

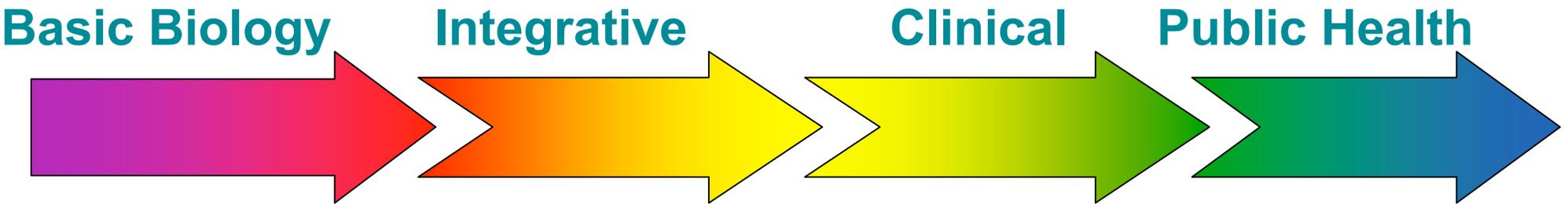
Mainstreaming Environmental Health Sciences



- **Progress and Challenges**
- **Hopes and Dreams**



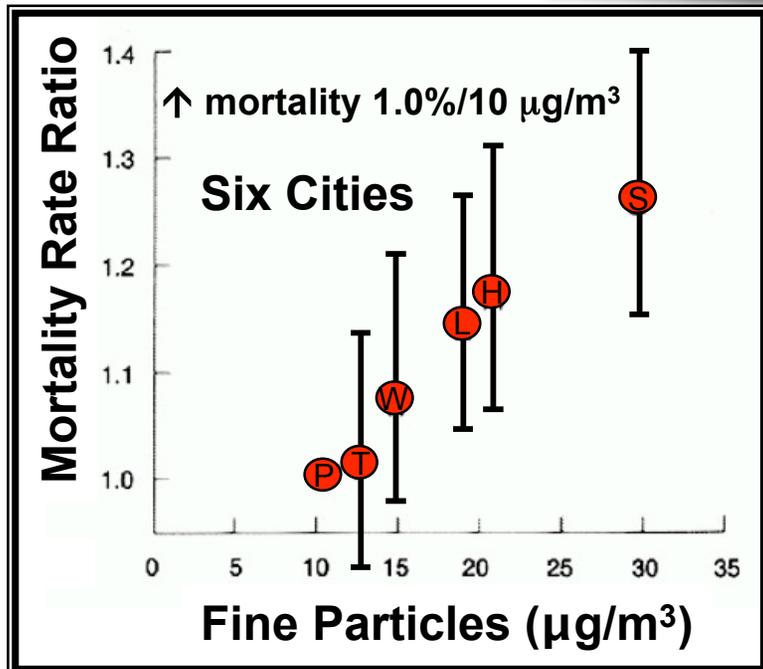
Scientific Accomplishments



- **AH receptor**
- **Endocrine disruptors**
- **Cell signaling**
- **Oxidative stress**
- **Metal biology**
- **DNA repair/mutagenesis**
- **Development**

- **Air pollution and mortality**
- **Air pollution and lung development**
- **Lead and IQ**
- **Arsenic and cancer**
- **Aflatoxin and liver cancer**
- **Community outreach**

Air Pollution and Public Health



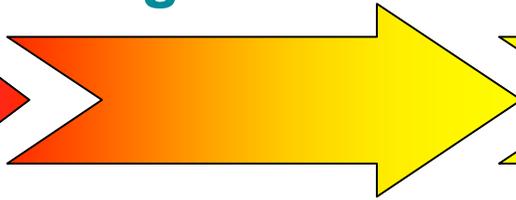
- New standard for PM in the U.S. and a rethinking of guidelines internationally
- 10 yr f/u - improved mortality with decreased concentration of PM

