



# Expanding the Capacity to Conduct Gene X Environment Experiments

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Director

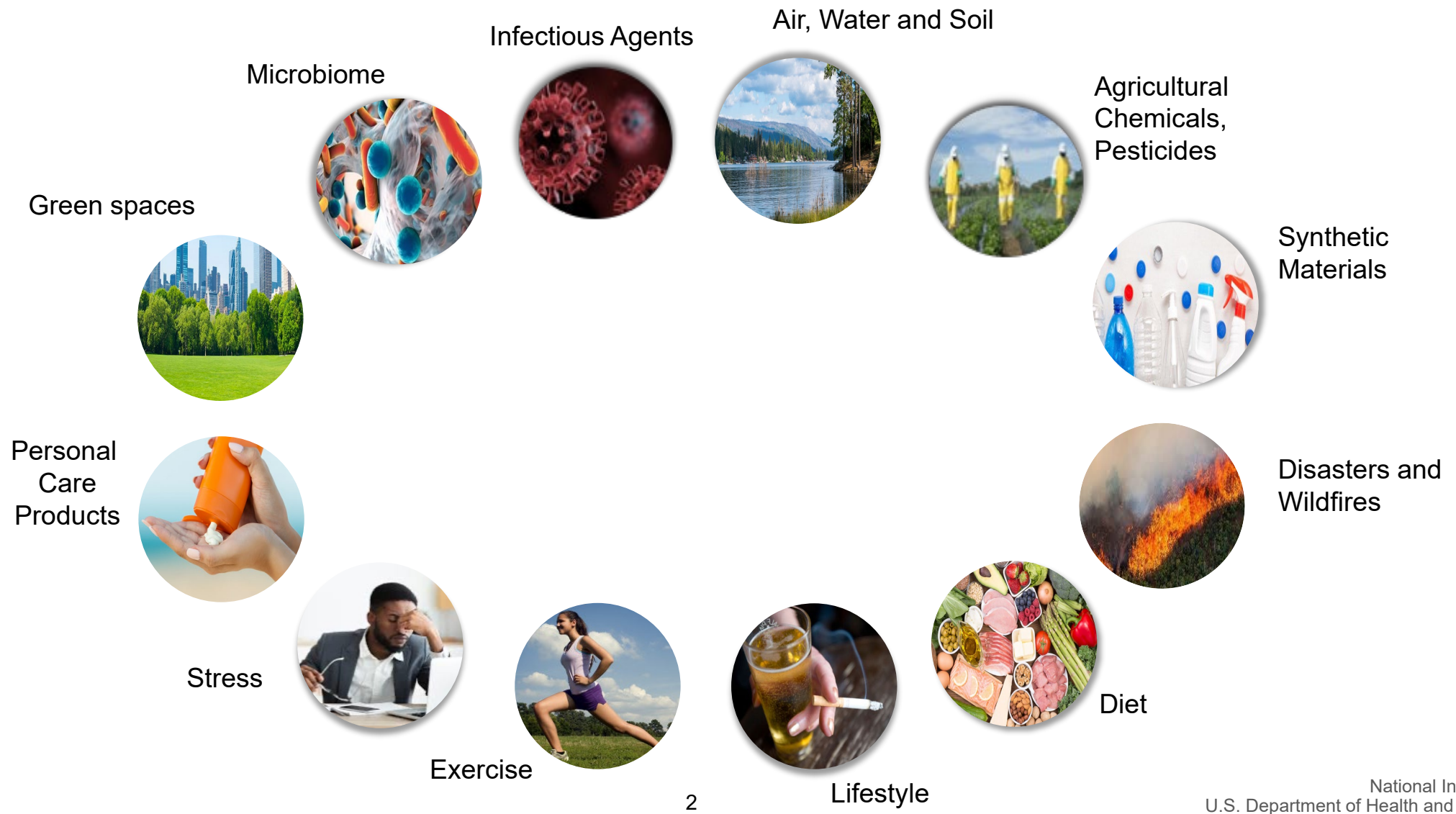
*National Institute of Environmental Health Sciences*

*National Toxicology Program*

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NHGRI Advisory Council Meeting

