

Session IV: Biologic Responses as Indicators of Exposure, Pathobiology, Clinical Disease, and Genetic Susceptibility

“Current State of the Science”

Samuel H. Wilson

**National Institute of Environmental Health Sciences,
National Institutes of Health
Department of Health and Human Services**

**IOM Roundtable on Environmental Health Sciences, Research, and Medicine
Workshop: From Exposure to Human Disease: Research Strategies to Address Current Challenges
National Academy of Sciences Auditorium
September 15, 2006**

Genes and Environment Initiative (GEI)

**Integrated trans-NIH genetics program and
exposure biology program lead by NHGRI and NIEHS**

GEI: Practical implications of new research initiative

- **Supports more exposure research.**
- **Focuses need for and supports new exposure technology.**
 - **Supports sensitivity/validation research on methods.**
- **Forces integration across sectors: from macro-scale, to personal exposure, to internal dose/metabolism, and to molecular indicators of exposure-induced stress responses.**

Outline

- **Current base of exposure information & technology.**
- **Concept 1 for GEI: Why Gene X Environment analysis ?**
- **Why now for a new initiative in exposure ?**
- **Concept 2 for GEI: What should we measure ?**
- **Concept 3 for GEI: Exposure science must make linkages!**

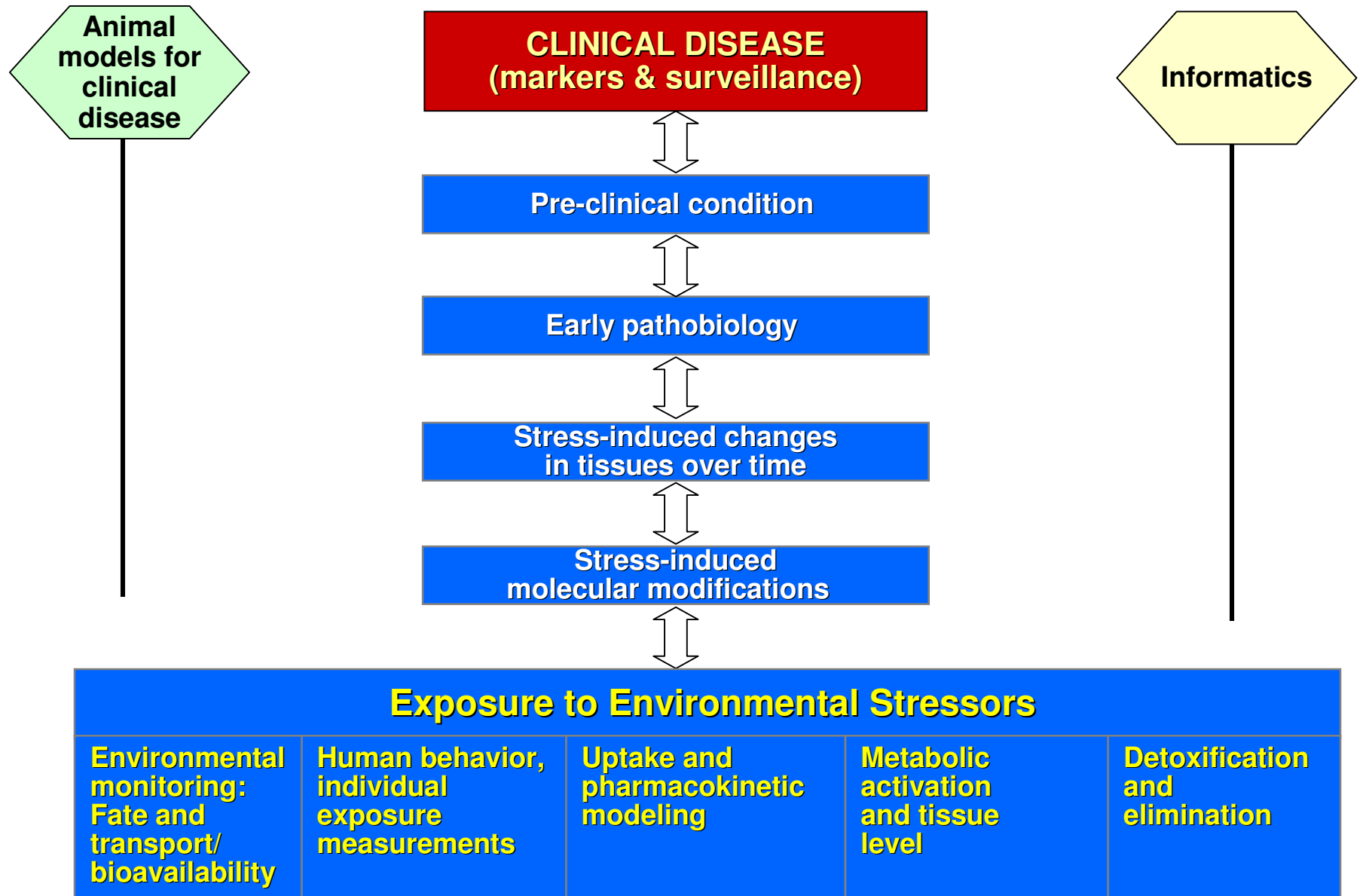
Summary

Abundant Background: Mature Field

- **Environmental Mutagen Society 37th Annual Meeting, September 16-20 in Vancouver, British Columbia, Canada**
100 platform presentations and 200 posters in the areas of biologic response to genotoxic stress and environmentally-induced disease risk analysis.
- **“Biomarkers of Environmentally Associated Disease-Technologies, Concepts, and Perspectives” CRC Press (eds., S. H. Wilson & W.A. Suk**

Thirty seven reference chapters on biomarkers in six categories, e.g., genomics-based; genetic toxicology; metal metabolism; organs and systems; chemical toxicants; nano-techniques.
- **Many other examples...(including recent NAS Reports)**

Background of information and technology to draw from:



Outline

- **Current base of exposure information & technology.**
- **Concept 1 for GEI: Why Gene X Environment analysis ?**
- **Why now for a new initiative in exposure ?**
- **Concept 2 for GEI: What should we measure ?**
- **Concept 3 for GEI: Exposure science must make linkages!**

