Methods and Applications of Functional Genomics to Health Effects Research

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The primary goal of this research program was to develop genomic and bioinformatic tools for application to assessing human health risks associated with low dose chemical exposure. In response to this goal, several tools have been or currently are being developed for broader use at the CIIT Centers for Health Research and within the toxicology community. These tools can be divided into six subprojects and are organized according to the traditional risk assessment paradigm. The first two subprojects (#1 and #2) focused on developing genomic tools for aspects of hazard identification. The next three subprojects (#3 through #5) focused on developing genomic and systems biology tools for application to dose-response assessment and understanding mode-of-action. The final subproject (#6) focused on developing genomic tools for identifying susceptible subpopulations. The tools developed in this program are providing opportunities for developing predictive models for toxicological endpoints, evaluating dose-dependent transitions, assessing the mechanistic bases of non-monotonic and hormetic dose-response curves, and developing more realistic models for responses at low-level exposures. These technologies promise to revolutionize the way we look at the old problems of risk assessment including identifying hazard, evaluating dose-response, mapping modes-of-action, and extrapolating to a diverse human population to estimate low-dose risks.

**Implications:** Functional genomics, the branch of genomic biology that studies the genome in a cellular and functional context, is usually characterized by high-throughput, large-scale experiments. The Functional Genomics Research Program developed tools to define the cellular signaling pathways involved in toxicity and to identify the cause-and-effect relationships among altered genes and toxicity. These functional genomic tools were used in research on reactive compounds that cause tissue damage and with compounds that alter cellular function by interacting with specific receptor molecules. Application of these tools permitted incorporation of more realistic dose response relationships into risk assessments with a variety of important industrial compounds.

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**Presentations:**


Thomas, R. S. (2004). Implementing a systems biology approach in toxicology. Presentation at Department of Environmental and Molecular Toxicology, North Carolina State University, Raleigh, NC, September 14; Department of Environmental Health, Colorado State University, Fort Collins, CO, November 1, 2004.

This abstract was prepared by the principal investigator for the project. Please see [www.americanchemistry.com/lri](http://www.americanchemistry.com/lri) for more information about the LRI.


Thomas, R. S. (2005). Application of functional genomics to toxicology research. Seminar at University of Texas Southwestern Medical School, Dallas, TX, November 9, 2005.


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