



National Institute of Environmental Health Sciences

Your Environment. Your Health.

Research Activities at NIEHS

Rick Woychik, Ph.D.
Director

National Institute of Environmental Health Sciences
National Toxicology Program

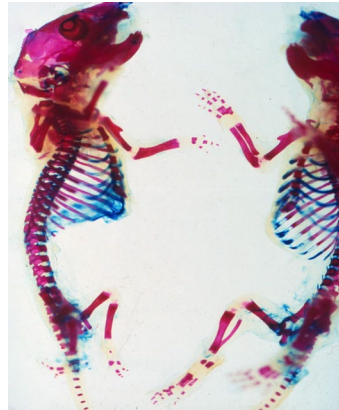
January 24, 2023

NICHD Council

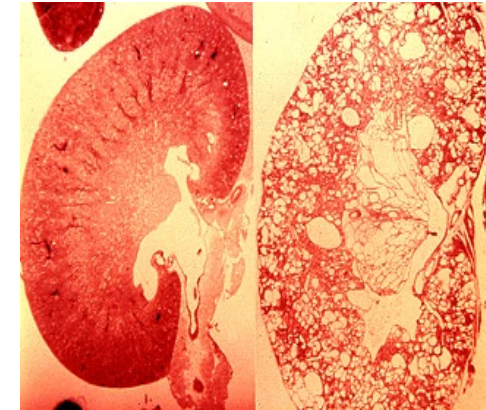
My First RO1 from NICHD - Insertional Mutagenesis in Transgenic Mice

Skeletal Abnormalities

Woychik et al *Nature* 1985
Woychik et al *Nature* 1990
Mass et al *Nature* 1990



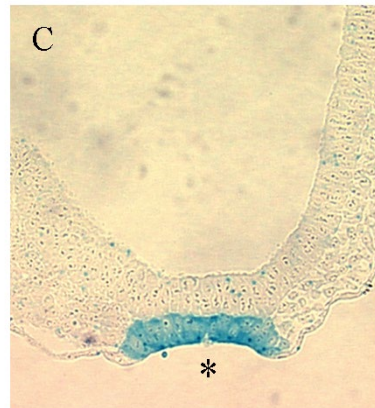
Hundreds of Transgenic Mice



Childhood PKD
Moyer et al
Science 1994

Polarity Defects

Murcia et al
Development 2000



Vice Chair Pediatric Research

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.

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



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

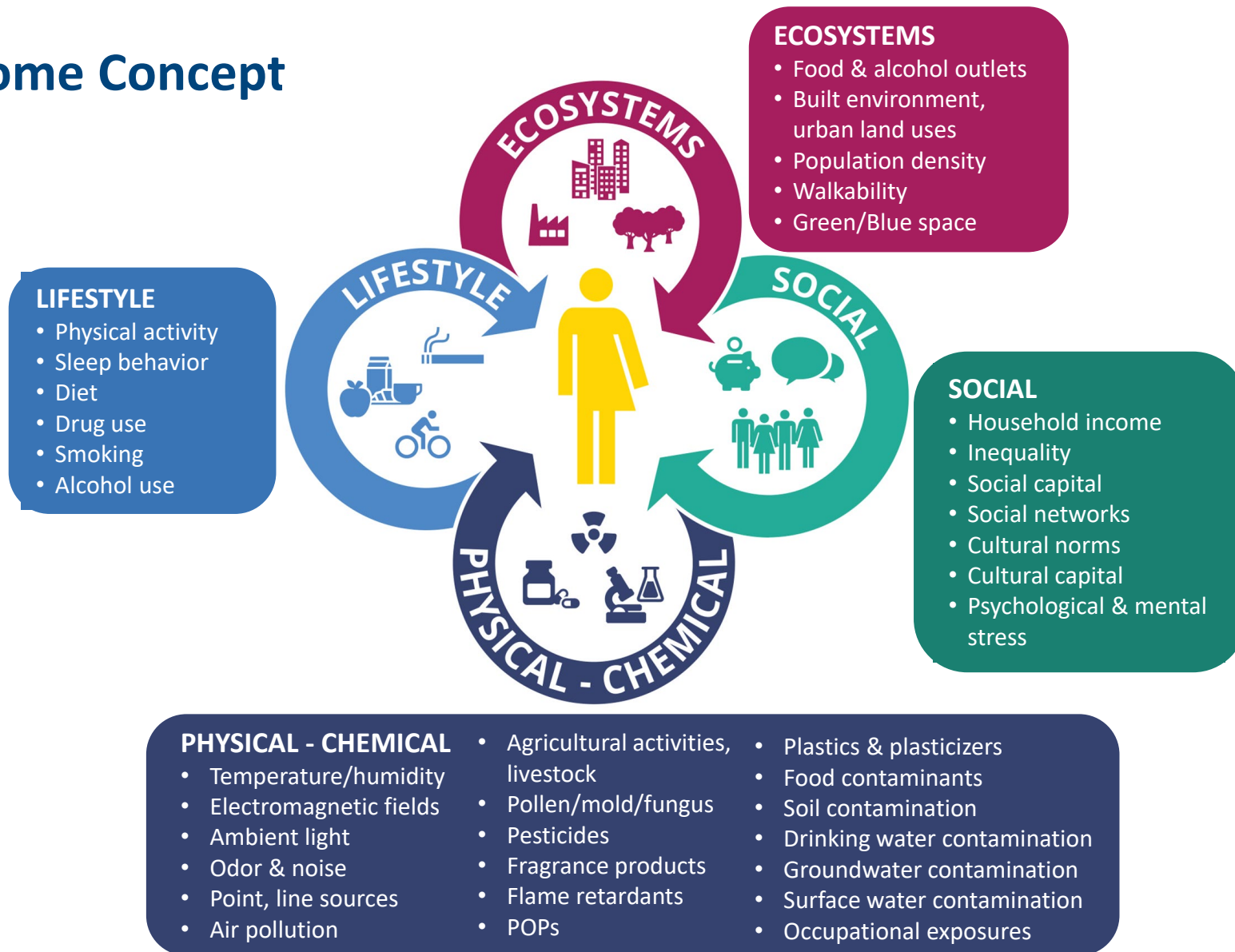
Inter-individual genomic and biological heterogeneity



