Welcome to the inaugural newsletter of the American Society for Cellular and Computational Toxicology. This first issue will provide you with some basic information about the society, its board of directors, mission, member benefits, and plans for the future. You can expect these newsletters on a quarterly basis, and we welcome input on the content and features that would be most helpful and interesting to you, and the events you would like to see your society hold. First, let’s hear from ASCCT president, Rodger Curren, co-founder and president of the Institute for In Vitro Sciences.

**Letter from the President**

Welcome to all the new members of the ASCCT! The response to this new society – as evidenced by the number of individuals joining and by corporate sponsorships received – has been extremely encouraging. To date we have more than 50 new members from 18 states and five countries. We are especially encouraged by the number of members from outside North America, because even though we refer to ourselves as the “American” society, we will be international in our views and will strive to develop strong collaborations with similar societies around the world.

As your first president, I am very confident that the time was right to organize such a society. Our formation comes at a time when the National Academy of Sciences 2007 Report “Toxicity Testing in the 21st Century: A Vision and a Strategy” is still discussed—event debated—at essentially every toxicology meeting, when new breakthroughs in computational methods occur almost monthly, and when new ways of growing or interrogating human cells and tissues *in vitro* are published in virtually every issue of our well-read journals. As a group of individuals who are looking toward the next, best steps forward in discovering what are the true hazards and risks from chemical substances to which the human population is exposed, we cannot have found a better environment in which to birth our society. It doesn’t matter whether we term our interest “the new toxicology” or “21st-century toxicology” or “human-based toxicology” or any of a plethora of other appellations, our research activities all complement each other in our search for better knowledge.

The next few years will be exciting ones, because it will be during this time that we will be challenged with how to use all the information – both computational and biologically based – in an integrated way to provide us with the most accurate prediction of the potential hazards to humans and the
There will be scholarly debates, impassioned arguments, and violent disagreements, but we will all come to sane, logical conclusions in the end, and our society will be in the midst of it all. What the ASCCT will provide, if my vision continues within the society, is a forum where input from all stakeholders can be heard, and where we all can participate in critically evaluating the various positions, rationales, and data presented.

Much of the context of my vision of the ASCCT’s role comes from the early days of a society known as the Genetic Toxicology Association (GTA). The milieu in which the GTA was founded was this: It was the late 1970s, nearly 10 years after Bruce Ames and colleagues had published their first papers, essentially establishing the Salmonella plate incorporation test as the standard assay for chemical mutagenicity, and what was speculated to be carcinogenicity as well. Both the FDA and EPA were seeking ways to incorporate this assay into the regulatory arena, and industry and academic scientists wanted a way to make sure that information from their laboratories was included in the discussions. This wish grew into a rather geographically localized society centered around the regulators’ location (Washington, D.C.), and a large part of the chemical and pharmaceutical industry (New Jersey, Pennsylvania, and Connecticut). The GTA’s organizers believed that constructive face-to-face scientific discussion could be had between researchers from the federal government, industry, and academe. In fact, the productive exchange of data and research techniques did occur between the various stakeholders, and as a consequence of the activities of this society – assisted by other supporting efforts – a rather orderly and informed progression to the regulatory use of \textit{in vitro} genetic toxicology assays occurred.

This is what I hope can be provided by a dynamic and effective ASCCT. Of course geographical exclusiveness is no longer an advantage or necessity. In fact, we need to have members from across the Americas and around the world. And there will be many other bodies that will collaborate on these topics, as well. But the ASCCT is now out of the blocks and striding forward, as evidenced by our growing number of members from regulatory agencies, industry, academic institutions, and advocacy organizations.

It has been a busy first few months getting all the logistical necessities (organizational papers, incorporation documents, website, descriptive literature, etc.) in place, but most of this has now been successfully completed, thanks mainly to the exhaustive efforts of two of your board members Erin Hill and Kristie Sullivan!

Please stop by the ASCCT booth – YOUR BOOTH – at the upcoming SOT meeting in Washington, D.C., introduce yourself, and ask what you can do for your society. We will be at Booth #971. See you then!

Rodger Curren
23 February 2011

**Mission Statement**

The Society aims to provide an organized forum for discussion of cellular (\textit{in vitro}) and computational toxicology approaches especially as replacements for animal-based toxicology methods. Through its meetings and activities, the Society will facilitate the development, acceptance, and routine use of cellular and computational methods through open dialog between industry, academic, advocacy, and regulatory scientists. The Society strives to include the participation of young scientists to promote their contributions to the field.