Scientific Challenges and Opportunities

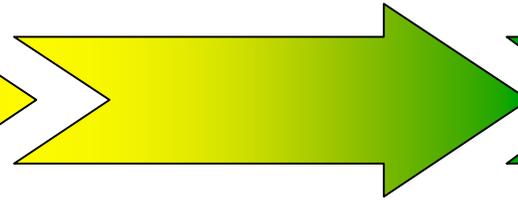
Basic Biology



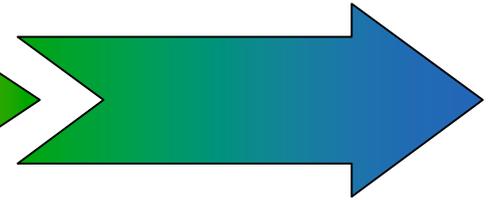
Integrative



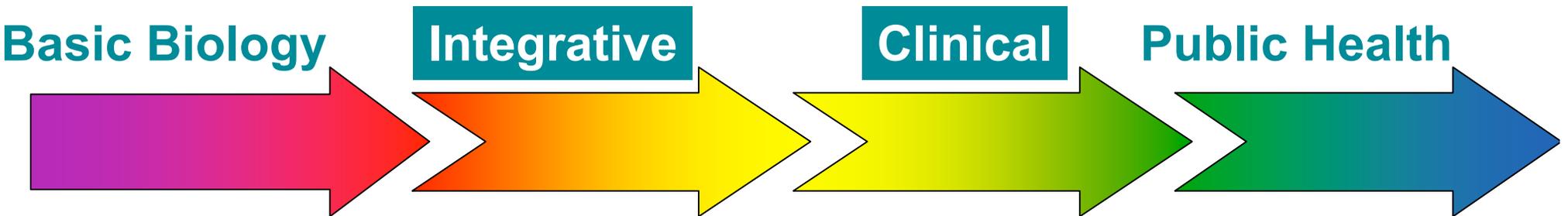
Clinical



Public Health



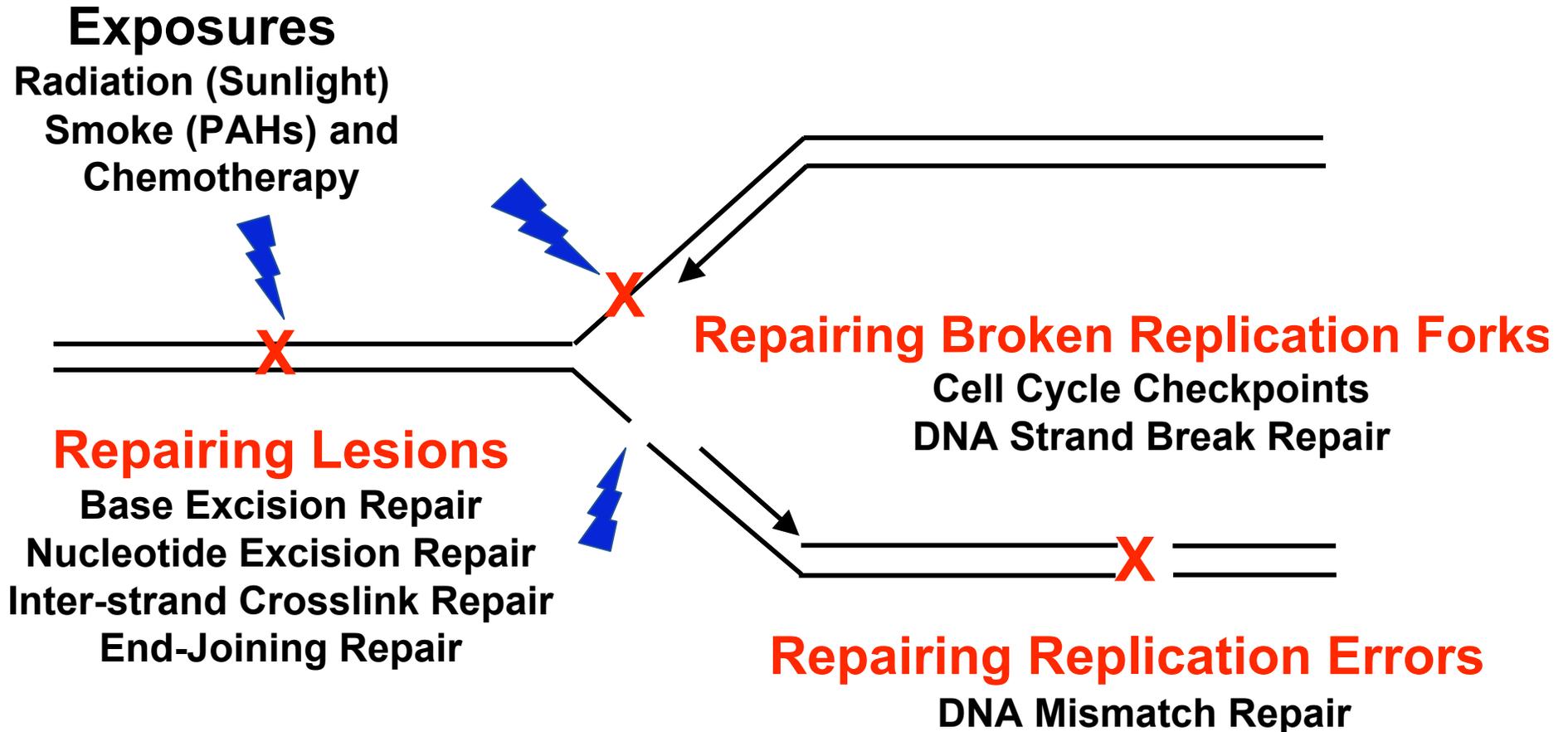
Scientific Challenges and Opportunities



Complex Human Diseases

