Genetics, Epigenetics and Public Health: A Primer

Muin J. Khoury MD, PhD

CDC Office of Public Health Genomics
Outline

- Public health in the genomics era

- Genetics and epigenetics 101

- Using epigenetics in public health: opportunities and challenges
What is the Role of Public Health in Translating Genomics into Health Impact?

Assessment - Policy - Assurance

The Public Health Role in Translating Advances in Genomics

Muin J. Khoury, M.D., Ph.D., and Scott Bowen, MPH

13 years after the completion of the Human Genome Project, an increasing number of genomic applications, including next-generation sequencing (NGS), are poised for clinical use. Fulfilling the promise of genomics to improve health in the real world requires a public health perspective.

As genomics reaches the bedside, a public health “post bedsidic” research agenda will be able to assess the contribution of genomics and other new markers to health and disease in the larger social and environmental context, evaluate promising genomic technologies for their potential to improve health and healthcare, design appropriate strategies for integrating genomics into clinical and public health practice and ensuring access, and continuously measure population health impact of these new technologies.

This research agenda is one part of the mission of public health, namely to ensure conditions by which people can be healthy. The three essential public health functions can be applied to genomics: policy development, assurance, and assessment.

Policy development: Public health serves as a convenor and honest broker, advising providers, the public, and policy makers on the potential net health impact of a particular health technology including genetic testing.

Assurance involves implementing appropriate programs (such as newborn screening), laws, and regulations, assuring access, and strengthening providers’ genomic competencies and the general public’s health literacy.

Assessment applies public health sciences to monitor and evaluate effectiveness, quality, and outcomes of deployment of genomic technologies in populations.

In 1997, the CDC established the Office of Public Health Genomics dedicated to the effective and responsible translation of genome-based science to improve population health in the United States. At that time, a new era of personalized healthcare seemed around the corner. However, the promise of the Human Genome Project was mixed with unrealistic expectations.

The public health community called for a scientific approach to explore the balance of benefits and harms of the new science. A major achievement for public health genomics has been to make these concerns central to the dialogue among the basic, clinical, and public health-related scientific communities. Public health genomics also has begun to prepare the workforce for integrating new tools in practice and for integrating genomics in public health’s essential functions.

So where are we after 17 years of public health genomics? There are five main areas of ongoing progress in public health genomics, where emerging information is making a real impact on improving health and preventing disease in populations:

- **Newborn Screening**
  Last year marked 50 years of saving lives through newborn screening, which remains the largest public health genomics program in the world. It is run by public health agencies in all 50 states in the U.S. and identifies more than 30 conditions that can affect a child’s long-term health or survival. Early detection, diagnosis, and intervention in more than 12,000 babies every year helps prevent death or disability.

- **Family history remains the simplest and most readily available genomic tool for disease prevention and healthcare across the lifespan.**

Each year millions of babies are routinely screened for certain genetic, endocrine, and metabolic disorders.

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CDC Office of Public Health Genomics

Mission
Provides timely and credible information for the effective and responsible translation of genome-based discoveries into public health & health care

1. Identify evidence-based applications
2. Inform & communicate
3. Integrate into practice & programs
CDC Horizon Scanning for Genomics and Health Impact

Public Health Genomics

Features of the Week
- Genomic Data Sharing
- Ebola
- Salmonella
- Severe Combined Immunodeficiency
- Epigenetics
- Genetic Counseling
- Surveillance & Registries
- Sickle Cell Anemia
- Prostate Cancer
- Gaucher Disease

Current Tweets
@DrKhouryCDC
More on #epigenetics & multigenerational effects of nutrition, chemicals & drugs @JillEscher @EpigeneticsGuy
https://t.co/Oj3RJqfVkR ...

Proposal for a minimal protocol for genome-wide association interaction analysis #genomics #complexity
http://t.co/XMpKTFNFJS
Public Health Genomics Priorities 2012-2017

2012
New Strategies in Public Health Genomics

Public Health Action in Genomics Is Now Needed Beyond Newborn Screening
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Key Words
Cascade screening  Evidenced-based recommendations  Health impact  Tier 1 genomics applications

Abstract
For decades, newborn screening was the only public health program in the US focused on reducing morbidity, mortality and disability in people affected by genetic conditions. The landscape has changed, however, as evidence-based recommendations are now available for several other genomic applications that can save lives now in the US. Many more such applications are needed.

