Looking Toward the Future of Environmental Health Sciences

Rick Woychik, Ph.D.
Director
National Institute of Environmental Health Sciences
National Toxicology Program

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The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects people in order to promote healthier lives.

The vision of the National Institute of Environmental Health Sciences is to provide global leadership for innovative research that improves public health by preventing disease and disability.
NIEHS Strategic Plan
What’s in our environment that can impact our health?
What’s in our environment that can impact our health?

Inter-individual genomic heterogeneity
What’s in our environment that can impact our health?
Variability Among Inbred Strains

Acetaminophen Toxicity

Benzene Clearance

Threadgill and colleagues
UNC, JAX and NCSU

French et al., EHP, 2014
Genes, Environment and Health Initiative

Develop technology and biomarkers

- Diet
- Physical Activity
- Environmental Exposures
- Psychosocial Stress and Addictive Substances

GxE

Identify genetic variants

- GWA Studies
- Data Analysis
- Replication
- Sequencing

- Database
- Function
- Translation
International Common Disease Alliance (ICDA)

- **ICDA:** Working together to accelerate common complex disease discovery and translation

- **M2M2M Challenge:** working together to eliminate the bottlenecks and accelerate progress in moving from maps to mechanisms to medicine, to benefit people around the world
# Environmental Exposures Linked to a Range of Common Disease Phenotypes

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Potential Health Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lead</strong></td>
<td>Decreased IQ, Behavior problems, ADHD, Delayed puberty, Decreased growth, Cardiovascular effects, Nerve disorders, Kidney dysfunction, Fertility problems</td>
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<tr>
<td><strong>Arsenic</strong></td>
<td>Cancer (skin, bladder, lung), Diabetes, Heart disease, Skin lesions, Cognitive development, Poor birth outcomes, Kidney failure</td>
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<tr>
<td><strong>PFAS</strong></td>
<td>Immunotoxicity, Liver injury and dysfunction, Altered metabolism, Obesity, Fertility problems, Reduced fetal growth</td>
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<tr>
<td><strong>Flame retardants</strong></td>
<td>Liver cancer, Neurologic function, Endocrine and thyroid disruption, Immunotoxicity, Reproductive toxicity, Reduced fetal and child development</td>
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<tr>
<td><strong>Pesticides</strong></td>
<td>Parkinson’s disease, Asthma, Diabetes, Thyroid disease, Cancer (prostate, kidney), Autoimmune diseases, Respiratory illness</td>
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<tr>
<td><strong>PM 2.5</strong></td>
<td>Respiratory outcomes (emphysema, asthma, COPD), Heart disease, Autism, Diabetes</td>
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</tbody>
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Air Pollution and Health

- Household and ambient air pollution are significant contributors to global burden of disease

- Each year, nearly 4 million people die prematurely from illness attributable to household air pollution (World Health Organization)

- Ambient PM2.5 was 5th ranking mortality risk factor in 2015, leading to 4.2 million deaths (Lancet 2017)

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Lower respiratory infections, asthma, lung cancer, COPD</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Blood pressure, vascular function, systemic inflammation</td>
</tr>
<tr>
<td>Neurological</td>
<td>Neuro-inflammation, behavioral problems, CNS diseases, Autism</td>
</tr>
<tr>
<td>Immune</td>
<td>Inflammation, impaired T-cell function</td>
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<tr>
<td>Metabolic</td>
<td>Type 2 diabetes, obesity</td>
</tr>
<tr>
<td>Neonatal</td>
<td>Fetal growth, birth outcomes</td>
</tr>
</tbody>
</table>
Integrating the Environment into an All of Us Study

- Geospatial capacity development
- Geospatial data and functionality tool for AoU workbench
- Conduct a G x E/S study

Examples of Geospatial Exposure Data

**Environment**
- Global Air Quality Models

**Climate**
- Daily Weather

**Social**
- CDC Social Vulnerability Index
Epigenetics

• The study of changes in DNA expression that are independent of the DNA sequence.

• A person’s DNA base sequence doesn’t change, but expression of DNA is affected by changes in DNA “packaging.”

• Environment is critical factor in DNA expression; we’re born with genes, but environment affects epigenetic changes.
Epigenetics in Action

Michaud et al., Genes & Dev 1994
The Roadmap Epigenomics Program: 
a public resource of reference epigenomic maps of normal human cells

Adult cells/tissues, fetal cells/tissues, pluripotent (ESC and iPS) cells
The Exposome

What is it?
Totality of exposures across life course, includes external and internal exposures

How to measure it?
Untargeted assessment via mass spectrometry, sensors, bioinformatics, and other tools

Adapted from: Vermeulen et al., Science, 2020
The totality of exposure an individual is subjected to from conception to death...the ‘environmental’ correlate to the genome.

The Challenges to Defining the Exposome

How do we define it?

How do we measure it?

How do we operationalize it?
PEGS
Personalized Environment and Genes Study
Participants: 19,672

Genotype
Whole Genome Sequencing
Candidate Gene SNPs
Epigenetic Chip*

Environment
Questionnaires
• Health & Exposure
• Internal Exposome
• External Exposome
GIS - Geographic Information Systems

Phenotype
Self-reported diseases/conditions
Electronic Health Records
Genetic Data

• Whole genome sequencing n = 4737
• Nucleotide variants
• Copy number and structural variants
• High resolution HLA complex variation
• Telomere length (in progress)

• Epigenetic Data – available early 2023
  – Return of Results
    – Les Biesecker’s Group NHGRI
Contacts for the NIEHS PEGS Program

• Dr. Janet Hall
  – Clinical Director
  – Chief, Clinical Research Branch
  – Janet.hall@nih.gov

• Dr. Alison Motsinger-Reif
  – Chief, Biostatistics and Computations Biology Branch
  – Alison.motsinger-reif@nih.gov
Proposed NIH-wide Initiative on Climate Change and Health

• Executive Orders Impel Renewed Focus on Climate Change Across Agencies
  – Executive Order 14008 Tackling the Climate Crisis at Home and Abroad

• President’s Budget & Congressional Markup
  – President's Budget, House & Senate Markup for Fiscal Year 2022 includes $100 Million to NIEHS for CCH Research

• Seven Institute and Center Directors as NIH Leaders
  – Drs. Bianchi (NICHD), Gibbons (NHLBI), Glass (FIC), Gordon (NIMH), Perez-Stable (NIMHD), Woychik (NIEHS), and Zenk (NINR)

• Re-energized NIH Working Group, co-chaired by NIEHS and FIC
Strategic Framework

• Reflects inputs from
  – Feedback on RFI
  – Portfolio Analysis
  – Strategic whiteboard session with NIH WG Staff
  – Landscape Analysis
NIEHS Research Priorities

• Climate Change and Health
• Precision Environmental Health
  – Exposomics
• Environmental Justice and Health Disparities
• Computations and Data Science
• Mechanistic and Translational Toxicology
Thank you!