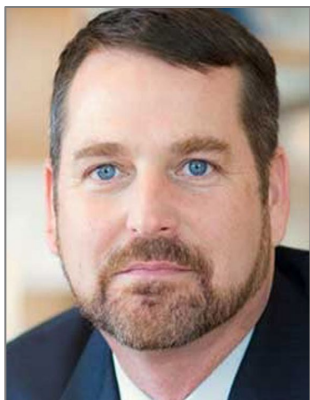
Precision Environmental Health



The Exposome Concept



The Challenges to Defining the Exposome



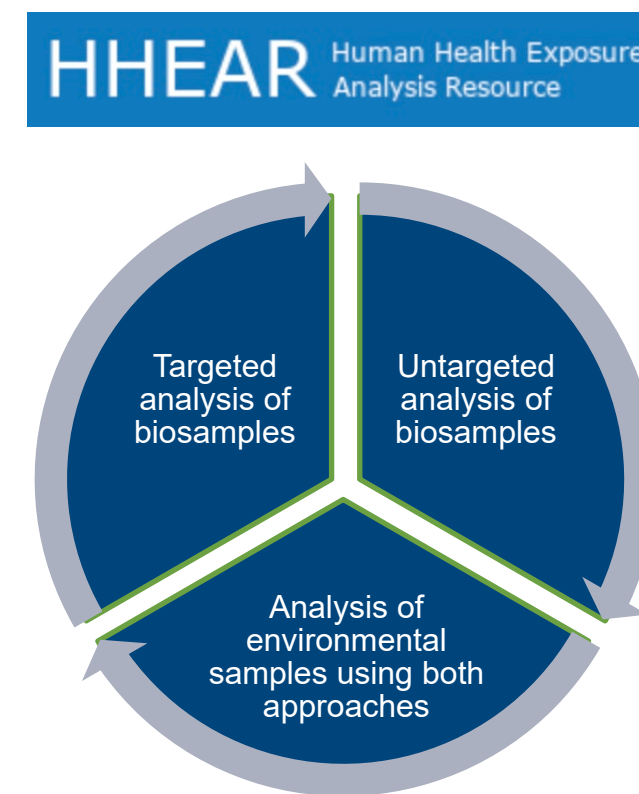
Gary Miller

We need:

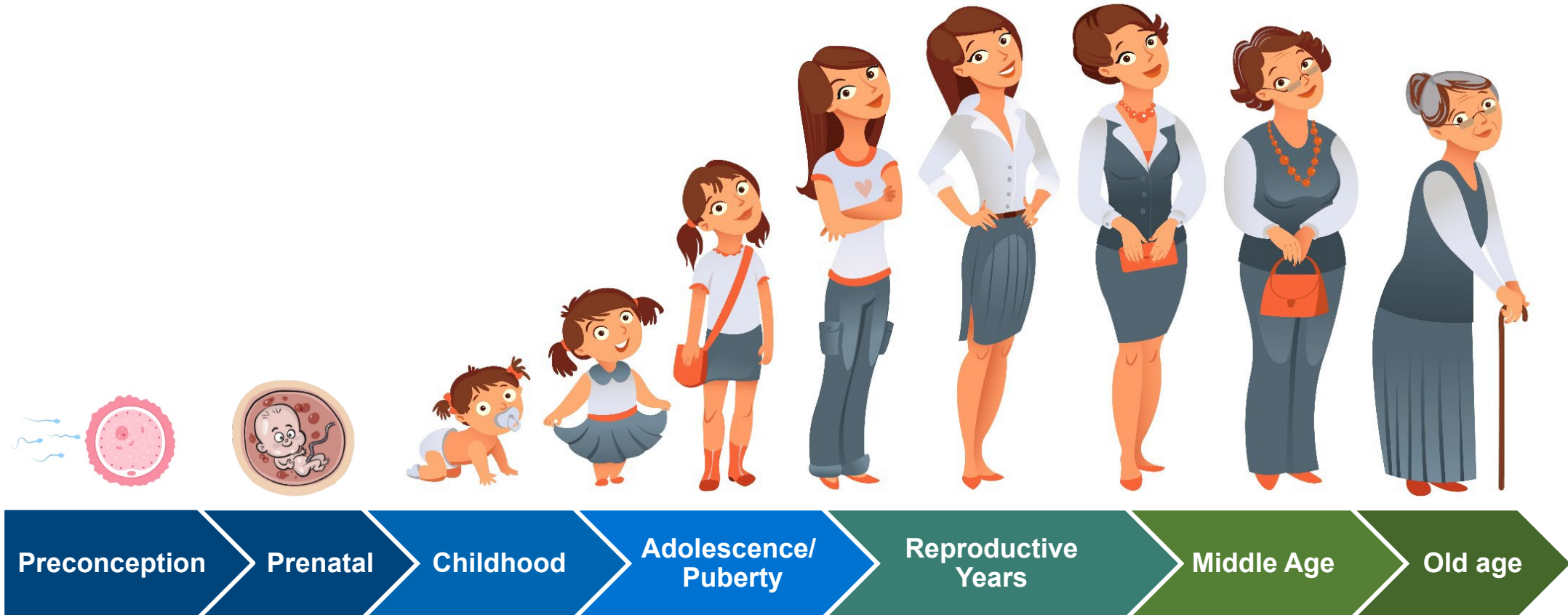
- An operational definition of the exposome
- To build the technology capabilities to study the exposome
- To study the pragmatic exposome – focus on what we can do now, e.g., high resolution mass spectrometry
- To model this on the genomics community

How are we implementing the exposome into the NIEHS research?