Background
Advances in genomics and related fields created expectations for a flood of new health-related applications, such as tests and interventions that could reduce the burden of common complex diseases in populations. However, while there are an increasing number of genomic applications that are progressing from bench to bedside (a total of 419 were identified from horizon scanning on May 1, 2012), few have actually been widely adopted in clinical practice, mainly because of the insufficient evidence base to support their use [1].

3-Tiered Classification of Evidence for Action
Genetics 101

All Diseases Result from Gene-Environment Interaction

Genetic variation

Environmental risk factors

Human Disease

Genetic Diseases: (Mendelian disorders-PKU Example, 5000+ conditions, 5%-10% of human disease)

“Complex” Diseases (heart disease, cancer, diabetes, environmental & infectious agents – 90%-95% of human disease)

Potentialmodifiable hence public health interest

3 billion base pairs, millions of mutations & variants, Non-Modifiable
Genetics 101
Interactions Getting More Complex
What Genomes?

**Genetic variation**
- Inherited (germ)
- Acquired (somatic) (e.g. cancer)
- Symbiotic (microbiome)
- Vectors

Human Disease

Environmental risk factors
- What Environments?
  - Infection
  - Chemicals
  - Physical agents
  - Diet
  - Behavioral
  - Social
Genetics 101
Interaction Getting Even More Complex
Epigenetics!!

What Genome?
- Inherited
- Acquired (e.g. cancer)
- Symbiotic (microbiome)
- Vectors

Genetic variation

Environmental risk factors

Human Disease

Epigenetic and post-genomic modification

Potentially modifiable hence public health interest

What Environments?
- Infection
- Chemicals
- Physical agents
- Diet
- Behavioral
- Social
“Epigenetics” in the Scientific Literature
A Tale of Two Mice (Agouti gene & Epigenetics)

Identical twins: In yellow mouse, Agouti gene is unmethylated and turned on all the time, while in the brown mouse, the gene is completely methylated and shut down.

Effect of BPA exposure

Effect of Folic acid

http://www.pbs.org/wgbh/nova/body/epigenetic-mice.html
Two Biological Codes

**Genetic code:** sequence of DNA (nucleotide sequences) that tells a cell how to build one protein. Set for life.

**Epigenetic code:** chemical modifications in the structure of the chromosomes that influence which genes can be expressed and in which tissues. Potentially altered in response to environments (especially early environments).

From C. Kuzawa
EPIGENETICS

3 Types of Epigenetic alterations – transcriptional, translational, or post-translational levels without change in DNA sequence

Methylation of DNA

Modifications of histones

RNA-mediated modifications

Genomic Imprinting

- RNA-directed DNA methylation
- RNA-interference mediated chromatin remodeling
- RNAi, siRNA, miRNA ...

- acetylation
- methylation
- phosphorylation
- ubiquitination
Epigenetics, Environment and Development

A. Germline epimutation
   Parental genomic demethylation
   Epigenetic drift/somatic epimutation
   Developmental tissue-specific epigenetic programming

B. Gametes → Zygote → Embryo → Fetus → Baby/child → Adolescent → Adult → Elderly
   Paternal imprinting established
   Maternal imprinting established

C. Stochastic + environmental exposure
   Maternal factors
   Diet/lifestyle
   ART, Assisted Reproductive Technology

D. CVS, Amniocentesis
   Placenta
   Umbilical cord
   Cord blood
   Urine
   Stool
   Blood
   Buccal/saliva
   Skin
   Sperm

Maternal Transgenerational Epigenetic Inheritance

Also applies to fathers!

Drake & Liu (2009), Trends Endocrinology Metab 21(4)
Can you inherit experiences? Inside the weird world of epigenetics

Updated by Susannah Locke on August 15, 2014, 10:21 a.m. ET  @susannahlocke  susannah@vox.com
Paternally Induced Transgenerational Environmental Reprogramming of Metabolic Gene Expression in Mammals

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SUMMARY

Epigenetic information can be inherited through the mammalian germline and represents a plausible transgenerational carrier of environmental information. To test whether transgenerational inheritance of environmental information occurs in mammals, we carried out an expression profiling screen for genes in mice that responded to paternal diet. Offspring of males fed a low-protein diet exhibited elevated hepatic expression of many genes involved in lipid and cholesterol biosynthesis and decreased levels of cholesterol esters, relative to the offspring of males fed a control diet. Epigenomic profiling of offspring livers revealed numerous modest (−20%) changes in cytosine methylation depending on paternal diet, including reproducible changes in methylation over a likely enhancer for the key lipid regulator Ppara. These results, in conjunction with recent human epidemiological data, indicate that parental diet can affect cholesterol and lipid metabolism in offspring and define a model system to study environmental reprogramming of the heritable epigenome.