# What's in our environment that can impact our health?

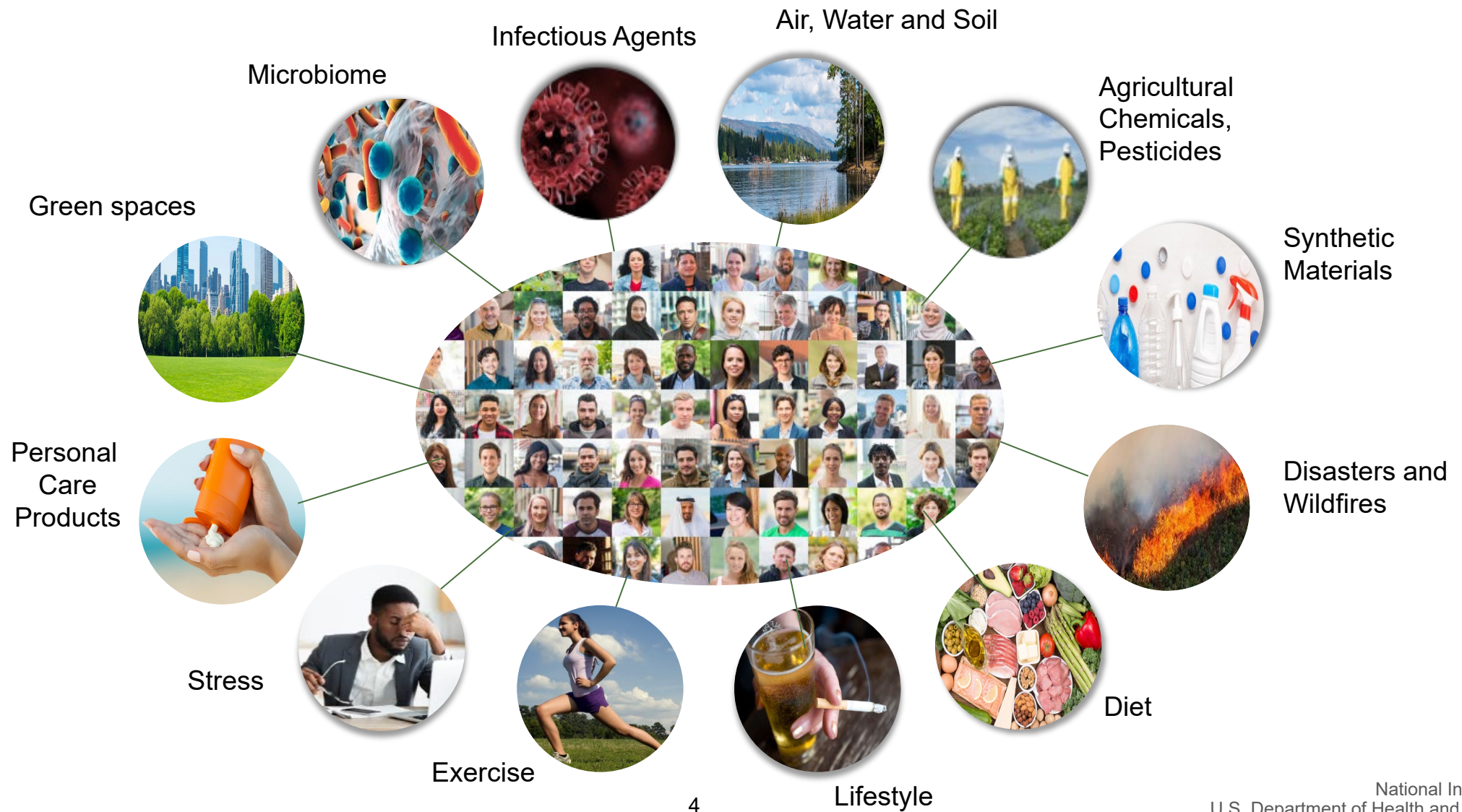


# What's in our environment that can impact our health?

Inter-individual genomic heterogeneity

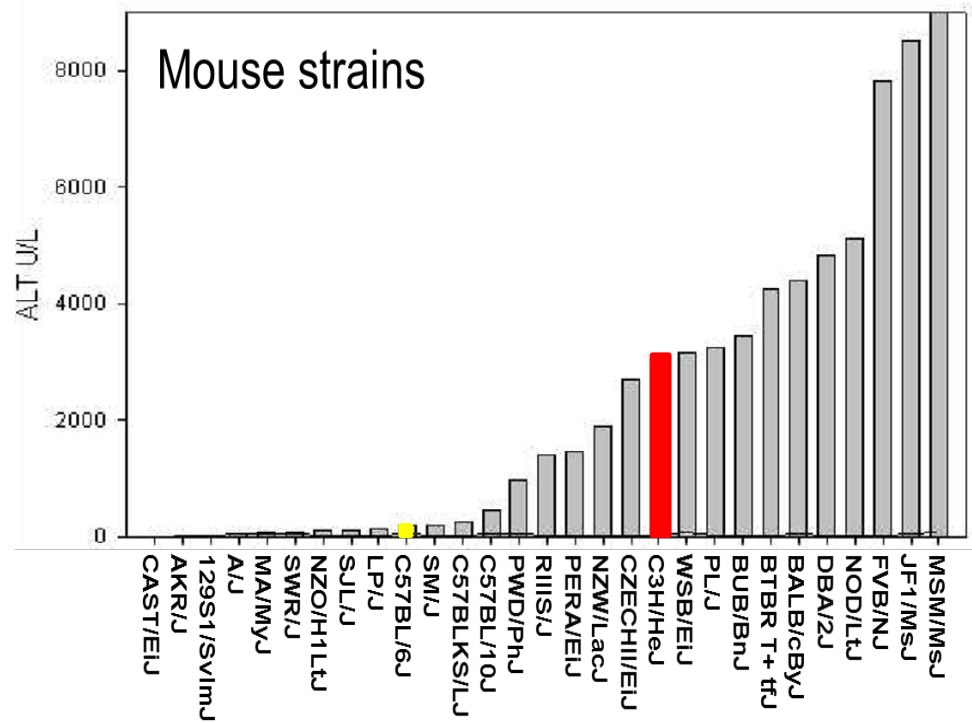


# What's in our environment that can impact our health?



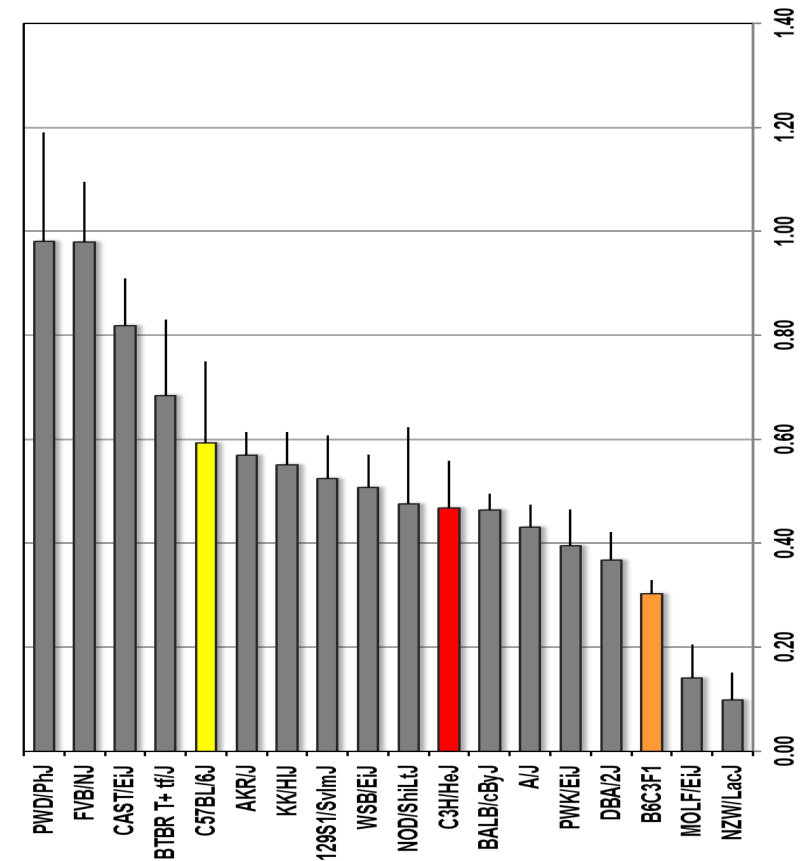
# Variability Among Inbred Strains

Acetaminophen Toxicity



Threadgill and colleagues  