- **Human Health Exposure Analysis Resource (HHEAR)** is an infrastructure available to NIEHS, NHLBI, NCI, and ECHO funded investigators to add or expand exposure analysis in biological and environmental samples and provide a public access data repository.
- The resource offers both:
 - traditional biomonitoring for **targeted**, hypothesis driven research involving analyses for specific contaminants, markers of exposure, and other substances that are known or suspected of affecting health,
 - and **hypothesis-free exploratory analyses** utilizing advanced technologies to discover new associations between chemicals or metabolites and health.
- Techniques used by HHEAR includes nuclear magnetic resonance (NMR) and mass spectrometry (MS).



Windows of Susceptibility and Developmental Origins of Health and Disease (DOHaD)



NIEHS DOHaD Targeted Programs

Preconception Exposure (2017-current)

- Investigates pre-fertilization exposures and later-life phenotypic outcomes in the first generation offspring.
- Including environmentally-induced germ cell alterations by endocrine disruptors, pesticides, components of air pollution, combined exposures, etc.



Environmental Influences on Placental Origins of Development (2014-current)

- Development and application of new models and methods for placental assessment.
- Focused on exposures effects on early-stage placental physiology, endocrine, immune, and metabolic functions and effects on fetal and maternal health.



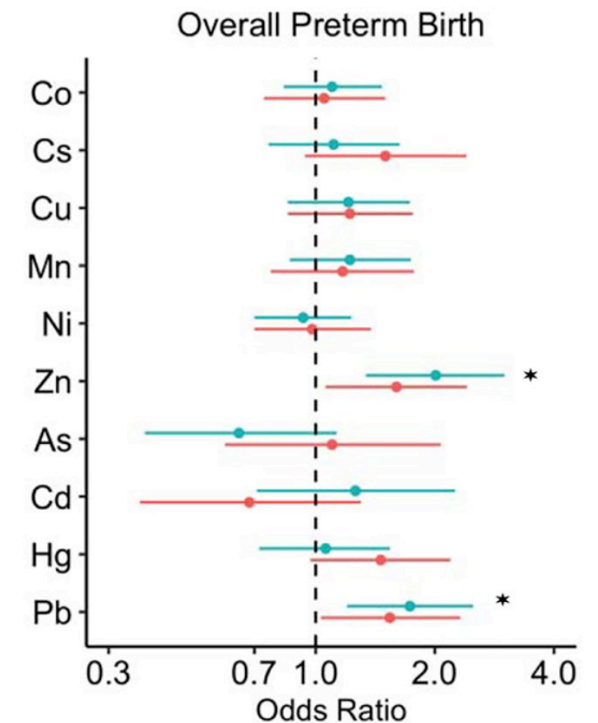
Pregnancy as a Vulnerable Time Period for Women's Health (2020-current)

- Exposures during pregnancy and the postpartum period with impacts on maternal health.
- Determine the life-long effects of these exposures on a woman's health.



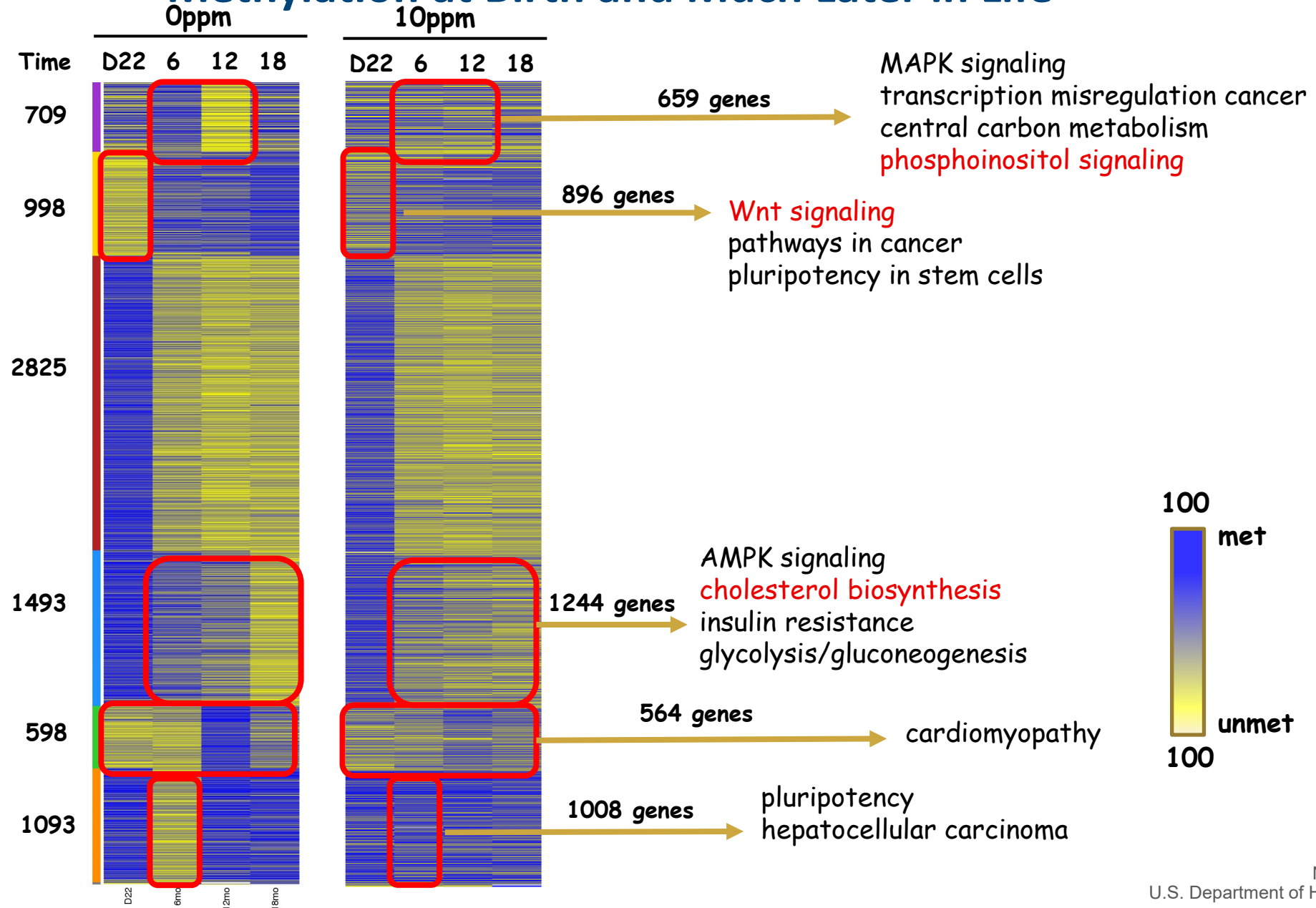
Exposures to Mixtures, Oxidative Stress, and Adverse Pregnancy Outcomes in Puerto Rico

