



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

Silent Dangers: The Impact of the Environment on Women's Health

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.
Director

National Institute of Environmental Health Sciences and
National Toxicology Program

July 28, 2014
Mercy College
Dobbs Ferry, New York



The NIEHS mission is to discover how the environment affects people in order to promote healthier lives.

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



“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

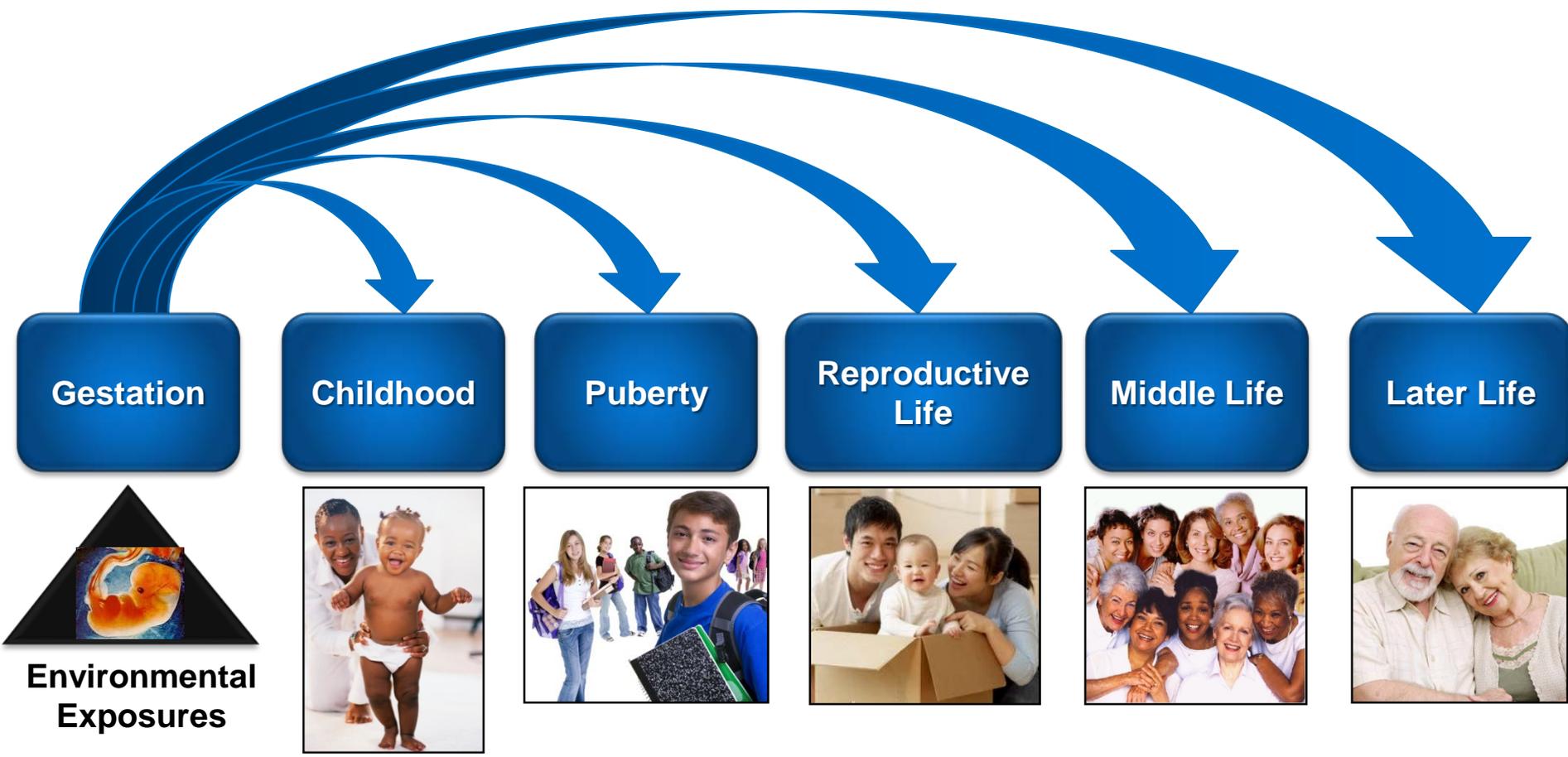


Environmental Exposures: One Size Does Not Fit All

- Thousands of chemicals in our environment:
 - EDCs, Mixtures...
- Many modes of exposure:
 - Air, water, food, pathogens, etc...
- Exposures differ depending on,
 - Dose, timing, the individual
- Disease and dysfunctions are not the same:
 - Many disease endpoints and mechanisms
 - Occur over a long range of time



Lifelong Effects of Early-Life Exposures



Gestation

Childhood

Puberty

Reproductive
Life

Middle Life

Later Life

Environmental
Exposures



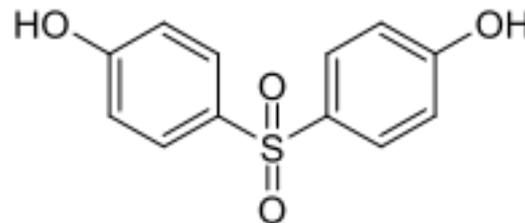
Early Life Exposures Can Have Lasting Effects: Developmental Basis of Adult Disease

- 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



