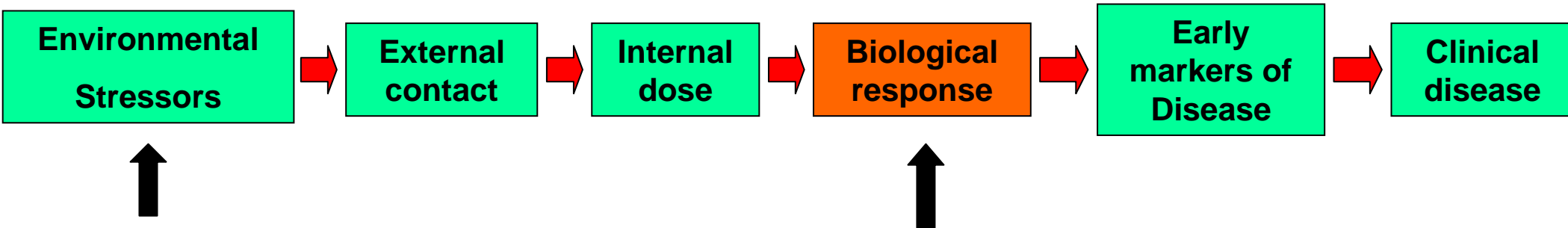


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Biological Response Indicators of Environmental Stress

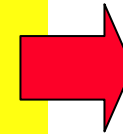
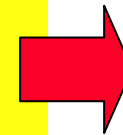


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- Nutrition
- Physical Activity
- Environmental Agents
Tobacco, PAHs, PCBs,
DEP, Pesticides,
Phytoestrogens, Metals,
Alcohol, Ethanol,
Addictive Substances
- Psychosocial Stress

- Oxidative stress
- Inflammation
- DNA damage and repair
- Epigenetics
- Apoptosis
- Immunity
- Endocrine disruption
- Xenobiotic Transformation
- Mitochondrial perturbations



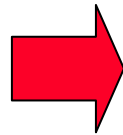
**U01
Biomarkers**

**U54
Biomarkers
Biosensors**

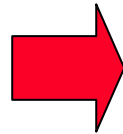


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**U01
Biomarkers**

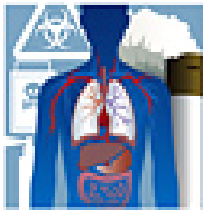


**U54
Biomarkers
Biosensors**



**Product- oriented:
develop, confirm, and apply
measures of key biological
pathways affected by
environmental stressors.**

Goal: products available for confirmation in and application to large-scale studies soon after the end of the four-year funding period.



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Definition of Biomarker

A biomarker is an indicator of biologic response to an environmental exposure or stressor that is objectively measured.

Multiple markers may be necessary to characterize the full response of the pathway to the stressor, e.g., molecular signatures composed of profiles of gene expression, proteins or metabolites.



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Definition of Biosensor (U54)

A biosensor is defined as a device or technology that measures markers of biological response to environmental stressors.

Examples of biosensors include lab-on-a-chip, microarrays, and new technologies to measure changes in genes, proteins and metabolites.



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Research Continuum

Discovery

Predictive
Analysis

Assay
Refinement

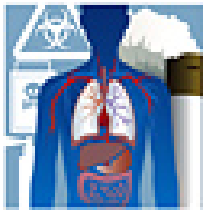
Sensor
Dev. (U54)

Identify
reproducible
patterns of
response to
environmental
stressors

Capacity of
biomarkers to
distinguish
between
homeostasis and
response to
challenge

Confirmatory
studies on
test sets of
specimens

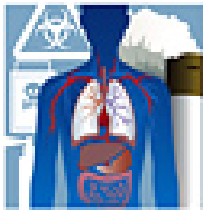
Devices/systems
that can measure
single/multiple
markers with
accuracy,
reliability and
technical validity



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Research Topics of Interest

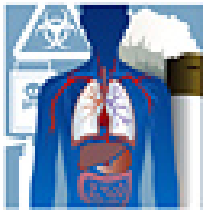
- Development of single or multiple biomarkers of response to environmental stressors
- Comparison of patterns of response across species, including humans
- Comparison of panels of biomarkers progressing from invasive to noninvasive specimens
- Acute vs. chronic exposure
- Study of biological responses under different exposure conditions – dose, frequency and timing of exposure



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Requirements for U01 Applications

- Single Principal Investigator
- Approach
 - Multidisciplinary
 - Animal models or human specimens
- Objective
 - Identify panels of biomarkers
 - Product-oriented approach



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Requirements for U54 Applications

- Multidisciplinary teams
- Central theme that links biomarker research with biosensor development
- Minimum of three projects
 - human specimens in at least one research project
- Biosensor development
 - measure biological responses *in vivo* or in banked biological specimens.
 - improved quantitation, accuracy and reliability



NIH Genes and Environment Initiative Exposure Biology Program

Budget

- **U01**
 - \$4 million (total costs) per year over 4 years
 - 6-8 awards are anticipated
 - individual awards

- **U54**
 - \$4.5 million (total costs) per year over 4 years
 - 3-4 awards are anticipated
 - program awards



NIH Genes and Environment Initiative Exposure Biology Program

Key Dates

- **Letters of Intent Receipt:** **November 22, 2006**
- **Application Receipt:** **December 22, 2006**
- **Peer Review:** **March-April 2007**
- **Council Review:** **May 2007**
- **Earliest Start:** **July 2007**



NIH Genes and Environment Initiative Exposure Biology Program

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