- Compared to the United States overall, significantly higher rates of preterm birth exist in Puerto Rico, where nearly 12% of all births are preterm.
- There are 19 Superfund sites on the island.
- Findings suggest that low-level prenatal Pb exposure, as well as elevated Mn and Zn exposure, may adversely affect birth outcomes, lead to preterm birth. (Ashrap, et al.)
- Phthalates may also play a role, as DBP and DiBP metabolites have also been associated with increased odds of preterm birth. (Ferguson, et al.)
- Through our support, PROTECT is discovering much needed information on the magnitude, sources, and impacts of exposures in pregnant women.



DOHaD: Developmental Rotenone Exposure Alters the Patterns of Liver DNA

Methylation at Birth and Much Later in Life



NIEHS Intramural Research Updates

Genomics and the Environment in Respiratory and Allergic Health Group

(PI: Stephanie London, M.D., Dr.P.H)

- The Pregnancy and Childhood Epigenetics (PACE) consortium, using 39 studies, is comprised of researchers at NIEHS and around the world who are interested in studying the early life environmental impacts on human disease using epigenetics.
- The primary aim is to identify differences in DNA methylation in relation to a wide range of exposures and outcomes pertinent to health in pregnancy and childhood.

Fetal exposures in pregnancy

- Air pollution
- Alcohol use
- Body mass index
- Diet
- Diseases
- Gestational weight gain
- Smoking
- Stress

Methodologic topics

- Causality
- Cell composition adjustment
- Differentially methylated regions
- Integrative omics analyses



PACE

Pregnancy And Childhood Epigenetics

Birth, infancy and childhood exposures/outcomes

- Birth weight, gestational age
- Cardio-metabolic: body mass index, blood pressure
- Eczema, atopy
- Neuro-developmental
- Otitis media
- Respiratory: wheezing, asthma, lung function

Collaborative Centers in Children's Environmental Health Research and Translation

Drs. Kimberly Gray and Lindsey Martin, NIEHS



- NIEHS developed *a new vision* for children's environmental health with 6 centers.
- Purpose:
 - **Facilitate interaction** among experts
 - **Engage partners** to move the science into public health and clinical practice
 - **Synthesize and translate** extant children's environmental health (CEH) research
 - Stimulate **pilot projects**
 - Test and implement new **tools, methods, intervention/prevention strategies**
 - **Collaborative** network to respond to and protect children from environmental threats

Environmental Health Disparities Centers (2020-2025)

NIEHS, NIMHD, NICHD

Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) Center

- **Population:** Low-income, predominantly Hispanic women
- **Center Goal:** To investigate how environmental and psychosocial stressors affect the health of mothers Depression; Cardiovascular health; and Postpartum allostatic load



Maternal and Infant Environmental Health Riskscape (MIEHR) Research Center

- **Population:** African American women
- **Center Goal:** To elucidate contributions of the biological, physical, social and built environments of the environmental riskscape to EHD in pregnant women and their infants.



Center for Native American Health Equity Research

- **Population:** Navajo Nation, Absaalooke (Crow), Cheyenne River Sioux Tribe Communities
- **Center Goal:** To examine toxicities of metal mixtures and strive to build research capacity and improve the understanding and interpretation of data across tribal communities



NIEHS Clinical Training

Pediatric and Reproductive Environmental Health Scholars Program (PREHS)

- Provides research experience in environmental health to pediatricians, OB/GYNs, and other healthcare professionals.
- Award Start Date: December 1, 2021
- 3 awards funded at \$500,000 each
- Awards are funded up to 5 years



EMORY
UNIVERSITY



Scholars



Environmental
Health Research



Scholars



Research Translation
& Communication



Scholars



Healthcare
Knowledge & Skills



**Well-rounded
Scholars:**
Research,
Resources, and
Leaders

NIEHS Community Outreach on Children's Health

Environmental Health Chat: Podcasts



[Climate Change, Air Pollution, and Children's Health](#) (2022) – Kari Nadeau, M.D., Ph.D. talks about how climate change and air pollution affect children's health. She also discusses what health care professionals, policy makers, and parents can do to better protect kids from climate change- and air-pollution-related health impacts.



[The Shrinking Salton Sea and Children's Health](#) (2022) – Shohreh Farzan, Ph.D., and Esther Bejarano discuss a community-engaged research project that aims to understand how the rapid drying of the Salton Sea will impact local levels of particulate matter and affect children's lung health.



[Why Neighborhoods Matter: Brain Development in Children](#) (2021) – Megan Herting, Ph.D., discusses why neighborhoods matter when it comes to brain and cognitive development, and what it may mean for health later in life.



[Using Culturally Appropriate Messages to Promote Smoke-free Homes](#) (2021) – Patricia Nez Henderson, M.D., shares her experience working with tribal communities to encourage smoke-free homes, with the goal of improving their health.



[Wildfire Smoke and Children's Health](#) (2021) – Stephanie Holm, M.D., discusses children's health risks from wildfire smoke exposure. She also offers advice to pediatricians and parents on how to keep kids safe during a wildfire event.



[PFAS and Children's Health](#) (2019) – This podcast discusses a complex group of “forever” chemicals known as PFAS and how researchers are working to understand how they may affect early development in children.

