Society of Toxicology

# Immunotoxicology Specialty Section Newsletter

## President's Message

*by Scott Burchiel*

Greetings from your elected officers. We hope that this newsletter finds you well. There are several information items that I would like to share with the membership.

First, I would like to encourage everyone with eligible predoctoral students and post docs to participate in our competition for awards for this year's annual meeting. The deadlines and other details are specified later in this newsletter. We want to maintain the excellent tradition of high quality posters and platform presentations by our students and members in-training and want to see good competition for these awards.

Second, SOT has been invited to provide names to NIH Staff of qualified individuals who might be willing to serve on NIH Study Sections. The Alcohol and Toxicology-4 (ALTX-4) study section is currently reviewing immunotoxicology grants. Therefore, we have been invited to submit names of potential reviewers and members for the Study Section. The procedure for submitting names has been left up to Specialty Sections, so please plan on giving us your input at our annual business meeting in Seattle.

Third, we were also invited to comment on the SOT Long Range Plan, and I participated in a conference call with Specialty Section Presidents and the SOT Council representative, Linda Birnbaum. Input was solicited from your elected officers, and we basically told Council that we would like more effective communication, including better use of web pages, and that we would like more involvement in communicating with the public.

Finally, many of you know that SOT will launch a new journal this spring to replace *Fundamental and Applied Toxicology*. The new journal will be titled *Toxicological Sciences* and will be edited by Curtis Klaassen. The ITOX Specialty Section has received letters and e-mails from the Publication Board and from SOT President Michael McClain requesting manuscripts. There will be a section of the Journal devoted exclusively to immunotoxicology, so let's plan on supporting this new journal.

We are looking forward to seeing you at the Specialty Section annual meeting in Seattle, which will meet Tuesday, March 3rd from 5:00 - 6:30 PM, tentatively scheduled for the West Ballroom AB. Please plan on attending our reception and business meeting, in which we will discuss business and announce our award winners.

## Vice President's Message

*by Kathleen Rodgers*
*Chair of Program Committee*

Greetings from sunny Southern California! Despite expectations to the contrary, we have not, as yet, been washed into the ocean by El Nino. All is well with the program for the Immunotoxicology Specialty Section for 1998. In the last newsletter, we informed you of our submissions to the SOT Program Committee and Continuing Education Committee, and I

will now report on those which have been accepted for presentation at the March meeting. These programs include: (1) a Continuing Education program entitled "Cytokines as Indicators of Toxicity: The Immune System and Beyond"; (2) a symposium entitled "Alterations in Cytokine Receptors by Xenobiotics"; (3) a workshop entitled "the Toxicology of Protein Allergenicity: Prediction and Characterization"; (4) a workshop entitled "Chemical Contact Allergy Structure Activity Relationships"; (5) a workshop entitled "Woodsmoke: Toxicological Impacts and Human Health Risks"; and (6) a workshop entitled "Immunotoxicity: Strategies to Identify Risk of Autoimmune Disease Associated with Chemical Exposure." As you can see, we had great success with our program and will be well represented in 1998. I extend my sincere gratitude to all the members of last year's Program Committee and the individuals that put together all the necessary pieces to allow such exciting presentations. I look forward to seeing all of you in March. If the above list generated any ideas for the 1999 program, please let Judith Zelikoff know so she can incorporate your ideas. My thanks again to everyone!

## Vice President-Elect's Message

*by Judith Zelikoff*

Even though the 1998 meeting has not yet come, it's time to begin thinking about the 1999 program. As Vice-President Elect and head of the Immunotoxicology Specialty Section (ISS) Program Committee for 1998, I would like to invite anyone interested to submit to me (judyz@charlotte.med.nyu.edu) a title and outline of a topic that you would like to see presented as either a Workshop, Symposium, Roundtable, or Continuing Education Course at our National meeting in Seattle in 1998.