Important Questions To Ask of Environmental Chemicals

- Are new or “replacement” chemicals safer than the chemicals they are replacing?
- How long are these chemicals going to remain in the environment after they are banned or no longer used in commerce?
- Can exposure to certain chemicals hurt me or my family? How can I protect myself?



BPS



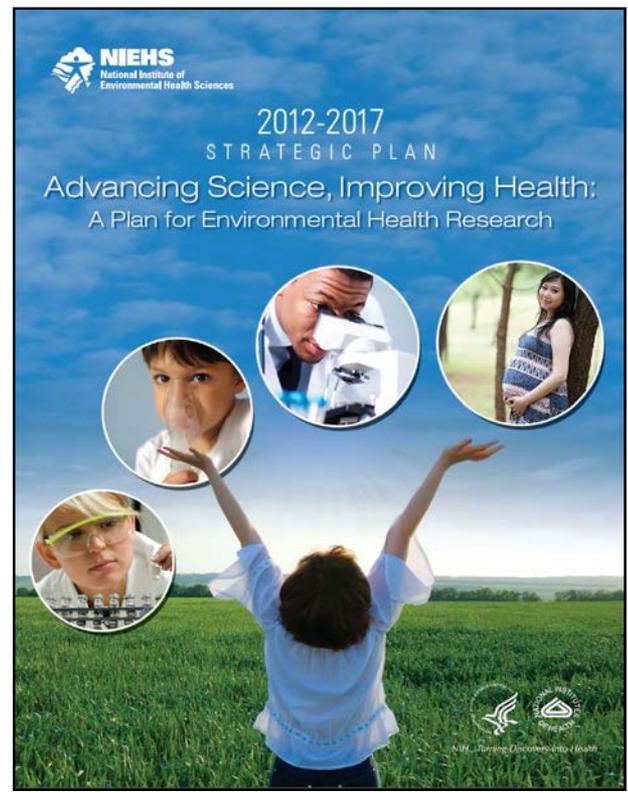
NIEHS is helping answer these questions!

New Strategies for 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 multi-generational effects



Autoimmune Diseases

- Novel estrogen target gene that plays a role in inflammation may contribute to higher systemic lupus erythematosus (SLE) incidence in women
- SLE prevalence 10-fold higher in females and 2.3-fold higher in black participants of large, diverse MI population
- Potential new therapeutic target in rheumatoid arthritis (RA) identified
- International Multiple Sclerosis Genetics Consortium identified 48 new genetic susceptibility variants for multiple sclerosis (MS)

Autoimmune Disease and Occupational Silica Exposure

	Autoimmune Disease	Risk Estimate
	Rheumatoid Arthritis	—
	Systemic lupus erythematosus (lupus)	●
	Systemic sclerosis (scleroderma)	●
	Systemic vasculitis (ANCA+)	●