UNC, JAX and NCSU

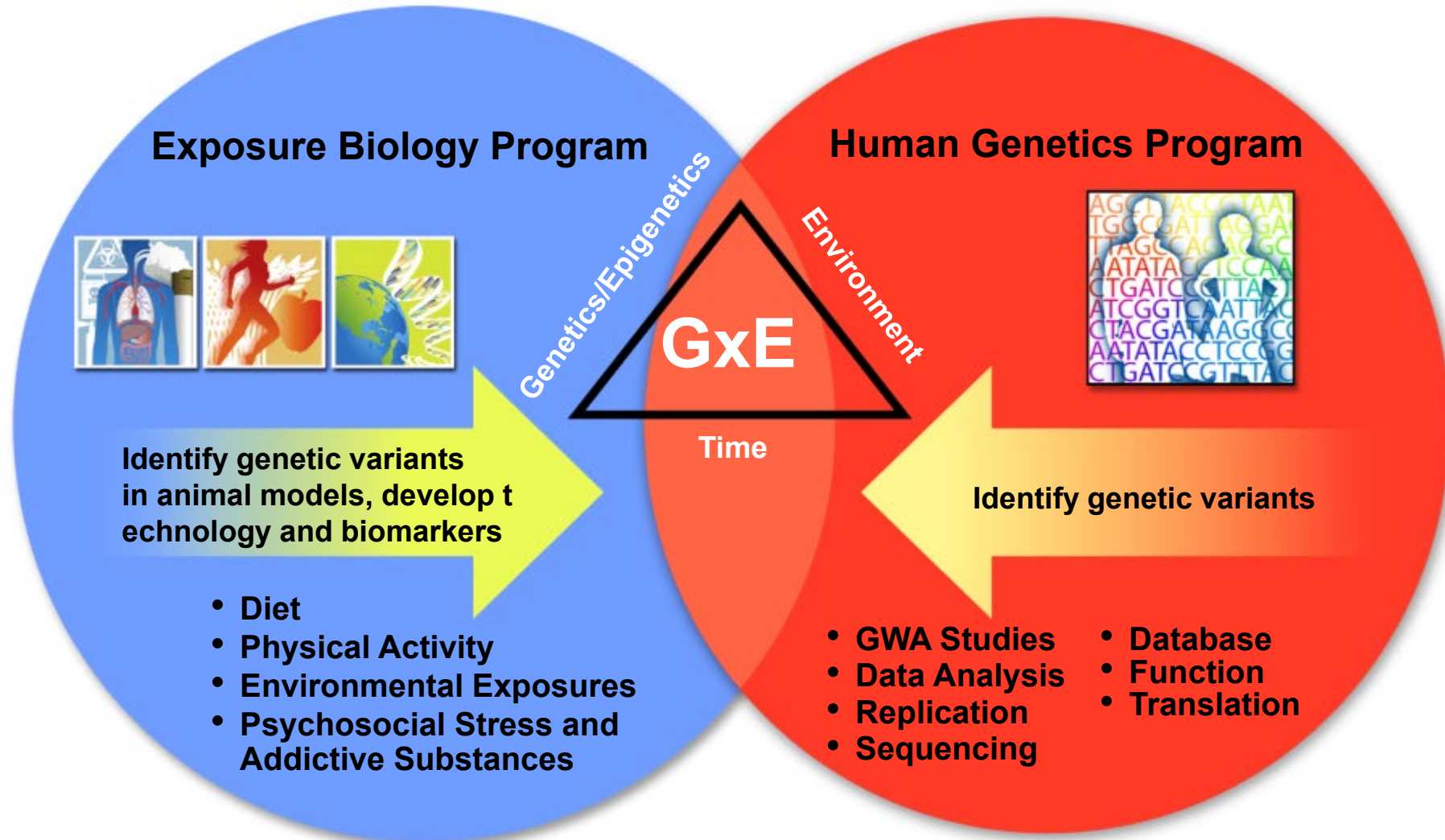
Benzene Clearance



French et al., EHP, 2014

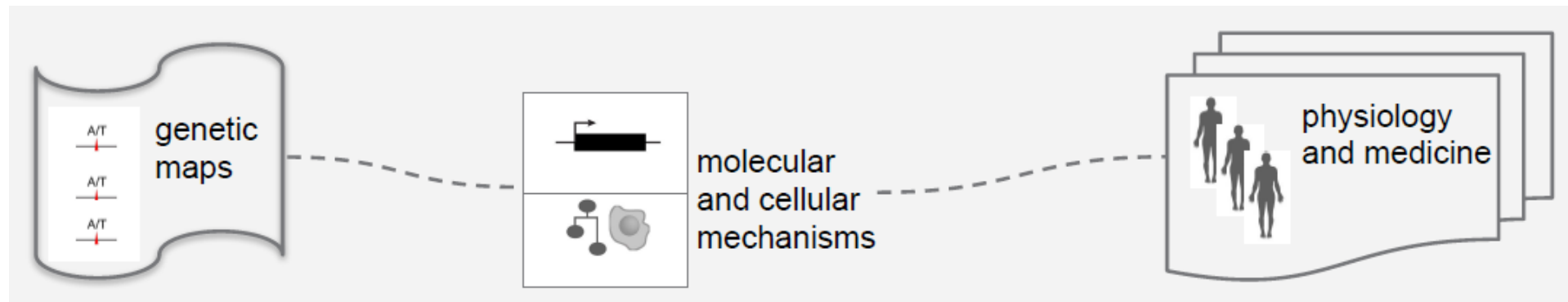
# The Genes, Environment, and Health Initiative

*Genetic Susceptibility - Linking Exposure to Disease*



## 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

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



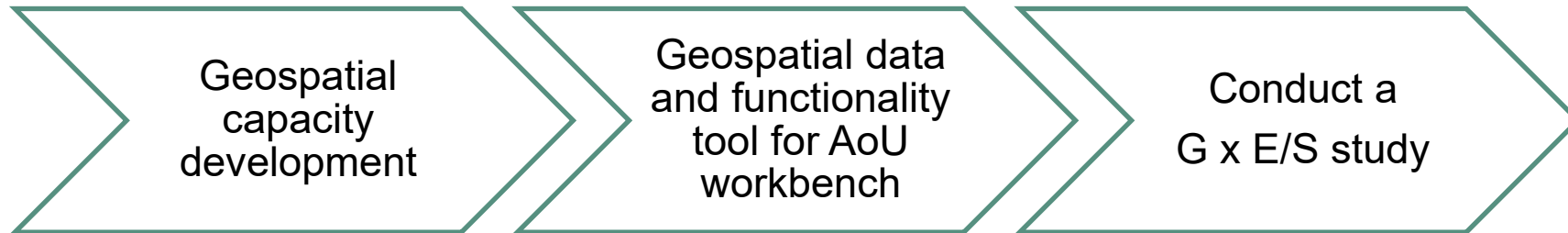
## Air Pollution and Health

- 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)



<b>Respiratory</b>	Lower respiratory infections, asthma, lung cancer, COPD
<b>Cardiovascular</b>	Blood pressure, vascular function, systemic inflammation
<b>Neurological</b>	Neuro-inflammation, behavioral problems, CNS diseases, Autism
<b>Immune</b>	Inflammation, impaired T-cell function
<b>Metabolic</b>	Type 2 diabetes, obesity
<b>Neonatal</b>	Fetal growth, birth outcomes