INTRODUCTION

The past few decades have seen an important expansion of our understanding of inheritance, as a wide variety of epigenetically inherited traits have been described (Jablonka and Lamb, 1996; Hurst and Zakin, 2005; Rando and Verstrepen, 2007). One implication of epigenetic inheritance systems is that they provide a potential mechanism by which parents could transfer information to their offspring about the environmental experience. In other words, mechanisms exist that could allow organisms to “inform” their progeny about prevailing environmental conditions. Under certain historical circumstances—perhaps, repeated exposure over evolutionary time to a moderately toxic environment that persists for tens of generations—such non-Mendelian information transfer could be adaptive in primates (Jablonka and Lamb, 1996; Rando and Verstrepen, 2007). Whether or not organisms can inherit traits induced by ancestral environments has far-reaching implications, and the type of inheritance has come to be called “Lamarckian” inheritance after the early evolutionary theorist J.B. Lamarck, although it is worth noting that both Darwin and Lamarck believed in the inheritance of acquired characters.

Despite these theoretical considerations, at present there is scant evidence for transgenerational effects of the environment, particularly in mammals. The majority of examples of transgenerational environmental effects described have been maternal effects (see Harris and Seal, 2010; Whitehead and Whitehead, 2008; Youngson and Whitelaw, 2008 for review), including in vitro passage of phenotypic information in various rodents (Horton, 2003), cultural inheritance of stress reactivity and maternal grooming behavior in rats (Massey et al., 2007; Weaver et al., 2006), and metabolic and psychiatric sequelae of fetal malnutrition in humans and rodents (Hales and Barker, 2001; Harris and Seal, 2010; Symonds et al., 2009). However, maternal effects are difficult to separate from direct effects of in utero environmental exposure on offspring.
Epigenetic Transmission of the Impact of Early Stress Across Generations

Tamara B. Franklin, Holger Rüssig, Isabelle C. Weiss, Johannes Gräff, Natacha Linder, Aubin Michalon, Sandor Vizi, and Isabelle M. Mansuy

Background: Traumatic experiences in early life are risk factors for the development of behavioral and emotional disorders. Such disorders can persist through adulthood and have often been reported to be transmitted across generations.

Methods: To investigate the transgenerational effect of early stress, mice were exposed to chronic and unpredictable maternal separation from postnatal day 1 to 14.

Results: We show that chronic and unpredictable maternal separation induces depressive-like behaviors and alters the behavioral response to aversive environments in the separated animals when adult. Most of the behavioral alterations are further expressed by the offspring of males subjected to maternal separation, despite the fact that these males are reared normally. Chronic and unpredictable maternal separation also alters the profile of DNA methylation in the promoter of several candidate genes in the germline of the separated males. Comparable changes in DNA methylation are also present in the brain of the offspring and are associated with altered gene expression.

Conclusions: These findings highlight the negative impact of early stress on behavioral responses across generations and on the regulation of DNA methylation in the germline.

Key Words: Brain, depression, DNA methylation, early stress, epigenetic, germline.

Contemporary models of developmental psychopathology suggest that adverse environmental, psychosocial, or physical experiences during early life are predisposing factors for the development of behavioral and emotional disorders in adulthood. In humans, primates, and rodents, insecure attachment and untrustworthy, disorganized, poor parental care negatively influence appropriate behavioral responses and cause maladaptive behaviors (1–3). Epidemiological studies have further shown that the offspring of people with such behavioral alterations, and sometimes the generation following that offspring, are often similarly affected even if they themselves, did not experience the trauma (4–7). The observation that stress-induced behavioral alterations can be transmitted across generations is intriguing and of fundamental importance; yet this phenomenon has not been well studied in mammals. Because it implicates environmental factors, it is suggested to be of epigenetic nature (8,9).

