

Report 79: Exposure Science and the Exposome

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Brief History:

We know that exposure and disease are complex. The concept of the exposome captures this complexity and recognizes the need to develop measurements that integrate multiple exposures across domains and incorporate a temporal component. It provides a conceptual framework for strategic development of biologically relevant exposure metrics and systems-based exposure models. Developing this framework will advance understanding of exposure-response relationships and toxicology.

Exposure science has not been well addressed by NIEHS or NIH and lags behind GWAS. A large fraction of chronic disease is due to environment, so poor characterization of exposure is a barrier to progress. Exposure is a weak link in environmental health science that is impairing progress in gene-environment science.

Discussion Highlights:

National Academy workshops have discussed the exposome and opportunities to harness technology to characterize the exposome. That discussion needs follow-up.

The exposome concept creates a framework for discovery of exposures we don't know to look for rather than "looking under the lamppost."

We are not adequately using existing tools and we also need new tools.

A strength of the exposome concept is that it focuses attention on the need to measure the entire pathway from exposure to disease, developing measures that are early markers of the effects of exposure. For cohort studies, it is desirable to develop measures that are markers of exposure years ago and to develop low-cost measures that can be collected repeatedly in large numbers. Measurements are needed to integrate exposures over many years and to measure exposure in critical windows of development. Currently there are cost and technology barriers to environmental exposure measures that are not questionnaire-based in cohort studies.

The exposome concept is needed to move us from linear to complex network approaches consistent with systems biology.

A critique of the exposome is that it seems unbounded. In addition, regulation is chemical by chemical, creating a tension with conceptions of multiple exposures.

NIEHS is a good place to explore the exposome because it is not engaged in regulatory issues.

Advances in bioinformatics will be needed to deal with data generated in exploration of the exposome.

In parallel to the exposome concept, we need to move beyond old models of disease diagnosis to a more complex, molecular definition of disease. Exposome measurements are needed to evaluate perturbation in a biological pathway that may lead to disease.

Observing biological perturbation in a population with unique exposures, such as after the Gulf oil spill, can lead to back-analysis to identify the responsible exposure source.

Interdisciplinary skills, including informatics and toxicology, are important and require training and incentives for investigators to work together.

Development of the exposome must be “open sourced,” with shared databases that don’t wait for publication.

Recommendations:

NIEHS should use the exposome concept to frame a research agenda that (a) elevates characterizing exposure to an end point rather than an ad hoc adjunct to other ends, (b) supports discovery science, and (c) reflects coordinated strategic priorities.

NIEHS should fund the development and validation of cost-effective exposure measurement technologies (platforms) for population surveillance, epidemiology, and emergency response.

NIEHS should fund proof-of-concept studies in existing cohorts or add-ons to cohorts.

NIEHS should facilitate data sharing, development of repositories for environmental and biological samples and data, repositories for measurement standards, and bioinformatics support to encourage rapid advances in understanding of exposure. Development of guidelines to ensure quality and consistency will enhance these shared resources.

NIEHS should promote the concept that exposures that perturb a biological pathway should be considered relevant to health, with the understanding that we must also investigate long-term meaning.

NTP should develop a program of pilot-testing in animals for biomarker discovery. Metabolomic and genomic profiling in exposed animals can lead to discovery of biologically-relevant metrics and disease pathways. These can be targets for human biomarker development and feed into high-throughput screening programs.

NIEHS should serve as a convener of workshops to develop a coordinated, strategic approach to the exposome concept and should explore collaborations with NSF, DOD, NASA, and NHANES.

NIEHS should work to ensure that the National Children’s Study contributes to understanding of health effects of environmental chemicals and understanding the exposome.

Discussion Participants:

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