ASCCT | www.ascctox.org | info@ascctox.org
Goals

• Facilitate the development, acceptance, and routine use of cellular and computational methods

• Increase the routine application and use of computational and in vitro methods for prioritization, classification, and risk assessment purposes

• Foster open dialog between industry, academic, advocacy, and regulatory scientists

• Include the participation of young scientists to promote their contributions to the field

• Strengthen cooperation between cosmetic, pharmaceutical, and chemical industry scientists and professionals

Membership Details

We offer memberships for students, individuals, and organizations. All members will receive:

• Our quarterly e-newsletter
• A discounted subscription to ALTEX and Toxicology in Vitro
• Discounted registration for ASCCT events
• Free educational webinars or seminars on related topics or tools
• News and event updates in the in vitro and computational toxicology field
• The chance to network with regulators, scientists, and policymakers on the cutting edge of nonanimal toxicology

Organizations that contribute by Aug. 31, 2011, will be considered Founding Sponsors and will receive one lifetime complimentary individual membership, display of their logo on the ASCCT website, and other advertising benefits over the life of the society.

All members will be helping to build a strong, active society and contributing to the future of toxicology.
President Rodger Curren
Dr. Rodger D. Curren, president of the Institute for In Vitro Sciences, Inc., received his B.S. in biology from Purdue University, his M.S. from Ohio University and a Ph.D. from the Institute of Microbiology at Rutgers University. After more than 10 years of specializing in genetic toxicology, he created an in vitro toxicology division as part of Microbiological Associates (now BioReliance) in 1988. This activity was subsequently incorporated as a nonprofit institute, the Institute for In Vitro Sciences, Inc. Since 1997 the Institute has provided educational and laboratory-based resources to industry, government, and animal welfare organizations. Dr. Curren serves on many national and international committees and science advisory boards of organizations focused on alternative methods to animal testing. Among other activities, he is currently a member of the Scientific Advisory Committee for the European Union’s validation authority, ECVAM. Dr. Curren’s efforts in optimizing and promoting new alternative methods have earned him several honors in the in vitro field, including the Russell and Burch Award, the Bjorn Ekwall Memorial award, and the William and Eleanor Cave award for outstanding achievements in the development, validation and advancement of humane alternatives for product testing.

Treasurer Erin Hill
Erin Hill received her bachelor’s degree in 1990 in cell biology and biochemistry from the University of California, San Diego, then joined Advanced Tissue Sciences and assisted in the marketing and sales of 3-D human skin constructs to the personal care and household products market. In 1995, she joined the in vitro toxicology division at Microbiological Associates with Dr. Rodger Curren. In 1997, she became a co-founder of the Institute for In Vitro Sciences, Inc., where she is currently an officer and a member of the board of directors. As vice president of program development, Erin is responsible for education, outreach, and fundraising activities, including interactions with industry, regulatory agencies and animal protection organizations. In 2010, Erin co-founded the ASCCT where she serves as treasurer.

Secretary Kristie Sullivan
Kristie Sullivan, M.P.H., is a science policy adviser with the Physicians Committee for Responsible Medicine. Since 2006, she has served on the EPA’s Pesticide Program Dialog Committee, a public advisory committee to EPA on pesticide issues. Ms. Sullivan also serves as Secretariat of ICAPO, a coalition of international organizations that advocate for policies that will reduce and replace animals in chemical testing guidelines at the Organisation for Economic Co-operation and Development. Ms. Sullivan received a B.S. in biological anthropology in 2001 and a Master of Public Health in Toxicology in 2003, both from the University of Michigan. Before joining PCRM, Ms. Sullivan worked at the University of Michigan Occupational Safety and Environmental Health Environmental Laboratory and the NYC Department of Health and Mental Hygiene.