Here, using an experimental paradigm for chronic and unpredictable stress in early life in C57BL/6J mice, we provide evidence that the transgenerational transmission of complex behavioral alterations induced by early stress can be modeled in animals. We show that chronic and unpredictable maternal separation during early postnatal development in mice induces depressive-like behaviors and alters the animals’ response to novel and aversive environments. Most of the observed behavioral alterations are transmitted to the offspring of males subjected to maternal separation and to the subsequent generation. Further to disturbing behavior, early stress is also shown to alter DNA methylation of several candidate genes in the germline of males subjected to maternal separation, as well as in the brain and, for some genes, the germline of the offspring. These results suggest that early stress persistently alters behavior and modifies the epigenetic profile of genes across generations, providing a behavioral and molecular correlate to complex traits induced by early stress.

Methods and Materials

Animals

C57BL/6J females and males (2.5 months) were obtained from Elevage Janvier (Le Genest Saint Isle, France) and maintained in a temperature- and humidity-controlled facility on a 12-hour reversed light-dark cycle with food and water ad libitum. All procedures were carried out in accordance with Swiss cantonal regulations for animal experimentation.

Maternal Separation

Dams and litters were subjected to unpredictable maternal separation combined with unpredictable maternal stress (MSIS) for 3 hours daily from postnatal day 1 through 14 (PND 1–14) or were left undisturbed except for cage change once a week (control) until weaning (PND21). Maternal behaviors were monitored during the first 2 weeks after delivery by noting the behavior occurring each minute during 30 min, three times per day (morning before, shortly after, and 2–3 hours after separation; see Supplement 1, Supplementary Methods). Once weaned, pups were reared in social groups (3–4 mice/cage) composed of animals subjected to a similar treatment but from different dams to avoid litter effects. To produce a second generation, F1 females were housed with naive, primiparous C57BL/6J females following behavioral testing. Maternal behaviors were monitored during the first 2 weeks after delivery by noting the behavior occurring each minute during 30 min, three times per day (morning before, shortly after, and 2–3 hours after separation; see Supplement 1, Supplementary Methods).
Developmental Origins of Adult Health
Barker, DP (1997) *Nutrition*: 13(9) 807-13

- Fetal Stress or Undernutrition
- Developmental response
  - Inflammation
  - Insulin resistance
  - Visceral fat
  - Hypertension

Cardiovascular Disease

From C. Kuzawa
Early Environments Can Influence Development & Adult Health

- Developmental biology is sensitive to prenatal and early postnatal conditions.
- Parental psychosocial and nutritional stressors lead to durable biological changes in offspring that elevate future risk for cardiovascular and other common diseases.
- Allows environmental experiences of one generation to have lingering impacts on adult health disparities in future generations.
- Epigenetics is a biological mechanism mediating such effects

- From C. Kuzawa
Epigenetics: Relevance and Implications for Public Health

Research
- Laboratory and field measurements of exposures
- Evaluation of exposed populations and observation of adverse effects

Risk assessment
- Hazard identification
  - Does the agent cause adverse health effects?
  - Structure-activity analysis
  - In vitro tests
  - Animal bioassays
  - Epidemiology
- Risk characterization
  - What is the nature and estimated incidence of adverse effects in a given population?
  - How robust is the evidence?
  - How certain is the evaluation?
  - Are susceptible populations characterized?
  - Is there a relevant mode of action?
- Dose-response assessment
  - What is the relationship between dose and response?
  - Susceptibility
  - Age
  - Gene/environment
- Exposure assessment
  - What types, levels, and duration of exposures are experienced or anticipated?

Risk management
- Development of regulatory options
  - Control
  - Substitute
  - Inform
- Evaluation of public health, economic, social, and political context for risk management options

Policy decisions and actions

Acquired DNA damage/mutation

Inherited genetic make-up

Acquired DNA damage/mutation

Inherited epigenetic make-up

Acquired epigenetic changes

Adverse Effects
Methylation

Epidemiology studies have measured both methylation of specific genes and global methylation (e.g. benzene, pollutants, lead, arsenic)

Both hypo and hypermethylation results found

Perhaps most intriguing are studies that explore associations between social or behavioral factors and epigenetic regulation (e.g. economic deprivation, work stress, and inflammation)

To date, studies that incorporate epigenetic measurements have rarely validated biological effects of epigenetic changes via RNA or protein expression

Impact of perinatal exposures on long term outcomes (BPA)
Using Epigenetics in Public Health

- **Histones**: a few studies have investigated the influence of environmental exposures on global levels of specific histone modifications.