Topics submitted will then be discussed at our ISS Program Committee meeting in Seattle. Those members' ideas that have been selected for further discussion and presentation to the ISS Executive Board will be contacted and requested to submit an expanded outline (including presenters) for submission to the SOT Program Committee and/or Continuing Education Committee. As a member of the ISS Executive Board, as well as of the SOT Program Committee, I can tell you that those ideas which are most well-worked out at the time of submission fare the best. Furthermore, cross-fertilization and sponsorship by another Specialty Section also leads to increased enthusiasm by the "powers that be."

You should also be aware that a considerable amount of time and work goes along with the glory of presenting a Symposium, Workshop, Roundtable, or Continuing Education Course at the National Meeting. In addition to preparing the appropriate forms, lining up the potential speakers and making sure their abstracts are in on time (a grueling task even for the most persistent of us), if your topic is selected by the SOT Program Committee, you will be working closely with a Program Liaison to ensure the best possible presentation. Thus, please consider the "glory" as well as the time involved when making a decision.

Again, since the competition amongst our own ISS members is quite stiff, and not all proposed programs that make it to the SOT Committee will be selected, please have your ideas as well thought-out as possible prior to submission. If you have any specific questions or comments concerning the submission of a topic, I will be happy to discuss them with you.

# COMMITTEE REPORTS

## Education Committee

*Mitchell Cohen, Chair*

With the approaching unveiling of our ISS website, I thought that it might be a nice concept for those members who are in academia and have active courses in immunotoxicology to post

their curricula and currently-used textbook(s) on the website so that students who might be interested in pursuing a graduate career in toxicology/ immunotoxicology might have an inkling of the types of courses (as well as the locations offering them) available around the country and the world. As with the keyword setup that is being established on the site, the teacher(s)'s name(s) could be made linkable to their e-mail address so that potential students may contact them directly.

Apart from aiding potential graduate students, the posting of the various curricula will also allow fellow academicians/ISS members to get an idea of what they might want to include (or even delete) from their own current curriculum. This is not a clarion call for uniformity of teaching the subject of immunotoxicology, but rather an opportunity for those of us in academia to sort of "compare notes."

Please feel free to contact me with feedback on this idea or even to provide me with suggestions of your own regarding ways to enhance the teaching of immunotoxicology. If you are already won over by the concept, please send your curriculum to me by e-mail (send to cohenm@charlotte.med.nyu.edu) and I will forward it to our own ISS webmasters.

See you all in Seattle (?) in March!!

## Membership Committee

*Michael McCabe, Chair*

Hopefully, all members of the ISS have received a Membership Directory. If you have not received yours and would like one please contact Michael McCabe (M.J.McCabe.Jr@wayne.edu). In an effort to keep the membership directory updated, please contact Michael McCabe with information regarding changes of address, telephone numbers, area codes, email addresses, etc. Also, please take a few moments to find, and to admire, your ISS membership directory, and please ensure that your "vital statistics" are correct as listed. Remember, the next deadline for new SOT membership applications is April 1, 1998. Encourage your colleagues and students to join the National SOT and the Immunotoxicology Specialty Section.

## Awards Committee

*Dori Germolec, Chair*

The Awards Committee of the Immunotoxicology Specialty Section of the Society of Toxicology is pleased to announce that once again we will be granting up to five awards at the Annual SOT meeting in Seattle in 1998. These awards are given in recognition of the scientific excellence of the research conducted by graduate students and postdoctoral fellows in the specialty of Immunotoxicology. Presentations will be judged on the scientific merit and significance of their work, the soundness of their experimental approach and methodology, and the quality of their writing and data presentation.

Candidates for these awards are requested to submit copies of their entire presentation, including abstracts, introduction, all figures and data tables, summary and conclusions. It is important that all of the above be included, as the decision on the awards will be based upon the written submission only, and not on the actual presentation at the meeting. The submission will be evaluated by the Awards Committee prior to the annual meeting and the winners will be announced at the Specialty Section meeting in Seattle. To be eligible the student or postdoctoral fellow must be first author on the paper.

