



Immunotoxicology Specialty Section Newsletter

**2014-2015
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The ImTox SS Newsletter is published 3 times/year (Summer, Fall, and Winter). If you would like to share an item of interest with members of the ImTox SS, please send it to the Communications Committee Chair. All comments on, or suggestions to, the newsletter are welcome.

Ashwini Phadnis-Moghe
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President's Message

In the last issue of the Newsletter I noted that the ITSS is approaching its 30th anniversary in 2015. This milestone in the history of our specialty section has inspired me to reach out to Dr. Jack Dean, Founding President, Dr. Daniel Wierda, 11th President and Dr. Kenneth Hastings, 21st President, and ask if they would be willing to share their thoughts and highlights from the ITSS history. I am delighted to say that they responded enthusiastically to my request and wrote three articles for a mini-series entitled "History of the Immunotoxicology Specialty Section" that is published in this issue. I would like to express my great appreciation to Jack, Dan and Ken for their contributions and hope that our "seasoned" members will enjoy the memories and our young members will learn about key players and the main work areas covered by this specialty section from its beginning to the present time. Enjoy the reading!

*Danuta Herzyk,
President, ITSS (2014-2015)*



**Dr. Danuta Herzyk
President, ImTox SS
2014-2015**

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Student & Postdoctoral Report

As the end of the year approaches, I hope that you are all getting excited for the 54th annual SOT meeting in San Diego, CA. Remember that there are many great opportunities for students and postdocs to get involved, including creating a video for the YouTox challenge. Students and postdocs are invited to submit a short video answering the question “Why did I become a toxicologist?” Cash prizes will be awarded, so get creative and have some fun! (Deadline is Jan 14; more information available at <http://toxicology.org/ai/spd/studentservices.asp>).

At the 54th annual SOT meeting, immediately after the ITSS reception, members of the ITSS Executive committee (on Tuesday, March 24, 2015) will be hosting a Networking/Mentor panel discussion with students and postdocs. Be sure not to miss out on speaking with immunotoxicologists from academia, industry, and the government!

Don't forget, the deadline for award nominations is quickly approaching. Awards available to students and postdoctoral ITSS members include Best Presentation by a Student, Best Presentation by a Postdoctoral Trainee, and Best Paper of the Year. Many travel awards are also available through the specialty section and through SOT; check out the websites for details and deadlines. <http://www.toxicology.org/ISOT/SS/imtox/Index.asp>

Lastly, I'd like to remind everyone to make sure their SOT member information is current and correct so you don't miss email reminders of the numerous events and activities available to students and postdocs! Upcoming events include Chat with an Expert, Poster Tours, and Student/Postdoc Mixers at the annual SOT meeting. If you would like to get involved in planning these great events, or have any comments/suggestions, please contact **Aimee Hillegas** (ahillegas@mail.usciences.edu) or **Ashwini Phadnis** (phadnisa@msu.edu).



Announcements!

Immunotoxicology networking event for graduate students and postdoctoral researchers

Wish there was more time to network with immunotoxicologists?

Join us for the first 'Immunotoxicology Networking Event' where you can meet a panel of immunotoxicologists from industry, academia, government and consulting firms. It is an opportunity not to be missed especially if you are a graduate student or postdoc wondering about a future career in this field. This event will be held on March 24, 2015 following the ITSS reception. More details of the event will follow soon. Please watch this space for more information in the next newsletter. Email reminders and a link for signing up will be sent to the graduate student and postdoctoral members of the specialty section soon!



ITSS-sponsored sessions at the 2015 SOT Annual Meeting

The sessions submitted by our membership for consideration at the annual meeting were fantastic and well received. Among 19 sessions that the ITSS sponsored for review by the program committee, eight were ultimately accepted as sessions at the annual meeting. This reflects the general interest in our discipline and the science we pursue, the broad interactions immunotoxicology has with other areas of toxicology, and the high quality work conducted by our membership.

The sessions sponsored by the Immunotoxicology Specialty Section at next year's meeting promise to be extremely compelling and timely. Stay tuned as the final program develops for when these sessions will be presented, but in the meantime I'm pleased to share the approved sessions, below.

Congratulations to those who had sessions accepted, and many thanks to all who submitted session proposals! Your efforts in putting these session proposals together are highly appreciated and extremely valuable to our discipline and the broader community. In addition, I want to thank those volunteers who helped review these proposals as we put them forward for consideration by the SOT Program Committee.