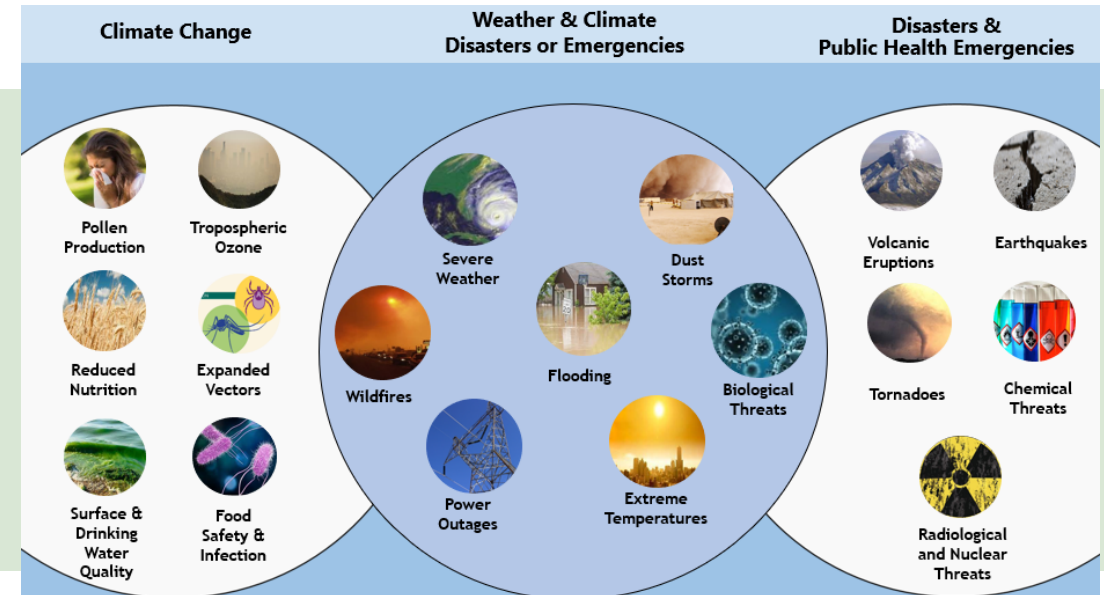
President's Task Force on Environmental Health Risks and Safety Risks to Children

- Asthma Disparities Subcommittee
- Chemical Exposures Subcommittee
- Subcommittee on Climate, Emergencies, and Disasters
- Lead Exposures Subcommittee



Subcommittee on Climate, Emergencies & Disasters (SCED) Purpose

To provide a **convening** and **coordinating** role to empower federal partners to collectively assess and address current gaps and inequities in **health protection and research related to children and pregnant/lactating mothers** resulting or arising from climate change, public health emergencies, and disasters



- Goal 1: Strengthen Federal Interagency Coordination and Collaboration
- Goal 2: Build External Partnerships and Public Health Awareness
- Goal 3: Provide Expert Consultation and Guidance
- Goal 4: Facilitate Development and Coordination of a Federal Research Agenda

Co-Chairs:
Cinnamon Dixon
(NICHD)
Kimberly Thigpen-Tart
(NIEHS)
Amelia Nguyen
(EPA)

Proposed ALL of NIH Initiative on Climate Change and Health (CCH)

- **Executive Orders Bring Renewed Focus on Climate Change Across Agencies**
 - Executive Order 14008: Tackling the Climate Crisis at Home and Abroad
- **President's Budget & Congressional Markup**
 - Congressional Appropriation of \$40M for FY23
- **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



Climate Change Affects Health Directly and Indirectly

Direct Effects

- Heat-related illness
- Respiratory disease
- Heart disease
- Food-, water-, and vector-borne diseases
- Injury
- Premature death
- Mental health impacts
- Poor maternal and birth outcomes

Indirect Effects

- Chemical releases into environment
- Changes in air, water, food quality and quantity
- Population displacement
- Interruptions to health care
- Infrastructure and supply chain disruption
- Economic impacts – more people living in poverty



Climate Change Affects Us Unequally



Under-served populations with health disparities

(Some communities of color; Low-income populations; Low-educational attainment groups; Immigrant groups; Indigenous populations)



Exposed workers

(e.g., farmers, construction workers)



Persons with disabilities



Vulnerability by life stage

(Fetal/pre-natal, infants, young children, pregnant women, elderly)



Vulnerability associated with chronic medical conditions

(e.g., diabetes, asthma, cardiorespiratory diseases, psychiatric diseases)