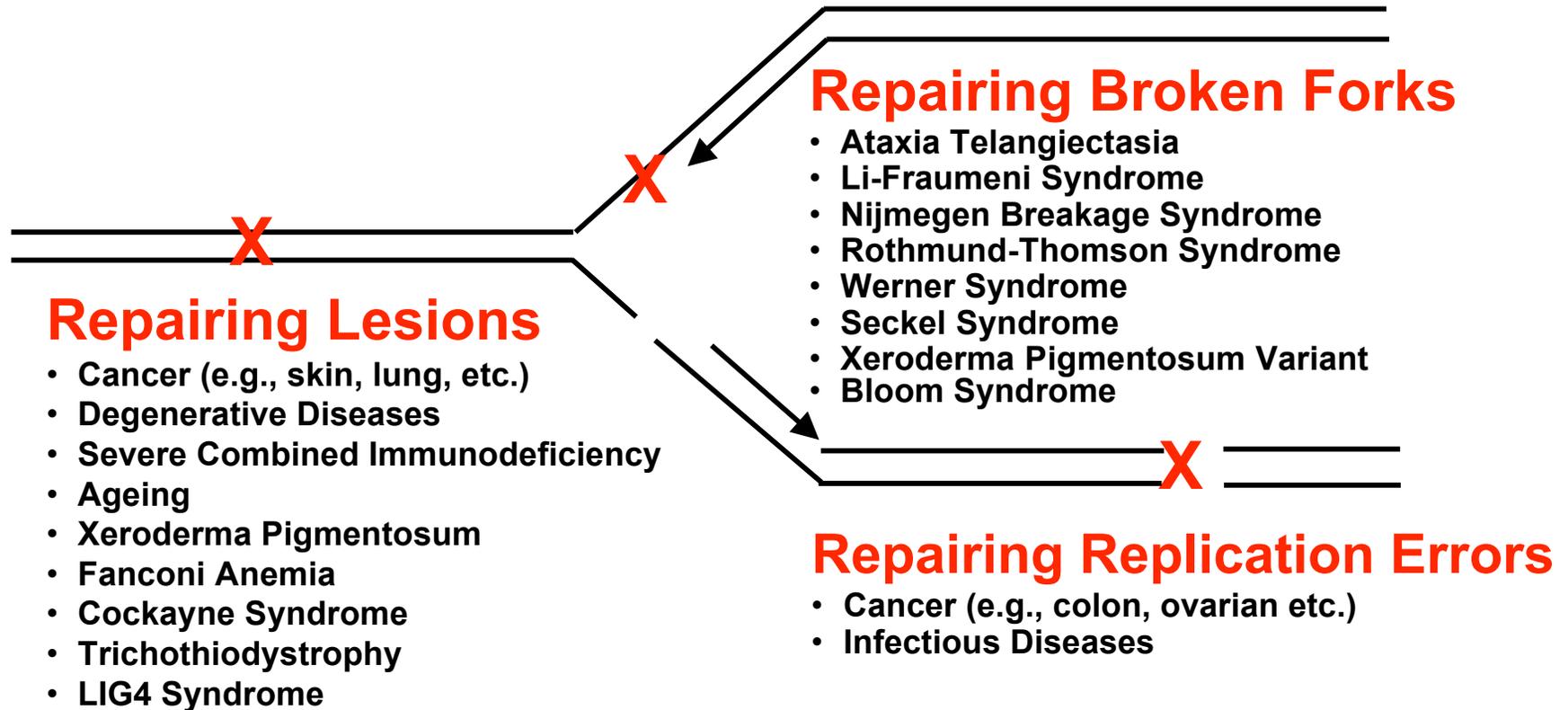
- Acute and chronic lung diseases
- Neurodegenerative conditions
- Reproductive disorders
- Several types of cancer
- Metabolic disorders - obesity
- Immune mediated diseases

DNA Repair: Fundamental to Homeostasis



More than 100 DNA repair genes discovered so far

Defects in DNA Repair Cause Human Diseases



Opportunities:

