

Report 20: Systems Framework Approach to Integrate Environment, Genetics, and Temporal Susceptibility

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Brief History: Etiology of common disease is complex involving multiple low level environmental factors in combination with low penetrant genetic elements and influenced by life-stage of exposure. The NIEHS uniquely among NIH Institutes is poised to spearhead the discovery of environmental factors causing common diseases.

Discussion Highlights: It would be useful to develop a systems framework to quantitatively aggregate and model environmental factors in the context of genetics, and temporal susceptibility. The illumination of nodes and their connectivity (edges) is crucial to identifying priority environmental inputs of focus.

The enormous advancement in genetic and genomic tools has enabled and driven the successful infusion of a genetics/genomics perspective and investment across the efforts of other NIH institutes. Through a systems framework model such as proposed here, NIEHS would be poised to propagate environmental health perspectives and datasets to other institutes and agencies. In return, this will create opportunities for other groups to populate this systems framework model. This will add value to currently existing efforts.

It was discussed that a recent eWAS study utilizing NHANES data with recognized limitations in data collection and biological analyses experienced success in identifying greater than 40 environmental factors associated with disease. Information such as this can be used to populate the model and can be validated using animal models. The proposed systems framework model builds upon this early success and will extend and enhance the value towards understanding of the environment's complex contribution to health. It was also recognized that all data added to the model should undergo quality control based on accepted guidelines generated by NIEHS.

Recommendations: We recommend that a phased staging begin the development of a system framework model. This framework model will then be populated with existing environmental and genetic data, generated from animal models as well as human populations. Subsequent to initial data population, the framework will highlight important gaps can then be prioritized. This framework will continue to increase in value as more data is added can serve as a innovate guide for the environmental health research community and to translate science to public health.

This systems framework approach provides an integrated problem that would benefit from the synergistic collaboration of the three arms of NIEHS (Intramural, Extramural and NTP).

Discussion Participants: David Balshaw, Jose Cordero, Michael Fessler, Lynn Goldman, Michael Gould, James Kiley, Cheryl Marks, Patrick Mastin, Carolyn Mattingly, Craig Newschaffer, Richard Paules, Robert Sills, Raymond Tice, Fred Tyson, Thomas Vogt, Leroy Worth