Environment

Understanding how Earth systems will change is a critical scientific challenge that has elevated "environmental observation" to a key goal of the Administration's research and development agenda for fiscal year 2005.

The science associated with the discovery and use of environmental biomarkers will fundamentally change the field of environmental science, and lead to better detection, management, and prediction of complex environmental systems.

Environmental Biomarkers

Pacific Northwest National Laboratory (PNNL) is discovering and using biomarkers to transform environmental science. Environmental biomarkers are biomolecular signatures that display a unique pattern of molecular change in an organism, such as a set of expressed proteins, and that identify an exposure or response to a specific environmental stressor. They may signal a specific biological response to pollution, subtle changes in the environment, or deliberate releases of toxic substances as an act of terrorism. Environmental biomarkers are the next generation of risk assessment tools, replacing whole-organism measures of response with directly measured sub-cellular responses from first exposure through terminal disease state.

The Challenge

The United States and others are facing major challenges in the areas of environmental quality, energy, and national security. We must meet these global challenges by managing natural habitats, water, air, food, and energy wisely. In so doing, we shape our future environmental and economic security. How we respond to terrorist threats, meet our energy needs, promote environmental quality, and respond to naturally occurring diseases and disasters will be determined largely by how we assess and manage the risks associated with alternative management strategies. Environmental biomarkers are the improved risk assessment tools necessary to build a more secure future.

The economic security of industrialized nations is closely linked to the growing need for energy, which is estimated to double by the year 2050. The question is not *whether* increasing fossil energy use will produce changes in the environment, but rather *how* our environment and ecosystems will change. There is agreement among scientists that energy by-products are global human and environmental health challenges. Unfortunately, our current approach to assessing environmental change by monitoring pollutants and species is inefficient, expensive, and often non-predictive. New approaches to threat surveillance are also urgently needed to detect novel agents before they reach human receptors. Environmental biomarkers will be the basis for rapid, broad-spectrum, effects-based monitoring systems for early detection of environmental change, early detection of terrorist threats, improved risk management, and prediction of final endstates.

Systems biology and cellular biology tools (including proteomics) will change the paradigm by which we study and manage complex ecosystems. For example, airborne particulate matter and chemicals produced by fossil energy use are a complex mixture composed of hundreds of constituents. Many of these chemicals are implicated as cancer agents or as disruptive agents to the endocrine system. Exposure to these chemicals activates a biochemical pathway that can eventually lead to disease and damage. The challenge is to identify unique biomolecular signatures throughout the biochemical pathway. Signatures early in the pathway will allow corrective actions to be undertaken before disease and damage occur. Signatures later in the pathway will improve the ability to assess the extent of change or damage, and to predict future change and damage with and without intervention.

Science and Technology Direction

The key science and technology challenge is to use systems biology tools, cellular biology tools, bioinformatics, and mechanistic studies at the molecular and cellular

levels to develop technologies for better understanding, predicting and protecting ecosystems and human health. This multidisciplinary approach increases the likelihood of showing a strong relationship between measures of exposure, effect and genetic susceptibility and the underlying causal factors of declining ecosystem health. As we understand the cellular dynamics that link environmental stimuli to tissue and organism response, use of biomolecular signatures will identify early exposures, identify doses required to initiate cascading biological effects, provide early disease detection, and improve controls and intervention strategies. Systems biology will define more accurately human and ecosystem response to environmental pollutants and mixtures of those pollutants, while reducing our reliance on laboratory animals for testing and model validations. The result will be extremely powerful pattern recognition and prediction technologies in the face of newly released chemicals whether intentionally disseminated or unleashed as acts of terrorism. We believe that these technologies will provide the best predictive power in tomorrow's market and are the key to sound decisions that support environmental and economic security.

PNNL's Role

PNNL's recognized expertise in environmental sciences and system biology positions the laboratory be a leader in the development of environmental biomarkers. We recognize that the complexity, uniqueness, and diversity of ecological systems are major challenges to understanding and predicting ecosystem health. And, we are well positioned to advance the area based upon 1) our existing scientific and technical strengths in analyzing exposure (e.g., environmental modeling, bioavailability research, and inhalation quantification and modeling), systems biology and cell signaling, data mining, visualization tools and information analytics; 2) our traditional strengths and breadth in environmental sciences, from biogeochemistry to ecological studies, integrated modeling, and risk assessment; 3) the nation's emerging emphasis on proteomics and our lead in developing high-throughput proteomics; and 4) our ability to integrate and apply these technical capabilities across mission areas. Through Laboratory level internal investments and external programs, we intend to develop and apply capabilities to

- Create protein assay systems to identify and classify environmental signatures of cellular injury that link fundamental science mechanisms to ecosystem damage;
- Identify and use biomarkers for early detection of terrorist threats and activities;
- Develop predictive strategies to differentiate between perturbations that initiate cascading cellular response leading to ecosystem damage and those that have no adverse ecosystem effect; and
- Develop and validate computational and pattern recognition strategies to integrate diverse, complex information to support science-based risk analysis and risk management for environmental health and interventional strategies.

Associations and partnerships with government agencies, other national laboratories, universities, and industries will be an integral part of PNNL's efforts to build an Environmental Biomarkers capability. Inquiries should be directed to

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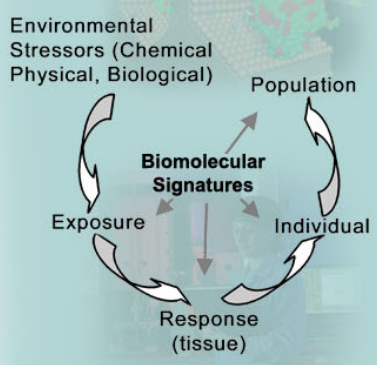
A novel 220-probe chemical exposure array developed at PNNL uses the bacterial Pseudomonas aeruginosa genome to quantify subsurface environmental contaminants based on dose-response behavior in bacterial messenger RNA expression. This capability would not exist without DOE's investments in genome science a decade ago.



Facing the Challenges:

- **What determines differential sensitivity or exposure among individuals?**
- **What are the norms of reaction in natural populations?**
- **What are the interactions among stressors?**
- **What are the reliable signatures of exposure and response among all levels of organization?**