The NIEHS - Our Future, Our Health: Research Opportunities

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and National Toxicology Program

8 April 2015
University of Illinois at Urbana-Champaign

The National Institute of Environmental Health Sciences

- One of the 27 National Institutes of Health, but located in RTP, NC
- Wide variety of programs supporting our mission of environmental health:
  - Intramural laboratories
  - Extramural funding programs
  - Disease Prevention
  - Clinical research program
  - National Toxicology Program
  - Public Health Focus

NIEHS Strategic Plan

Mission

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

Strategic Themes for Environmental Health Sciences

Vision

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.

Strategic Goal #1:

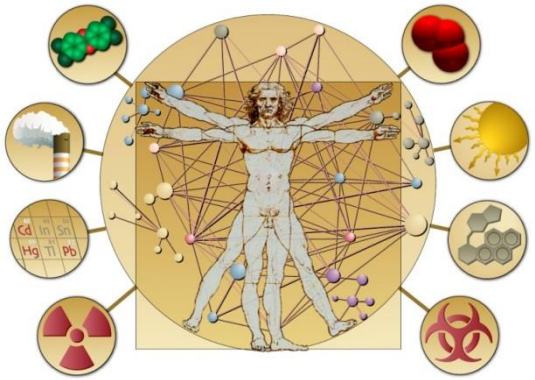
Identify and understand fundamental shared mechanisms or common biological pathways (e.g., inflammation, epigenetic changes, oxidative stress, mutagenesis) underlying a **broad range of complex diseases**, in order to enable the development of broadly applicable prevention and intervention strategies.

Strategic Goal #2:

Understand **individual susceptibility across the life span** to chronic, complex diseases resulting from environmental factors, in basic and population-based studies, to facilitate prevention and decrease public health burden.

Strategic Goal #3:

Transform exposure science by enabling consideration of the totality of human exposures and links to biological pathways and create a blueprint for incorporating exposure science into human health studies.



Strategic Goal #4:

Understand how **combined environmental exposures** affect disease pathogenesis.

Strategic Goal #5:

Identify and respond to **emerging environmental threats** to human health on both a local and global scale.

Strategic Goal #6:

Establish an **environmental health disparities** research agenda to understand the disproportionate risks of disease and to define and support public health and prevention solutions in affected populations.

Strategic Goal #7:

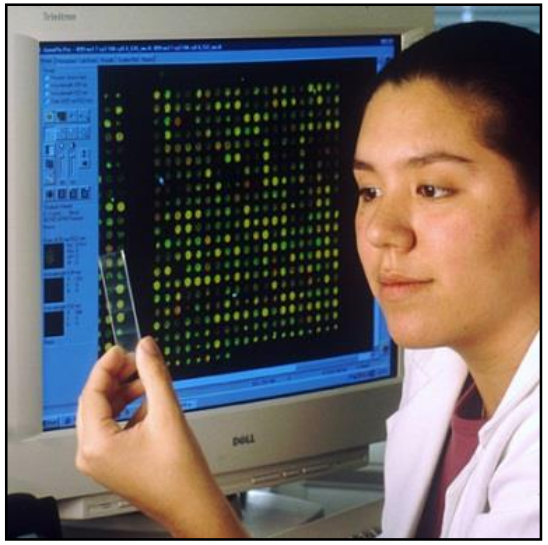
Use **knowledge management** techniques to create a **collaborative environment** for the EHS community to encourage an **interdisciplinary approach** to investigate, analyze, and disseminate findings.

Strategic Goal #8:

Enhance the teaching of EHS at all levels of education and training (K-professional) to **increase scientific literacy** and **generate awareness of the health consequences** of environmental exposures.

Strategic Goal #9:

Inspire a diverse and well-trained cadre of scientists to move our transformative environmental health science forward; **train the next generation of EHS leaders** from a wider range of scientific disciplines and diverse backgrounds.



Strategic Goal #10:

Evaluate the **economic impact of policies, practices, and behaviors** that reduce exposure to environmental toxicants through prevention of disease and disabilities; invest in **research programs to test how prevention improves public health and minimizes economic burden**.

Strategic Goal #11:

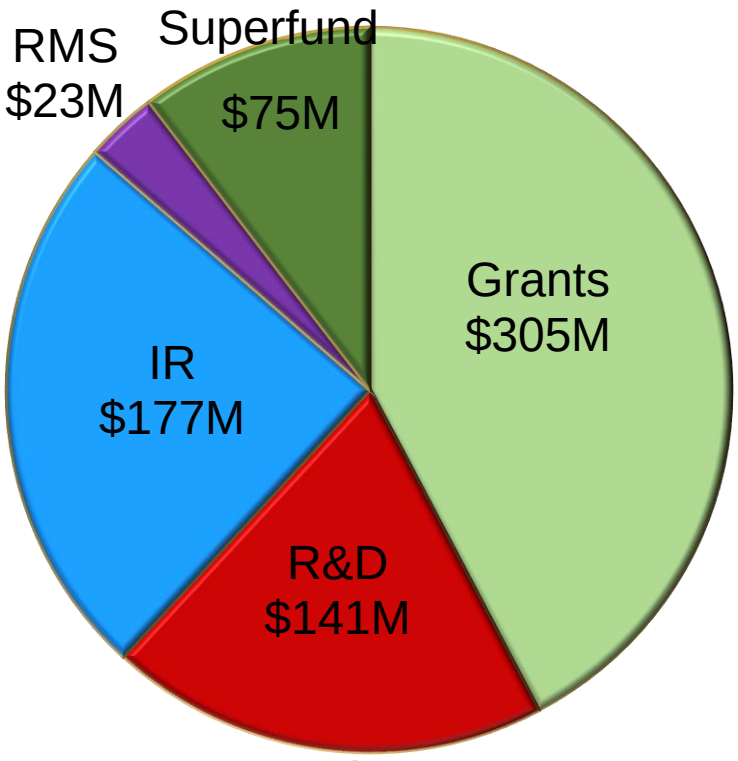
Promote bidirectional communication and collaboration between researchers and stakeholders (policy makers, clinicians, intervention/prevention practitioners, and the public) in order to advance research translation in the environmental health sciences.

ONE-NIEHS: Meeting Challenges with Big Ideas

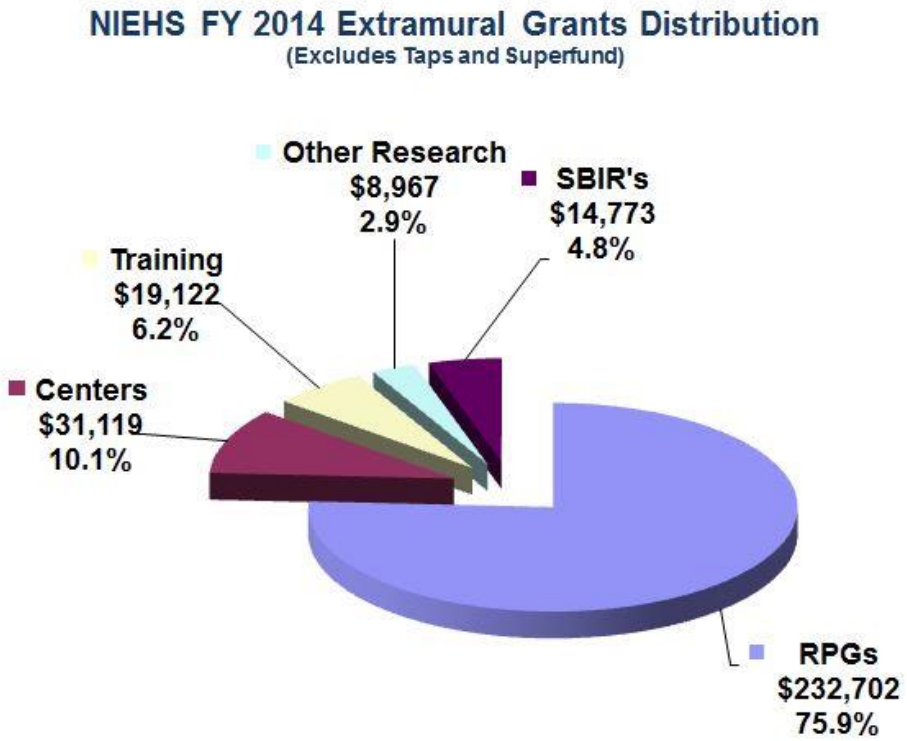
- Identified eight ***science focus areas*** within the new strategic plan, where we can work collectively to have a significant impact on public health
- *The **ONE-NIEHS*** process,
  - Cross-divisional teams formed
    - DIR, DERT, DNTP
  - Assessing long- and short term scientific impacts
  - Identifying activities, outputs, costs & benefits

Science Focus Areas
Epigenetics
Inflammation
Stem Cells
Exposome
Predictive Toxicology
Knowledge Management & E-Science
Website and social media
Global Environmental Health