To be considered for the awards, students and postdoctoral fellows should submit a copy of their entire presentation (poster or platform) to

be received NO LATER THAN FRIDAY, JANUARY 16, 1998 to:

Dori Germolec
Environmental Immunology Laboratory
National Institute for Environmental Health Sciences
PO Box 12233, RTP, NC, 27709
Telephone: (919) 541-3230
germolec@niehs.nih.gov

## Methods Committee

*Bob Luebke, Chair*
*(Update Provided by Robert House)*

Progress on the ISS Home Page has been much slower than anticipated. A skeleton version has been available for several months, but is essentially serving as a place-holder until the final version is finished. As most of you are aware, we have the ambitious goal of including a "Resources" subdirectory in which the e-mail address of participating members of the Section will be linked with key words. The goal is the dissemination of information on concepts, techniques, reagents, troubleshooting and other issues. This will aid in the identification of Specialty Section members willing to act as consultants to individuals with questions on methods, as well as fostering greater cooperation between individuals within the Section.

There have been two problems associated with this effort. First, although there is a lot of support for this effort, the National SOT Council has had a few reservations; not as much in concept as in implementation. There are legitimate questions surrounding the inclusion of direct links to personnel and other web sites via the SOT Home Page. Our solution to this, we hope, is getting explicit permission from each linked person prior to instituting this service. Most of you have already been contacted.

Which leads me to our next major difficulty, namely the lag time we have experienced in peoples' responses to our communications. Mitchell Cohen took the lead in this area, and did yeoman's service in compiling a membership directory and individually contacting all members regarding their willingness to participate. Responses have been slow to trickle in, but we now have a critical mass of participants to make this thing work. The initial Resources page is now complete, and most of the participants have been contacted directly from the page to confirm that the links will work. We hope to have the Resources section operational and uploaded by year's end.

Another feature of our web site will be the inclusion of links to other sites relevant to immunotoxicology, although National SOT at present is excluding commercial sites. If you know of sites that should be included, please forward the URL to either Bob Luebke or Robert House.

To date, we have received strong verbal support for our ideas regarding the Home Page. Please remember that we depend on the cooperation and support of the membership to make this work.

## Regulatory Committee

*Liz Sikorski, Chair*

**FDA Center for Devices and Radiological Health (CDRH)**

The CDRH announced the availability of a draft guidance document entitled the *Immunotoxicity Testing Framework* for public comment in the Federal Register on March 18, 1997. A copy of the draft guidance document can be obtained by calling 1-800-638-2041. During the comment period, CDRH received comments from approximately 25 companies and organizations in the U.S. and abroad. A revised version of the document is almost completed and will go through an in-house FDA review. The final document is

anticipated to come out in Summer of 1998. Upon finalization of the document, it will be announced in the Federal Register and available on the Internet (FDA Home Page).

**FDA Center for Drug Evaluation and Research (CDER)**

Dr. Ken Hastings has provided an update on the CBER guidance document for immunotoxicity testing (see May 1997 newsletter for additional information). The document has been circulated within the FDA for comment and the internal review has been completed. The current discussion within the FDA regards the format in which the document should be provided for outside comment. When the draft guidance document is available for public comment, it will be announced in the Federal Register and will be available on the Internet on the FDA Home Page. No date was given for the availability of the draft document.

The three fundamental recommendations that are proposed in the draft guidance document are: (1) recommended use of flow cytometric analysis of blood and/or spleen as a backup assay if a dose-dependent alteration in routine toxicological assessment of the immune system (*i.e.*, histopathology) is observed; (2) use of the murine local lymph node assay (MLLNA) as an acceptable alternative to guinea pig assays for testing the contact sensitization potential of topical drugs; and (3) the introduction of the popliteal lymph node assay to test for immunostimulation.

**FDA Center for Biologics Evaluation and Research (CBER)**

CBER reviews the safety of a variety of products such as monoclonal antibodies, recombinant proteins, vaccines, gene therapy and xenotransplants. This branch of the FDA deals with many immunotoxicology issues, as some of the biologics they evaluate directly or indirectly affect the immune system. A draft guideline containing information on CBER immunotoxicology testing was made available for public comment in April 1997. This guideline was prepared under the auspices of the International Conference on Harmonization (ICH) on Technical Requirements for Registration of Pharmaceuticals for Human Use.

