

Immunotoxicology Specialty Section Newsletter



2000 - 2001

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The Immunotoxicology Specialty Section Newsletter is published 3 times/year (May, August and November). If you would like to share a book review, meeting report, interesting web site or any other item of interest with members of the Specialty Section, please send it to us by the middle of the month preceding the planned publication date. All comments on, or suggestions for, the newsletter are welcome.

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P r e s i d e n t ' s M e s s a g e

Dori Germolec

This is my last chance to speak with you via the newsletter before the annual meeting and I want to thank those of you who responded to my request for feedback in the July newsletter. After hearing from a number of you regarding our annual reception/business meeting, it appears that the majority opinion is to continue to have the meeting at the conference hotel. Our Specialty Section Reception will be held on Wednesday, March 28 from 6:00 p.m. to 7:30 p.m. at the San Francisco Marriott. We have been assured that we will be assigned a room large enough to accommodate our numbers, so please plan to attend.

Beginning next year, SOT is asking the specialty sections more than three years old to become self-supporting, meaning that our expenditures will need to match the monies we take in. This is going to mean increasing our revenues (such as seeking corporate gifts/sponsorship for our reception and/or awards) or significant belt tightening (providing the newsletter in electronic format only), as we are currently running a deficit of more than \$3,000 for the year 2000. This will be the number one priority on our agenda for the Specialty Section Executive Committee Meeting which also takes place during the national meeting. If you have any items which you would like to see addressed by the executive committee please contact myself or Bob Luebke so that we can see that they get on the schedule.

A positive aspect of the new budgetary structure is that the costs of nonmember speakers who participate in our symposia, workshops and roundtables at the annual meeting will be now covered by the National program committee. This should allow us more freedom in developing scientific programs for the meeting.

We are still seeking nominations for the Career Achievement, Young Investigator and Best Paper Awards. Please see the Awards Committee report elsewhere in this newsletter for nomination guidelines and deadlines. Because of changes in the ballot distribution schedule at National Headquarters the deadline for nominations for next year's officers was moved up to October 30. The quality of the nominees and the fact that we received at least 7 nominations for each opening made the selection of candidates extremely difficult. Please watch your e-mail for the ballots; please let us know right away if you do not receive this by the second week of November. The following names have been submitted to SOT as nominees for our 2001-2002 officers:

Vice President-Elect: Tom Kawabata and Steve Pruett
Secretary/Treasurer: Don Frazier and Jean Regal
Councilor: Greg Ladics and Jean Meade

Once again, I encourage you to contact me with any questions, suggestions or concerns that you have regarding our Specialty Section. I look forward to seeing you in San Francisco and don't forget to vote!

Education Committee Report

Submitted by David Lawrence

We have been having informal discussions regarding the development of an on-line text for the teaching of immunotoxicology. We have not received any decision from SOT Council whether an immunotoxicology textbook would be acceptable for publication on the SOT web site, but Dan Acosta was encouraging and thought that we should continue with the development of the idea. There are other possible options including our own web site for the text as well as dissemination of other ideas, procedures etc. An outline for the text will soon be released to all members of the Immunotoxicology Specialty Section for comment. Once the Education committee reviews the comments and finalizes the format for the text, we will be requesting authors. As originally suggested, we would like to have most first authors being predocs and postdocs with guidance from their sponsors.

Membership Committee Report

Submitted by Paige Lawrence

You likely all received an email plea from the Immunotoxicology Specialty Section Membership Committee requesting that you do three simple things:

1. When you pay your SOT annual membership dues, please check the Immunotoxicology Specialty Section Membership box. SOT Members can join a Specialty Section annually upon payment of their membership dues (\$15/Specialty Section)

2. Please encourage your students and postdocs to join this Specialty Section. Students and postdocs who are not members cannot be considered as recipients of poster and platform awards. Students can join one Specialty Section for free.
3. Please pay your SOT membership dues before December 31, 2000. Timely payment of dues on your part has an enormous monetary impact on our Specialty Section. For all Specialty Section dues paid in a given fiscal year, we receive \$13 of that \$15 to support our Specialty Section. We receive \$13 for every student who checks that box, regardless of the fact that a student can join for free. These monies go toward awards and the reception.

