

## **NIEHS holds high throughput toxicogenomics platforms workshop**

*By Kristen Ryan*

Leaders in the field of toxicogenomics met at NIEHS Sept. 16-17 to discuss the best methods for prioritizing approximately 1,000 genes for use in high-throughput toxicogenomics platforms.

The genes will be used for determining the effects of environmental toxins on cells or tissues from humans, rats, mice, zebrafish, and *Caenorhabditis elegans*. The High Throughput Transcriptomics Workshop - Gene Prioritization Criteria gave presenters an opportunity to summarize their respective gene sets, and discuss how these sets have been used to screen disease or toxic agent-related responses in cells from humans or rodents.

### **Advancing predictive toxicology with gene expression profiles**

NIEHS Deputy Director [Richard Woychik, Ph.D.](#), welcomed the group. NTP Biomolecular Screening Branch Chief [Raymond Tice, Ph.D.](#), then addressed the workshop goals and how the gene list would be used to advance **Tox21**, a collaboration between several federal agencies to research and test chemicals using high throughput screening methods.

"In our next phase of Tox21, we plan to focus on high content screens and high throughput gene expression platforms, which is where this workshop comes in," Tice said. "We want to identify a set of genes that could be applied to virtually any cell type, whether it is *in vitro* or *in vivo*, and would allow us to screen large numbers of cell samples in a short time at low cost."

Joel Dudley, Ph.D., of the Icahn School of Medicine at Mount Sinai, discussed how large scale data integration could be used to select genes of interest. Justin Lamb, Ph.D., of Genometry Inc., described the development of the Broad Institute L1000 assay, and performance of the platform for detecting toxic responses in cultured human cells.

NTP molecular toxicologist [Scott Auerbach, Ph.D.](#), gave his presentation remotely, and asked the audience, "How does one balance data-driven versus knowledge-driven gene selection?" He argued that it is important to include chemical genomics data when selecting genes - a practice he uses to weight his gene selections.

The remainder of the first day included talks from Richard Judson, Ph.D., of the U.S. Environmental Protection Agency (EPA); David Gerhold, Ph.D., of the National Center for Advancing Translational Sciences (NCATS); Henghong Li, M.D., Ph.D., of Georgetown University; and Lena Smirnova, Ph.D., of the Johns Hopkins Bloomberg School of Public Health.

### **Setting the stage for the project's future directions**

[Daniel Shaughnessy, Ph.D.](#), a health scientist administrator in the NIEHS Division of Extramural Research and Training, outlined the workshop's focus for the second day, and set the stage for the morning's scheduled speakers. These included Ruili Huang, Ph.D., of NCATS; Avrum Spira, M.D., of the Boston University School of Medicine; Julia Gohlke, Ph.D., of the University of Alabama; Carolyn Mattingly, Ph.D., of North Carolina State University; and Christopher Willis, Ph.D., of Thomson Reuters.



*"Hopefully, by the end of this workshop, we will have identified the kinds of criteria we think are optimal for this gene prioritization process," Tice said. (Photo courtesy of Steve McCaw)*



*Lamb said large-scale gene expression profiling, using the L1000, yielded results that were similar to those produced using microarray studies. (Photo courtesy of Steve McCaw)*

The afternoon was reserved for discussion, which was led by NTP Deputy Division Director for Science [Nigel Walker, Ph.D.](#) Walker moderated several discussions ranging from the goals of the workshop, biological systems, technologies to be utilized, and the types of approaches best suited to select and prioritize genes.

One audience member wondered whether the central goal was to predict toxicity or disease. The majority of the group believed that predicting toxicity from a gene set was best suited for the proposed screening program. However, [John Bucher, Ph.D.](#), NTP associate director, said the aim was to determine overlap of chemically induced toxicity and disease pathways, to increase the probability of finding chemicals of interest to human health.

Tice concluded the workshop by providing a sequential set of future directions for the project, including the development of gene prioritization criteria based on responses to a request for information, publications, workshop presentations, and discussions.

(Kristen Ryan, Ph.D., is an Intramural Research Training Award fellow in the NTP Toxicology Branch.)



*Richard Paules, Ph.D., of the NIEHS Laboratory of Toxicology and Pharmacology, was particularly interested in using some of the gene sets to study the molecular mechanisms of response to environmental stresses. (Photo courtesy of Steve McCaw)*



*Judson summarized the EPA1000, a group of genes chosen because they are altered by chemicals and because of the pathways they affect. (Photo courtesy of Steve McCaw)*



*Gerhold laid out the pros and cons for an optimal method of picking genes for screening. He said, using an unsupervised, unbiased, mathematical approach is valid, but advocated that a supervised approach, using data from the literature and personal experience with genes, may be more useful. (Photo courtesy of Steve McCaw)*

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