The document has now been finalized and can be obtained by calling 1-800-835-4709 (CBER Voice Information System) or via the Web (http://www.fda.gov/cder in the "Regulatory Guidance" section). This guidance document provides general principles for the design of internationally acceptable preclinical safety evaluation programs for biopharmaceuticals. Briefly, this document states that new therapeutic agents will be evaluated for immunotoxicity on a case-by-case basis rather than by a routine tiered testing approach.

**EPA**

The EPA has undertaken a harmonization of its pesticides and toxics guidelines for testing of health effects, environmental effects and chemical fate. The rationale for this harmonization is to incorporate state of the art science and to minimize variations among the protocols contained in: (1) test guidelines by the EPA Office of Pesticide Programs (OPP); (2) the series of TSCA test guidelines which exists in the Office of Pollution Prevention and Toxics (OPPT); and (3) guidelines published by the Organization for Economic Cooperation and Development (OECD).

Harmonization has improved the guidelines but certain problems were created by trying to write a single set of guidelines which can be used by both OPP in its administration of FIFRA and the Federal Food, Drug and Cosmetic Act and the Office of Pollution Prevention and Toxics (OPPT), which administers TSCA. Further discussion on this issue can be found in the Federal Register announcement of the TSCA Test Guidelines on August 15, 1997.

**TSCA Immunotoxicity Testing Guidelines**
The Toxic Substances Control Act (TSCA) was enacted by Congress in 1976 and is an act "to regulate commerce and protect human health and the environment by requiring testing and necessary use restrictions on certain chemical substances, and for other purposes." TSCA regulates the use of certain chemical substances in the U.S. but excludes the following classes of chemicals: pesticides, food, food additives, cosmetics, and drugs.

The TSCA Test Guidelines have recently been finalized and were announced in the Federal Register on August 15, 1997. For the TSCA Immunotoxicity Test Guidelines, the Agency has used the OPPTS harmonized health effects test guidelines (870.7800) developed using the public notice and comment process as well as certain OECD guidelines to create the TSCA-specific test guidelines.

Therefore, as indicated in the OPPTS guidelines, the Agency requires that in addition to information obtained from routine toxicity testing (*i.e.*, histopathology, organ weights,) they will require an immune function assay in Tier 1 testing - the sheep red blood cell (SRBC) assay. This assay can either be quantitated by enumeration of plaque forming cells or the measurement of antigen-specific antibody by ELISA. If there is a positive response in the SRBC assay, the guidelines suggest flow cytometry of the spleen as an optional assay. If the SRBC assay is negative, the guidelines suggest the NK cell assay as an option to assess non-specific immune effects. These optional assays will not be requested by the EPA on a regular basis but will be discussed on a case-by-case basis.

**FIFRA Immunotoxicity Testing Guidelines**
The EPA is in the process of finalizing OPPTS 870.7800 Immunotoxicity Health Effects Test Guidelines (see the May 1997 newsletter for additional background). This document will be very similar to the TSCA immunotoxicity testing guidelines that were announced in the Federal Register on August 17, 1997 (see section above on TSCA Immunotoxicity Test Guidelines). No date was given as to when the finalized document will be available, but it will be announced in the Federal Register.

**OECD (Information supplied by Karen Kohrman, Procter & Gamble Co.)**
OECD has been working with OECD National Authority representatives over the past two years to harmonize classification and labeling systems. This process has involved the development and finalization of classification criteria proposals for various toxicity endpoints. The proposals outline the rationale and criteria for classification of chemicals as sensitizers, for example. The two proposals of importance to the Immunotoxicology Specialty Section are: (1) sensitization; and (2) systemic toxicity which currently includes immunotoxicology.