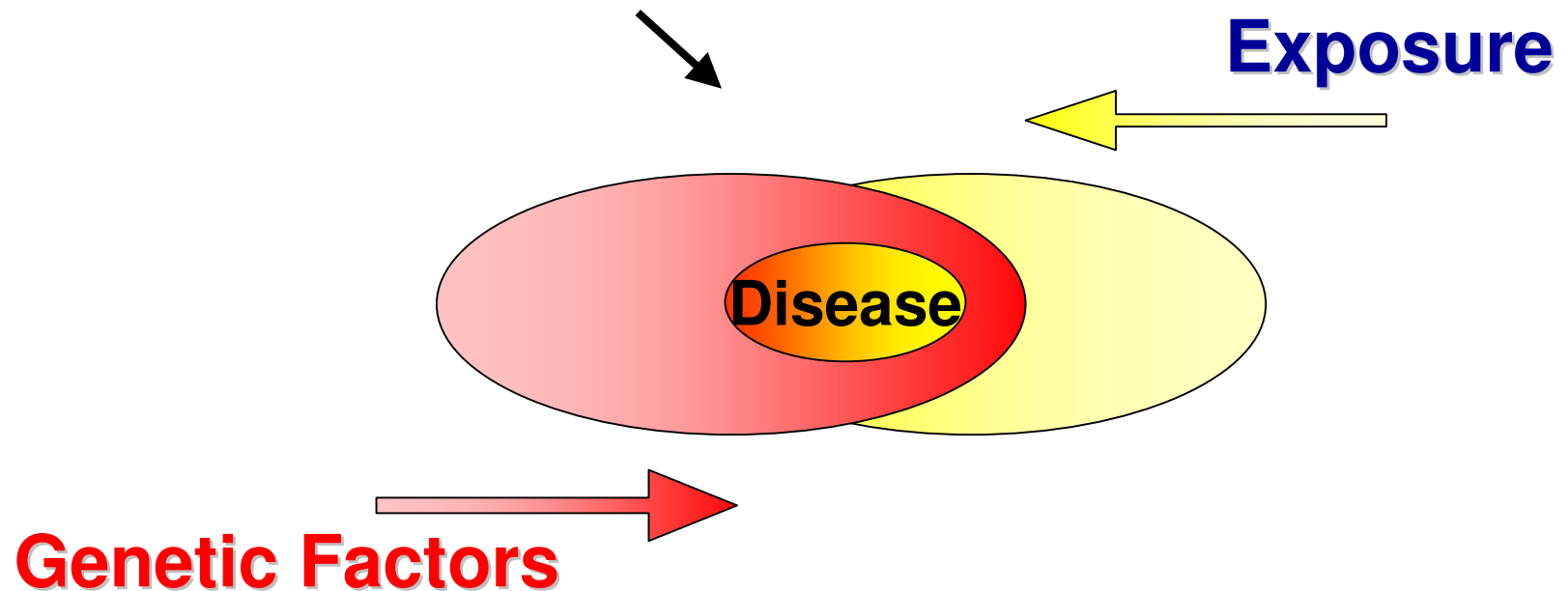
Summary

Concept 1: GXE informs on risk of common disease

Environment:

Toxicants; Metals; Toxins;
Radiation; Diet; Stress;
Infectious diseases; others.

Gene x Environment Interaction



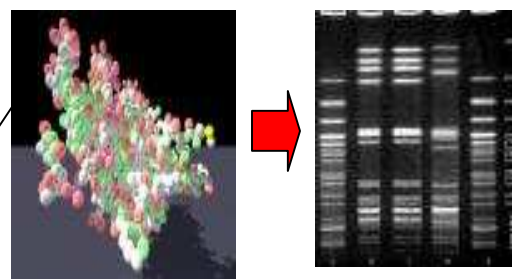
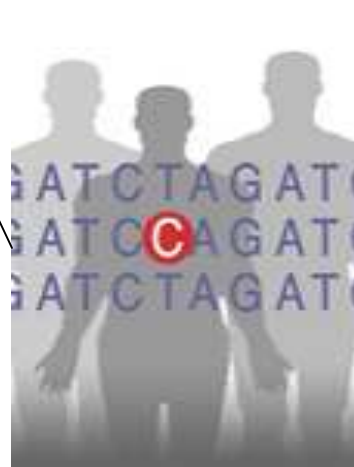
Outline

- **Current base of exposure information & technology.**
- **Concept 1 for GEI: Why Gene X Environment analysis ?**
- **Why now for a new initiative in exposure ?**
- **Concept 2 for GEI: What should we measure ?**
- **Concept 3 for GEI: Exposure science must make linkages!**

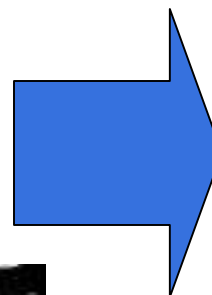
Summary

Precision of genetic and exposure measurements

SNP (single-nucleotide polymorphism)