Typical occupational exposures: fracking, mining, heavy construction, masonry, farming, and manufacturing of tile, pottery, glass





Air Pollution Contributes To:

OBESITY
Asthma
Diabetes **COPD**

Autoimmunity

Behavioral Effects

Autism

Developmental Disabilities

Pneumonia

Cancer

Lower Respiratory Infections

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 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



Autism, Genes, and Environmental Exposures

- Traffic-related air pollution during pregnancy and during first year of life is associated with autism
- Prenatal exposure to selective serotonin reuptake inhibitors (SSRI) prescribed for depression is associated with autism in boys
- Children of mothers living within one mile of fields where organophosphates pesticides were used at some point during pregnancy have a 60% increased risk for ASD
- Higher maternal intake of certain nutrients and supplements has been associated with reduction in autism risk, with strongest evidence for folic acid supplements



IQ and Environmental Exposures

	Number of IQ points lost
Major medical and neurodevelopmental disorders	
Preterm birth	34 031 025
Autism spectrum disorders	7 109 899
Paediatric bipolar disorder	8 164 080
Attention-deficit hyperactivity disorder	16 799 400
Postnatal traumatic brain injury	5 827 300
Environmental chemical exposures	
Lead	22 947 450
Methylmercury	1 590 000*
Organophosphate pesticides	16 899 488
Other neurotoxicants	Unknown

IQ=intelligence quotient. Data from from Bellinger.³⁴ *From Grandjean and colleagues.³⁵

Table 3: Total losses of IQ points in US children 0–5 years of age associated with major risk factors, including developmental exposure to industrial chemicals that cause neurotoxicity

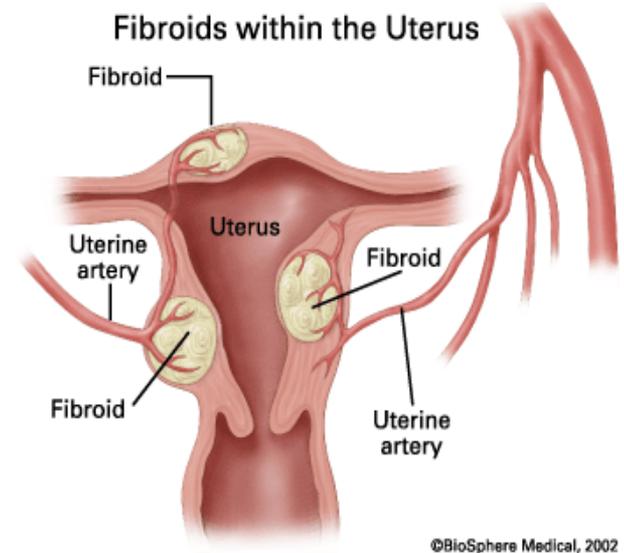
Parkinson's Disease & Paraquat Exposure

- Paraquat, one of the most widely used herbicides, produces PD in rodents and is associated with PD in humans.
- Study shows exposure to paraquat in men with functional GSTT1 gene increases odds ratio to 1.5 for PD
- In men with deletion of GSTT1 gene, exposure increases odds ratio to 11.1
- GSTT1 deletion is common and could potentially identify a large population at risk for PD after exposure to paraquat.
- Genetic variation in ALDH2 increases risk of PD in patients exposed to ALDH-inhibiting pesticides
- Women with PD had lower mortality after hip/pelvic fracture than men with PD, but higher mortality than those without PD
- Women had a lower odds of receiving deep brain stimulation treatment for PD compared with men