As we prepare for the year ahead, it is not too soon to begin thinking about important, high impact areas of immunotoxicology research that should be discussed in 2016 – the clock for these session proposals begins at the end of the annual meeting, with formal proposals due at the end of April, 2015! I'm looking forward to seeing you all in what promises to be a fascinating meeting.

All the best.

Rafael Ponce, Program Committee Chair

Workshop Session (Chairs)

Current Understanding of Immune-Mediated Adverse Drug Reactions (Arno Siraki, University of Alberta and Alison Harrill, University of Arkansas)

Strengths and Weaknesses of Mouse Models in Studies of Immunological Effects of Drugs and Chemicals (Courtney Sulentic, Wright State University and Bindu Nanduri, Mississippi State University)

Continuing Education (Chairs)

The New World of Cancer Immunotherapy: Challenges in Bench to Bedside Translation (Rodney Prell, Genentech and Rafael Ponce, Amgen)

Skeletal System Endocrinology and Toxicology (Alan Hoberman and Susan Smith, Charles River Laboratories)

Roundtable Session (Chairs)

Should Respiratory Sensitizers Be Listed As Substances of Very High Concern (SVHC) under REACH? (Jon Hotchkiss, Dow Chemical Company and David Basketer, DABMEB Consultancy, Ltd.)

Symposium Session (Chairs)

Epigenetics, Developmental Programming, and Immune Function: Where Do We Go from Here? (Berran Yucesoy, University of Cincinnati and Victor Johnson, Burleson Research Technologies)

Immune Responses to Different Classes of Inhaled Particulates: Unique vs. Shared Responses and Mechanisms (Andrij Holian, University of Montana and Seishiro Hirano, National Institute for Environmental Risk, Japan)

Immunostimulant Cancer Treatments: Toxicology Programs with an Autoimmune "Twist" (Lauren Black, Charles River Laboratories and Helen Haggerty, Bristol-Myers Squibb)

Call for Nominations from the Awards Committee

Did you read an outstanding immunotoxicology paper this year? Read a presentation abstract that was amazing? Work with someone who you think embodies excellence in the field of immunotoxicology? If you answered yes to any of these questions, I urge you to nominate the author, the presenter, or the colleague for an award from the Immunotoxicology Specialty Section.

Recognizing these important contributions of our Specialty Section's students, postdoctoral scientists, and colleagues is one of the most important undertakings of our Specialty Section. Additionally, acknowledging the excellence of the scientists within our Specialty Section helps to demonstrate how our science furthers the mission of the SOT.

Please make it difficult for the Awards Committee to choose recipients for these awards. Please nominate a student, postdoctoral scientist, or colleague for one of the Immunotoxicology Specialty Section Awards. You also may nominate yourself for one or more awards. Descriptions of awards, Awards Committee contacts, and due dates are listed below. **For a more detailed description of the awards and their nomination criteria, please visit the Immunotoxicology Specialty Section web site (<http://www.toxicology.org/ISOT/SS/imtox/deadlines.asp>).**

Jamie DeWitt, Awards Committee Chair



Vos Lifetime Career Achievement Award in Immunotoxicology

This award was named for the late Professor Jeff Vos and will be presented to a senior investigator whose body of work represents an outstanding career in immunotoxicology. Please submit nominations to Danuta Herzyk by January 16, 2015.

Outstanding Senior Immunotoxicologist Award

This award will be presented to a senior investigator with more than 10 years of experience since obtaining the highest degree and whose work has made significant contributions to the field of immunotoxicology. Please submit nominations to Rafael Ponce by January 16, 2015.

Outstanding Young Immunotoxicologist Award

This award will be presented to a young investigator with 10 years of less of experience since obtaining the highest degree and whose work has made significant contributions to the field of immunotoxicology. Please submit nominations to Rafael Ponce by January 16, 2015.

Best Paper of the Year Award

Authors of the paper deemed to be the best paper in immunotoxicology will receive this award. The paper must have been published between January 1 and December 31 of the previous calendar year and the first publication date (paper or e-version) will be considered the publication date. Immunotoxicology papers published in any peer-reviewed journal are acceptable. Please submit nominations to Jamie DeWitt by January 16, 2015.

