

Computational Systems Biology and Dose Response Modeling Workshop

September 22 – 26, 2008

Division of Computational Biology

The Hamner Institutes for Health Sciences

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The recently published National Academy of Sciences (NAS) report “Toxicity Testing in the 21st Century” recommends a new approach to toxicity testing, based on evaluating cellular responses in a suite of toxicity pathway assays in human cells or cells lines *in vitro*. Such a paradigm shift would benefit from mechanism-based computational modeling of the molecular circuitry involved in the targeted cellular pathways, which should produce improved dose response assessment of the toxic actions of compounds. In accordance with the goals set forth by the NAS report, an inaugural 5-day workshop on Computational Systems Biology and Dose Response Modeling was offered by the Division of Computational Biology at The Hamner Institutes for Health Sciences September 22 – 26, 2008. The course was attended by 36 students of varied backgrounds from regulatory agencies, academia, and industry, as well as internal members of the institute. The focus of the course was on common themes in signal transduction and gene regulatory networks that underlie systems-level cellular behaviors, including linear and nonlinear response motifs, homeostasis, adaptation, binary cell fate decisions, and stochasticity in gene expression. A number of specific biological examples were discussed in detail, including ultrasensitivity and bistability in MAP kinase signaling cascades, checkpoint control in the eukaryotic cell cycle, and oxidative/electrophilic stress response. Lectures on the various topics were accompanied by exercises on computational modeling of cellular responses using the Berkeley Madonna simulation program. Implications for toxicology and dose-response modeling were emphasized throughout the course. *This presentation may not reflect the official policies of the U.S. EPA.*