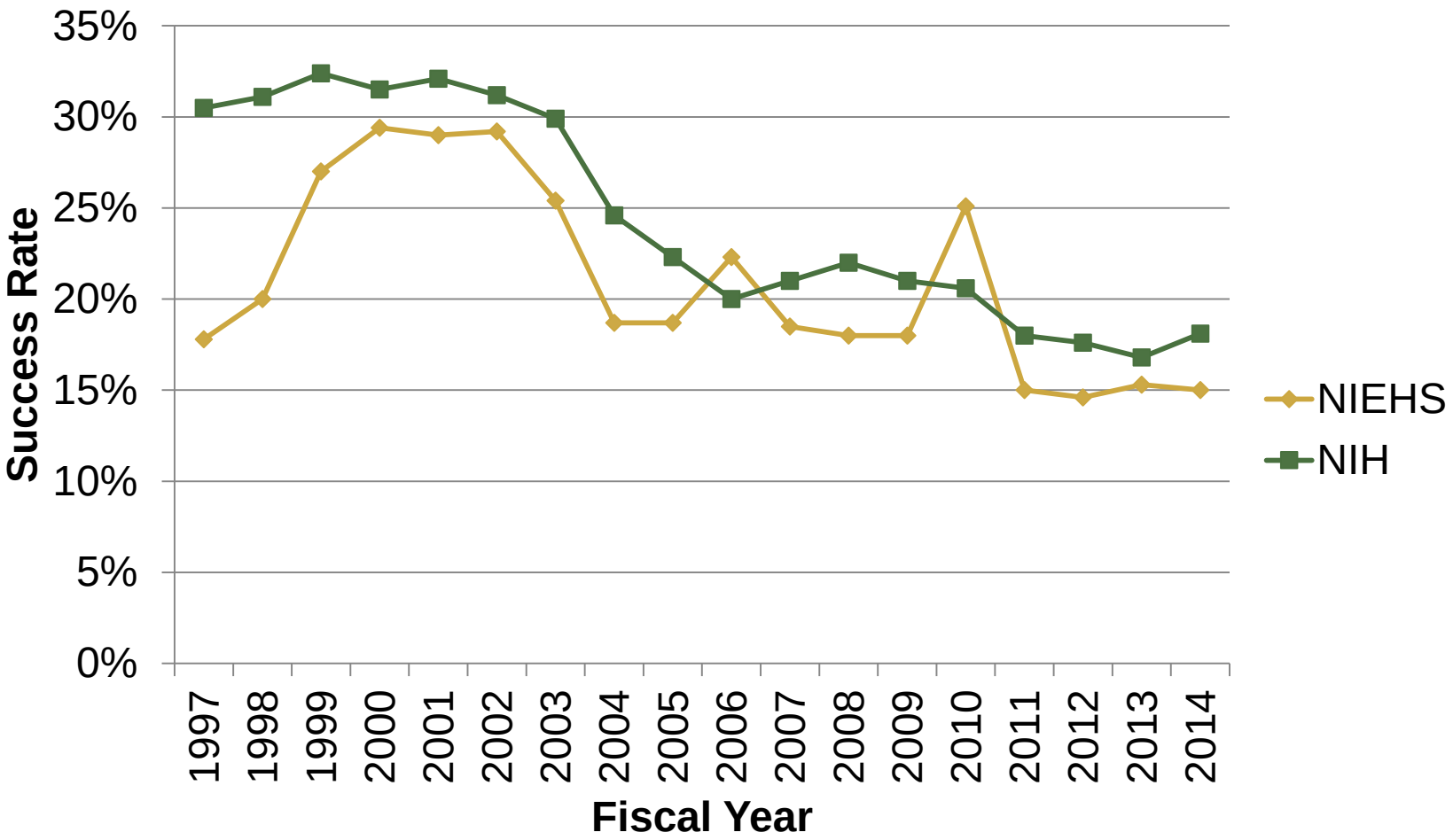
NIEHS FY2013 Budget (Dollars in Millions)



Type of Funds



FY 2014 Success Rates: Research Project Grants



The number of applications for competing RPG awards increased during the NIH budget "doubling period" (FY 1998 through FY 2002).

NIEHS Grant Type Success Rate Comparison (2014)

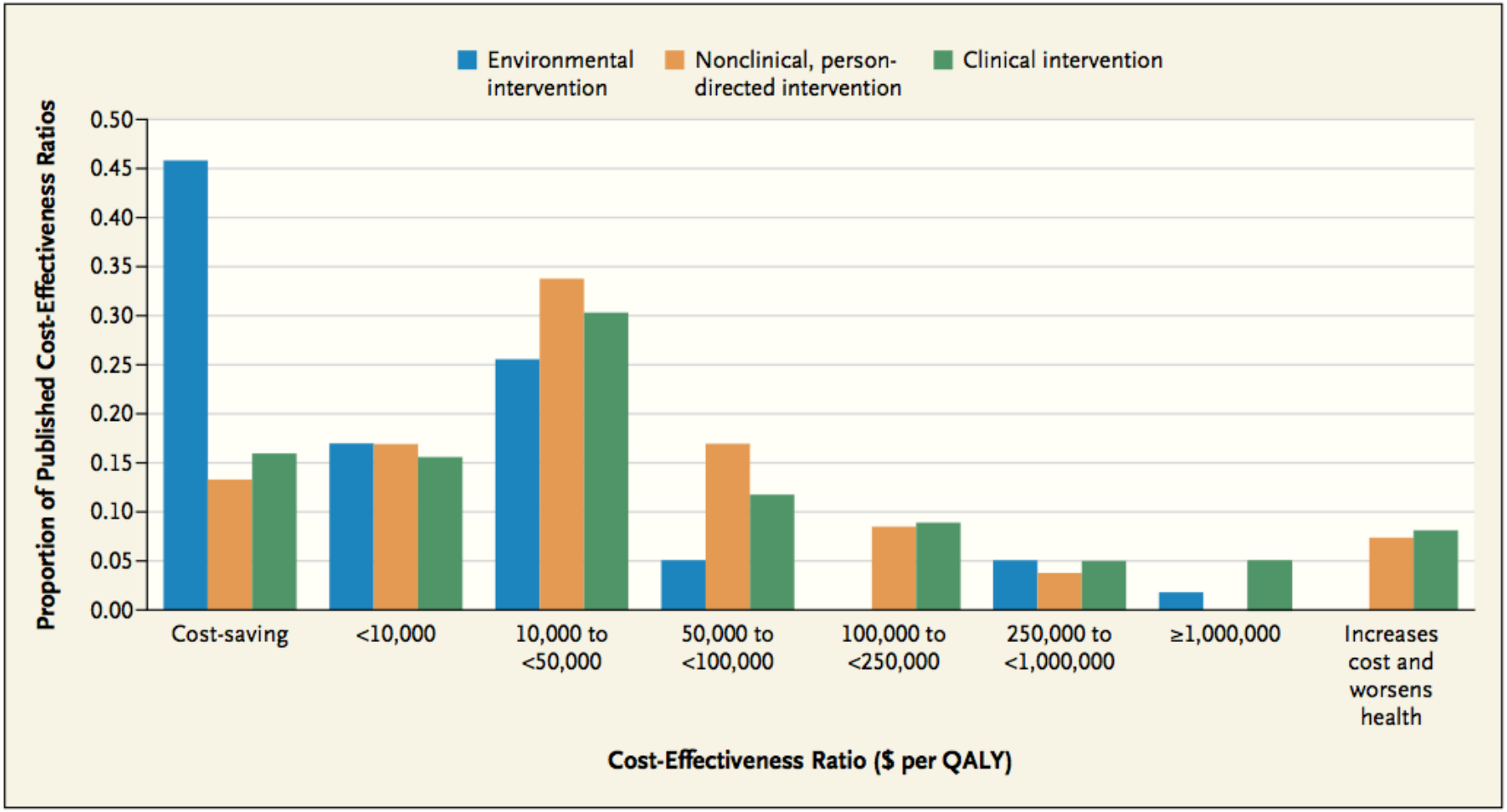
Activity Code	Success Rate Base	Number Awarded	Total Cost Awarded	Success Rate
DP2	0	0	$1,500.000	0%
R01	496	83	$37,383,378	16.7%
R03	63	7	$541,956	11.1%
R15	62	10	$3,822,192	16.1%
R21	515	66	$15,568,810	12.8%
R56	5	5	$1,085,614	100%
Total	**1141**	**171**	**$59,901,950**	**15%**

Why Environmental Health Matters

- 13 million deaths could be ***prevented*** per year by improving our environment
- Environmental factors influence 85 out of the 102 non-communicable diseases in WHO report
- Environmental factors account for at least 2/3 of cancer cases in the United States
- You can't change your genes, but you ***CAN*** change your environment

WHO Global Health Report (2010); Horton, R., Lancet (2013)

Public Health Implications of Environmental Effects

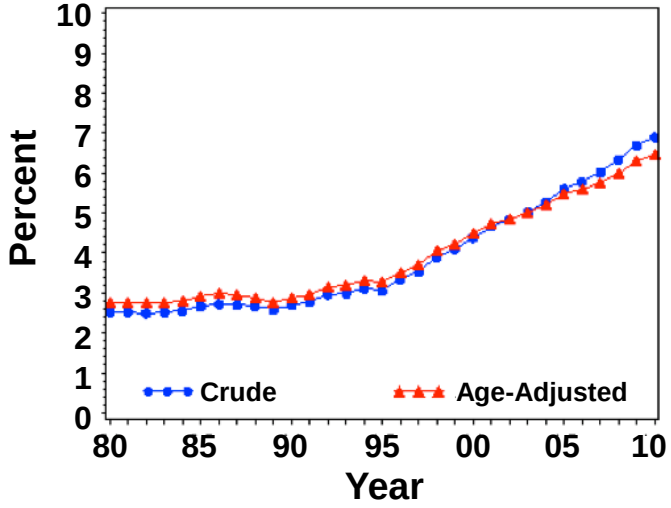


Cost-Effectiveness of Categories of Preventive Interventions.