Throughout these classification efforts, the Business and Industry Advisory Committee (BIAC) and the National Authorities have provided input to the OECD. The BIAC consists of representatives/experts from the chemical, consumer products and metals industries. Industry has not been able to directly provide input to the OECD but has been working with BIAC to influence the OECD, and with U.S. Regulators to influence the OECD via the National Authorities.

In October 1997, OECD held the fifth Advisory Group meeting to discuss and finalize as many of the classification proposals as possible. Three classification proposals were finalized at this meeting including the proposal for sensitization. This document will be made available. It should be noted that there is controversy surrounding the finalized sensitization proposal. There are two issues of concern. For respiratory sensitization, the current OECD proposal does not adequately separate a response caused by sensitization from a response caused by a non-

immunologic mechanism (*i.e.*, asthma or contact urticaria). To classify a chemical as a respiratory sensitizer, it is important to show that it operates via an immune-mediated mechanism.

The second controversy is with contact sensitization and the use of human data in the risk assessment process. The finalized proposal states that human data should not normally be used to negate positive animal studies in the assessment of contact sensitization potential. This is inconsistent with the U.S. Federal Hazardous Substance Act. Some scientists argue that good human data should have preference over animal or other data and is the most pertinent information to consider. In support of this position, there are many examples of potentially inappropriate labeling of chemicals based on the guinea pig maximization test where substances such as sulphanilic acid would be classified with R 43 but clearly has a very low sensitization potential in humans as evidenced by its safe widespread use.

Regarding use of human data, BIAC proposed that either human experience or ethical human testing should be allowed and used for classification purposes. This position is also supported by the U.S. National Authority. The current OECD position is that human testing conducted within the Helsinki Agreement should be considered in classification. The key issues that remain include how human data will be integrated, and gaining support for the idea that valid, robust human data takes precedence over data obtained from different species. OECD is preparing a preamble on human testing and use of human data for classification.

The OECD classification proposal on Immunotoxicology is currently being developed and finalization of the harmonized classification criteria proposal is anticipated by Spring 1998. The current debate is whether immunotoxicology should be included with systemic toxicology or treated as a separate endpoint.

In addition to the harmonization of classification and labeling efforts discussed above, OECD is continually upgrading test guidelines. Regarding immunotoxicology test guidelines, discussions have begun to update Guideline 407, Repeated Dose 28-day Oral Toxicity Study in Rodents, which includes routine toxicity endpoints that can identify effects on the immune system (*i.e.*, histopathology, organ weights). A discussion of this effort was included in the May 1997 newsletter.

Briefly, in December 1996, OECD convened an *ad hoc* working group meeting on Immunotoxicity to review the currently available test methods for immunotoxicity safety evaluation of substances, consider minimum test requirements and make recommendations for test method development. This group concluded that assessment effects on the immune system would be via routine toxicity endpoints such as histopathology of immune organs, spleen and thymus weights, and hematology. If this analysis produces any indication of treatment-related effects on the immune system at any dose tested, the sheep red blood cell assay will be required. An OECD report on the meeting is not yet available.

Regarding OECD Guideline 406 on Skin Sensitization testing, a Toxicology Shadow Group from an OECD Member Country (UK) is preparing a proposal that will be submitted to the OECD asking for review of the local LLNA and possible incorporation in Guideline 406. This assay would be used as an alternative test for assessing the skin sensitization potential of chemicals.

**Validation of the MLLNA**

In the May 1997 newsletter, the validation of alternative methods was discussed. An *ad hoc* Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was established by the NIEHS/NTP and pub-

lished a report outlining criteria and procedures for the validation and regulatory acceptance of toxicological testing methods. The report entitled "Validation and Regulatory Acceptance of Toxicological Test Methods" was recently published (NIH Publication No. 97-3981). This document outlines: (1) validation criteria for new or revised test methods for regulatory risk assessment purposes; (2) criteria for regulatory acceptance of new or revised methods; and (3) regulatory acceptance process recommendations.