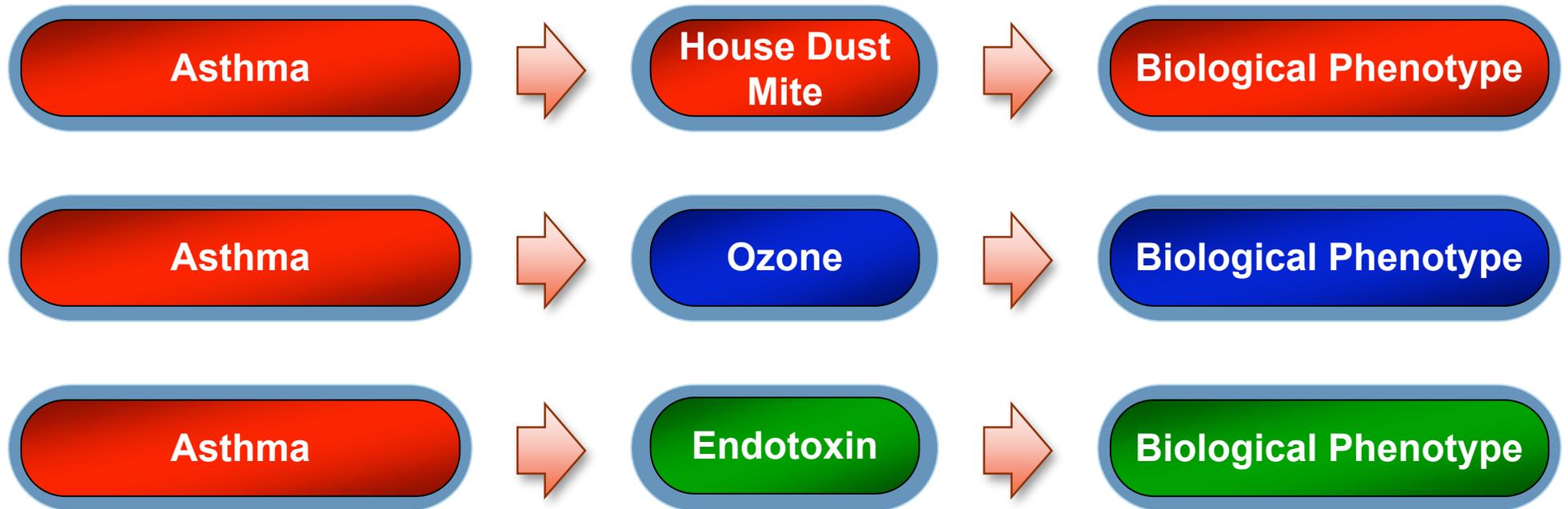
- Individual susceptibility based on DNA repair capacity
- Develop targeted/allele-directed therapeutic agents

Many Loci and Genes are Associated with Asthma

- Multiple exposures
- Complex biology
- Many phenotypes

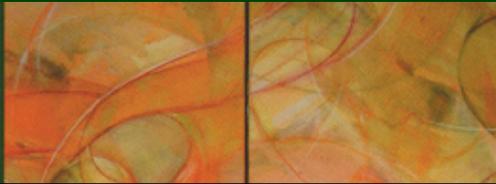
Stylinou I. “Comparative Genomics of Asthma.” In: *Genetics of Asthma*. In press