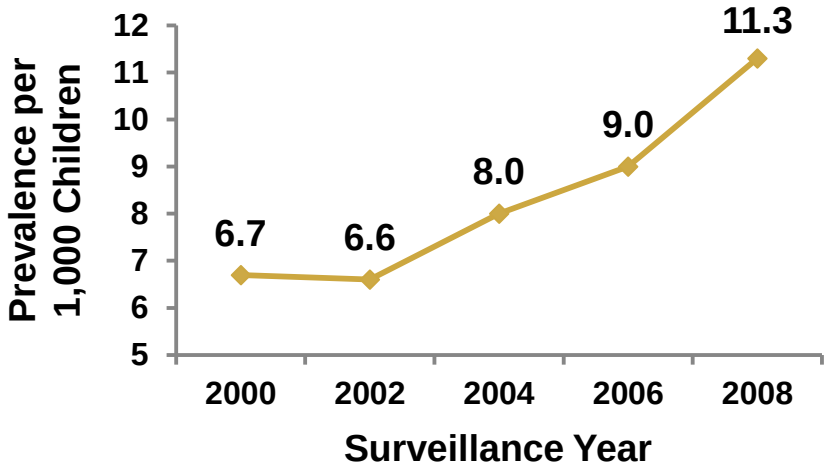
Chokshi and Farley, N Engl J Med 2012; 367:295-297.

Should We Be Concerned?

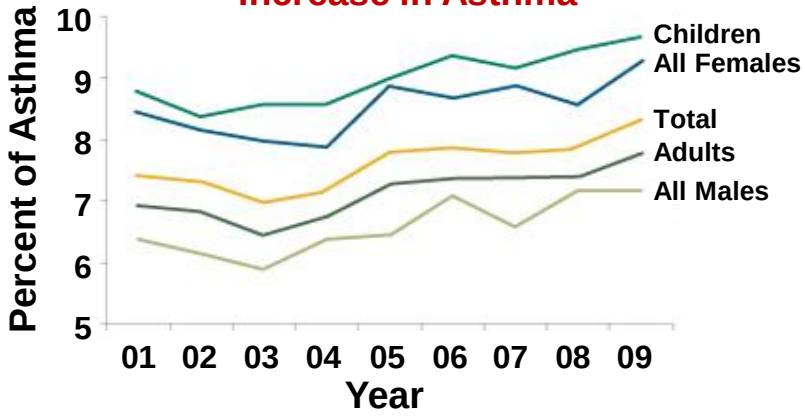
Increase in Diabetes (1980-2010)



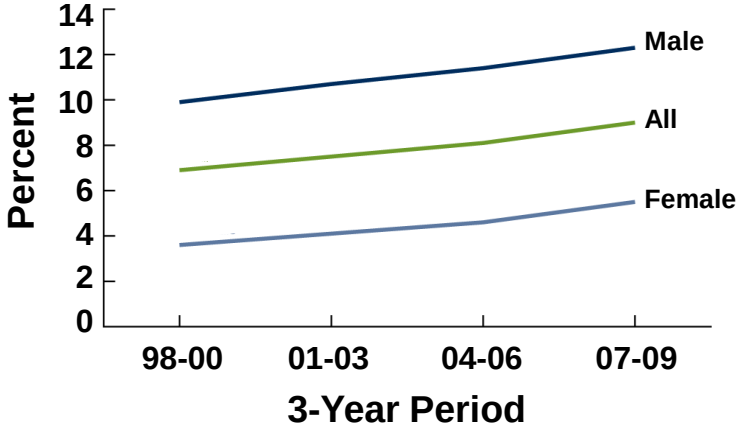
Increase in Autism Prevalence



Increase in Asthma



Increase in ADHD



Data from CDC / National Center for Health Statistics

"ENVIRONMENT" Includes:

- Industrial chemicals
- Agricultural chemicals
- Physical agents (heat, radiation)
- By-products of combustion and industrial processes (dioxin)
- Infectious agents
- Microbiome (gut flora)
- Foods and nutrients
- Prescription drugs
- Lifestyle choices and substance abuse
- Social and economic factors

Diseases with a Known or Suspected Environmental Component Include:

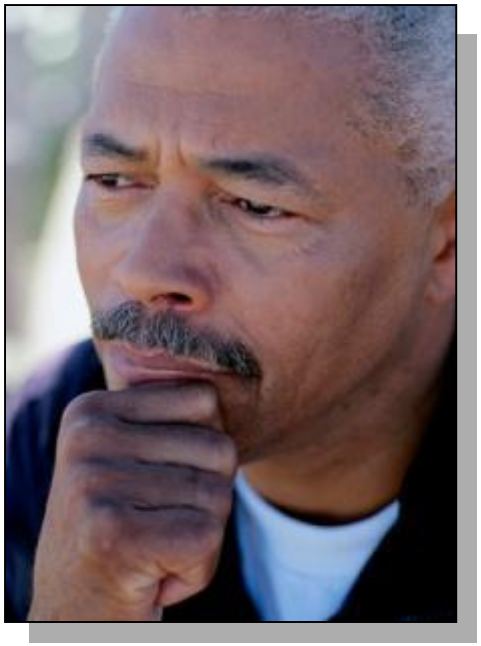
- Cancers
- Birth defects (cleft palate, cardiac malformations)
- Reproductive dysfunction (infertility)
- Lung dysfunction (asthma, asbestosis)
- Neurodegenerative diseases (Parkinson's)
- Neurodevelopmental disorders (autism)
- Cardiovascular disease (air pollution, dioxins)
- Endocrine disorders (diabetes)

New ways of thinking about environmental health sciences…

OLD… chemicals act by overwhelming the body's defenses by brute force at very high doses

NEW… chemicals can act like hormones and drugs to disrupt the control of development and function at very low doses to which the average person is exposed

NEW… susceptibility to disease persists long after exposure **(epigenetics)** and may lead to transgenerational effects



…and about disease causation

- Complex diseases have complex causes.
- Cancer and birth defects are not the only endpoints.
- The environment is a contributor to: obesity, diabetes, cardiopulmonary disease, autoimmune disease, reproductive dysfunction, neurodevelopmental disorders, schizophrenia, addiction, Alzheimer's Disease, and depression, and cancer and birth defects .

Science Advances

The concordance between RNA-seq and microarray data depends on chemical treatment and transcript abundance.

Wang C, B Gong, PR Bushel (DIR), J Thierry-Mieg, D Thierry-Mieg, J Xu, H Fang, H Hong, J Shen, Z Su, J Meehan, X Li, L Yang, H Li, PP Labaj, DP Kreil, D Megherbi, S Gaj, F Caiment, J van Delft, J Kleinjans, A Scherer, V Devanarayan, J Wang, Y Yang, HR Qian, LJ Lancashire, M Bessarabova, Y Nikolsky, C Furlanello, M Chierici, D Albanese, G Jurman, S Riccadonna, M Filosi, R Visintainer, KK Zhang, J Li (DIR), JH Hsieh (NTP), DL Svoboda, JC Fuscoe, Y Deng, L Shi, RS Paules (NTP), SSAuerbach (NTP) and W Tong. Nat. Biotechnol. (2014) [ePub] **SP Goal 1**

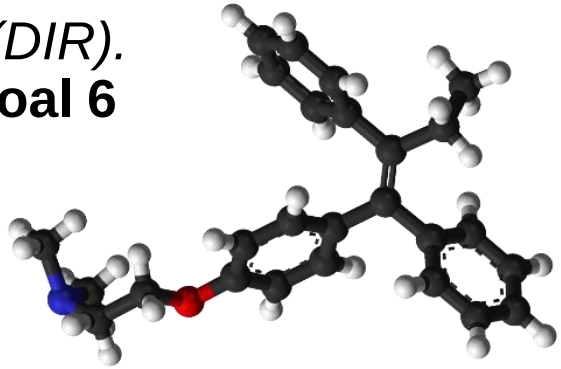
Diversity Outbred Mice Identify Population-Based Exposure Thresholds and Genetic Factors that Influence Benzene-Induced Genotoxicity.

French, JE (NTP), Gatti, DM, Morgan, DL (NTP), Kissling, GE (DIR), Shockley, KR (DIR), Knudsen, GA (OD), Shepard, KG, Price, HC, King, D (NTP), Witt, KL (NTP), Pedersen, LC (DIR), Munger, SC, Svenson, KL and Churchill, GA. Environ. Health Perspect. (2014)[ePub] **SP Goal 2**

Science Advances

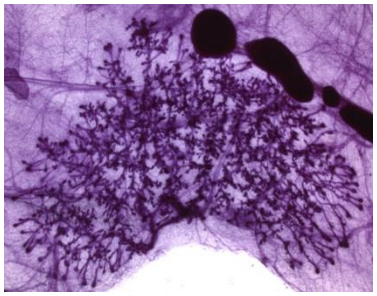
Ambient Air Pollution Exposure and Incident Adult Asthma in a Nationwide Cohort of U.S. Women.
Young, MT, Sandler, DP (DIR), DeRoo, LA (DIR), Vedal, S, Kaufman, JD and London, SJ (DIR). Am. J. Respir. Crit. Care Med. (2014) **SP Goal 2, 6**

Risk-benefit profiles of women using tamoxifen for chemoprevention.
Nichols HB, LA DeRoo, DR Scharf and DP Sandler (DIR). Journal of the National Cancer Institute (2015) **SP Goal 6**



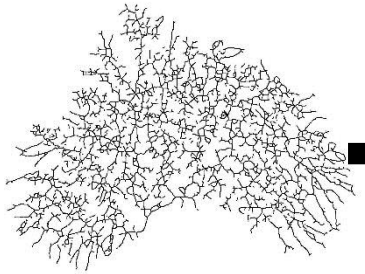
Science Advances

Application of Sholl analysis to quantify changes in growth and development in rat mammary gland whole mounts.
Stanko JP, Easterling MR, Fenton SE. Reproductive toxicology. 2014. Epub 2014/11/15 **SP Goal 1**