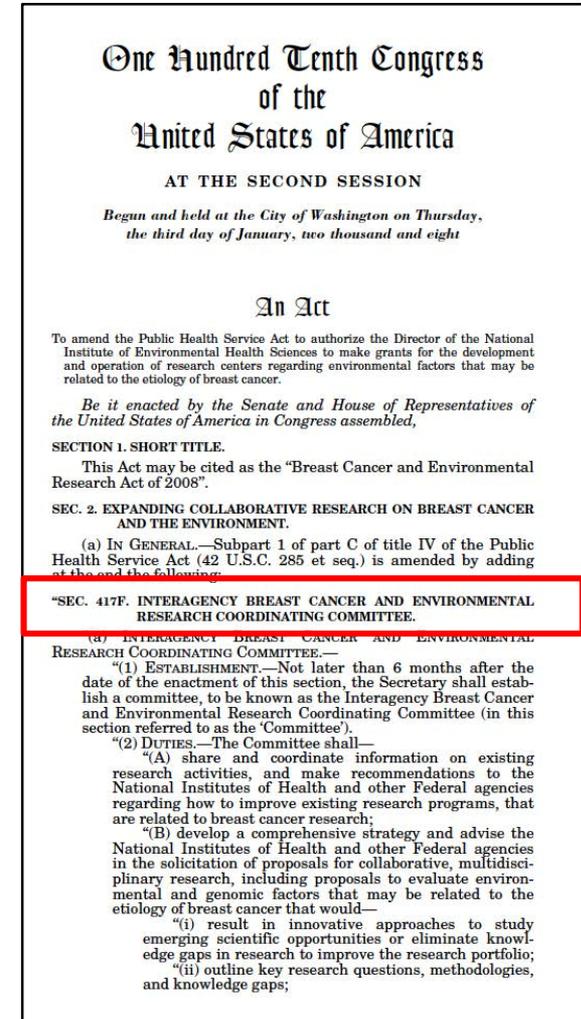
Uterine Fibroids

- Fibroids are the leading cause of hysterectomy in the USA
- Only 10% of blacks and 50% of whites have sufficient levels of vitamin D. Women with sufficient vitamin D have an estimated 32% lower odds of fibroids
- Greater risk of early fibroid diagnosis associated with soy formula during infancy, maternal diabetes, low childhood socioeconomic status, and being born at least 1 month early
- First trimester DES exposure may be associated with increased risk



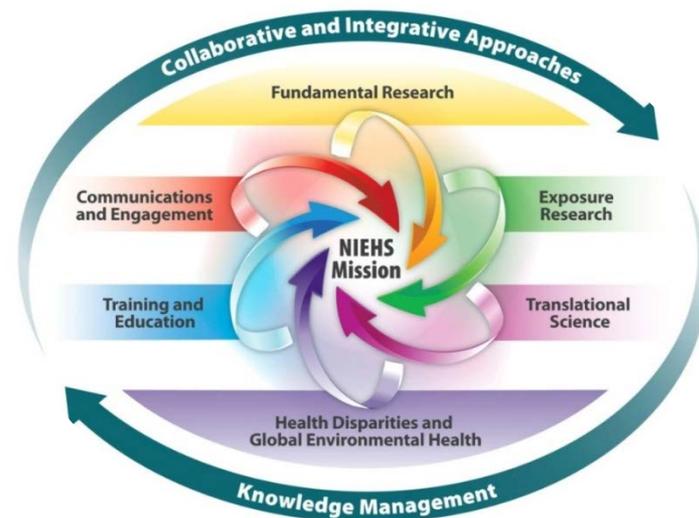
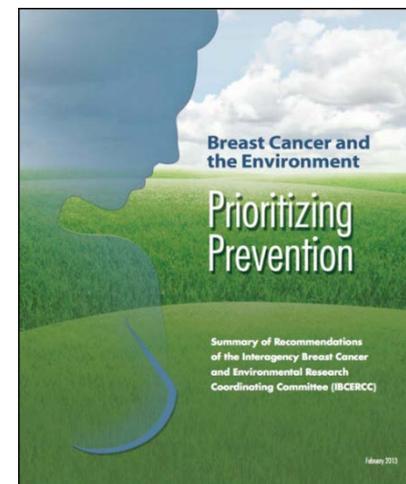
An Act of Congress