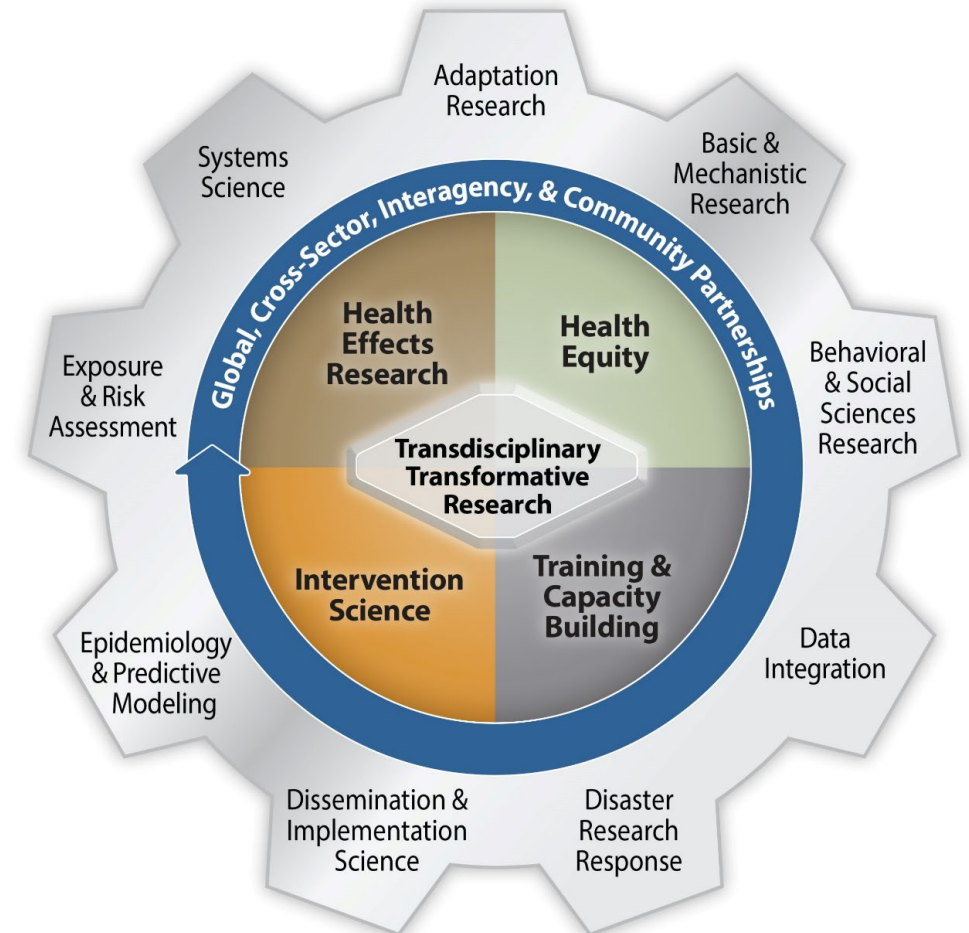


Populations in LMICs

(Higher rates of existing diseases, malnutrition, and extreme poverty)

Framework Guides Future Climate Change and Health Research

- Outlines four core elements
 - Health Effects Research
 - Health Equity
 - Intervention Science
 - Training & Capacity Building
- Goal is to reduce health threats from climate change across the lifespan and build resilience
- New Funding Announcements posted: www.nih.gov/climateandhealth

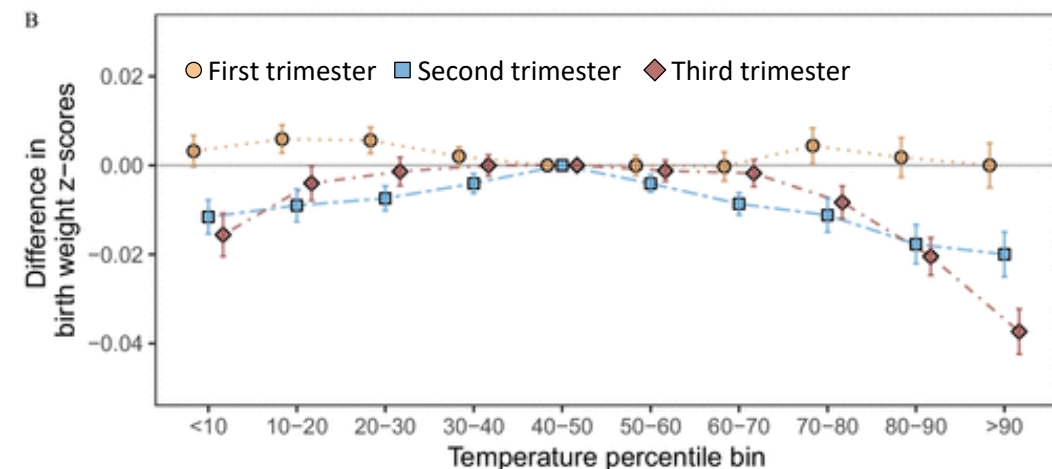
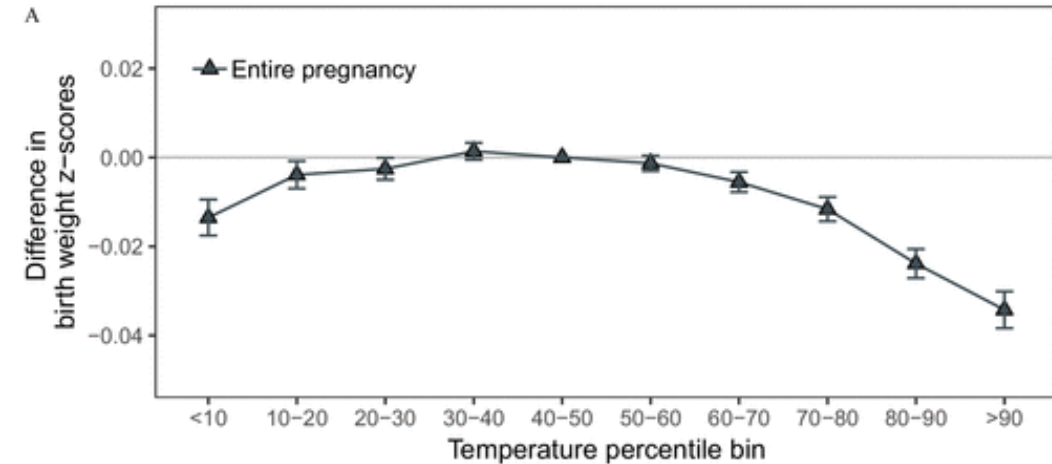


Climate Change Affects Reproductive Health

Exposure	Physiologic and biologic vulnerabilities	Disparate health impacts
Extreme heat	Women have higher working metabolic rate and reduced heat dissipation through sweating	Heat-related morbidity and mortality
Poor air quality	Women experience greater deposition of particles in the lungs	Respiratory and heart disease
Poor air quality	Air pollutants can cross placenta	Poor birth outcomes
Disasters	Women are more likely to have poor baseline nutritional status and physical health	Higher rate of mortality during disasters, birth complications, poor maternal and neonatal health
Food insecurity	Increased nutritional needs during menstruation, pregnancy, and nursing	Malnutrition, anemia, poor neonatal outcomes
Waterborne diseases	Dehydration and infection during pregnancy	Preterm birth, poor maternal and neonatal outcomes
Vector-borne diseases	Women produce higher CO ₂ which attracts mosquitos; Hormone changes during pregnancy reduce immune response	Poor reproductive, maternal, and neonatal outcomes