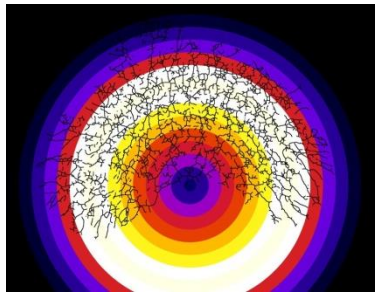


Prepare mammary whole mount and capture image

Threshold image, remove noise



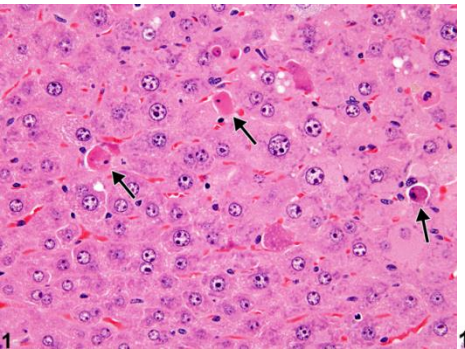
Skeletonize image, set parameters

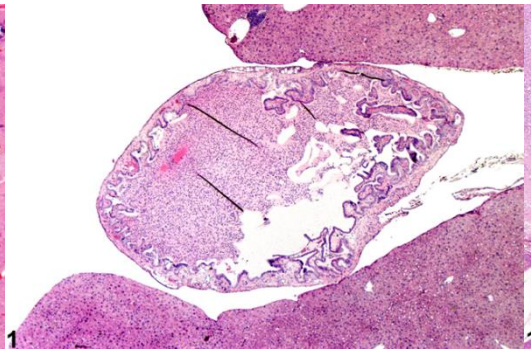


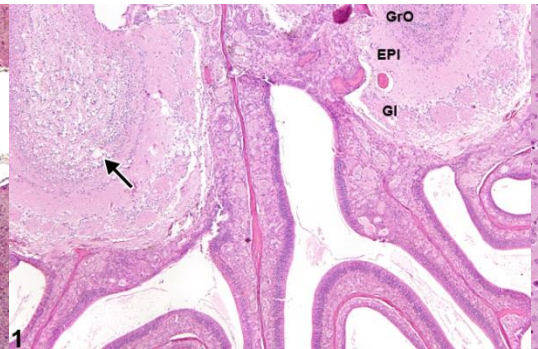
Heat map of ring/branch intersections

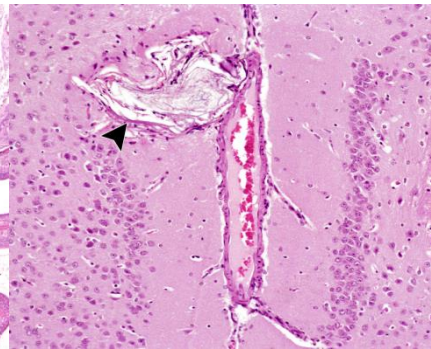
NTP: Nonneoplastic Lesion ATLAS

- Guide to allow identification of human carcinogens in rodent bioassays
- Captures large amount of data on tissue changes & presents in user - friendly platform
- Dynamic Document; regular updating
- http://ntp.niehs.nih.gov/nnl/index.htm









Science Advances

The commonly used antimicrobial additive triclosan is a liver tumor promoter. *Yueh M-F, Taniguchi K, Chen S, Evans RM, Hammock BD, Karin M, and Tukey RH.* 2014. *Proc Natl Acad Sci U S A 111(48): 17200-17205.* **SP Goal 5**

Dissecting neural differentiation regulatory networks through epigenetic footprinting. *Ziller MJ, Edri R, Yaffe Y, Donaghey J, Pop R, Mallard W, Issner R, Gifford CA, Goren A, Xing J, Gu H, Cacchiarelli D, Tsankov AM, Epstein C, Rinn JL, Mikkelsen TS, Kohlbacher O, Gnirke A, Bernstein BE, Elkabetz Y, Meissner A. Nature. 2014 Dec 24.* **SP Goal 1**

Prenatal Arsenic Exposure and the Epigenome: Identifying Sites of 5-methylcytosine Alterations that Predict Functional Changes in Gene Expression in Newborn Cord Blood and Subsequent Birth Outcomes. *Rojas D, Rager JE, Smeester L, Bailey KA, Drobná Z, Rubio-Andrade M, Stýblo M, García-Vargas G, Fry RC. Toxicol Sci. 2015 Jan;143(1):97-106.* **SP Goal 1**

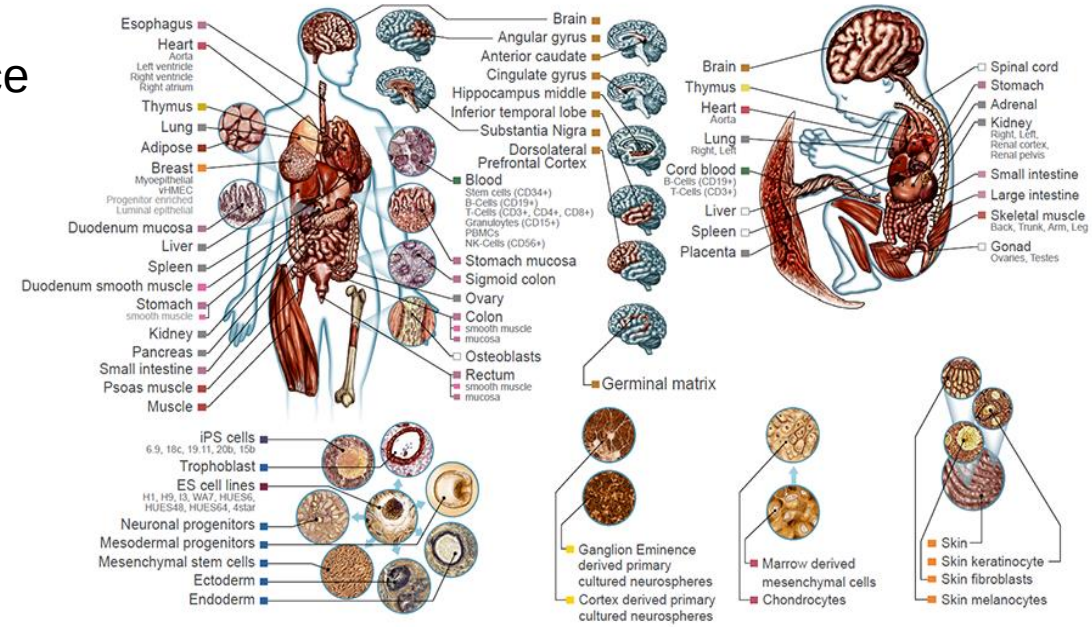
The Resilience Activation Framework: a Conceptual Model of How Access to Social Resources Promotes Adaptation and Rapid Recovery in Post-disaster Settings. *Abramson DM, Grattan LM, Mayer B, Colten CE, Arosemena FA, Bedimo-Rung A, Lichtveld M. J Behav Health Serv Res. 2015 Jan;42(1):42-57. doi: 10.1007/s11414-014-9410-2* **SP Goal 5**

Science Advances

NIH Roadmap Epigenomics Program

Integrative analysis of 111 reference human epigenomes.
Roadmap Epigenomics Consortium. 2015. Nature; doi: 10.1038/nature14248

- First of 20+ papers, < 200 authors
- NIH Roadmap Epigenomics Program (Common Fund) is co-led by NIEHS and NIDA
- Major goal of program: generate a public resource of reference epigenomic maps from normal human cells and tissues
- This is the most comprehensive catalog of epigenomic data from primary human cells and tissues to date
- Data available at NCBI



Data Management and Technology

- Comparative Toxicogenomics Database Enhancements

The Comparative Toxicogenomics Database

- New Tox21 Chemical Screening Data Released

Tox21

- DREAM Toxicogenetics Winners

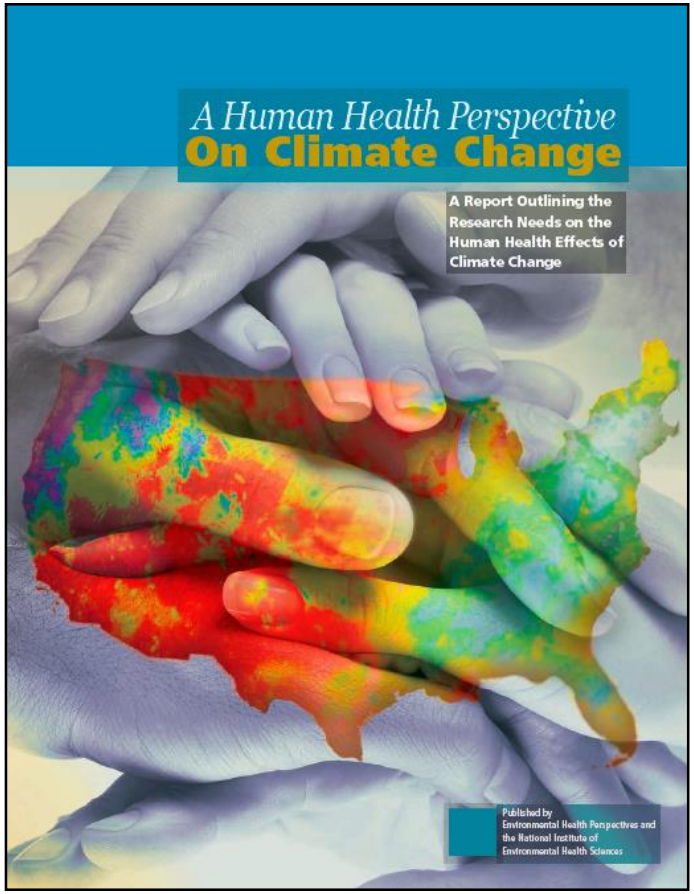
DREAM

- IOM Roundtable Workshop on Data Sharing for Environmental Health

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Climate Change: Research Needs