Best Presentation by a Postdoctoral Trainee Award

Postdoctoral trainees who are presenting (poster or platform) at the 2015 SOT Annual Meeting are eligible for this award. Nominees are asked to submit a written version of an immunotoxicology presentation to be made at the Annual Meeting and a letter of nomination from the trainee's advisor. Please submit materials to Jamie DeWitt by January 16, 2015.

Best Presentation by a Student Award

Students who are presenting (poster or platform) at the 2015 SOT Annual Meeting are eligible for this award. Nominees are asked to submit a written version of an immunotoxicology presentation to be made at the Annual Meeting and a letter of nomination from the student's advisor. Please submit materials to Jamie DeWitt by January 16, 2015.

HESI Immunotoxicology Young Investigator Travel Award

ILSI HESI sponsors this award to assist young investigators (≤ 5 years from completing a graduate dissertation) in attending SOT and presenting their research. Both US and international investigators are encouraged to apply. Please submit nominations to Danuta Herzyk by January 16, 2015.

NEW AND NOTEWORTHY

Dr. Rodney Dietert, Professor of Immunotoxicology at Cornell University College of Veterinary Medicine appears in the recently-released documentary film, Microbirth (www.microbirth.com). Filmed partly at Cornell University, the movie deals with the impact of the microbiome, birth delivery mode, and immune development on later-life health risks. In October, the film won the Grand Prix at the 2014 Life Sciences Film Festival in Prague among 39 entries (<http://www.lsff.cz/en>).

SAVE THE DATE!

54th Annual Society of Toxicology Meeting
March 22-26, 2015
San Diego, California

Late Breaking Abstract Submission- January 12, 2015

Early Registration Deadline- January 31, 2015

Housing Reservation- February 19, 2015

Standard Registration Deadline- February 28, 2015



Immunotoxicology: The Early Years 1977-1995

Submitted by the Founding President of the ITSS – Dr. Jack Dean

It is important to understand how the interest in immunotoxicology developed and flourished among toxicologists within government regulatory agencies and the pharmaceutical, chemical and consumer product industries. The earliest interest in immunology among toxicologists started with the observation that certain environmental chemicals (e.g., dioxins, PCBs, some pesticides, etc.) appeared to target the immune system and alter its function as was highlighted in an early publication by J. Vos (1977). In parallel, the discipline of immunopharmacology caught the interest of many in the 70's, including this author, as the search for new chemical entities (NCEs) possessing immunological activity and therapeutic potential flourished. In many pharmaceutical companies, immunologically active NCEs and cytokines became a development target for the treatment of cancer, viral diseases and immune deficiencies.

During the 1980's toxicologists in industry were confronted for the first time with the safety assessment of protein therapeutics (e.g., monoclonal antibodies, IFNs, lymphokines, cytokines, etc.) and NCEs possessing novel immune activity. Consequently, most of the scientists working in the developing discipline of immunotoxicology during this period got their training in pharmacology, immunology or immunopharmacology, and rarely toxicology.

Recognizing the importance of this emerging field, the Gordon Research Conference on Drug Safety in the summer of 1978 devoted two days to immunotoxicology which represented the first symposia on this topic. Shortly thereafter, the first Workshop on Methods and Approaches for Assessing Immunotoxicology was organized in Williamsburg, VA, and was attended by over 50 scientists and physicians. The Williamsburg meeting was immediately followed by an NIH/NIEHS Consensus Meeting in Research Triangle Park, NC, with the objective of defining specific research needs for this newly emerging field of immunotoxicology. During 1979-1982, the National Institute of Environmental Health Sciences/NIH directed a major study on the immunobiological and toxicological effects of polybrominated biphenyl contamination in Michigan farmers and chemical workers. This was one of the earliest examples of environmental exposure to a potentially immunotoxic agent.

This followed in 1981 with NIEHS awarding contracts for the development and validation of method in rodents for immunotoxicology assessment. These contracts went to A. Munson, et al., at the Medical College of Virginia and P. Thomas, et al. at The Illinois Institute of Technology.

The discipline of immunotoxicology soon captured the imagination of the International Program on Chemical Safety (IPCS) of the World Health Organization (WHO) and the first WHO sponsored international meeting was held in 1984. During this meeting a formal definition was developed.

By the mid- to late-80's most major pharmaceutical companies began recruiting toxicologists or immunologists trained in immunotoxicology and established small groups to monitor for inadvertent immune side-effects of new drug candidates. In 1998 it was reported that there were 12 pharmaceutical companies with groups involved in the safety assessment of NCEs for immunotoxic potential.