Exposures Can Simplify Complex Diseases



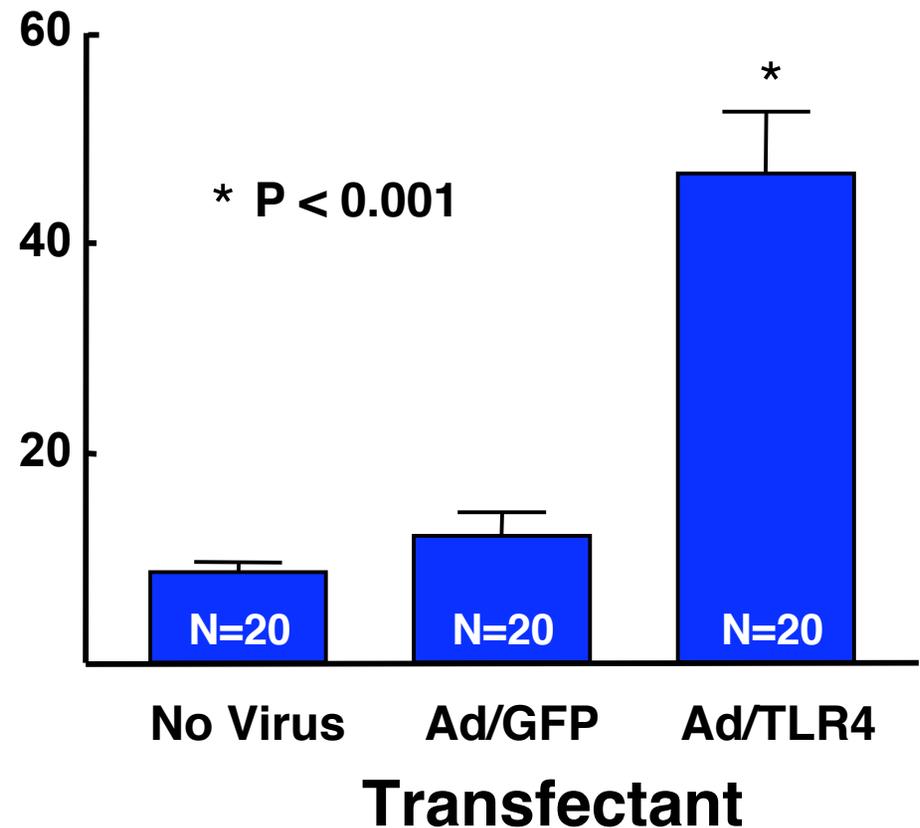
nature
genetics

Volume 25
June, 2000



**Polymorphisms in *TLR4*
blunt the response to
inhaled LPS in humans**

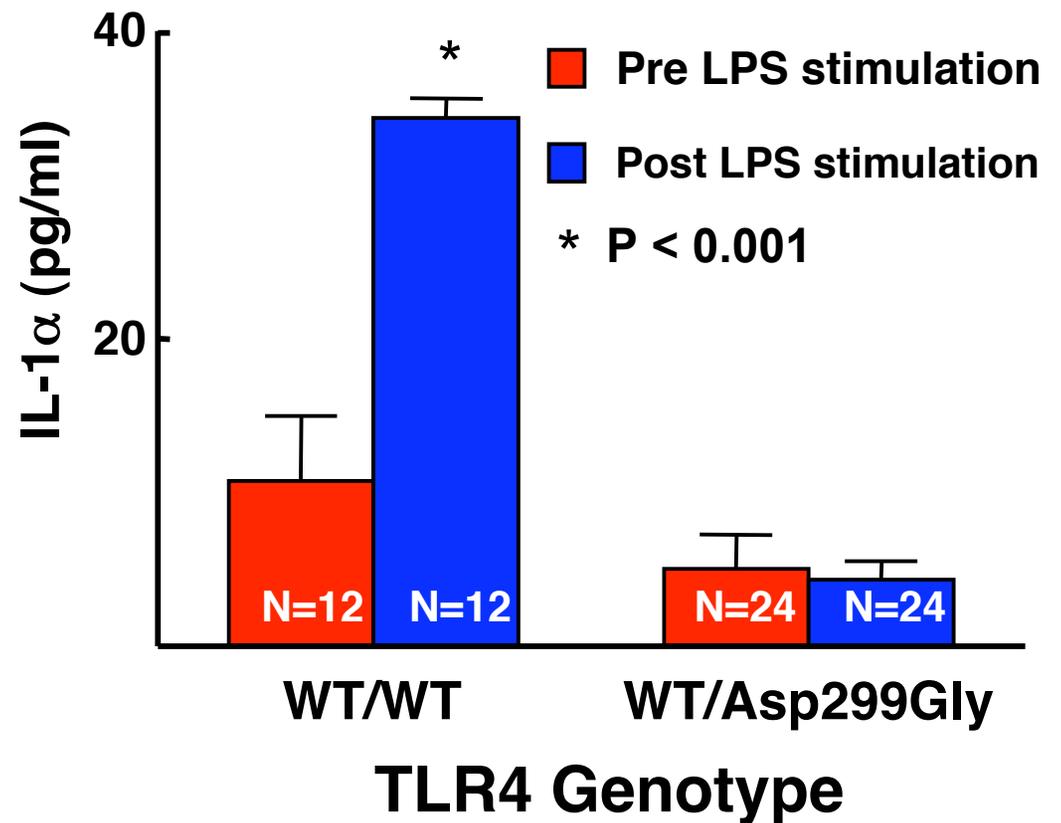
Brian Schutte et al.





**Polymorphisms in *TLR4*
blunt the response to
inhaled LPS in humans**

Brian Schutte et al.





The
New England
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Volume 347

July 18, 2002

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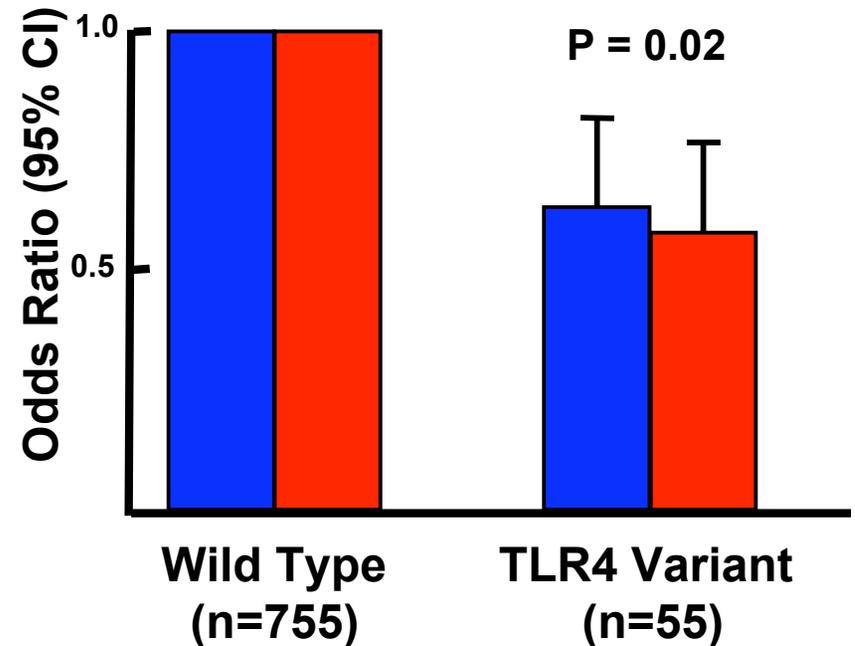
CLINICAL IMPLICATIONS
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Long-Term Effects of Early Genetic Influences
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R. FREEDMAN

Polymorphisms in *TLR4* protect humans from atherosclerosis

Steven Kiechl et al.