- Asthma, respiratory allergies and airway diseases
- Cancer
- Cardiovascular disease and stroke
- Foodborne diseases and nutrition
- Heat-related morbidity and mortality
- Human development effects
- Mental health and stress-related disorders
- Neurological diseases and disorders
- Vectorborne and zoonotic diseases
- Weather related morbidity and mortality



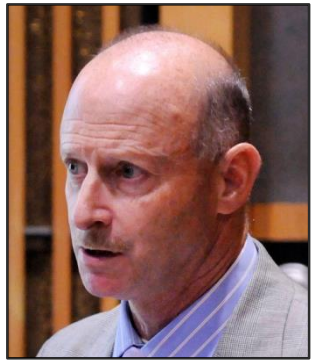
NIH Disaster Research Response (DR2) Initiative

- Pilot project
  - NIEHS leading and administering — research networks, field experience
  - NLM supporting — organization, public interface, communication
- Ready-to-go research data collection tools
- Network of trained research responders

Aubrey Miller, ODB

Chip Hughes, WETP

Stavros Garantziotis, CRU



Les Reinlib, DERT

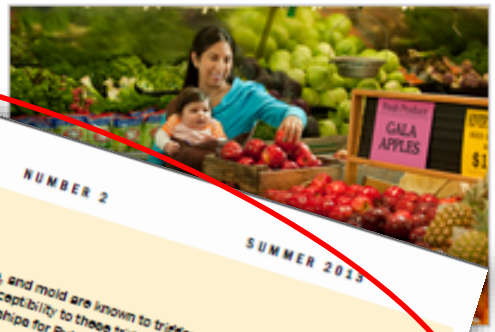
National Institute of Environmental Health Sc
Your Environment. Your Health.

Environmental Health

- Episodes highlight way
  work in partnership with
  to understand and addr
  health issues.
- Podcasts feature the w
  within the PEPH netwo
- Available on iTunes as
- Topics include: Frack
  Radon, Native Amer
  Cancer, Epigenomi
  and most recently, Citiz

Fighting Asthma with ... a Healthy Diet?
Partnerships for Environmental Public Health (PEPH)

May 17, 2013



VOLUME 11 NUMBER 2 SUMMER 2013

PODCAST:
Fighting Asthma with... a Healthy Diet?

Environmental factors like air pollution, cigarette smoke, and mold are known to trigger asthma attacks, but new research suggests that the quality of your diet can affect your susceptibility to these triggers. We learn why a healthier diet might help reduce asthma attacks in this podcast from Partnerships for Public Environmental Health, part of the National Institute for Environmental Health Sciences.

http://www.niehs.nih.gov/research/supported/dert/ephb/programs/peph/podcasts/asthma/index.cfm

RESEARCH ARTICLES

New Study Finds Pediatricians Will Integrate Environmental Management into Asthma Care

Following a brief, targeted educational intervention, pediatricians reported a significant increase in knowledge about environmental triggers of asthma and a willingness to incorporate exposure history questions and remediation recommendations in their routine practice. These improvements persisted at a 3-6 month follow-up interval compared to baseline levels. The findings were published in Clinical Pediatrics http://cpj.sagepub.com/content/early/2013/03/27/0009922813484752.abstract. The study was conducted by NEEP's Pediatric Asthma Faculty Champions using a standardized PowerPoint presentation based on NEEP's Environmental Management of Pediatric Asthma: Guidelines for Health Care Providers

http://www.neehsus.org/health/asthma/

Climate Change Linked to More Pollen, Allergies, Asthma

Carbon dioxide, a heat-trapping greenhouse gas emitted by burning coal, gasoline, oil, and other fossil fuel products, is seen in increasing levels in the atmosphere. More carbon dioxide means more plant growth and thus more pollen production. If carbon dioxide emissions continue to increase, allergic conditions will most likely worsen. "There's clear evidence that pollen season is lengthening and total pollen is increasing," says George Luber, associate director for climate change at the CDC. "It's one of the ways climate change is already affecting your community."

http://www.usatoday.com/story/news/nation/2013/05/30/climate-change-allergies-asthma/2183693/

Study Finds Pain Relievers Do Not Cause Asthma

Some parents have been worried about giving their children pain relievers like ibuprofen and acetaminophen, based on reports that children who take the drugs are more likely to develop asthma. But a new study suggests that the relationship may be little more than a statistical oversight, finding that children suffering from respiratory infections — which often lead to asthma — are simply more likely to be given over-the-counter pain relievers.

http://well.blogs.nytimes.com/2013/05/21/pain-relievers-do-not-cause-asthma-study-finds/?hpw

PAGE 7

continued from page 1

Asthma Medication Posters

Parents/students who have asthma experience difficulty talking their asthma inhalers at home and school health staff must assist those students in managing their asthma by having them take medications in the school health office. Identifying which asthma inhalers a student is taking can be a challenge—especially if they're taking more than one. The names of prescription drugs are often difficult for children to remember and pronounce. These full-color posters will help students in identifying which inhaler(s) they use.

The posters display a photo of each inhaler; the generic and brand name of the medication; the delivery dose; and manufacturers' name for all currently available inhaled asthma medications commonly prescribed in the US.

The posters are available in two sizes: a double sided 8.5 x 11 for hands-on use, and an 11 x 17 poster size to place on the wall in an exam room or school health office.

Both posters are available for download and printing from the MDH Asthma website at http://www.health.state.mn.us/asthma/asthmaMedsPosters.html

of racial and

and NIEHS-supported

Research Program

focused on yielding insights

about asthma and many other

NIEHS Kids Page: Asthma & Allergies

Find kid-friendly stories and games exploring the role indoor po play in asthma and allergies.

Scientific Focus Areas in Global Health

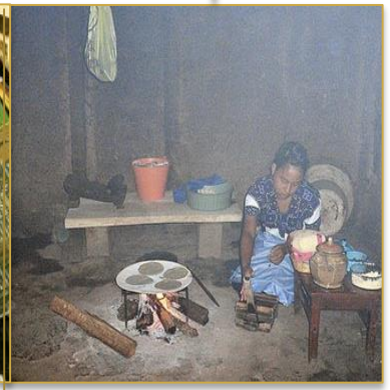
Training and Capacity Building

Children's Environmental Health

Climate Change

Developmental Origins of Health and Disease

Electronic Waste

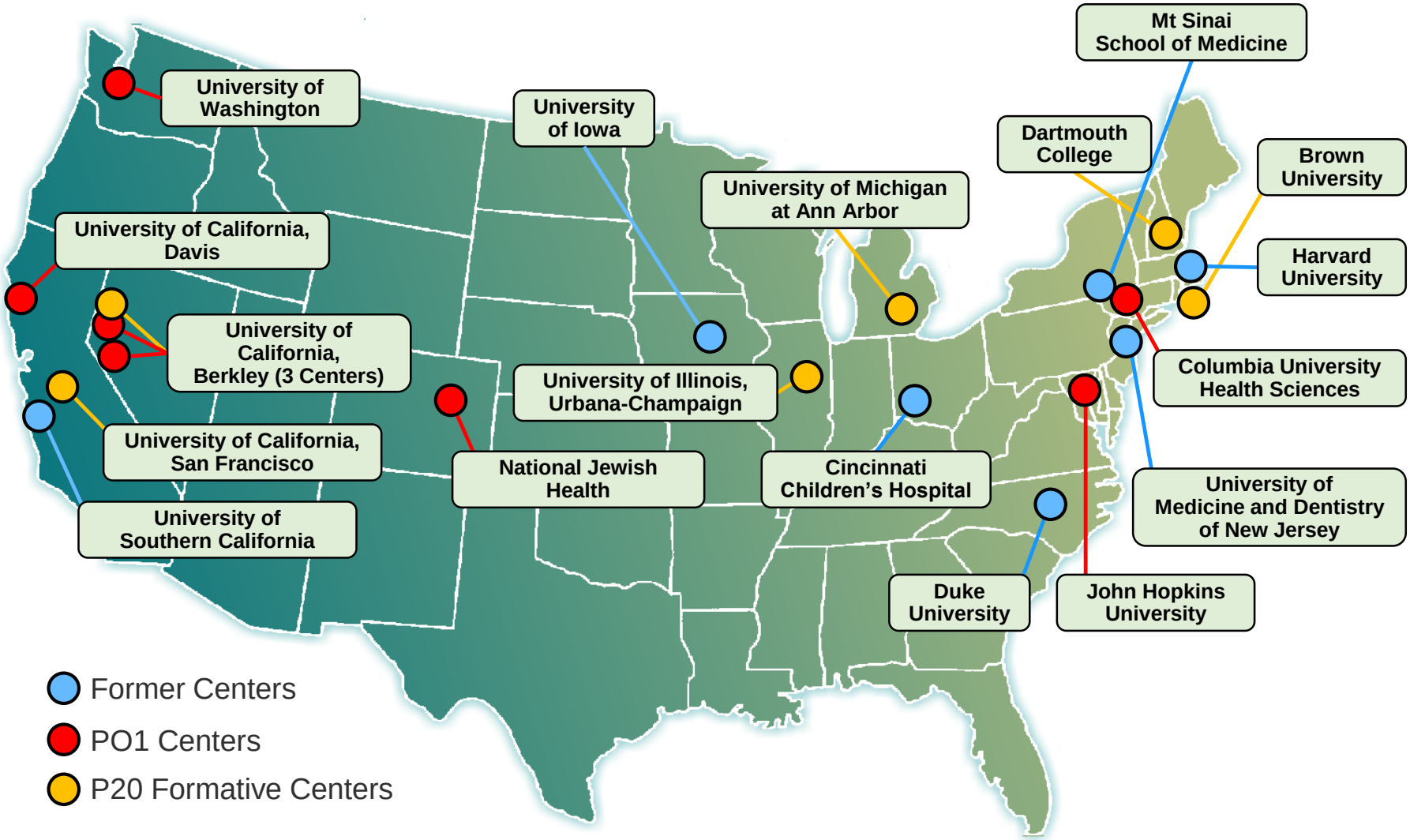


Indoor Air Pollution and Cookstoves

Early Life Exposures Can Have Lasting Effects: Developmental Basis of Adult Disease