Mel Andersen
Dr. Mel Andersen is the director of the Institute for Chemical Safety Sciences at the Hamner Institutes for Health Research in Research Triangle Park, N.C. Over a 40-year career in toxicology, he held positions in the federal government (U.S. Navy, Department of Defense, and EPA), private industry (vice-president of ICF Kaiser Consulting) and academia (Colorado State University). His research career has focused on computational approaches for dose response modeling and human health risk assessments for environmental chemicals and increasingly is closely aligned with accelerating toxicity testing approaches outlined by the 2007 NAS report, Toxicity Testing in the 21st Century: A Vision and Strategy.
Enjoys Reduced Subscription Rates for Two Top Journals

As a member of the ASCCT, you are entitled to reduced subscription rates to two top journals covering the cellular and computational toxicology fields: *Toxicology in Vitro* and *ALTEX-Alternatives to Animal Experimentation*. *ALTEX* is published by the Center for Alternatives to Animal Testing and is a “quarterly journal for new paths in biomedical science.” *TIV* is published by Elsevier and publishes articles on the use of “in vitro systems for assessing or predicting the toxic effects of chemicals and elucidating their mechanisms of action.”

Please contact ASCCT secretary Kristie Sullivan for more information or to subscribe.

Thomas Hartung, M.D., Ph.D., has studied biochemistry, medicine, and mathematics in Germany at the Universities of Cologne, Hagen, Tübingen, Freiburg, and Konstanz. In 2002, he became head of the European Centre for the Validation of Alternative Methods at the EU Joint Research Center in Italy. In 2003, he was appointed full professor of the University of Konstanz, Germany, for Pharmacology and Toxicology. He is endowed chair (Doerenkamp-Zbinden Foundation) for Evidence-based Toxicology, Department of Environmental Health Sciences, Bloomberg School of Public Health, Johns Hopkins University, and director of their Center for Alternatives to Animal Testing. In 2010, he received a joint appointment for medical microbiology and immunology at this institution. He has authored more than 350 publications.

Dr. Chad Sandusky is director of research and senior toxicology adviser at the Physicians Committee for Responsible Medicine. He promotes alternatives to the use of animals in research and coordinated the review of and preparation of comments on the Environmental Protection Agency’s High Production Volume Challenge Program. Dr. Sandusky also served as a core expert panel member for the EPA’s Voluntary Children’s Chemical Exposure Program. Before joining PCRM he was employed by the EPA, where he served on the Pesticide Research Committee, worked as toxicology team leader, and served as senior author of numerous EPA documents.

Dr. Chihae Yang, vice president of toxicology and predictive modeling, joined Leadscope, Inc., in 2000 from her position as a tenured chemistry professor at Otterbein College and adjunct professor at the Ohio State University. She brings 25 years of experience in computational chemistry applied to lipid membranes, colloidal systems, and polymeric materials. At the Clorox Company, she invented and successfully commercialized innovative polymeric films to the national market, leading a team of product development chemists and engineers. She also has served as a consultant in statistical design and analysis, and currently teaches at the Ohio State University in statistical design and molecular informatics. Dr. Yang received her B.S. from Seoul National University and her Ph.D. from the Ohio State University.
A Little Bit of Background ...

Stephanie Ringeissen: “I am a chemist by training who discovered the field of toxicology during my thesis. At that time I knew little about computational toxicology. It is when I started to work at L’Oreal in Research & Innovation that I uncovered this challenging and exciting discipline.”

Chihae Yang: “I have been in the area of computational modeling for a couple of decades, but had to learn toxicology to be able to solve real problems. Through the collaborations with FDA, I realized that if computational methods were to be employed in the risk assessment, they must be intuitive, interpretable, and transparent. After ten years, I humbly admit that I still strive to bring suitable methods to the reviewers.”

Collaboration Important

Developers of in silico models should work hand-in-hand with both in vivo and in vitro toxicologists - they know the experimental assays and have an understanding of the factors that influence the biological response. They should also be involved in constructing structured databases suitable for structure-activity studies.

Indeed, what makes our job exciting on a day-to-day basis are the multiple and stimulating interactions with safety evaluators and chemists to develop in silico alternatives to animal testing. Safety evaluators need alternatives to animal testing for hazard identification and human health risk assessment (e.g., building of dossiers for regulatory bodies). Chemists need tools to screen and prioritize new chemical series. Experts in specific fields are also very much involved (e.g., characterization of physicochemical properties).

We recently benefited from such interactions to develop a safety assessment workflow to predict the severity of skin irritancy where mechanisms of toxicological action were considered to build intuitive mode-of-action models. Mechanistic knowledge was used to develop relationships between physicochemical properties of compounds and toxicological hazard. Another illustration of how valuable multi-expertise interactions are comes from the building of Integrated Testing Strategies (ITS) with in vivo/in vitro toxicologists, physical chemists, in silico model developers and statisticians. Indeed one can only feel humble about the challenges and thus appreciate expertise of others.