- Age and gender adjusted
- Age, gender, cholesterol, smoking, and HTN



- Significantly less MI deaths
- Lower serum concentrations of C-reactive protein, IL-6, and fibrinogen

Progress in Program Development

- **Integrative Research on Complex Human Diseases**
 - ❑ Office of Translational Research – Bill Martin, MD
 - ❑ Extramural DISCOVER Centers and Interdisciplinary RO1s
 - ❑ Intramural Director's Challenge
 - ❑ Clinical Research Unit at NIEHS
- **Recruit/Train the Next Generation**
 - ❑ R25 Science education grants – high school and undergrads
 - ❑ Re-engineer training and career development (T32, K12, and K/R)
 - ❑ ONES Program – new independent RO1 investigators

Progress in Program Development

- **Global Environmental Health**
 - **Katrina Research Program**



Progress in Program Development

- Global Environmental Health
 - Katrina Research Program
 - Public-private partnerships



The
**New England
Journal of Medicine**

Volume 329 December 9, 1993

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Case Records of the
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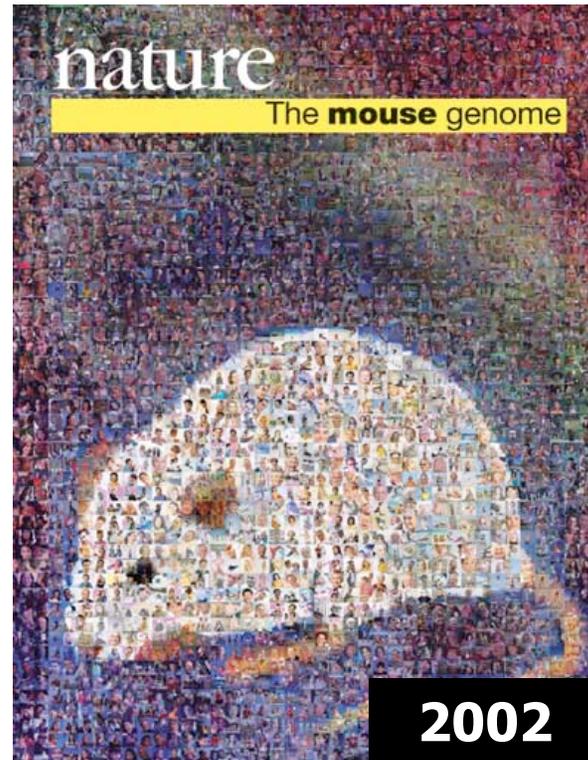
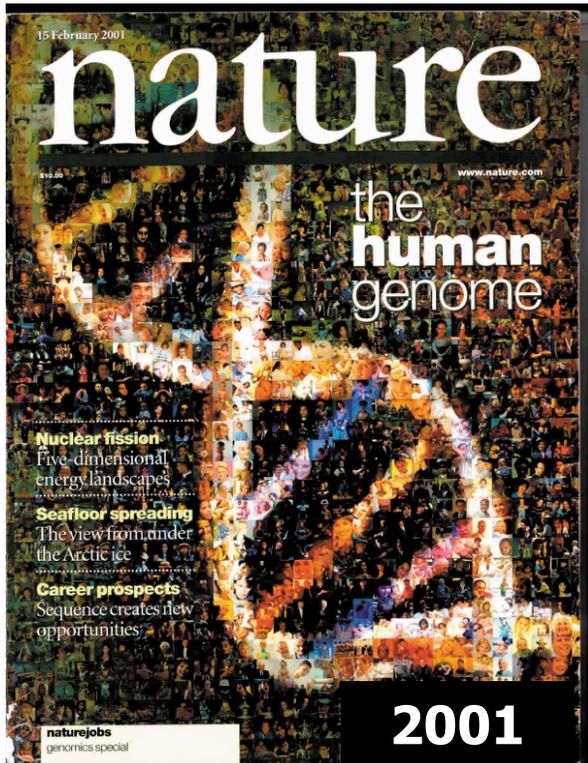
**Air pollution
causes excess
morbidity and
mortality**

Doug Dockery et al.