- Early life is a sensitive time for exposure:
  - Organs are forming
  - Gene expression programs are being established
  - Epigenetic reprogramming is occurring
  - Changes occurring during development permanently alter the potential of an organ

NIEHS and EPA Children's Centers



Children's Environmental Health

- Roadway Air Pollution – asthma, IQ, autism
- Prenatal polycyclic aromatic hydrocarbons (PAHs) - lower IQ
- Phthalates – asthma, ADHD, male reproductive tract
- Pesticides – lower IQ, behavior, autism
- Flame retardants – lower IQ, behavior, reproductive
- And Many others…

Air pollution contributes to:

Autoimmunity

OBESITY

Behavioral Effects

Asthma

Autism

Diabetes

COPD

Stroke

Developmental Disabilities

Pneumonia

Lower Respiratory Infections

Cancer

DECREASED IQ

Pulmonary Disease

Cardiovascular Disease




Research on Air Pollution and Child Health

- Living within 75m of a major roadway associated with increased risk of asthma. This is particularly the case for children without a family history of asthma.
- Genetic variations in immune response to air pollutants may offer protection or make a child more susceptible to asthma. Some genetic differences vary between ethnic groups, could contribute to health disparities.
- Mothers exposed to urban air pollutants, known as polycyclic aromatic hydrocarbons (PAHs), had children with lower IQ's

Improving Indoor Air

- 4 Million deaths per year (Lancet 2013)
- NIEHS is largest funder of cookstove research at NIH
  - NIEHS provided ~$3.66M in cookstove research in FY2013
- Part of the Global Cookstove Alliance
- **Guatemala**: Using ventilated wood stoves significantly reduced rates of severe childhood pneumonia (Smith, *The Lancet*, 2011)

Health Disparities and Vulnerable Populations

We need to protect the most vulnerable, not just the average!

- **Children** – size, respiration rate, and development stage all create vulnerabilities
- **Elderly** – compromised immune systems, less able to compensate
- **Race** – genetics, behaviors, and medicine can all influence individual susceptibility
- **Socio-Economics** – may dictate where you live, what you eat, and thus your exposure
- **Occupation** – influences not only your exposure but also your family's

Funding Opportunities

- Understanding and Promoting Health Literacy R03, R21
  - Program Announcement PAR-13-132
  - Open until May 8, 2016
- ViCTER: Virtual Consortium for Translational / Transdisciplinary Environmental Research R01
  - Program Announcement PAR-14-050
  - Open until March 5, 2016
- ONES: Outstanding New Environmental Health Science Investigator R01
- DIR, DERT, DNTP Transdisciplinary Environmental Health Fellowships (RTP, NC)

NIEHS Core Centers (P30): Building Collaborations

- **Purpose to provide infrastructure and core facilities to EHS research** - *annual RFA; new sliding scale funding*
- **Working Group on Emerging Environmental Health Issues** - *Provides guidance, gauges interest*
- **COEC Webinars** - *Topics of Community Concern*
- **NIEHS Core Center Meetings** - *Facilitates Collaboration, NIH Updates, Working Group Activities*

Redistribution of the Funding for the National Children's Study

- Tools to measure environmental exposures in children's health research
  - **CHEAR** – Building a resource for exposure assessment for studies of children's health for studies supported across NIH; NIEHS ($48M)
  - **PRISMS** – Development and deployment of personal sensors in studies of children's health; NIBIB and other ICs ($28M)
  - **PROMIS** – Validation of Pediatric Patient Reported Outcomes in Chronic Diseases Consortium (U19); NIAMS ($12M)
- Enhance understanding of in-utero and post natal development
  - **Tox21** – Development and deployment of development biology assays in the Tox21 program; NCATS and NTP ($8M)
  - **Human Placenta Project** - Developing Paradigm Shifting Innovations in Human in-vivo Placental Assessments in Response to Environmental Influences; NICHD and NIBIB ($39M)
- Leverage existing programs
  - Expansion of Extant Children's Health Research – NIEHS ($5M)

Children's Health Exposure Analysis Resource (CHEAR) Purpose

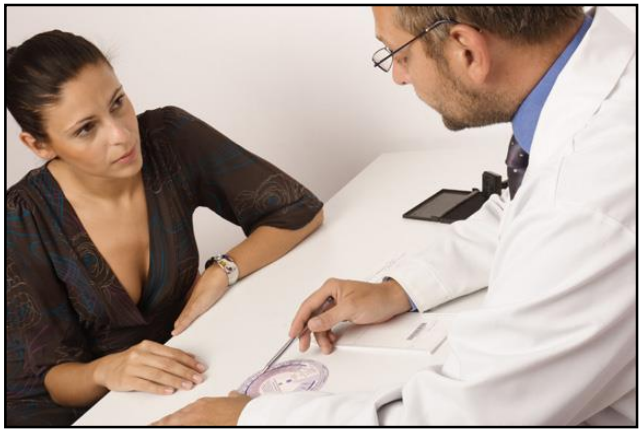
- Advance our understanding of the impact of environmental exposures on children's health and development.
- Provide infrastructure for adding or expanding exposure analysis to studies involving research in children's health.
- Exposures measured encompass the breadth of the exposome, the totality of biological, psycho-social, chemical, and physical exposures.

Funding Opportunity Announcements for CHEAR

- **National Exposure Assessment Laboratory Network (U2C)**
  - **ES 15-009 Applications due: April 30, 2015**
- **Exposure Data Repository and Resource for Statistical Analysis and Methods Development (U2C)**
  - **ES 15-010 Applications due: April 30, 2015**
- **Coordinating Center (U24)**
  - **ES 15-011 Applications due: April 30, 2015**
- **$48M to be spent in FY15 to run the CHEAR program for 4 years**

Prevention is the Key

- Genetic and environmental factors individually contribute and interact with each other to increase risk
- The impact of exposures can vary based on timing of the exposure within critical windows
- Identifying the hazards associated with chemicals to which humans are exposed is critical
- *Environmental factors are more readily identified and modified than genetic factors and therefore present a tremendous opportunity to prevent non-communicable disease*



Thank you!

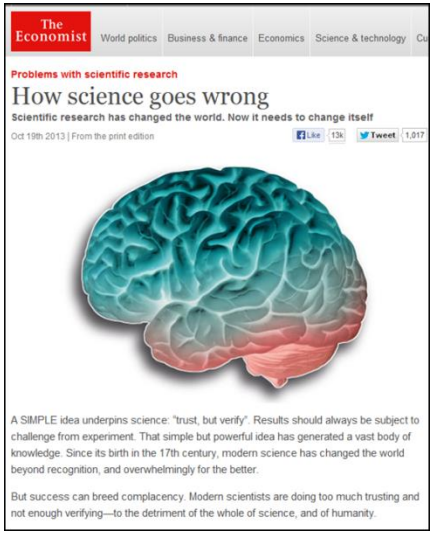
National Institute of Environmental Health Sciences

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

NIEHS Strategic Plan Website
http://www.niehs.nih.gov/strategicplan

Focused Efforts at the NIH

- Reproducibility
- Big Data and Scientific Computing
- Increased Diversity
- Training
- New Resubmission Policy



The Economist — World politics | Business & finance | Economics | Science & technology

Problems with scientific research

How science goes wrong

Scientific research has changed the world. Now it needs to change itself

Oct 19th 2013 | From the print edition

A SIMPLE idea underpins science: "trust, but verify". Results should always be subject to challenge from experiment. That simple but powerful idea has generated a vast body of knowledge. Since its birth in the 17th century, modern science has changed the world beyond recognition, and overwhelmingly for the better.

But success can breed complacency. Modern scientists are doing too much trusting and not enough verifying—to the detriment of the whole of science, and of humanity.

The Economist — World politics | Business & finance | Economics | Science & technology

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not

Oct 19th 2013 | From the print edition

"I SEE a train wreck looming," warned Daniel Kahneman, an eminent psychologist, in an open letter last year. The premonition concerned research on a phenomenon known as "priming". Priming studies suggest that decisions can be influenced by apparently irrelevant actions or events that took place just before the cusp of choice. They have been a boom area in psychology over the past decade, and some of their insights have already made it out of the lab and into the toolkits of policy wonks keen on "nudging" the populace.