- The Breast Cancer and Environment Research Act was signed into law by the President on October 8, 2008
- Amends the **Public Health Service Act** to establish a committee composed of federal officials, scientists, health professionals, and non profit groups who represent individuals with breast cancer
- DHHS Secretary Sebelius delegates this activity to NIH, IBCERCC formed



IBCERCC Report: Prioritizing Prevention Aligns with NIEHS Strategic Plan

- Studying basic mechanisms and windows of susceptibility
- Linking individual and population exposure to risk
- Creating better predictive models and 21st Century tools
- Enhancing diversity in all aspects of breast cancer research
- Training a multidisciplinary group of scientists
- Improving coordination between gov't agencies and other groups



NIEHS Breast Cancer Research

- NIEHS invested > \$31 million on Breast Cancer research in FY 2013
 - Breast Cancer and the Environment Coordinating Center
 - 3 Puberty Studies
 - 8 projects on Windows of Susceptibility
 - Collaborating Center
 - Over 20 Breast Cancer Research Grants
 - 12 Intramural Programs investigating BC
 - NTP programs
 - RoC, Tox21, Toxicity studies



The NIEHS Sister Study and Two Sister Study

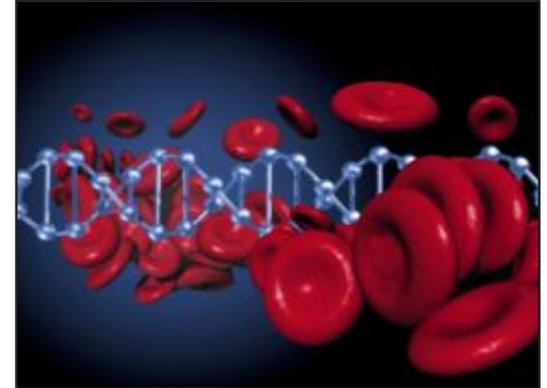
- The Sister Study examines environmental and familial risk factors for breast cancer in sisters of women who have had breast cancer
- This study enhances the ability to assess the interplay of genes and environment in breast cancer risk and to identify potentially preventable risk factors
- Between 2004-2009 the study had recruited nearly 51,000 women aged 35-74
- Two Sister Study! More than 1600 remarkable women have volunteered to help us get some answers to questions about early onset breast cancer



Findings from The Sister Study and Two Sister Study

Sister Study

- Blood markers may be used for early diagnosis of breast cancer
- Early life exposures associated with early puberty, which could lead to higher rates of breast cancer later in life
- Epigenetic changes, genes, and the risk of breast cancer



Two Sister Study

- Fertility drugs associated with reduced risk of young-onset breast cancer
- Early menopause-associated symptoms associated with markedly reduced risk of young-onset breast cancer



Breast Cancer Prevention and Research

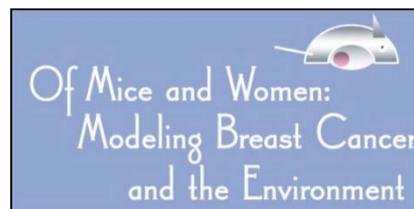
- Onset of breast development found to occur earlier among white, non-Hispanic girls than observed 10-20 years ago
- Association of breast feeding with age of onset of girls' puberty varied by environment
- Polyfluoroalkyl compound serum concentrations higher in young girls in Cincinnati vs. San Francisco suggesting water treatment systems are effective at reducing exposure
- CYP19A1 biomarker used to assess risk of early puberty

Breast Cancer Prevention and Research

- Long Island Breast Cancer Study showed post-diagnosis physical activity associated with improved survival among women with breast cancer
- Proteomics used to investigate effects of prepubertal chemical exposure
- Early life body weight and abdominal obesity associated with increased risk of breast cancer in Carolina Breast Cancer Study
- High fat diet during puberty likely related to enhanced breast cancer development

