Systems Toxicology 2013 - From Basic Research to Human Risk Assessment

Centro Stefano Franscini, Monte Verità, Ascona Switzerland, 28 April - 1 May 2013

http://www.systox2013.ch

Background

Humans are exposed to thousands of chemicals with potentially adverse effects, from the environment, diet, drugs and consumer products. At present, human risk assessment relies on animal studies and an empirical one-by-one approach to identifying and characterizing risks. This approach is costly in terms of time, money and animals, and it is far too limited in scope for the innovations of modern industry and the complexities of multiple exposures. In addition, there is increasing public reluctance to accept continued reliance on animal tests, and increased demands on risk assessors due to new chemical safety legislation.

Risk assessment is undergoing a paradigm shift with the development of new powerful and rapid systems-wide approaches, such as genomics, proteomics, metabolomics, molecular dosimetry, and computational biology. Based on these tools, the emerging systems toxicology paradigm relies more on *in vitro* and computational data, and changes the focus from empirical endpoints to modes of action and life stages. It also offers the potential to better define real human exposures to potentially harmful chemicals. However, the critical gap between these data and regulatory human risk assessment has not yet been bridged, and there are no harmonized global standards. It is therefore of vital importance to promote dialogue between basic scientists and experts in risk assessment and regulations, to clarify the needs, potential, and limitations of the systems toxicology approach.

Objectives

To evaluate how state-of-the-art systems biology tools are or can be used to elucidate toxic modes of action and provide realistic exposure and biological impact assessments.

To establish a framework for interpreting and applying systems toxicology data that will result in a major positive impact on risk assessment policy and regulation of chemicals.

Programme and key topics

The meeting uses an innovative 3-day workshop format that combines cutting-edge basic science presentations with highly interactive discussion and debate platforms, to address relevant current concerns in human toxicology.

The scientific cooperation inherent in cross-disciplinary systems toxicology (i.e. from basic science to data handling to risk assessment) is best facilitated in a focused, efficient, and interactive forum, and is a major driver of the conference format and objectives. The meeting will unite international forward-thinking senior and junior researchers with high-level European and American experts in human risk assessment and regulation of chemical hazards.

Four key topics are bridged in the meeting programme:

Key Topic #1: Framework for Systems Toxicology

Key Topic #2: Platforms, Basic Science, and Data Integration

Key Topic #3: Applications of Systems Toxicology (including posters, oral presentations and breakout sessions)

Key Topic #4: The Role of Systems Toxicology in Risk Assessment and Regulation

Programme details

Day 1: Sunday, 28 April 2013	
16:00	Registration open (until 19:00)
17:30	*Welcome apero*
18:30	*Buffet dinner*
20:00-21:00	**Opening Keynote Lectures** "**Transforming Toxicology: The Case for Change"** *Bob Kavlock*, EPA Office of Research & Development, USA and *Maurice Whelan*, EU JRC Systems Toxicology + ECVAM, Italy

Day 2: Monday, 29 April 2013	
08:45	Centro Stefano Franscini welcome
09:00	**Systems toxicology platforms** "**Toxome and -Omics in Systems Toxicology**" *Thomas Hartung*, Johns Hopkins, USA *"***EPA's Computational Toxicology Program: Predicting Chemical Toxicity, Exposure and Disease**" *Kevin Crofton*, EPA Integrated Systems Toxicology Division and National Center for Computational Toxicology, USA "**IMI eTOX**" *François Pognan*, Novartis Institutes for BioMedical Research, Basel, CH
10:30	*Coffee break*
11:00	"**Systems toxicology in pharmaceutical development**" *Thomas Singer*, Roche Pharmaceuticals, Basel, CH **"Metabolomics in vivo - importance of reference data to predict toxicity"** *Hennicke Kamp*, BASF Metanomics Health, DE "**Systems toxicology: gaining mechanistic insight through a more integrative omics approach**" *Nigel Skinner*, Agilent Technologies, Wokingham, UK
12:00	*Lunch break*
13:30	**Experimental enablers of systems toxicology** **"Enzyme Response Profiling: Integrating proteomics and genomics with xenobiotic metabolism and cytotoxicity"** *Shana Sturla*, ETH Zurich, CH **"Adductomics: DNA biomarkers in exposure, risk assessment and cancer prevention"** *Robert Turesky, NY State Department of Health, USA* **"Toxicogenomics in Hazard Assessment"** *Joost van Delft*, Maastricht University, NL
15:00	*Coffee break*
15:30	**Computational enablers of systems toxicology** "**Data Management, Normalization and Integration**" *Ioannis Xenarios*, Swiss Institute of Bioinformatics, CH *"***Reverse Engineering Disease Pathways***"* *Gustavo Stolovitzky*, IBM Research, USA *"***Computational Systems Toxicology: Network-based Biological Impact Assessment***"* *Manuel Peitsch & Julia Hoeng*, PMI R&D, CH "**The Virtual Patient: Multiscale modeling of disease processes**" *Thomas Paterson*, Entelos, USA
17:30	**Current Research in Systems Toxicology: Poster session** *with refreshments*
19:00	*Dinner*