The first proposed alternative method that will be formally reviewed by ICCVAM according to the criteria outlined in their document is the MLLNA. To begin the process, several scientists from various companies proposed an interagency peer review of this assay as an alternative method in contact hypersensitivity testing. Their request was approved by ICCVAM who agreed to establish an ICCVAM Immunotoxicity Working Group (IWG) composed of knowledgeable scientists nominated by the participating ICCVAM agencies. The function of the IWG is to: (1) develop a request for the information needed for the test method peer review; (2) assess the submitted information to ensure that it is adequate and complete; (3) identify suitable independent reviewers for the peer review panel; (4) formulate questions to be addressed by the peer review panel; and (5) develop recommendations on the use of the method based on the conclusions of the peer review panel.

To date, the IWG has completed the first step. At their first meeting, the IWG discussed the proposal and developed a set of submission guidelines that outlined the information that should be provided to them for the review. Several Companies are participating in the compilation of the requested information. Once sufficient data is received, the IWG will schedule the peer review. Following the peer review, ICCVAM will compile their recommendation on the use of the MLLNA method which will be forwarded to the appropriate federal agencies. These agencies will then evaluate the recommendation and determine how the LLNA will fit into their sensitization testing schemes. For further information contact Dr. Frank Gerberick (513) 627-2909.

**Immunotoxicology Research**

There are a number of regulatory issues and data gaps that are driving immunotoxicology research interests. In this column of the newsletter, we will provide some information on research efforts that may ultimately be of importance to the regulatory community and/or useful for hazard identification or risk assessment of sensitizers and immunotoxicants.

**COLIPA Sensitization Task Force**

The COLIPA (The European Cosmetic, Toiletry and Perfumery Association) Skin Sensitization Task Force is chaired by David Basketter (Unilever, UK) with members from U.S. and European industries. The Task Force has recently approved funding for two proposals. The objective of the first proposal is to assess whether measurement of IL-1β mRNA expression in Langerhans/dendritic cells can be used to predict the sensitization potential of a chemical. The first year of this project will be funded under an ECVAM contract plus a contribution from COLIPA. The second proposal is in the area of metabolism and skin sensitization. The objective of this proposal is to identify the major metabolic pathways and enzymes in the skin that are important for skin sensitization and consequently for the development of *in vitro* assays to assess contact sensitization potential.

**European Union**

The European Union developed the 4th Framework Program which runs from 1994 to 1998. One part of this program consists of funding *in vitro* testing projects. A call for proposals in

this area was released in the Summer of 1996 and the chosen proposals were announced in October of 1996. Two *in vitro* proposals were funded on the topic of hypersensitivity. One proposal is entitled "New Immuno-Pharmaco-Toxicological Model: Human Reconstructed Epidermis Containing Langerhans Cells." The objective of this proposal is to integrate Langerhans cells into reconstructed epidermis. The goal is to create an *in vitro* model to evaluate the sensitization potential of new compounds and drugs. The coordinator of this project is Dr. Rainer Schmidt from L'Oreal. This laboratory has recently published a manuscript on this project (Regnier et al. 1997. *J. Investigative Dermatology* 109:510). The second proposal was entitled "Development of *in vitro* tests for drug allergenicity and B cell switching to IgE." The objective of this proposal is to develop *in vitro* tests for induction of the primary human B cell antibody response to drugs, characterize the cellular and molecular mechanisms involved in these responses and identify conditions required for *in vitro* B cell switching to IgE. The coordinator on this project is Dr. John Coleman, Department of Pharmacology and Therapeutics, University of Liverpool.

## A Sampling of Recent Immunotoxicology Publications


Gehrs, BC, Riddle, MM, Williams, WC and Smialowicz, RJ. (1997). Alterations in the developing immune system of the F344 rat after perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin: II. Effects on the pup and the adult. *Toxicology* 122: 229-240

Burchiel, SW, Kerkvliet, NL, Gerberick, GF, Lawrence, DA and Ladics, GS. (1997). Assessment of immunotoxicity by multiparameter flow cytometry. *Fund Appl Toxicol* 38: 38-54.

Beaunne, PH and Lecoeur, S. (1997). Immunotoxicology of the liver: adverse reactions to drugs. *J Hepatol* 26 Supp. 2: 37-42.