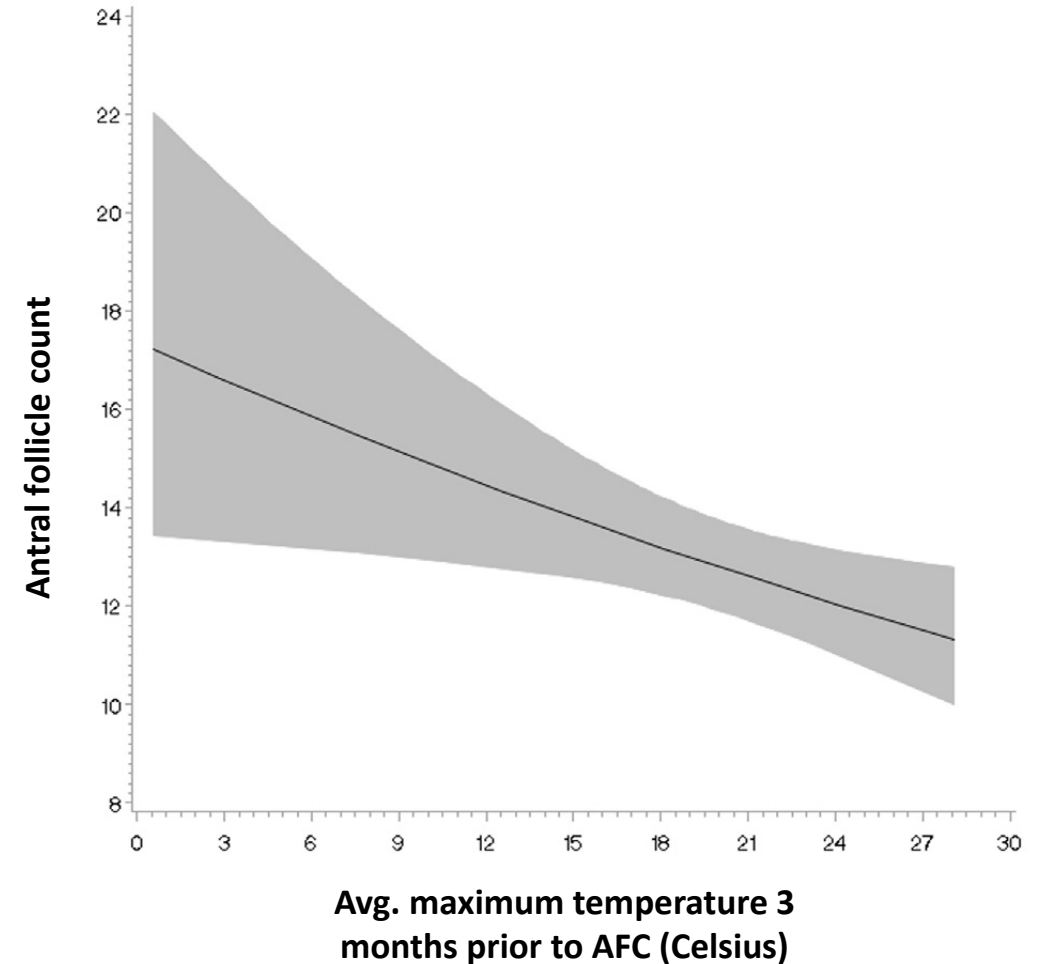
Hotter Temperatures During Pregnancy Linked to Lower Fetal Growth

- Study included data from nearly 30 million births across the U.S. between 1989 and 2002
- High ambient temperatures across pregnancy were associated with **higher risk of term small for gestational age (SGA) and lower birth weight**
- Risks were more strongly associated with temperatures during the 2nd and 3rd trimesters, and in cold climates
- Study provides evidence that **temperature may be novel risk factor for lower fetal growth**



Higher Temperatures Linked to Lower Ovarian Reserve

- Assessed antral follicle count (AFC), a measure of ovarian reserve, in 631 women aged 18-45 years in Massachusetts
- Estimated daily ambient temperature exposures 3 months, 1 month, and 2 weeks before AFC examination
- **A 1-degree C increase in average maximum temperature 3 months before ovarian reserve testing was associated with a 1.6% lower AFC**
- Results suggest that the steady increase in temperature due to climate change may result in **accelerated reproductive aging in women**



Climate Change Associated Natural Disasters Disproportionately Affect Women, Children, People with Disabilities

- Women, teens and young adults, and children more vulnerable to **post-traumatic stress after Indian Ocean tsunami**
- Children with chronic health conditions, and those who needed mental health care, experienced **health care disruptions and unmet care needs after Hurricane Katrina**
- At-risk children with higher exposure to natural disaster experienced **more longer-term problems controlling aggression**



Pregnancy Outcomes Before and After Hurricane Harvey

- Study included data from nearly 30,000 pregnant women – 3,842 of whom delivered within 40 weeks after Hurricane Harvey
- Women delivering after the hurricane were more likely to have adverse outcomes, as were their newborns, compared to women delivering before the storm:
 - **27% higher maternal morbidity**
 - **50% higher neonatal morbidity**
- Women of low socioeconomic status were most affected