Progress/Interactions at the International Level

Due to numerous international regulatory initiatives, a real need in computational toxicology is recognized. Developing alternatives to animal testing including computer-based approaches has been the main focus. The following is a short example of the list of supporting activities:
• The OECD and regulatory authorities (OECD QSAR Toolbox with ECHA)
• The EU (Framework programs such as OSIRIS, OPENTOX, ORCHESTRA)
• The EU and industry partners (EPAA, FP7/COLIPA program on systemic toxicity)
• Regulatory agencies (US EPA: DSSTOx, ToxCast; US FDA: CERES)

Challenges Facing Computational Toxicologists

No single computational model is capable of “covering” or predicting the entire range of biological activities (e.g., ADME properties and toxicity profiles) needed to consider for safety testing under multiple exposure scenarios. Examples include absorption in multiple organs (e.g., skin and GI tract), abiotic metabolism (e.g., autoxidation reactions encountered during air exposure of some chemical entities), biotic metabolism in multiple tissues (e.g., skin and liver), and toxic effects (from skin irritation/skin sensitization to target-organ toxicity), among others. It is just not practically possible to be able to understand and represent the vast knowledge domain in one brush stroke.

One major challenge faced by members of the computational toxicology community is the delivery of tools that are flexible and intuitive, but robust enough to cover all that are necessary during the risk assessment process. These methods and tools must be utilized by wide variety of users—from chemists to safety evaluators—on a routine basis within their workflow. Only by working in a collaborative manner can we succeed. We truly hope that ASCCT will provide us such a collaborative forum.

Meet Other Members of Your Society

You can find the ASCCT in Washington and Montreal

We have garnered a booth at the Society of Toxicology meeting in Washington, D.C., March 6-11, 2011. Stop by Booth #971 for a visit—and bring your colleagues!

We are also planning an event at the 8th World Congress for Alternatives and Animals in the Life Sciences. This international conference take place every two years and brings together scientists and policymakers in all fields related to alternatives to animals in science. You can find out more information about the congress here: www.wc8.ccac.ca. The ASCCT has been brainstorming with the European Society for Toxicology In Vitro (ESTIV) to plan a co-sponsored event that will showcase the goals of the societies, encourage their members to get to know each other, and educate attendees on key issues in the field. Stay tuned for more details.
Selected Upcoming Events and Key Dates

**U.S. EPA/OPPT Sustainable Futures Training Workshop**
*April 27-29, Cincinnati, Ohio*
Sustainable Futures™ is a voluntary U.S. EPA initiative that aims to promote the incorporation of Pollution Prevention methods through stakeholder education on the proper use and interpretation of EPA/OPPT assessment models and methods. During this workshop you will learn to use a variety of EPA/OPPT computerized models and assessment techniques to evaluate the potential hazard and exposure of a chemical substance, as well as learning how to incorporate those components into a screening-level risk assessment. For more information, contact Ms. Kelly Mayo at U.S. EPA at mayo.kelly@epa.gov or by phone at 202-564-7662.

**Third International Conference on Alternatives for Developmental Neurotoxicity**
*May 10-13, Varese, Italy*
The DNT3 Conference is being held to discuss the adverse outcomes of altering critical processes in human neurodevelopment and how they can be mimicked under *in vitro* conditions, the available alternative methods and their capabilities, the role of systems biology approaches and how they will impact testing for DNT, and how to use *in vitro* data in decision-making processes. For more information: [http://ihcp.jrc.ec.europa.eu/events_workshops/dnt3conference](http://ihcp.jrc.ec.europa.eu/events_workshops/dnt3conference).

**Evidence-based Toxicology (EBT) Collaboration**
*March 10, Washington, D.C.*
A group of toxicologists with backgrounds in industry, government oversight, academia, and animal welfare have created the EBT Collaboration to foster the development of a process, based on the Cochrane Collaboration in Evidence-based Medicine (EBM), for quality assurance of new toxicity tests for the assessment of safety in humans and the environment. To start the collaboration and solicit input from the stakeholder community, the EBT Collaboration steering group is organizing a kick-off meeting immediately following SOT. The EBT Collaboration is anticipated to be a long-range activity and be pivotal in helping to influence the development and implementation of new toxicity tests. For more information: [http://caat.jhsph.edu/programs/workshops/ebt.com](http://caat.jhsph.edu/programs/workshops/ebt.com).