During this period most of the focus was an ongoing efforts to standardize and validate these methods in rodents using a tiered or phased approach in addition to multiple ring studies.

The field of immunotoxicology has matured considerably since this early period when most of the focus was on methods development and validation in rodents. The field was successfully natured by the Society of Toxicology (USA) in 1985 with the formation of the Immunotoxicology Specialty Section with 50 charter members and J. Dean as the founding President. ITSS became one of the largest specialty sections within the SOT. This was followed in 1992 with the formation of the Immunotoxicology Technical Committee by the Health and Environmental Scientists Institute (HESI).

J.G. Vos, in CRC Crit. Rev. Toxicol. 5:67-101, "Immune Suppression as related to toxicology", 1977.

The second decade of ITSS (1995-2005)

Submitted by the 11th President of the ITSS- Dr. Daniel Wierda

I would characterize the decade from 1995-2005, in immunotoxicology terms, as the era of immunotoxicity regulations. In 1996-1997, the FDA Center for Devices and Radiologic Health, as well as the Office of Science and Technology, and the Office of Device Evaluation were working on guidance documents for immunotoxicity testing. Dennis Hinton reported that his final draft of the Red Book II was almost ready for publication. Ken Hastings and the FDA Center for Drug Evaluation and Research (CDER) began drafting an immunotoxicity guidance document while Joy Cavagnaro was leading FDA Center for Biologics Evaluation and Research (CBER)'s efforts in writing the Guideline for Preclinical Testing of Biotechnology Derived Pharmaceuticals. The Environmental Protection Agency (EPA) was intent on promulgating the Federal, Insecticide, Fungicide and Rodenticide Act (FIFRA) Immunotoxicity Testing Guideline in harmony with the Organization for Economic Co-operation and Development (OECD) which proposed that chemical pesticides should undergo immunotoxicity testing in rodents, and these tests should include the sheep red blood cell (SRBC) assay, serum IgG levels and thymus weights. On a similar front the EPA was working on test rules for analyzing air pollutants under the leadership of Vicki Dellarco and Mary Jean Selgrade. There were other regulatory initiatives underway as well: The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was developing criteria for utilizing the mouse local lymph node assay. It represented the 1st effort to determine how a weight of evidence approach might be used in immunotoxicity screens. In 2000, the Japanese Ministry of Health and Welfare proposed immunotoxicology as a safety topic for International Conference on Harmonization (ICH).

Other highlights of this decade: Bob Luebke organized an ITSS Methods Committee to promote the development, standardization, and validation of assays useful in the detection of immunologic impairment following exposure to chemicals. Mitch Cohen and Judy Zelikoff were leading ITSS in the development and promotion of lectures and continuing education courses in immunotoxicity at the NYU Environmental Immunotoxicology Department. Student Awards began in 1996 with George Shopp as one of the 1st organizers. Mitch Cohen launched the ITSS's first website along with a membership directory. The book Immunotoxicology and Risk Assessment was authored by Dennis Flaherty and published in 1999. Judy Zelikoff and Peter Thomas edited a book entitled Immunotoxicity of Metals in 1998 and the first edition of Jacques Descotes' book An Introduction to Immunotoxicology followed a year later. Jacques' Summer School in Immunotoxicology symposium series, held in France each year, was also in full swing.

The book Developmental Immunotoxicology edited by Steve Holladay was published in 2004. A workshop on environmental agents and autoimmune diseases was hosted by the National Toxicology Program (NTP) also that year. In 2003, the Northwest Immunotoxicology Conference was held at the University of Montana to explore the effects of synthetic and natural chemicals on the immune system.

Immunotoxicology hot topics during this decade reflected by publications and symposia, included benzene, TCDD, formaldehyde, neuroimmunotoxicity, autoimmunity, allergy, respiratory and aquatic toxicology. The immunotoxicology theme was also picking up interest among regional SOT meetings as evidenced by an increase in presentations on immunotoxicity. There was a steady increase in immunotoxicology publications related to asthma, allergy, and hypersensitivity, especially by Ian Kimber and colleagues, and the beginning crescendo of cytokine/chemokine-related immunotoxicity papers, as well as interest in the immunotoxicology of autism.