The Membership Committee also seeks input on ways to recruit more student and post-doctoral members. If you have any ideas, please share them with us. We can be contacted by email at:

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IN MEMORIAL



Dr. Robert Colinas, an Immunotoxicology Specialty Section member, recently passed away after a long and valiant battle against cancer. Rob earned his Ph.D. in Microbiology and Immunology from Albany Medical College in 1990. He pursued his postdoctoral research, which was NIEHS-funded, at Wadsworth Center on a project to assess the mechanisms by which benzene metabolites alter hematopoiesis. Even during multiple bouts of poor health, he courageously strove ahead. He had recently received his first RO1 grant to investigate the molecular mechanisms of cytokine-mediated protection against the hematotoxicity of benzene metabolites. Rob is survived by his wife Dr. Anne Walsh, who is also a member of the Society of Toxicology and the Immunotoxicology Specialty Section.

An Important Announcement Concerning the Newsletter

Beginning with this issue, the Specialty Section newsletter will be distributed to all members electronically, and posted on the Immunotoxicology Specialty Section page of the SOT website. You will need Adobe Acrobat Reader (available at no cost from www.adobe.com) to view or print the newsletter. The cost of having the newsletter printed and mailed to all members has become one of the larger items in our budget. By switching to electronic distribution, we eliminate both of these costs, and save a few trees along the way.

Awards Committee Report

Submitted by Liz Sikorski

The available awards in the Immunotoxicology Specialty Section for 2000-2100 are Career Achievement, Outstanding Young Investigator, Best Presentation by a Post-doctoral fellow, Best Presentation by a Graduate Student and Best Paper of the Year Award in an SOT journal. The Nominating Committee (President, last three Past Presidents, and Vice President-Elect) judges the Career Achievement Award. The Awards Committee judges the Best Presentation by a Post-doctoral Fellow and the Best Presentation by a Graduate Student awards. The Councilors judge the Young Investigator and Best Paper of the Year in an SOT journal Awards.

Below is a description of the various awards that will be presented at SOT 2001, as well as the requirements for the awards and the deadlines for submission. Most submissions are due by December 1, 2000. However, the submissions for the graduate student and post-doc awards are not due until February 15, 2001. [Please take time to look over the available awards and nominate those individuals that you feel are most deserving of recognition for their contributions to the field of Immunotoxicology!](#)

Career Achievement Award

An engraved plaque will be awarded to a Senior Investigator whose body of work represents an outstanding achievement in Immunotoxicology. The nominator should provide a discussion of the role that the individual's work has played in advancing the field of Immunotoxicology. A *curriculum vitae* and bibliography should also be

included. A second letter of recommendation from another investigator in the field would be helpful. Nominations of candidates will be considered for two additional years unless the nomination is withdrawn by the sponsor. Final decisions will be made by the Nominating Committee (Dori Germolec, Judith Zelikoff, Kathleen Rodgers, Scott Burchiel and Robert House). Please send your nominations to any member of the Nominating Committee. The address for Dr. Dori Germolec is: NIEHS, Environmental Immunology, PO Box 12233, Research Triangle Park, NC 27709 (T) 919-541-3230, (F) 919-541-0870, Email: germolec@niehs.nih.gov. The deadline for submission is December 1, 2000.

Best Paper of the Year in an SOT Journal Award

An engraved plaque will be awarded to the author(s) of the best paper in the area of Immunotoxicology, published either in *Toxicological Sciences* or *Toxicology and Applied Pharmacology* between July 1, 1999 and June 30, 2000. Dr. MaryJane Selgrade has put together a list of eligible Immunotoxicology articles from these two journals. This will be sent out via email to Immunotoxicology Specialty Section Members and can be perused to nominate the 'Best Paper of the Year in an SOT Journal Award'. Please make sure you look over this list and submit your nomination.

The nomination for this award should provide a full citation of the paper and a short discussion of the value of the research to the field of Immunotoxicology. Decisions on this award will be made by the Specialty Section Councilors. Please send your nominations to Dr. Elizabeth E. Sikorski, The

Procter & Gamble Company, Miami Valley Laboratories, PO Box 538707, Cincinnati, OH 45253 (T) 513-627-1360, (F) 513-627-1612, E-mail: sikorski.ee@pg.com. The deadline for submission is December 1, 2000.

Outstanding Young Investigator Award

An engraved plaque will be awarded to a scientist who has made significant contributions to the field of Immunotoxicology. The recipient must have less than 10 years of experience since obtaining his/her highest earned degree at the time when the award is presented. The nomination should summarize the contributions of the candidate scientist and should include a *curriculum vitae* and a bibliography. Decisions will be made by the Specialty Section Councilors. Please send your nominations to Dr. Elizabeth E. Sikorski. The deadline for submission is December 1, 2000.