Personalized exposure indicator



Need high level of precision for both genetic and exposure data

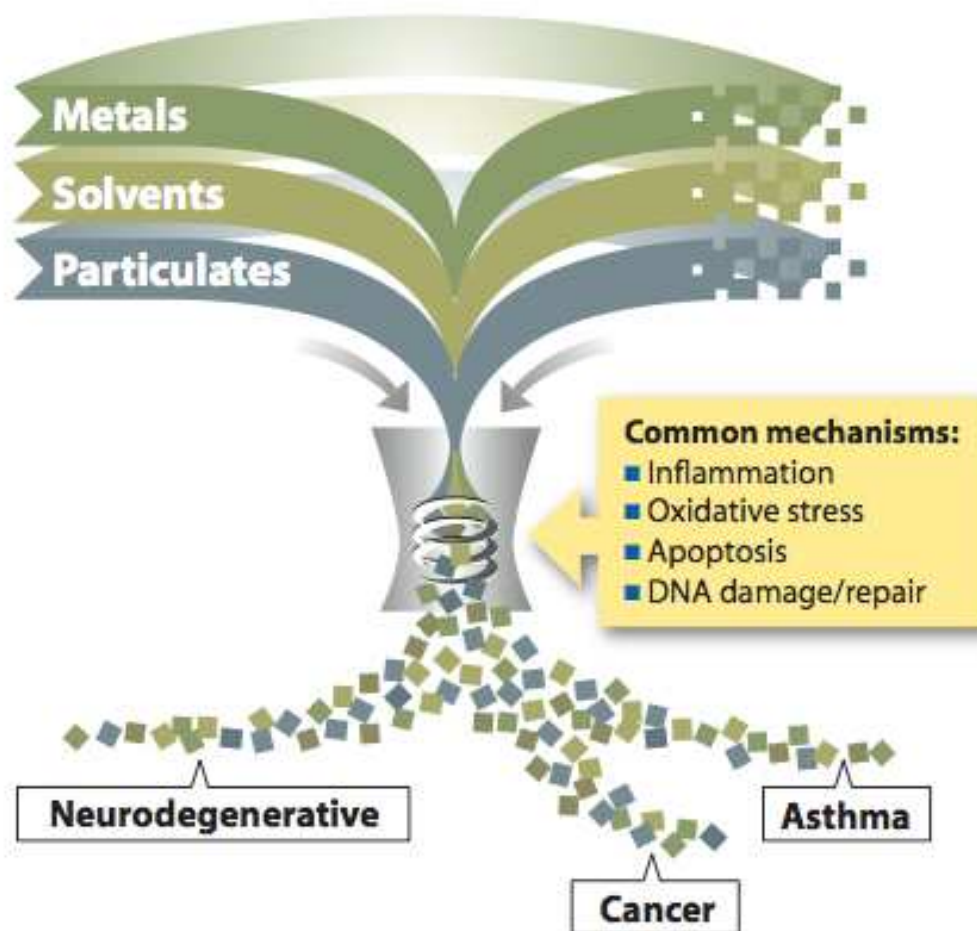
Outline

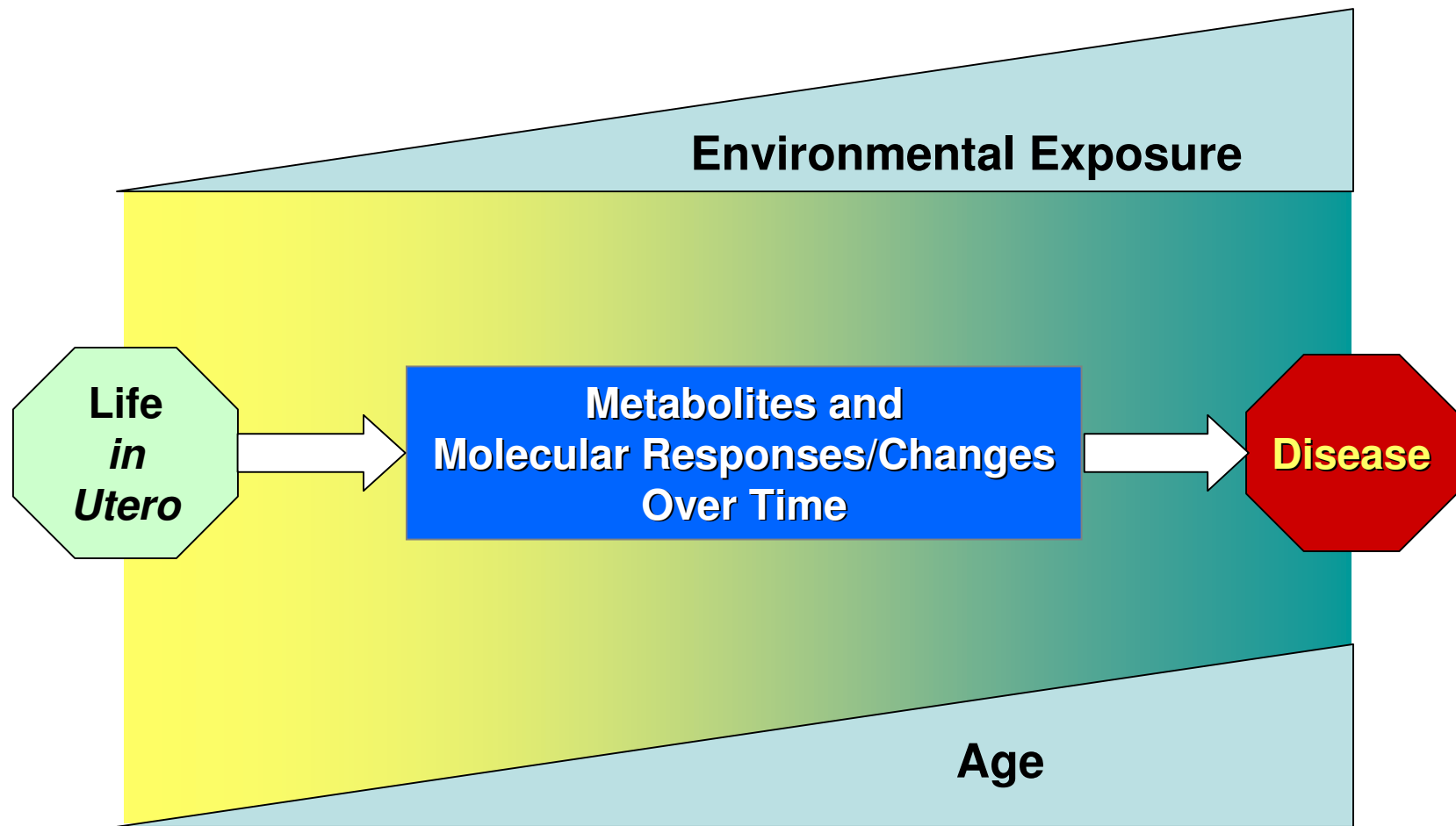
- **Current base of exposure information & technology.**
- **Concept 1 for GEI: Why Gene X Environment analysis ?**
- **Why now for a new initiative in exposure ?**
- **Concept 2 for GEI: What should we measure ?**
- **Concept 3 for GEI: Exposure science must make linkages!**

