
- Encourage appropriate patenting and licensing practices to benefit the public
- Understand the relationship of genomics, race, and ethnicity, and bring this to bear usefully on the often contentious dialog about race
- Assess the ramifications of advances in understanding genetic factors that influence behavior
- Define boundaries of the appropriate application of genomics in the non-medical arena

## Genomics and Public Health in the 21<sup>st</sup> Century

“Genomics will be to the 21<sup>st</sup> century what infectious disease was to the 20<sup>th</sup> century...Genomics should be considered in every facet of public health: infectious disease, chronic disease, occupational health, environmental health, in addition to maternal and child health.”

Gerard et al. Journal Law, Medicine , Ethics  
2002; vol 30(suppl):173-176

## Health People 2010: The Promise / Benefit of Genetic Advances

- Improve disease risk assessment.
- Make earlier, more accurate diagnoses.
- Enhances medical care and public health practices.

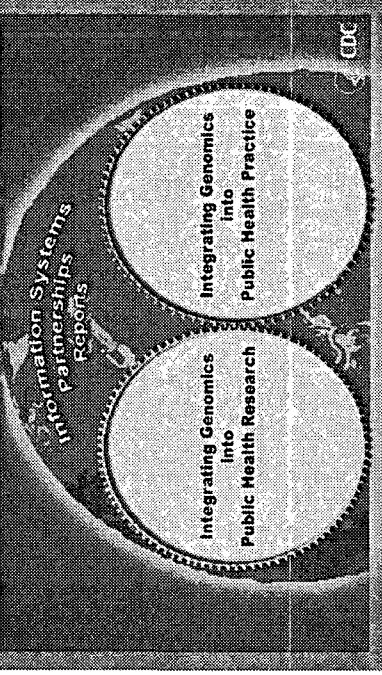
Source: Partnership for Prevention, 2003  
"Harnessing Genetics to Prevent Disease and Improve Health"

## Public Health Preparedness

- Training of the public health workforce
- Development and maintenance of the public health infrastructure
- Communication
- Policy development
- A sustainable, long-term solution to public health needs

## CDC Genomics & Disease Prevention

Using Genetic Information to Improve Health & Prevent Disease



## Summary

- Genome epidemiology can contribute to public health by disease prevention and health promotion
- Genome epidemiology contributes most by identifying modifiable environmental factors that interact with the genome structure and function