Dr Kahneman and a growing number of his colleagues fear that a lot of this priming

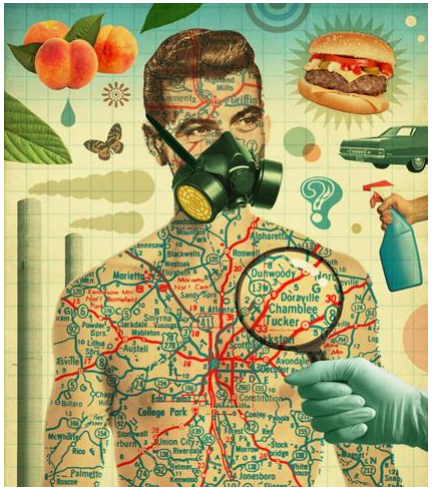
NIEHS Strategic Plan Cross-Divisional Implementation: Priority Activities

- Scientific Data and Knowledge Management: IT governance, establish SIO, data science needs workshop
- Epigenetics: Core facility, systematic review by OHAT, training opportunities
- Stem Cells: Training opportunities
- Exposome: Internal faculty meetings, workshop
- Predictive Toxicology and Disease: Workshop held, organize internal faculty, catalog biobanked human samples
- Inflammation: Workshop planning
- Global Environmental Health: WHO Coordinating Centre and other activities
- Website and Social Media: Web content for mobile users; initial efforts towards search engine optimization

One NIEHS Initiatives

Disaster Response Research (DR2)

PEPH



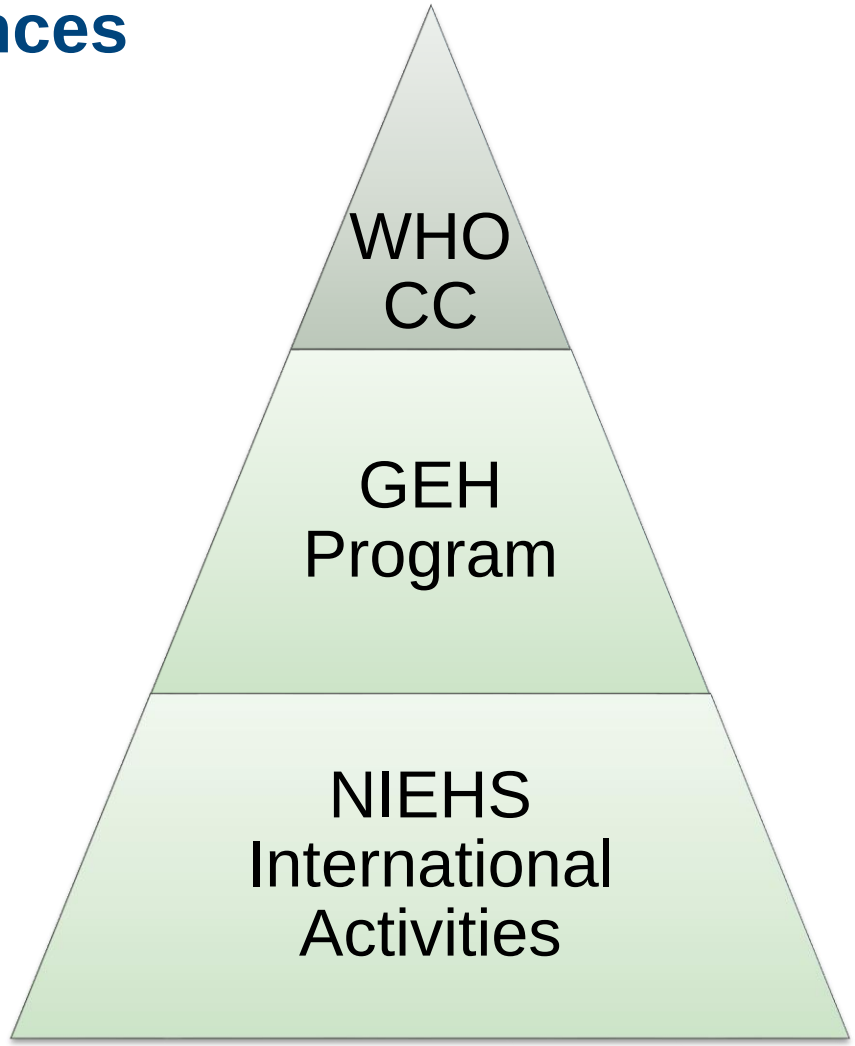
Exploring the Exposome

NTP Nonneoplastic Lesion Atlas

WHO Collaborating Center

The NIEHS WHO Collaborating Centre for Environmental Health Sciences

- Designated September 2013
- Emphasis on research translation and capacity building activities
- Activities organized by "focus areas"
  - NIEHS staff designated as focus area leads and co-leads



A New Vision for NIEHS and NTP

- Our ***vision*** is to provide global leadership for innovative research the improves public health by preventing disease and disability
- Our ***mission*** is to discover how the environment affects people in order to promote healthier lives.

Strategic Themes

- Studying ***basic mechanisms*** and ***windows of susceptibility***
- Linking ***individual and population exposure*** to risk
- Creating better ***predictive models*** and 21st Century tools
- Enhancing ***communication*** and ***diversity*** in all aspects of research

- ***Training*** a multidisciplinary group of scientists
- Improving ***coordination*** between gov't agencies and other groups

Science Advances

Mimicking of estradiol binding by flame retardants and their metabolites: a crystallographic analysis

Gosavi RA (DIR), Knudsen GA, Birnbaum LS (OD), Pedersen LC (DIR). *Environ Health Perspect.* 2013 Oct;121(10):1194-9. doi: 10.1289/ehp.1306902. Epub 2013 Aug 13.

Science Advances

Temporal comparison of PBDEs, OH-PBDEs, PCBs, and OH-PCBs in the serum of second trimester pregnant women recruited from San Francisco General Hospital, California
Zota AR, Linderholm L, Park JS, Petreas M, Guo T, Privalsky ML, Zoeller RT, Woodruff TJ. 2013. *Environ Sci Technol.* 47(20):11776-11784.

Interplay between polymorphisms and methylation in the H19/IGF2 gene region may contribute to obesity in Mexican-American children M. A. Hernández-Valero, J. Rother, I. Gorlov, M. Frazier and O. Gorlova. 2013. *Journal of Developmental Origins of Health and Disease* v. 4 (6): pp. 499-506

Science Advances

Ancestral dichlorodiphenyltrichloroethane (DDT) exposure promotes epigenetic transgenerational inheritance of obesity.
Skinner MK, Manikkam M, Tracey R, Guerrero-Bosagna C, Haque M, Nilsson EE. *BMC Med.* 2013 Oct 23;11:228.

Maternal engineered nanomaterial exposure and fetal microvascular function: does the Barker hypothesis apply?
Stapleton PA, Minarchick VC, Yi J, Engels K, McBride CR, Nurkiewicz TR. *Am J Obstet Gynecol.* 2013 Sep;209(3):227.e1-11.

Science Advances

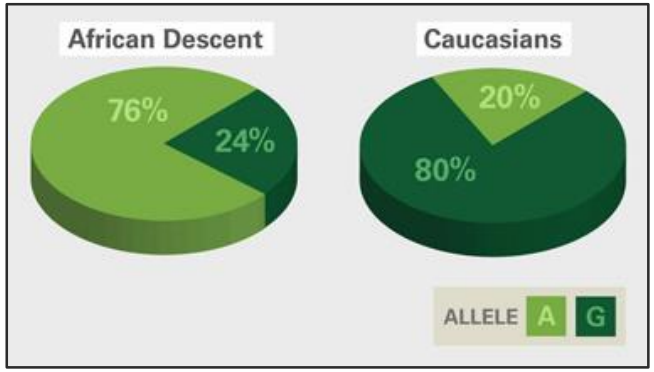
Report on the international workshop on alternatives to the murine histamine sensitization test (HIST) for acellular pertussis vaccines: State of the science and the path forward
Isbrucker R, Arciniega J, McFarland R, Chapsal JM, Xing D, Bache C, Nelson S, Costanzo A, Hoonakker M, Castiaux A, Halder M, Casey W (NTP), Johnson N, Jones B, Doelling V, Sprankle C, Rinckel L, Stokes W (NTP). *Biologicals (2014)*

Methylarsonous acid causes oxidative DNA damage in cells independent of the ability to biomethylate inorganic arsenic
Tokar EJ, C Kojima and MP Waalkes
Arch. Toxicol. (2013 Oct 5)

Science Advances

Global DNA methylation and one-carbon metabolism gene polymorphisms and the risk of breast cancer in the Sister Study

