

Report 9: Human Toxicology Project

Convener: Andrew Rowan

Brief History:

Following the NRC 2007 Toxicology in the 21st Century report, a consortium of NGOs and companies was put together to promote the establishment of an international big biology project (a la the Humane Genome Project) entitled the Human Toxicology Project. Toxicology has been an observational science for many years. Adverse effects in animals following chemical exposure are extrapolated to human experience using overly simplistic methods. The use of these animal-intensive approaches prohibits the evaluation of the tens of thousands of chemicals in commerce today. Over the past several decades, new technologies have been developed that have provided new insights into the normal biology of human diseases. Our challenge is adopting these new technologies and insights and applying them to the development of new predictive toxicology and risk assessment tools. These efforts will require multidisciplinary approaches involving toxicologists, bioinformaticists, geneticists, epidemiologists and many others. The challenge is how to develop and refine the new technologies coming on-stream to move forward in the most efficient and cost-effective manner to produce a quicker, cheaper and more predictive human risk assessment.

Discussion Highlights:

Robert Rickard – the HTP Consortium (6 multinationals, two NGOs, one research institute and one university) seeks to accelerate the transformation of human risk assessment away from the low and cumbersome animal methods to a new approach based on an understanding of key pathways elucidated by a range of high-throughput assays and improved bioinformatics tools and moving away from animals. Need international coordination and then international regulatory acceptance.

Develop a set of tiered approaches with HTS as first tier followed by different biological models to add depth to available data.

Discussion of mixtures led to a suggestion that one could begin to elucidate key pathways using SiRNA approaches to knock out genes in a cell one-by-one and identify key pathways that either protect from or sensitize to a particular toxicant.

Bioinformatic needs are a particular problem. New trainees are hired away as fast as they complete their training.

It is fairly obvious how the NP would be engaged and important in this idea but how would the intramural program be engaged? The intramural “reward” system does not necessarily encourage laboratories to support this type of activity. Possibility of developing better rewards and a “translational” health function to ensure that various NIEHS sectors all contribute to vision.

Recommendations:

1. Bio-informatics will be a key need as data volume increases. Address the need for producing more bioinformatics specialists and retaining them in NIEHS.
2. Look to change organizational culture to focus attention on translating new technologies (wherever developed within NIEHS) into the growing international attention to a new approach to toxicology.
3. Establish an extra-mural funding program to help coordinate and support the elucidation of critical pathways, new assays to follow those pathways, the use of functional genetics to support pathway elucidation and assay development.
4. Encourage and ease the dissemination of data to key publics such as epidemiologists and NGOs.

Discussion Participants:

Andrew Rowan, Janice Allen, John Cidlowski, Michael DeVito, Craig Newschaffer, Jerry Phelps, Robert Rickard, James Swenberg, Jack Taylor, Ray Tice,