Best Presentation by a Graduate Student and Best Presentation by a Post-doctoral Fellow

The award requirements are submission of a complete written version (including all graphs and tables) of an Immunotoxicology presentation to be made at the SOT 2001 meeting. This presentation is to be accompanied by a Letter of Nomination from the Student's or Post-doctoral Fellow's advisor. Electronic submissions are strongly encouraged. No manuscripts will be accepted. Please send your submissions directly to Dr. Elizabeth E. Sikorski. Winners will receive a plaque and cash award (generally \$250.00). The deadline for submission is February 15, 2001.

Regulatory Committee Report

Submitted by *Kenneth Hastings and Denise Sailstad*

CPMP

The European Agency for the Evaluation of Medicinal Products (EMA) Committee for Proprietary Medicinal Products (CPMP) has formally adopted the *Note for Guidance on Repeated Dose Toxicity (3BS2a; CPMP/SWP/1042/99)*. This new version of an old guidance (originally adopted in October, 1983) was written primarily to include information on immunotoxicity and novel excipient testing and to harmonize the document with relevant International Conference on Harmonization (ICH) guidelines. As was reported previously, this document appears to mandate inclusion of immunotoxicity evaluation in standard repeat dose toxicity testing of investigational drugs. According to page 5 of the document (under section 6.4: Guidance on Immunotoxicity) all new medicinal products should be screened for immunotoxic effects in at least one repeat dose toxicity study. The suggested length of exposure to the test drug is from 14 days to 3 months (although it appears that the 28 day rodent study is the standard). Interpretation should be based on "...analysis of changes in lymphoid tissues and immune cell populations..." as well as other general health indicators. What this means in practice is a little unclear: it could be interpreted to mean that standard histologic examination of lymphoid tissues and general clinical pathology parameters such as white blood cell counts and serum immunoglobulin levels would suffice. It could also be interpreted to mean

that immunohistochemistry for differentiation markers in lymphoid tissues and immunophenotype determination by flow cytometry should be performed. The guidance does state that if signs of immunotoxicity are observed in the screening phase, follow-on studies should be conducted on "...a case-by-case basis...". The document refers the reader to Appendix B for more information. It should be noted here that there is a list of tissues to be examined histologically (Appendix A): this list includes blood smears, lymph nodes (mesenteric and any peripheral), bone marrow (from sternum, femur, or vertebrae), thymus, Peyer's patches ("when relevant"), and spleen. Thus, the document provides a relatively complete list of immune system tissues for standard histologic examination. In the next section (6.5: Terminal monitoring) there are two items that should be noted. First, if the drug is administered via inhalation, the lungs and "associated lymphoid tissue" should be examined (all dose groups). Second: "Bone marrow cellularity, lymphocyte subsets and NK-cell activity or the primary antibody response to a T-cell dependent antigen should be monitored in at least one rodent study..." As a practical matter, this could be taken to indicate that either flow cytometry with NK cell activity *or* some variation in the plaque assay (such as ELISA) should be conducted in at least one rat study. It is not clear if the two sections of the guidance (6.4 and 6.5) are consistent in what is needed for evaluation of potential immunotoxicity.

Appendix B gives a much clearer picture of what is intended for immunotoxicity testing. Screening for immunotoxic effects should be conducted as part of a standard repeat-

dose study in mice or rats. This screen should include hematology, lymphoid organ weights, histologic examination of lymphoid tissues, bone marrow cellularity, and either distribution of lymphocyte subsets and NK cell activity or primary antibody response to a T-cell dependent antigen (e.g. sheep red blood cells). Thus, immunotoxicity testing appears to be recommended consistent with section 6.5. In addition, Appendix B recommends a tiered approach to immunotoxicity testing with a number of functional assays, depending on effects observed in the screening bioassay. In summary, it appears that CPMP will now expect immunotoxicity evaluation as part of the standard battery of toxicity testing of new drugs to support human clinical trials and marketing approval. This document can be obtained from the EMA web site at: www.eudra.org/emea.html

ICH

The Japanese Ministry of Health and Welfare (MHW) and the Japan Pharmaceutical Manufacturers Association have jointly proposed immunotoxicology as a safety topic for ICH. This proposal will be forwarded for consideration at the next ICH meeting (November, 2000) in San Diego. By the time you read this, the decision will have been made: it is not clear at this time if there is sufficient support for writing another ICH safety document. The draft concept paper prepared by MHW and JPMA notes that two conditions indicate the need for an ICH guidance: the CPMP document discussed above and the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) decision to accept the murine local lymph node assay

(LLNA) as a validated alternative for hazard identification of potential skin sensitizers. The concept paper also notes that other regulatory agencies are likely to adopt guidances on immunotoxicity testing. If immunotoxicology is adopted as a new ICH topic, the initial meeting to formulate a document would likely be scheduled for May, 2001. Stay tuned. (For further information, visit the ICH web site at: www.ifpma.org.)