- These studies require availability of intact protein fractions, and quantification is currently not cost-effective for large studies.

- For example, higher inhalational exposure to iron, arsenic, and nickel, as quantified by personal air monitors.
Cancer: Epigenetic Disease

- Remains the most actively studied field.
- A heterogeneous set of diseases, displaying both genetic and epigenetic etiologies.
- In general the epigenome is widely hypomethylated compared to normal tissue-inactivated tumor suppression genes (some exceptions)
- Animal and cell line models of specific pathways serve as critical tools
- Need integration of laboratory and epidemiological approaches
Epigenetic Research in Cancer Epidemiology: Trends, Opportunities, and Challenges

Mukesh Verma¹, Scott Rogers¹, Rao L. Divi¹, Sheri D. Schully¹, Stefanie Nelson¹, L. Joseph Su¹, Sharon A. Ross², Susan Pilch³, Deborah M. Winn¹, and Muin J. Khoury¹,⁴

Abstract

Epigenetics is emerging as an important field in cancer epidemiology that promises to provide insights into gene regulation and facilitate cancer control throughout the cancer care continuum. Increasingly, investigators are incorporating epigenetic analysis into the studies of etiology and outcomes. To understand current progress and trends in the inclusion of epigenetics in cancer epidemiology, we evaluated the published literature and the National Cancer Institute (NCI)–supported research grant awards in this field to identify trends in epigenetics research. We present a summary of the epidemiologic studies in NCI’s grant portfolio (from January 2005 through December 2012) and in the scientific literature published during the same period, irrespective of support from the NCI. Blood cells and tumor tissue were the most commonly used biospecimens in these studies, although buccal cells, cervical cells, sputum, and stool samples were also used. DNA methylation profiling was the focus of the majority of studies, but several studies also measured microRNA profiles. We illustrate here the current status of epidemiologic studies that are evaluating epigenetic changes in large populations. The incorporation of epigenomic assessments in cancer epidemiology studies has and is likely to continue to provide important insights into the field of cancer research. Cancer Epidemiol Biomarkers Prev; 23(2); 223–33. ©2013 AACR.
Table 3. Trends, opportunities, and challenges in the cancer epigenetics and epidemiology field

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<th>Trends</th>
<th>Opportunities</th>
<th>Challenges</th>
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<tr>
<td>Most of the studies have been conducted using methylation markers. The majority of the exposures evaluated for their impact on the epigenome were nutrition, smoking, drugs and treatments, and infectious agents. Most of the studies investigated epigenetic changes at specific individual loci, and very few studies explored changes at multiple loci or interactions among multiple loci. Few investigators explored histone modifications along with methylation, nucleosome remodeling, or miRNA expression changes in cancer epidemiology. Most epigenetic studies have been conducted in blood, which may not be an appropriate biospecimen.</td>
<td>Integrate epigenetic research with genetics, environmental predisposition, and lifestyle factors. Incorporate epigenetics into epidemiologic studies of cancer and the environment, which could contribute greatly to our understanding of cancer risk and development. Determine the stability of epigenetic marks in repeated biospecimen samples from the same people over time. Explore the use of epigenomic information to better define cancer subcategories. Develop improved strategies for epigenetic data analysis and interpretation. Conduct studies that examine the relationship between epigenetic marks in germline DNA and tumor DNA. Characterize all the components of the epigenome, which might help to understand the underlying mechanism of cancer risk and identify new biomarkers of cancer initiation and</td>
<td>Follow an individual’s epigenomic status, which changes spatiotemporally and compartmentally in tissues, and contributes to variations. Improve strategies for epigenetic data analysis and interpretation. Conduct large-scale epidemiologic studies to determine whether epigenetic changes detected using blood samples accurately reflect both inherent and acquired epigenetic changes that contribute to cancer risk and impact outcomes. Identify new chromatin abnormalities and their association with cancer. Develop high-throughput technologies for histone modifications and nucleosome remodeling. Distinguish between association and causality of epigenetic mark with disease. Evaluate relationships between epigenetic marks in germline versus tumor DNA. Distinguish age-related epigenomic</td>
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Folate and DNA Methylation: A Review of Molecular Mechanisms and the Evidence for Folate’s Role$^{1,2}$