Day 3: Tuesday, 30 April 2013	
09:00	**ACS/Chemical Research in Toxicology Keynote Lecture** **"Exposing the Exposome"** *Stephen Rappaport*, University of California, Berkeley, USA
09:45	**Breakout Sessions on Current Applications** Introduction, allocation of participants, moderator and rapporteur nomination. *"***Genotoxins in food***"*** "**Systems Toxicology in Drug Safety**" *"***Thyroid endocrine disruptors***"*
10:15	*Coffee break*
10:45	**Breakout Session Work** What is the basis of the current relevance/importance of the topic? Assess and critique any systems-oriented efforts to address the topic: who are leaders in this area and what has been accomplished? What information or tools are missing? How and to what degree can systems-oriented strategies impact this topic?
12:15	*Lunch*
13:45	**Current Research in Systems Toxicology** Selected oral presentations from submitted abstracts
14:30	**Systems Toxicology in Risk Assessment** **"What does Risk Assessment need from Systems Toxicology?"** *Alan Boobis,* Imperial College London "**Advancing the Next Generation of Risk Assessment**" *Ila Cote*, EPA, USA "**Translating Systems Toxicology-based Assessment into Risk Management**" *Marcel Leist*, University of Konstanz, DE
16:00	*Coffee break*
16:30	**Panel Discussion: "What data from biological systems-wide technologies will be needed in risk assessment and what can facilitate their interpretation?"**
18:30	*Conference dinner*

Day 4: Wednesday, 01 May 2013	
09:00	**CSF Award presentation**
09:15	**Breakout Session Reports -** Report presentations and Q&A (preparation for publication)
10:15-11:00	**Closing Remarks**: "**Transforming Toxicology: The Way Forward"** *Bob Kavlock*, EPA ORD, USA; *Maurice Whelan*, EC JRC, Ispra

Organizing committee

The meeting organizers represent critical domains of systems toxicology (i.e. data collection, data integration, and application to risk assessment) and a diversity of scientific and professional backgrounds.

Shana J. Sturla, PhD, is Professor of Toxicology at the ETH Institute of Food, Nutrition and Health in the newly established Department of Health Science and Technology. With a background in Chemistry, Professor Sturla leads research in developing innovative strategies for biomarker analysis. She is the Principal Investigator for the SNF Sinergia project "Systems-wide responses of colon cells to food components and impact on cancer drug action," in close collaboration with the University of Zurich Institute for Molecular Cancer Research, and ETH researchers in computational biology and systems biology. A recent recipient of a European Research Council Starting Investigator Award, she represents a basic science and academically oriented dimension of the program.

Manuel Peitsch, PhD, is Vice President for Biological Systems Research at Philip Morris International, as well as co-founder and Chairman of the Executive Board of the Swiss Institute of Bioinformatics (SIB). He has a background in biochemistry and computational biology and is currently very active in the area of systems biology-based toxicology. Over the past 15 years he has been an industry leader in informatics and biological networks, and has co-founded and co-organized the Basel Computational Biology Conferences.

Martin Wilks, MD PhD, is Director of the Swiss Center for Applied Human Toxicology (SCAHT), and has a background in Medicine and Clinical Toxicology. SCAHT is a network of Swiss scientists and toxicology professionals active in four core fields: regulatory toxicology, applied research, toxicology education, and third party services. The SCAHT is supported by the Swiss Confederation, namely the Federal Office of Public Health, State Secretariat for Education and Research, Federal Office for Agriculture, State Secretariat for Economic Affairs and the Swiss Agency for Therapeutic Products (Swissmedic). Dr. Wilks contributes a deep knowledge of human toxicology and risk assessment, and a high-level perspective of its many aspects on an international scale.

Rex FitzGerald, DPhil DABT, is Regulatory Toxicology Expert at the Swiss Centre for Applied Human Toxicology (SCAHT). He spent 10 years in academic research (zoology and functional neuroanatomy at Sussex, Groningen, and ETH Zürich), 10 years in industry (neuro- and reprotoxicology and gynecological endocrinology, Ciba-Geigy), and 15 years as an independent industry consultant in regulatory nonclinical toxicology and clinical safety.