Summary

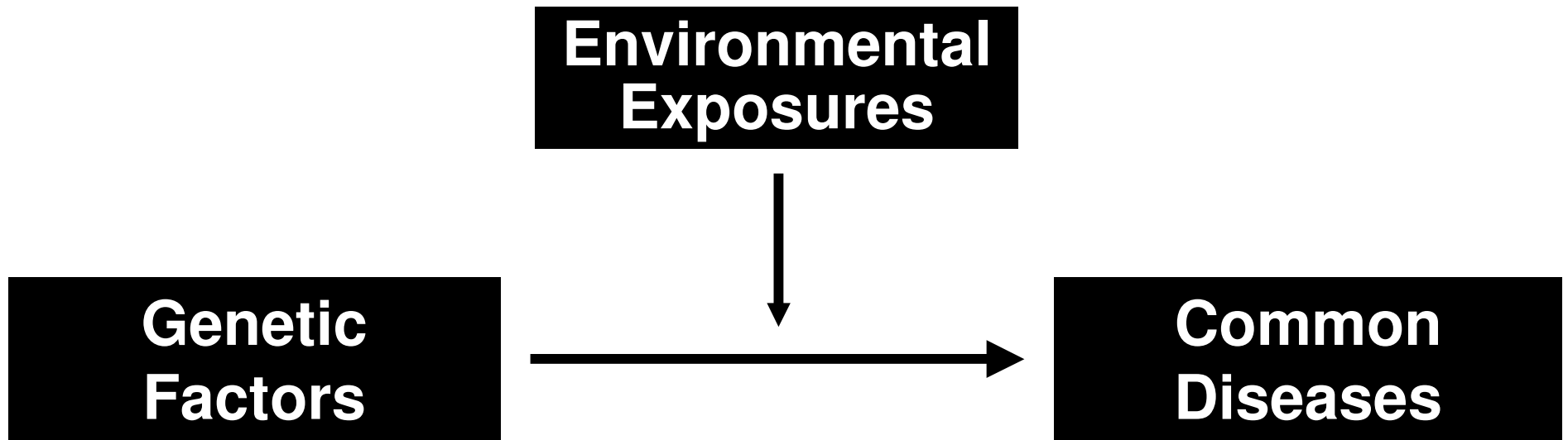
Concept 2: Common stress response mechanisms