Progress in Program Development

- **Global Environmental Health**
 - ❑ Katrina Research Program
 - ❑ Public-private partnerships
- **Re-focus environmental genomics on new opportunities**
 - ❑ Epigenetics, comparative genomics, and genetics/genomics of complex diseases
 - ❑ T32/K awards in environmental genomics/genetics

Why Don't We Know More?



We Simply Need More Precise Measures of Exposure

Genes and Environment Initiative



Research Policy ALERT
THE BIOMEDICAL RESEARCH COMMUNITY'S PREMIER DAILY POLICY RESOURCE
Formerly "The Blue Sheet" & Washington Fax

Feb 9, 2006

Genes, Environment And Disease Converge In Two Major NIH Initiatives

Building on the promise of recent advances in genomic research, NIH launched two major, multi-million dollar initiatives Feb. 8 to find the genetic and environmental roots of common diseases.

Genes and Environment Initiative

- Trans-NIH initiative developed by NHGRI and NIEHS
- 2007-2010: \$40 million/yr
 - ❑ \$26 million human genetic case-control studies
 - ❑ \$14 million environmental biology program
- Environmental Biology Program – environment, diet, and activity level
 - ❑ Environmental sensors
 - ❑ Biological response indicators
 - ❑ Technology development

**NIH coordinated
Centrally managed
Product oriented**

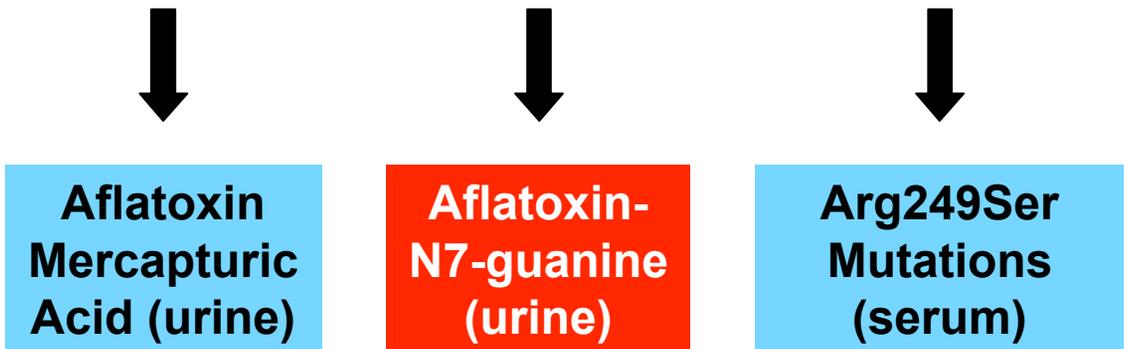
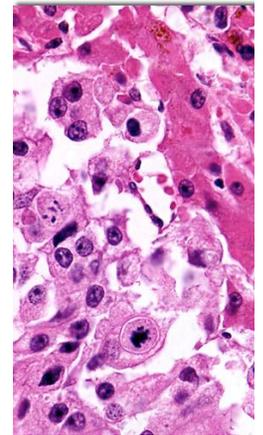
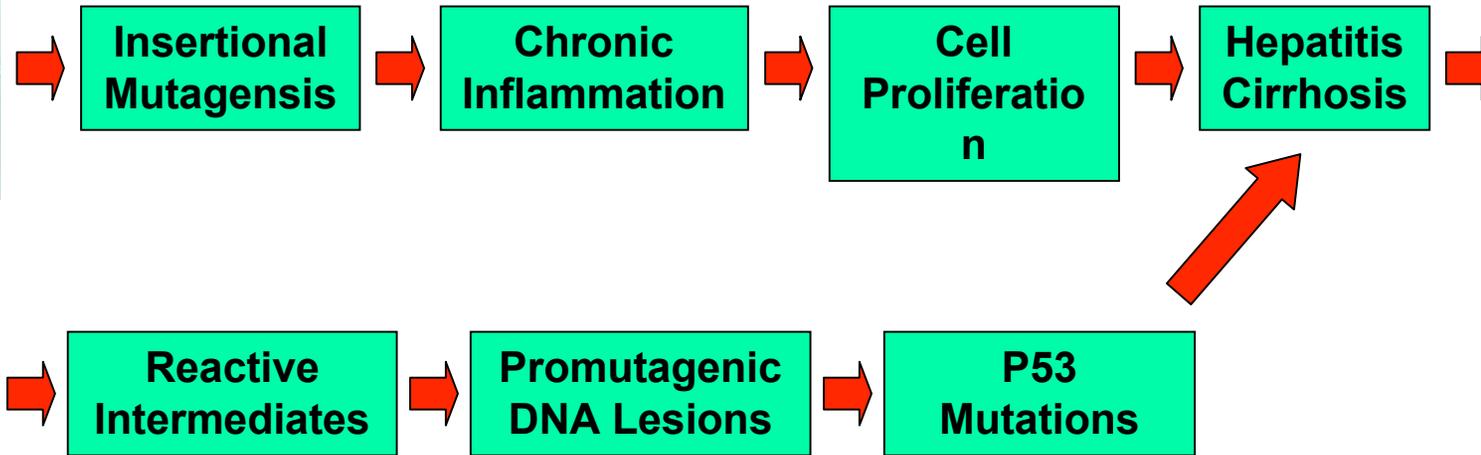
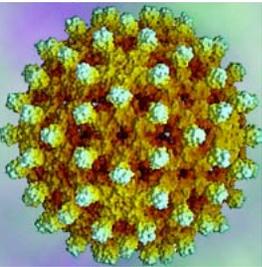
	2006	2007	2008	2009	2010	TOTAL
Appropriation	----	14	14	14	14	56
NIEHS	4	8	10	10	----	32