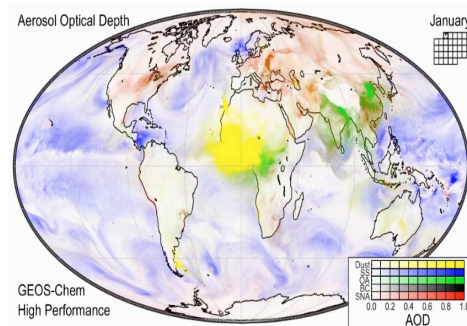
# Integrating the Environment into an All of Us Study



## Examples of Geospatial Exposure Data

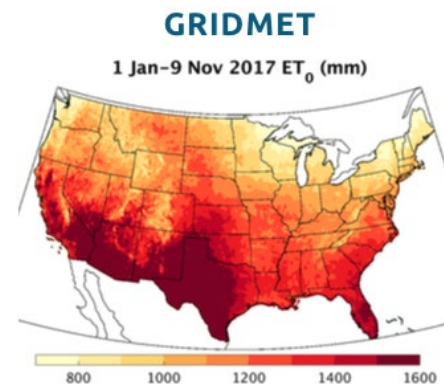
### Environment

Global Air Quality Models



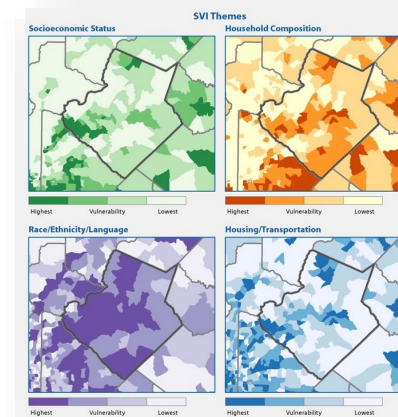
### Climate

Daily Weather



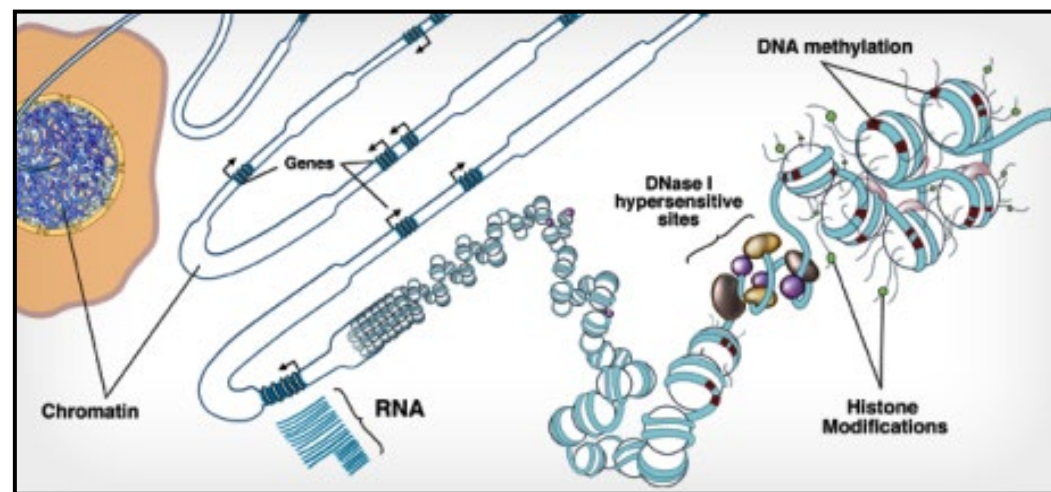
### Social

CDC Social Vulnerability Index