ICCVAM

(reported by Denise Sailstad)

A training workshop on the Local Lymph Node Assay (LLNA) is scheduled for January 25 – 26, 2001 at the National Institute of Health, Natcher Conference Center. The International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute's (HESI) Alternatives to Animal Testing Technical Committee has partnered with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to organize a training workshop for the LLNA. It has been acknowledged that in order to implement the use of new test methods, such as the LLNA, it is important to familiarize the regulated community with the method and the manner in which agencies expect the method to be conducted. Additionally, both users and agency staff need to become familiar with the technical procedures required to conduct the LLNA and understand its usefulness and limitations.

The primary objective of the workshop is to assist participants in gaining a practical understanding of the theory and application of the LLNA. Specific goals are to: 1) provide an overview of

the methods, applications, strengths and weaknesses of the LLNA, 2) provide information on the procedures for conducting and interpreting data in accordance with regulatory testing requirements and guidelines, 3) allow an opportunity to become familiar with data generated by the local lymph node assay, and 4) provide a forum for scientists to share information on the appropriate use of assay results in hazard, safety, and risk assessments. At this time the workshop is in the planning phase. More details and a preliminary program will be available soon. For more information, check the ICCVAM web site at: www.iccvam.niehs.nih.gov.

Program Committee Report

Submitted by Robert House

The Program Committee for the Immunotoxicology Specialty section is hard at work on programs for the 2002 annual meeting. Our Specialty Section has a long history of sponsoring interesting programs. However, we need your help in the process. We are soliciting suggestions for topics; naturally, we prefer having fully-developed proposals, but even suggested topics and recommended speaker suggestions would be welcomed.

Any of the members of this year's committee (Mitchell Cohen, Brian Freed, Robert House, Ian Kimber, Mike Lynes, Mike McCabe, David Shepherd) would be happy to help you develop an outline, put you in touch with potential co-chairs, or provide more information on the submission process. Since plans for 2002 will have to be finalized at the 2001 meeting,

there's no time to waste - please don't wait until the meeting to start thinking about this. If you have a topic in mind and ideas for a couple speakers let us know. We look forward to hearing from you!

Continuing Education ("hot topics" in toxicology that need to be reviewed)

- Basic courses are intended to familiarize investigators with a defined knowledge base or to assist them in developing, implementing or learning techniques or approaches.
- Advanced courses are intended to be of interest for those already working in the field.

Symposia ("cutting-edge" science, new areas for toxicologists; new concepts or approaches, new data)

- 3 hours or less
- Chairperson and 4-5 speakers (30 minutes per speaker)
- Summary of symposium by last speaker

Workshop (Topics requiring intensive study and discussion)

- 3 hours or less
- One to five speakers
- Informal, interactive presentations
- Emphasis on discussion

Roundtable (Controversial subject matter)

- ~1.5 hours
- Moderator and 2-4 speakers
- Moderator presents overview
- Each speaker makes a 3-5 minute statement (Moderator coordinates the comment)
- Balance of time for questions and discussion

Meeting Announcement

The PsychoNeuroImmunology Research Society (PNIRS) is an international organization for researchers in a number of scientific and medical disciplines, including psychology, neurosciences, immunology, physiology, pharmacology, psychiatry, behavioral medicine, infectious diseases, toxicology, and rheumatology, who are interested in interactions between the nervous and immune systems, and the relationship between behavior and health. An important goal is to conduct basic research that can be translated into clinically relevant health applications.

On behalf of the Psychoneuroimmunology Research Society and the 2001 Program Committee, it is our pleasure to invite you to submit an abstract for our 9th Annual Meeting to be held in Utrecht, Netherlands, May 16-19, 2001. The abstract deadline is January 5, 2001, and abstracts may be submitted on line at www.pnirs.org. Email should be sent to pnirs@pnirs.org.