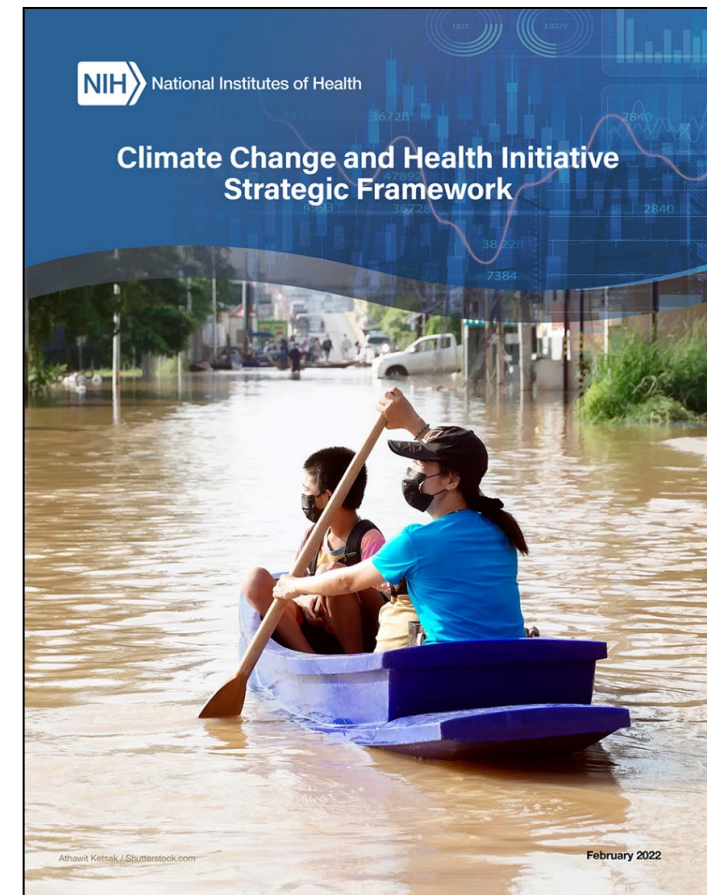


First Projects with FY 2022 Funds from all 7 NIH Initiative Partners

- **Research Coordinating Center for the Climate Change and Health Community of Practice**
 - RFA-ES-22-00
 - The Research Coordinating Center (RCC) will support the development of an inclusive Community of Practice (COP) of climate change and health researchers and trainees that fosters collaboration, capacity building, innovation and research.
- **Research Opportunity Announcement Alliance for Community Engagement- Climate and Health (ACE-CH)**
 - RFA-ES-22-003
 - NIH is soliciting applications from teams to conduct community-engaged research focused on climate change impacts on health and, the co-benefits of identifying the mitigation of climate change risks, vulnerabilities and adaptation.
- **Notice of Special Interest: Climate Change and Health**
 - NOT-ES-22-006
 - NOSI encourages applications that address the impact of climate change on health and well-being over the life course, including the health implications of climate change in the United States and globally.
- **Notices of Special Interest: Innovative Technologies for Research on Climate Change and Human Health (SBIR/STTR)**
 - NOT-ES-22-009 & NOT-ES22-010
 - NOSI to develop or adapt practical technologies for capturing the effects of climate change and extreme weather events on human health and to reduce the health threats posed by climate change across the lifespan.

2022-2023 NIH Climate and Health Scholars Program

- The program seeks to bring Climate and Health scientists from outside the U.S. federal government to work with NIH staff to share knowledge and help build our capacity in the scientific domains outlined in the NIH Climate Change and Health Initiative's [Strategic Framework](#).
- During their time at NIH, the scholars will be invited to collaborate with NIH staff on one or more of a diverse array of research, training, and policy activities that share their scientific knowledge with NIH laboratories, program offices, and the wider NIH community.
- 2022 applications closed, stay tuned!



Promoting Health Effects of Climate Change Research in the NIH Intramural Research Program



Supporting trans-
NIH research

Implement a new competitive funding program, the Intramural Targeted Climate Change & Health (ITCCH) program, that provides seed funding to stimulate research activities from NIH intramural investigators at multiple ICs.



Building
intellectual
capacity

Establish a new intramural Laboratory/Branch/Center at NIH that focuses on biological mechanisms of health impact of climate change. This branch will serve as a central hub to facilitate research in this area across the entire NIH Intramural Research Program.



Building
infrastructure

Build infrastructure within the NIH Intramural Research Program to begin to establish the tools necessary to conduct research into the health impact of climate change.

NIH Resources on Climate Change and Health

- **NIH Climate Change and Health Initiative**

- *Information on the Initiative and Framework*

www.nih.gov/climateandhealth

- **Funding Announcements**

- *Updated live as announcements are released*

www.nih.gov/climateandhealth

- **Public Seminar Series**

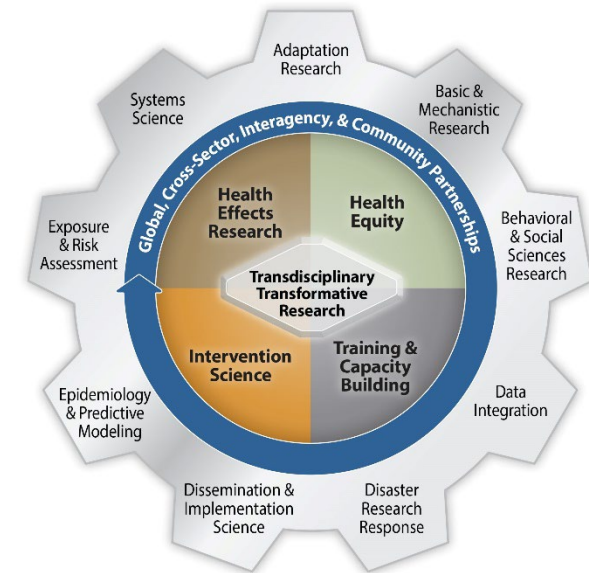
- *Promoting transdisciplinary discussion and collaboration against this threat to health.*

<https://www.nih.gov/climateandhealth#seminar-series>

- **Climate Change and Health Literature Portal**

- *Searchable database to provide access to the most relevant scientific literature*

<https://tools.niehs.nih.gov/cchhl/index.cfm>



Possibilities for Future Collaborations

- Bringing exposomics (HHEAR?) to bear on existing NICHD cohorts
- Existing tissue archives, bringing exposomic approaches to analyze these existing tissue samples.
- Utilizing samples to study epigenetic profiles.
 - Signatures that reflect exposures?
- Utilizing the NICHD's Data and Specimen Hub (DASH) repository



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Thank You!



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