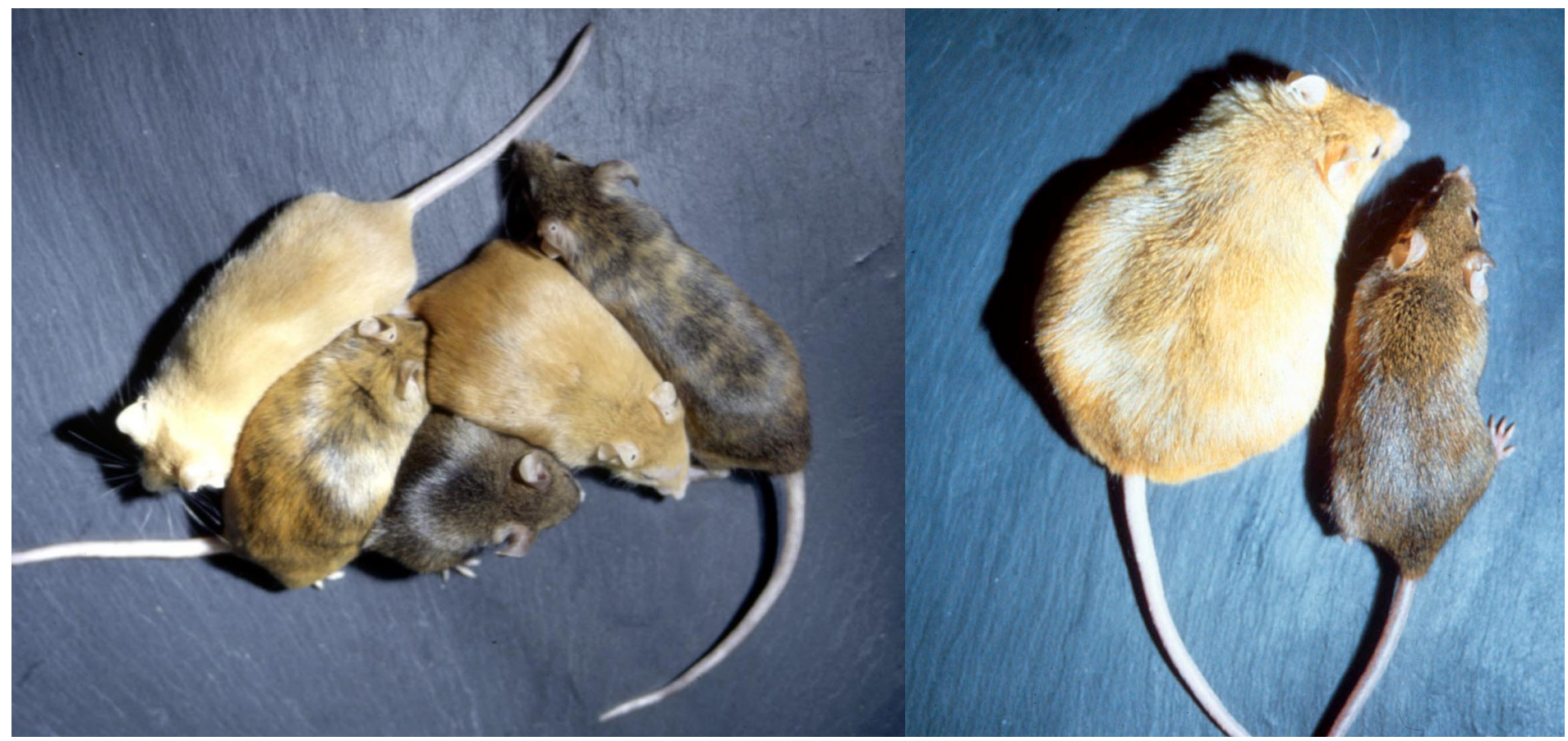


## Epigenetics

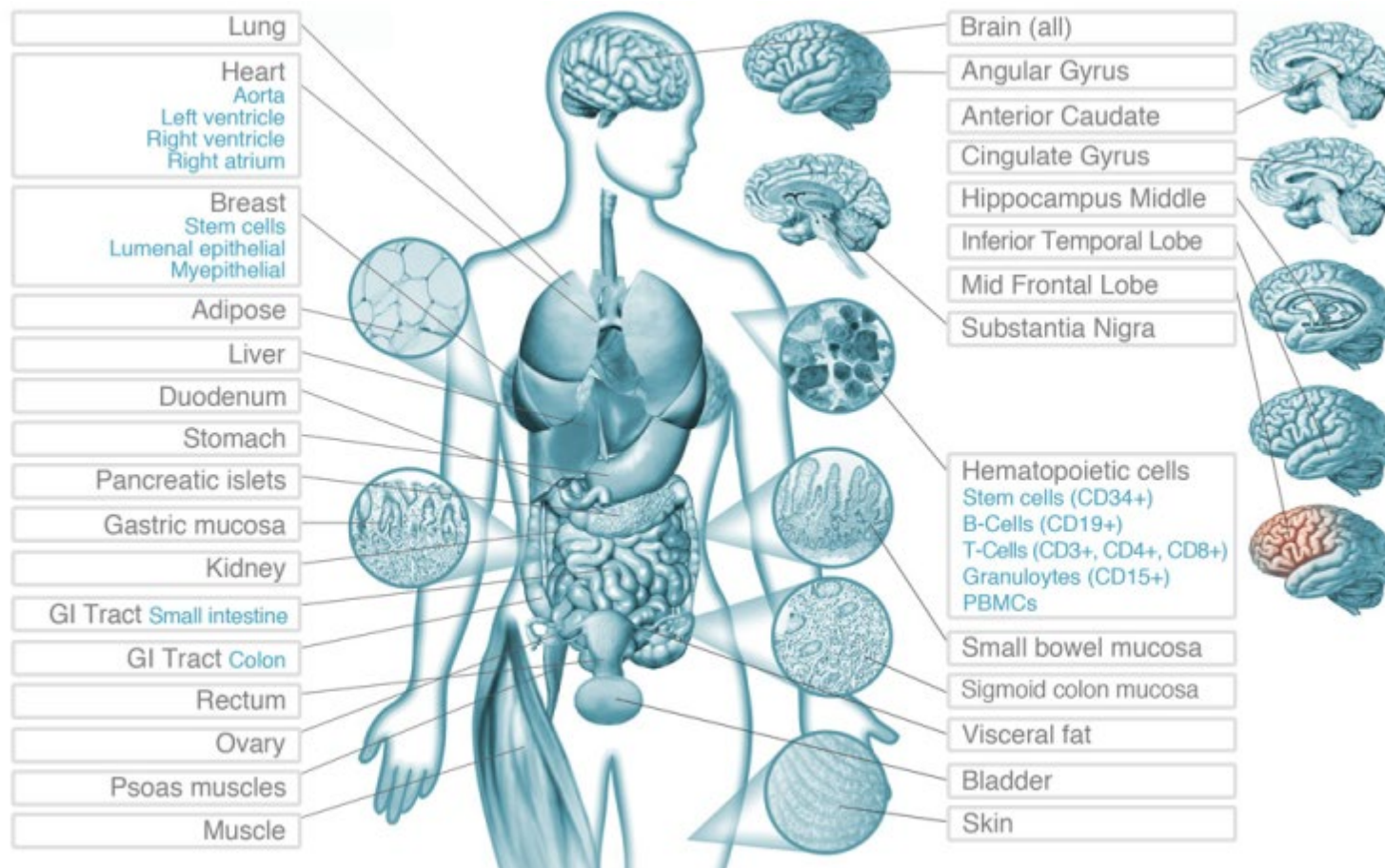
- The study of changes in DNA expression that are independent of the DNA sequence.
- A person's DNA base sequence doesn't change, but expression of DNA is affected by changes in DNA "packaging."
- Environment is critical factor in DNA expression; we're born with genes, but environment affects epigenetic changes.