Community Partners

- Zero Breast Cancer
- Michigan Breast Cancer Coalition
- Huntington Breast Cancer
- Komen for the Cure Foundation – Local Chapters
- Wisconsin Cancer Council
- Wisconsin Breast Cancer Coalition
- Pink Ribbon Girls
- Huntington Breast Cancer Action Coalition
- Great Neck Breast Cancer Coalition
- Central Carolina Nurses' Council
- First Calvary Baptist Church Health Ministry
- Save Our Sisters
- e-WATCH (Wellness for African Americans Through Churches)
- ACTS (Action in Churches in Time to Save Lives) of Wellness
- NC Breast and Cervical Cancer Control Program
- Breast Cancer Alliance of Greater Cincinnati



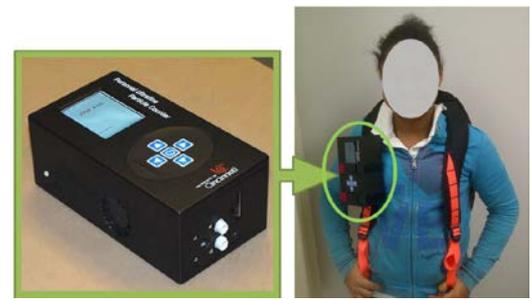
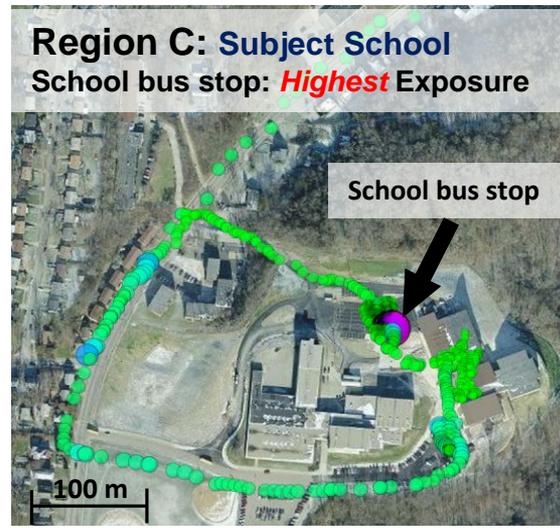


Better Methods for Diagnoses and Treatments

- NIEHS researchers have developed a compound that shows promise in preventing the immune system of autoimmune patients from attacking their bodies.
- NIEHS scientists discovered two partners in an immune cell—a tumor suppressor protein, the other a tumor growth stimulating protein—that work together in responding to cancer drugs to increase inflammation. Modifying this pathway could decrease inflammation in cancer treatment and in lung diseases like COPD.
- Discovery of epigenetic changes associated with pancreatic cancer might lead to early detection.

Better Tools for Research

- In 2014, researchers at Oregon State University developed a silicone bracelet that monitors a wide range of environmental exposures
- Scientists at University of Cincinnati developing personal ultrafine particle counter
- Field test indicated highest exposures at bus stop when worn by a child



Broad Categories of Botanical Dietary Supplements Under Study

- Multipurpose
 - Aloe vera, echinacea, gum guggul, kava, milk thistle, pulegone/pennyroyal, senna laxative
- Women's health
 - Black cohosh, gum guggul, dong quai
- Cancer chemopreventatives
 - Green tea extract, indole carbinol, milk-thistle extract, resveratrol, melatonin
- Anti-aging/wellness
 - Ginseng, glucosamine/chondroitin sulfate, Ginkgo biloba, vincamine, nanosilver
- Weight loss/sports aids
 - Usnea lichen/usnic acid, chitosan, garcinia cambogia, bitter orange extract, androstenedione



Herbal Medicines, Their Toxicity and Pathology

- The NTP conducted long term studies in rodents on 8 commonly used botanical based supplements
- No evidence of carcinogenic activity for ginseng, milk thistle, and green tea extract
- Liver tumors associated with ginkgo, goldenseal, and kava
- Thyroid tumors associated with ginkgo
- Uterine tumors associated with indole carbinol
- Intestinal tumors associated with aloe vera whole leaf nondecolorized extract



Prevention is the Key

- Genetic and environmental factors interact with each other to impact our health
- We can modify our environment, which presents us with a tremendous opportunity to support wellness in our communities





Thank you!



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