Although not comprehensive, I hope the above snap shot that I gleaned from the newsletter archives of the ITSS portrays the sense of growth and action prevalent during this decade. Building on the decade before, the immunotoxicological science of this decade grew a larger network of immunotoxicologists who helped mature the science of immunotoxicology and carried that knowledge forward to the next decade.

The third decade of ITSS (2005-present)

Submitted by the 21st President of the ITSS- Dr. Kenneth Hastings

Beginning in 2005, immunotoxicology was established as a mature science based on robust methodologies and sound underlying principles. By this time, many co-operative studies had been conducted and reported in peer-reviewed literature demonstrating intra- and inter- laboratory concordance using standardized methods (such as what became known at this time as the T-dependent antibody response assay: TDAR), appropriate predictability for human health (the murine local lymph node assay: LLNA), and validation of instrumental methods (such as flow cytometry) so that these could take a place beside other long-used tools (such as automated blood cell counters). What began as a long-term development and evaluation of methods was beginning to evolve into efforts to use these data for what we now call translational science (or medicine).

Three important trends began to develop after 2005. The first was increased interest in in vitro methods for immunotoxicology. The driving factors are more complex than generally appreciated. Political pressure to reduce the use of animals is certainly an important issue driving some of these efforts. In November, 2003, a workshop on "The use of in vitro systems for evaluating immunotoxicity" was held at the European Centre for The Validation of Alternative Methods (ECVAM), in Ispra, Italy. This meeting was a harbinger of things to come – such as efforts that are underway today to develop alternative methods (such as Tox21). But there were two other factors: tools were needed to develop biologic drugs where there were no adequate animal models (that is, lack of pharmacologic activity to the test article). The extreme example of this was the TeGenero disaster in which nonclinical safety studies failed to adequately warn of serious adverse effects in human volunteers. Finally, we are beginning to observe adverse effects on immune function that may be adequately modeled in animals, but for which other tools (computational toxicology, in vitro assays) may be at least as useful and may in fact be preferable for various reasons. Consider the issues of "anaphylactoid reactions" associated with both traditional as well as biologic drugs.

A second trend has been international outreach. Although SOT ITSS members had attended the Japanese Society of Immunotoxicology (JSIT) annual meeting in the past, at the 12th Annual Meeting in Tokyo in September, 2005, Mitch Cohen established with our colleagues there a standing relationship that is still thriving. Along with our long established collaborations with European members of SOT/ITSS, we assumed a more global presence.

Finally, the long-anticipated International Conference on Harmonization of Technical Requirements for Registration of Human Medicines (ICH) Guidance on Immunotoxicology was promulgated as S8 in the Spring of 2006 (actual date of adoption varies with the region). Although there is much to criticize about the guidance/guideline, it was (and still is) the only regulatory document on immunotoxicology that is *applied* internationally (yes, there are ISO, OECD, and WHO documents, but these do not have the same regulatory standing as an ICH guidance). ICH S8 needs, to use ICH parlance, “maintenance”, but it remains a useful document.

What has been most surprising to me has been that immunotoxicology has become an important issue in drug development. This may sound odd coming from someone who has a long career in pharmaceuticals, but my bias has always been that most drug-associated immunotoxic effects would likely be predictable based on known pharmacology of the test article. This isn't turning out to be true. First: drug allergy is a persistent problem in drug development and we still lack adequate tools to address this issue. Second: drugs intended to manipulate immune function (such as anti-inflammatories) continue to surprise. I can remember when JC virus was considered an “orphan virus”. We now know that it has pathogenic potential, unfortunately due to unanticipated drug-associated immunotoxicity. We now know that standard rodent carcinogenicity bioassays are inadequate to detect *known* human carcinogens that have effects on immunity, and we now have a much better understanding of why. Hopefully, this will lead to better methods for carcinogenicity assessment of, for example, biologics. Finally, thanks in no small part to Mitch Cohen and the *Journal of Immunotoxicology*, there is much more valuable cross-talk between immunotoxicologists and others who have been conducting related research. I suspect environmental immunotoxicology will remain the most important branch of the science, but we have experienced significant growth in many related areas over the last ten years and this is likely to continue.

Compiled by Haley Neff-LaFord. Anytime you have a new fully-published or electronically-available article to report, please send the citation to Haley Neff-LaFord at hnlaford@seagen.com

Asthma, Allergy, Autoimmunity & Hypersensitivity

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