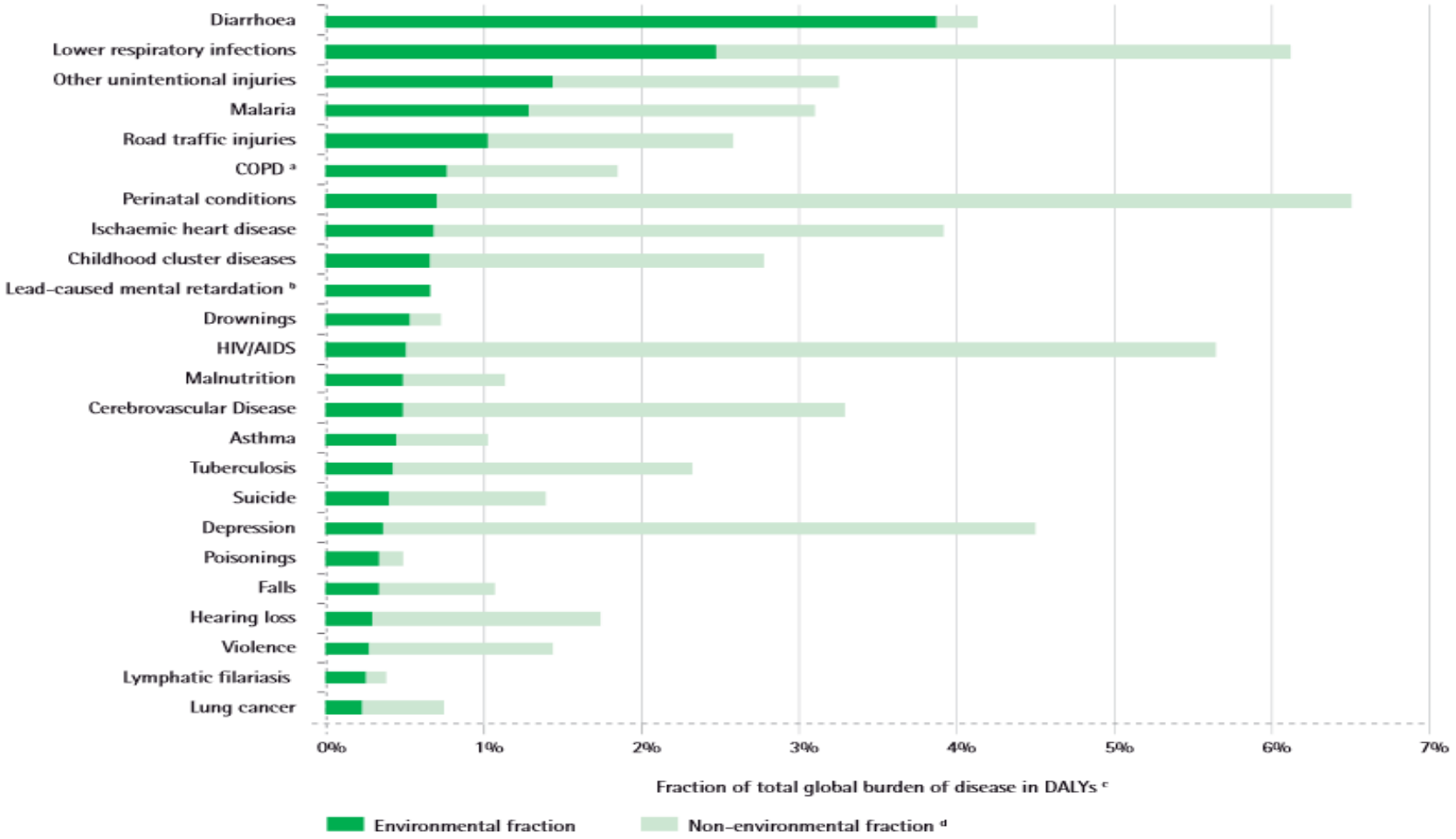
Deroo LA, SC Bolick, Z Xu, DM Umbach, D Shore, CR Weinberg, DP Sandler and JA Taylor *Carcinogenesis (2013 Nov 23)*



A polymorphic p53 response element in KIT ligand influences cancer risk and has undergone natural selection

Zeron-Medina, J, Wang, X, Repapi, E, Campbell, MR, Su, D, Castro-Giner, F, Davies, B, Peterse, EFP, Sacilotto, N, Walker, GJ, Terzian, T, Tomlinson, IP, Box, NF, Meinshausen, N, De Val, S, Bell, DA and Bond, GL *Cell (2013) v. 155 (2): pp. 410-422*

Diseases with the largest environmental burden



WHO Preventing Disease Through Healthy Environments 2006
http://www.who.int/quantifying_ehimpacts/publications/preventingdiseasebegin.pdf

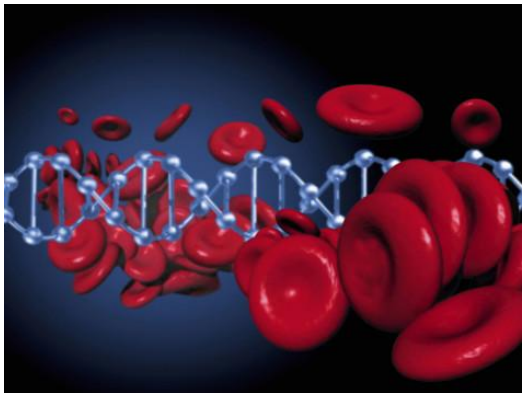
One NIEHS: Exposome Faculty

- Purpose: develop the concept and study of exposome science at NIEHS.
- Goal 3 of the NIEHS Strategic Plan
- The faculty is comprised of NIEHS staff across the institute.
- Provides a forum to discuss and define the exposome concept, foster collaborations across NIEHS.
- Bimonthly webinar series

The NIEHS Sister Study and Two Sister Study

Sister Study

- Blood DNA methylation profiles may be used for early diagnosis of breast cancer



- Early life exposures associated with early menarche, which could lead to higher rates of breast cancer later in life

- Increased DNA methylation have been associated with increased rates of cancer

Two Sister Study

- Early findings show fertility drugs associated with reduced risk of young-onset breast cancer

CHEAR: National Exposure Assessment Laboratory Network (U2C)

- Coordinated network of laboratories
- Variety of stored or newly collected biosamples (e.g., cord blood, blood, urine, teeth, and saliva) derived from extant or ongoing children's health studies.
- Expertise in providing analysis of environmental (e.g. metals, pesticides, substances of abuse) and endogenous (e.g. nutrients, hormones, cortisol) stressors through both targeted and untargeted approaches.
- Assessment of biological response indicators such as DNA damage, oxidative stress, immune/inflammation indicators, and other molecular markers
- Technical consultation on measurement and interpretation of data on the wide range of environmental measurements characterizing the exposome.

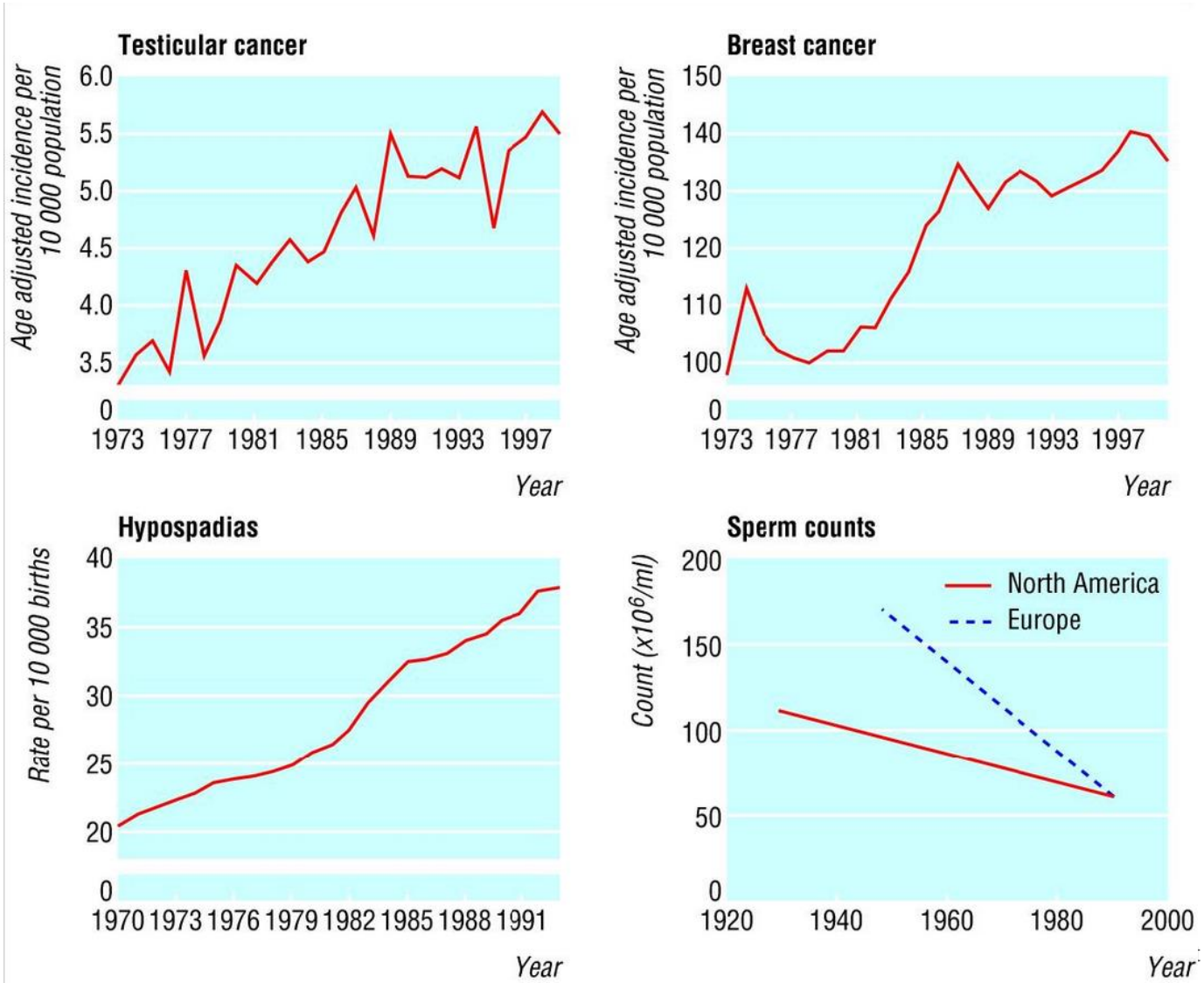
CHEAR: Exposure Data Repository and Resource for Statistical Analysis and Methods Development (U2C)

- Provide comprehensive consulting and support for the analysis and interpretation of data generated by the CHEAR resource.
- Development and application of statistical methodologies and informatics tools to analyze and integrate the diverse set of data generated and enhance the capabilities of the network.
- Create and manage a repository of exposure data that enables data sharing.
- Development of data standards and ontology as needed to maximize the value of the data generated by the CHEAR program.

CHEAR: Coordinating Center (U24)

- Responsible for managing the flow of materials, data, and analyses between CHEAR components and participating investigators.
- Coordination of the network of laboratories and statistical center/data repository regarding policies and procedures for this team effort.
- Outreach, marketing and communication with the children health community regarding all aspects of the resource.

Trends in human health



Sharpe *et al.* 2004

National Institutes of Health
U.S. Department of Health and Human Services