# Epigenetics in Action



# 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**

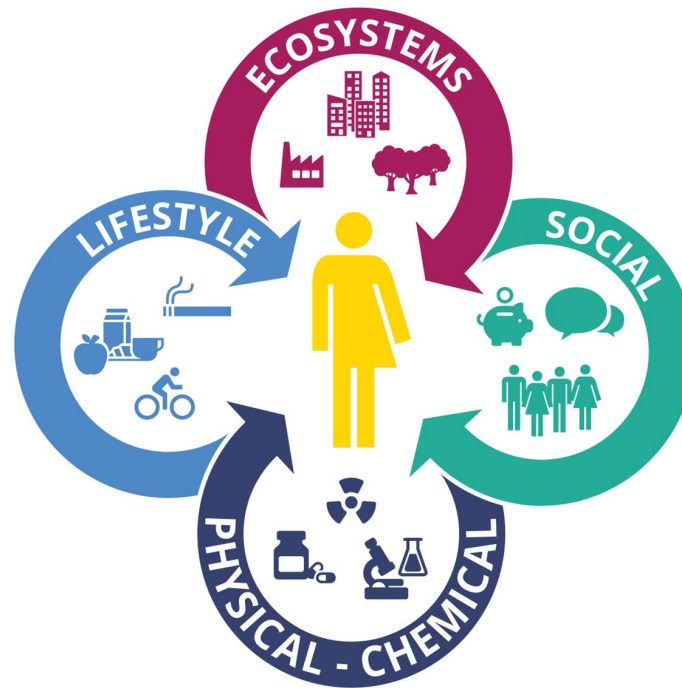
# The Exposome

## 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



- Food outlets, alcohol outlets
- Built environment
- Urban land use
- Population density
- Green space



- Physical activity
- Sleep behavior
- Diet
- Smoking
- Drug / Alcohol use



- Household income
- Inequality
- Social capital
- Cultural norms
- Psychological / mental stress



- Temperature / Humidity
- Electromagnetic fields
- Ambient light
- Pollen / Mold / Fungus

- Point, line sources
- Odor / Noise
- Air pollution
- Agricultural activities

- Pesticides
- POPs
- Plastics / Plasticizers
- PBDEs

- Water contaminants
- Soil contaminants
- Food contaminants
- Occupational exposures



# Implementing the Exposome into NIEHS Research

## The Human Health Exposure Analysis Resource:



### Goal

Provide infrastructure for adding or expanding exposure analysis to advance understanding of the impact of environmental exposures on human health throughout the life-course

# The Challenges to Defining the Exposome

## The Exposome

The totality of exposure an individual is subjected to from conception to death...the 'environmental' correlate to the genome.



How do we define it?

How do we measure it?