GEI: Focus on Common Mechanisms





Scientific Opportunities



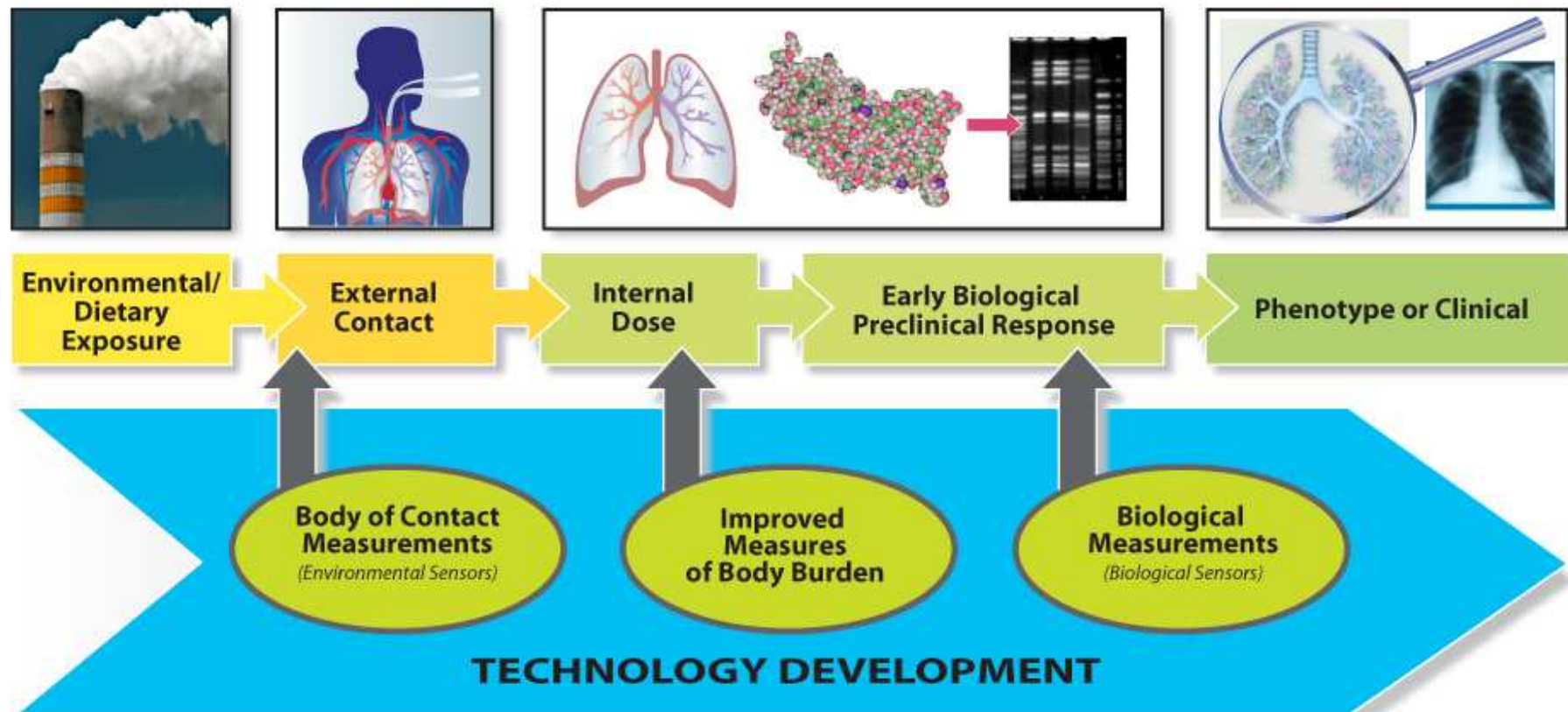
- **Disease pathogenesis**
 - **Homeostatic and adaptive mechanisms**
 - **Simplify phenotype of complex disease**
- **Individual susceptibility - including lifestyle, other diseases, age, social stress, psychological stress**

Outline

- **Current base of exposure information & technology.**
- **Concept 1 for GEI: Why Gene X Environment analysis ?**
- **Why now for a new initiative in exposure ?**
- **Concept 2 for GEI: What should we measure ?**
- **Concept 3 for GEI: Exposure science must make linkages!**

Summary

Conceptual Approach to Technology Development in the GEI



Link personal exposure to biological response

Suggestions from GEI Exposure Biology Program's Greensboro Workshop

- **Emphasize quantitative measurements**
- **Validation needed (technical & biological)**
- **Plans enabling replication by other groups**
- **Study designs boosting reliability (e.g., dose range)**
- **Include measurements that are not “hypothesis-limited”**
- **Also include hypothesis-testing (candidate GxE approach)**

Summary: Scientific Hopes and Dreams

- ***Exposure Science*** – understanding of source, personal exposure, and biological response to exposure

Sensors
Biomarkers

) 10-25 over the
next 5 years

Sufficient data management and analysis

- ***Complex Human Disease*** – exposure science helps target relevant genes, novel mechanisms and treatments, and strategies for prevention/intervention