Useful URLs

Volume 21 (8) of *Immunology Today* contains an article entitled "The Antibody Web", a summary of resources for immunology-related sites. The reference section is actually a list of 46 URLs to the various sites. If you have online access to the full text version via Elsevier's Science Direct site (www.sciencedirect.com), the URLs will appear as hotlinks in the HTML version of the article (not in the .pdf version). BTW, if your library subscribes to Elsevier journals, you can get full text access to all subscribed journals through your librarian.

OCCUPATIONAL CONCERNS

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Sugatani, J et al. (2000). Disorders in the immune responses of T- and B-cells in mice administered intravenous verotoxin 2. *Life Sci.* 67(9):1059-1072.

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RECENT IMMUNOTOXICOLOGY PUBLICATIONS

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RECENT IMMUNOTOXICOLOGY PUBLICATIONS

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NEUROIMMUNOLOGY

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SUPPLEMENTS AND SUCH

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BOOK REVIEW

Pulmonary Immunotoxicology

Editors: Mitchell D. Cohen, Judith T.

Zelikoff, Richard B. Schlesinger

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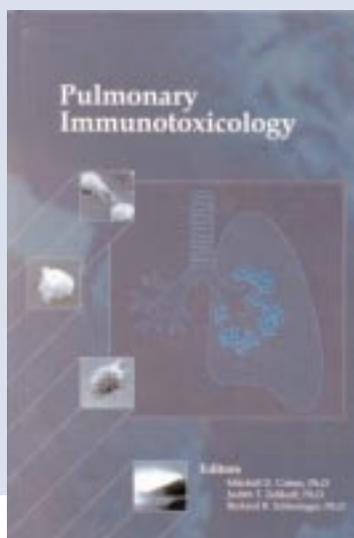
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Reviewed by Jean F. Regal

Many of us involved in immunotoxicology spend a great deal of time thinking about how substances can adversely affect the immune system. Those who identify themselves as pulmonary toxicologists spend a great deal of time thinking how substances can adversely affect the respiratory system. Another group, inhalational toxicologists, while away the hours examining how and when those nasty substances get into the lung.

Pulmonary Immunotoxicology combines the salient features of all of these viewpoints into a single volume.

The first section of the book deals with the respiratory tract itself, including a detailed view of the structure of the respiratory tract, with many informative tables comparing animal species commonly used in toxicology research. An overview of immunology is provided, especially as it relates to the response of the immune system to inhaled substances. In addition, the fate of inhaled particles is presented in a very organized and understandable fashion for a non-inhalational toxicologist. This first section of the book provides very good background information and includes references to pertinent reviews on each of the subjects

for more detailed information. The background chapters of the book would be quite useful in teaching either pulmonary toxicology or immunotoxicology.

In the second section of the book adverse effects of altered pulmonary immunity are divided into three chapters: Hypersensitivity and Asthma, Inflammation and Fibrosis, and Pulmonary Autoimmunity and Inflammation. In these chapters, the state of knowledge of the pathological mechanisms are considered. In addition, relevant examples of toxicant exposures which result in the particular adverse effect are provided. Missing from this list is a discussion of altered susceptibility to infection. However, in the following chapters of the book, the changes in susceptibility to infection are considered in detail for each of the immunotoxicants where data is available.

The third section of the book goes chapter by chapter through many of the agents which have been classified as pulmonary immunotoxicants. The toxicants chosen are logical and relevant. The authors are well respected scientists actively involved in research

in the area. A great deal of information is provided and each chapter serves as an excellent overview of the research for each immunotoxicant and provides an excellent jumping off point to examine the current research in the field.

I particularly found the fourth section of the book valuable. All of the information catalogued in the earlier chapters was put into a practical context in discussing such issues as "How do we arrive at reasonable exposure levels?" and "What do we measure to decide if a substance is harmful?"

Throughout the book, tables are used as the primary method of summarizing or compiling the information. One complaint regarding this book was the quality of the tabular material, as well as some housekeeping items: a number of publishing details (punctuation, hyphens, extra or missing words) escaped correction. In addition, a lack of indentation in the references sometimes made it difficult to locate the citation of interest.

Overall, this book provides a concise, yet thorough treatment of the subject matter of pulmonary immunotoxicology. It clearly fills an important niche, bringing information in the areas of pulmonary, inhalational and immunotoxicology together in one very useful volume.