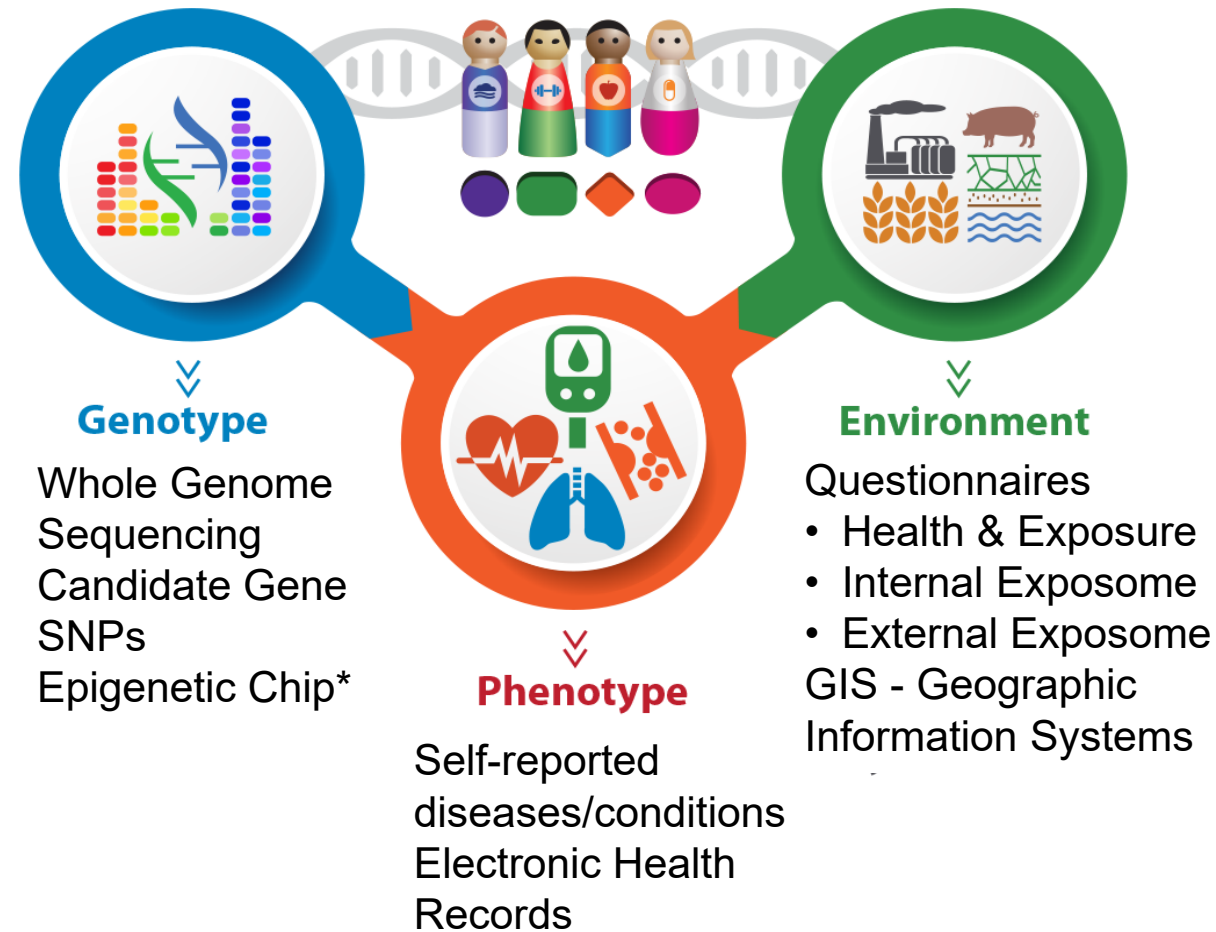
How do we operationalize it?



# PEGS

## Personalized Environment and Genes Study

Participants: 19,672



## 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](mailto:Janet.hall@nih.gov)
  
- Dr. Alison Motsinger-Reif
  - Chief, Biostatistics and Computations Biology Branch
  - [Alison.motsinger-reif@nih.gov](mailto: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
- [www.nih.gov/climateandhealth](http://www.nih.gov/climateandhealth)



## An Invitation for Your Participation

**Commit to explore and develop** the health impacts of CCH within the mission areas in your IC and with the extramural community and other stakeholders

- Bring those ideas to the NIH-wide CCH WG to help build the NIH-wide Strategic Plan going forward

**Identify staff** to join the CCH WG if not yet represented

**Your thoughts and ideas**

# Climate Change and Health Initiative Participants

## Executive Committee

- Rick Woychik, NIEHS – Chair
- Roger Glass, FIC
- Josh Gordon, NIMH
- Shannon Zenk, NINR
- Eliseo Pérez-Stable, NIMHD
- Diana Bianchi, NICHD
- Gary Gibbons, NHLBI

## Co-chairs and Advisor

- Joshua Rosenthal, FIC
- Aubrey Miller, NIEHS
- Gwen Collman, NIEHS –  
*Strategic Advisor*

## CCH Steering Committee

- Regina Bures, NICHD
- Flora Katz, FIC
- Megan Kinnane, NIMH
- Ivan Navarro, NIMHD
- Louise Rosenbaum, NINR
- Claudia Thompson, NIEHS
- Larry Fine, NHLBI

## Critical Contributors

- Abee Boyles, NIEHS
- Amit Mistry, FIC
- Kimberly Thigpen Tart, NIEHS
- Trisha Castranio, NIEHS
- Ann Liu, NIEHS (c)
- Betsy Eagin Galluzzo, NIEHS (c)
- Rachel Scheinert, NIMH
- Liz Perruccio, NINR
- Mike Sayre, NIMHD
- Shyamal Peddada, NICHD
- Andrew Liang, NINR
- Plus many others...



National Institute of Environmental Health Sciences  
*Your Environment. Your Health.*

*Thank you!*



National Institute of  
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National Toxicology Program  
U.S. Department of Health and Human Services