Etiology of Hepatocellular Carcinoma

No association between dietary aflatoxin and liver cancer

25-30 years

HBsAg (serum)



	RR
Aflatoxin	3.8
HBV	7.3
Aflatoxin + HBV	60.0

Genes and Environment Initiative: Exposure Biology Program

2

New Technology Development

Nutrition

Environmental Exposures

Physical Activity

Genetic Vulnerability

Complex Human Disease

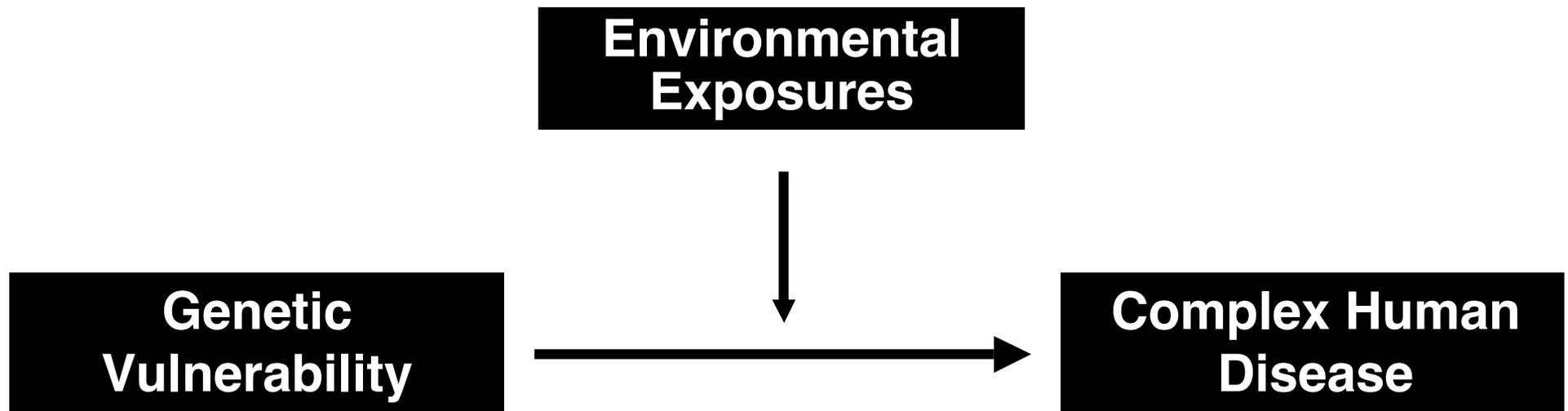
1

- Environmental sensors
- Biomarkers and sensors

3

Heart disease
Cancer
Neurodegenerative
Chronic lung disease
Metabolic disorders
Psychiatric conditions

Scientific Challenges and Opportunities



- Homeostatic Mechanisms
- Disease Pathogenesis
- Individual Susceptibility - including genetics, diet, other diseases, and age
- Simplify Phenotype of Complex Diseases
- Impact on Prognosis and Public Health

Scientific Hopes and Dreams

- ***Exposure Sciences*** – personalized measures of exposure
 - ❑ Environmental sensors
 - ❑ Biomarkers of response
- ***Complex Human Diseases*** – environmental exposures will identify relevant genes, novel mechanisms and treatments, and pathways for prevention
 - ❑ Chronic lung diseases, reproductive disorders, neurodegenerative conditions, and specific cancers
- ***Global Environmental Health*** – focusing on extraordinary environmental exposures that will have a profound impact on global health
 - ❑ Indoor air and childhood respiratory disease

10-25 over the next 5 years

NIEHS: An Institute on the Move



- **Lutz Birnbaumer – Director, DIR**
- **Perry Blackshear – Director, Clinical Research**
- **Allen Dearry – Interim Director, NTP**
- **Bill Martin – Director, Translational Research**
- **Chris Portier – Director, Risk Assessment Research**
- **Anne Sassaman – Director, DERT**
- **Brenda Weis – Senior Scientific Advisor**
- **Sam Wilson – Deputy Director**