Krista S. Crider,$^3*$ Thomas P. Yang,$^4$ Robert J Berry,$^3$ and Lynn B. Bailey$^5$

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**ABSTRACT**

DNA methylation is an epigenetic modification critical to normal genome regulation and development. The vitamin folate is a key source of the one carbon group used to methylate DNA. Because normal mammalian development is dependent on DNA methylation, there is enormous interest in assessing the potential for changes in folate intake to modulate DNA methylation both as a biomarker for folate status and as a mechanistic link to developmental disorders and chronic diseases including cancer. This review highlights the role of DNA methylation in normal genome function, how it can be altered, and the evidence of the role of folate/folic acid in these processes. *Adv. Nutr.* 3: 21–38, 2012.

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$^*$Corresponding author.
| **Assay** | DNA methylation patterns vary across genomic regions. These regions are differentially regulated and the consequences of changes in DNA methylation vary depending on the site and developmental time frame. It is important to consider:
|---|---|
| • Does the assay test individual sites (alone or a multiplex format) or “global” methylation?  
• Is the assay sensitive and specific? What % change in methylation level can be detected? Is the % change meaningful? Is this known?  
• Can the assay differentiate between 5 methyl cytosine and 5 hydroxymethycytosine? Is this of importance to the outcome of interest?  
• For the assay of choice what is the accuracy, reproducibility, labor intensiveness, and sample usage and cost (both for testing and analysis)? |
| **Individual sites:**  
• Single site or multiplex?  
• DMR, CpG islands, shores, promoter region, etc.?  
• Does change in DNA methylation occur at at sites known to affect gene expression or disease risk? Is the study sufficiently powered (number samples, assay variability, etc.) to detect these changes? | **“Global” Assays:**  
• Does the assay measure, repetitive DNA elements, total methylated cytosine, open CpG sites, etc.?  
• Are methylation changes associated with changes in disease risk? Is the study powered (number samples, assay variability, etc.) to detect these changes?  
• How well does the assay correlate with other global assays? |
| **Tissue** | DNA methylation patterns vary between tissues at specific loci. It is important to consider:  
|---|---|
| • Is the tissue being testing composed of one or more than one cell type?  
• Is the “normal” methylation pattern and level known for the CpG sites being testing? Is there methylation variation at those sites or regions among tissues/cell lineages?  
• Is there a known correlation between methylation in the tissue being assaying and the tissue/outcome of interest (e.g., blood vs. tumor or buccal vs. brain)? |
| **Type of Change** | The “normal” variation in DNA methylation is unknown for many regions of the genome (not just among tissues but in the same tissue between “normal” individuals within the population). It is important to consider:  
|---|---|
| • What is the normal methylation pattern at the site(s)/region of interest? Is the normal variation in methylation known?  
• Is the exposure of interest anticipated to increase or decrease the DNA methylation level?  
• Are the sites of change known to affect gene expression? |
| **Time** | Exposures at different developmental times could be expected to have differential impacts.  
|---|---|
| • Developmentally, are the DNA methylation patterns of specific interest set in the tissue at the specific time during development? Is it known?  
• Are the patterns set at the same developmental time in the tissue of interest and the tissue assayed (if different)?  
• Are both tissues/cells types replicating? |
Methodologic Issues

- How to make sense out of epigenetic data
  - Pattern and level may vary across tissues and cells
  - Impact of confounders
  - Selecting appropriate statistical models
  - Can DNA from specimen banks be used?
  - Need to link epigenetic changes and apical endpoints
Methodologic Issues
No Consensus How to Model Methylation

- Appropriate statistical model will depend on the scientific question of interest and knowledge about biological pathways.
- Since methylation CpG sites often exist in clusters and may show correlated methylation changes, analytical methods for summarizing correlated are needed.
- Since most epigenetic data summarizes methylation at individual CpG sites as proportions specific models for proportional data will be required.
- Disentangling genetic and epigenetic effects could be a challenge.
Summary

- Public health in the genomics era
  - We are paying more attention to how we can use pathogen and human to improve health & prevent disease

- Genetics and epigenetics 101
  - Epigenetics as a link between genes & environment and possible biological mediator for health disparities

- Using epigenetics in public health
  - Numerous opportunities and challenges, stay tuned
  - In the meantime, increasing number of genomic applications can be used to save lives today