**March 10: Deadline for application, Johns Hopkins Center for Alternatives to Animal Testing 2012-2013 grants**

**April 10: Deadline for abstracts, 8th World Congress on Alternatives and Animals in the Life Sciences**

**May 5: Deadline for application, US EPA STAR Program (Developing High-Throughput Assays for Predictive Modeling of Reproductive and Developmental Toxicity Modulated Through the Endocrine System or Pertinent Pathways in Humans and Species Relevant to Ecological Risk Assessment)**
NEWS

Animal testing alternatives come alive in US

In Europe, long-standing public opposition toward animal testing has led to a broad push to develop alternative means for assessing the potential hazards of drugs. But similar efforts across the Atlantic have often lagged far behind. Now, with the formation of a new society dedicated to finding nonanimal testing methods, as well as new government programs, many experts perceive a sea change in US policy.

“There just seems to be an uprising and enthusiasm in the US for finding these alternative methods,” says Erin Hill, vice president of program development at the Institute for In Vitro Sciences, a nonprofit testing center in Gaithersburg, Maryland.

Hill, together with Kristie Sullivan from the Physicians Committee for Responsible Medicine, unveiled the new ‘American Society for Cellular and Computational Toxicology’ at the In Vitro Alternatives Forum in Alexandria, Virginia this past October. Although only a handful of non-board members have signed up to the society thus far, “we’re getting a couple more each day as word gets out,” says Sullivan.

“It’s an important step,” remarks Thomas Hartung, director of the Center for Alternatives to Animal Testing at Johns Hopkins University in Baltimore and a member of the new society’s board of directors. He points to a “long-lasting tradition in Europe of alternative methods” for testing compounds, adding that “in the US involves the US Environmental Protection Agency (EPA) and the US National Institutes of Health, aims to determine an experimental compound’s safety earlier in the drug discovery process by comparing its molecular characteristics to a database of around 3,000 pharmaceutical compounds and 7,000 environmental chemicals with known toxicity profiles. Next, the initiative plans to add watersoluble compounds and complex mixtures of chemicals, too.

“The goal is to develop fingerprints for compounds,” explains Raymond Tice, chief of the Biomolecular Screening Branch at the US

As part of Tox21, the EPA has also completed the first phase of its ToxCast program, which involved rigorously testing around 300 chemicals (mostly pesticides) in close to 500 assays in multiple human and animal cell lines to determine which chemicals activate different metabolic pathways (Environ. Health Perspect. 118, 485–492, 2010). Comparing the results with in vivo data, the researchers found that the more cellular pathways perturbed by a chemical as observed in a lab dish, the lower the dose at which the chemical causes toxicity in animals.

According to Robert Kadlock, director of the Office of Environmental Health Assessment and Human Exposure Science at the EPA, the goal of Tox21 is to

...read the rest at nature.com (doi:10.1038/nm1210-1348).

Selected Online Resources

• OECD QSAR Application Toolbox: www.qsartoolbox.org
• Euroecotox: https://sites.google.com/a/euroecotox.eu/netwerkeuroecotox/HOME
• In Vitro Jobs Bank: www.invitrojobs.com
• International QSAR Foundation: www.qsari.org
• US EPA CompTox program: www.epa.gov/comptox

Have an idea for this section, or for an educational webinar or in person seminar? Let us know!
Founding Sponsors

Many thanks to our founding sponsor organizations for their support of cellular and computational toxicology development and implementation. Additional founding sponsors will be accepted until August 31, 2011.
How would you like to connect?

One of the main goals of the society is to increase coordination, cooperation, and communication between professionals and scientists from different fields, regulatory sectors, and points of view.

As Secretary, I hope to send ASCCT members communications from time to time sharing conferences, events, news articles, or scientific resources that might be of interest. Would you prefer to receive these updates via e-mail, through the LinkedIn discussion group, the ASCCT website, or even Twitter? What online discussion formats do you currently use and find useful? Please let us know.

Find us on LinkedIn

We have created a discussion group on LinkedIn (www.linkedin.com), a business-oriented social networking site. If you already use LinkedIn, or you plan to join, simply search for “American Society for Cellular and Computational Toxicology” on the website and join the group.

Contact the ASCCT

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