



The NIEHS-NCATS-UNC DREAM Toxicogenetics Challenge: Crowdsourcing Tox21 Qualitative High Throughput Screening Data

Monday, December 2, 2013

10:30 a.m. – noon

Building 101

Rodbell Auditorium

111 T.W. Alexander Drive, RTP, NC

Host: Raymond R. Tice, Ph.D.

**Part 1: The 1000 genomes toxicity screening project:
Utilizing the power of human genome variation for
population-scale in vitro testing**

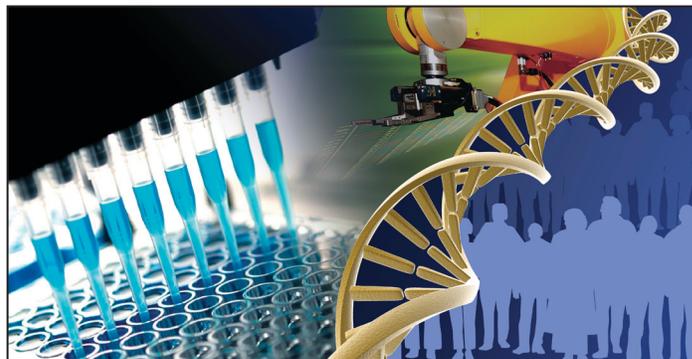
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This Tox21 project tested a hypothesis that population-wide in vitro screening has the potential to assess both the magnitude of and molecular causes for inter-individual genetic variability in toxicity of chemicals. Cytotoxicity data was generated on 1086 human lymphoblast cell lines, representing 9 populations from 5 continents, in a cell viability assay with 179 diverse environmental chemicals at 8 concentrations (0.3 nM-92 µM). The outcomes of this project demonstrate that population-based in vitro toxicity screening is more powerful than traditional in vitro testing because it enables: (i) quantitative assessment of both hazard and inter-individual variability in chemical toxicity; (ii) identification of susceptible sub-populations; (iii) understanding of the genetic determinants of the inter-individual variability; (iv) generation of testable hypotheses about toxicity pathways by leveraging genetic and genomic data from 1000 Genomes and HapMap Projects; and (v) can be used to build predictive in silico models for new individuals and chemicals.

Security Information: Any individual seeking access to the NIEHS campus will need to be prepared to show a photo ID (e.g., driver's license, or a company, government, or university ID) and provide pertinent information about the seminar (e.g., name of the speaker, host, or title of the seminar).

Individuals with disabilities who need accommodation to participate in this event should contact Debbie McCarley at 919-541-2384 or mccarley@niehs.nih.gov. TTY users should contact the Federal TTY Relay Service at 800-877-8339. Requests should be made at least 5 business days in advance of the event.



**Part 2: Estimating population-scale toxicities for
environmental chemicals from genomic and chemical
information**

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Using computational models to predict environmental chemical's toxicity risks is a very challenging task. The NIEHS-NCATS-UNC DREAM Toxicogenetics Challenge provided a valuable and unique opportunity for researchers worldwide to evaluate their prediction algorithms. Our team proposed to use hierarchical modeling workflows that emphasize the complexity of toxicity responses. To ensure model robustness and goodness-of-fit to the data, cross validation were used to identify the optimal model parameters, including descriptor types, machine learning methods, and consensus methods for the prediction. In this talk, I will discuss the approaches we used for winning both subchallenge 1 (predicting toxicities of compounds in new cell lines based on genomic information), and subchallenge 2 (predicting toxicities for new compounds based on chemical information). I will also talk about the lessons that we learned from this challenge and the future directions.