Farine, JC. (1997). Animal models in autoimmune disease in immunotoxicity assessment. *Toxicology* 119: 29-35.

Lovik, M. (1997). Mutant and transgenic mice in immunotoxicology: an introduction. *Toxicology* 199: 65-76.

Saint-Remy, JM. (1997). Epitope mapping: a new method for biological evaluation and immunotoxicology. *Toxicology* 119: 77-81.

Dean, JH. (1997). Issues with introducing new immunotoxicology methods into the safety assessment of pharmaceuticals. *Toxicology* 119: 95-101.

Selgrade, MK, Lawrence, DA, Ullrich, SE, Gilmour, MI, Schuyler, MR and Kimber I. (1997). Modulation of T-helper cell populations: potential mechanisms of respiratory hypersensitivity and immune suppression. *Toxicol Appl Pharmacol* 145: 218-229.

Luebke, RW, Hodson, PV, Faisal, M, Ross, PS, Grasman, KA and Zelikoff, J. (1997). Aquatic pollution-induced immunotoxicity in wildlife species. *Fund Appl Toxicol* 37: 1-15.

Phillips, KE and Munson, AE. (1997). 2'3'-dideoxyinosine inhibits the humoral immune response in female B6C3F1 mice by targeting the B lymphocyte. *Toxicol Appl Pharmacol* 145: 260-267.

Dozier, MM, Ratajczak, HV, Sothern, RB and Thomas, PT. (1997). The influence of vehicle gavage on seasonality of immune system parameters in the B6C3F1 mouse. *Fund Appl Toxicol* 38: 116-122.

House, RV, Thomas, PT and Bhargava, HN. (1997). Immunotoxicology of opioids, inhalants

and other drugs of abuse. *NIDA Red Monogr* 173: 175-200.

Kim, HM, Han, SB, Hong, DH, Yoo, BS and Oh, GT (1997). Limitation of Hu-PBL-scid mouse model in direct application to immunotoxicity assessment. *J Pharmacol Toxicol Meth* 37: 83-89.

Rodgers, K, Klykken, P, Jacobs, J, Frondoza, C, Tomazic, V and Zelikoff, J. (1997). Immunotoxicity of medical devices. Symposium overview. *Fund Appl Toxicol* 36: 1-14.

Prell, RA and Kerkvliet, NI. (1997). Involvement of altered B7 expression in dioxin immunotoxicity: B7 transfection restores the CTL but not the autoantibody response to the P815 mastocytoma. *J Immunol* 158: 2695-2703.

## Announcements

### A Word From the Editors

The newsletter and website are for you, so please use them! Any meeting announcements, news of note, important book releases, postdoctoral positions, or job openings in immunotoxicology are perfect for inclusion in both the newsletter and the web site. The web site will be of particular importance, since it can be regularly updated. Many of you already use the listserver for such announcements, so please send a notice along to us as well.

### New Student Representative Elected

Beth Vorderstrasse, a fourth year student in Dr. Nancy Kerkvliet's laboratory at Oregon State University, was recently elected as the new Student Representative to the Immunotoxicology Specialty Section Council. Beth takes over this position from Cynthia Graham, who is graduating. Beth is interested in the mechanisms of TCDD-induced suppression of T cell-dependent immune responses, and her research project specifically addresses the effects of TCDD on dendritic cells.

Beth can be reached at ALS 1007, Oregon State University, Corvallis, OR 97331. Her phone number is (541)737-2096, and her e-mail address is vordersb@ucs.orst.edu. Please join us in extending congratulations to Beth as she takes on this important job.

### A Book to Watch For. . .

Drs. Judith Zelikoff (New York University School of Medicine) and Peter Thomas (Covance Laboratories, Inc.) have edited a book for Taylor and Francis entitled *Immunotoxicology of Environmental and Occupational Metals*, which should be on sale sometime around the National meeting in Seattle. This book contains detailed information concerning the *in vivo* and *in vitro* immunomodulating effects of a number of environmentally/-occupationally-relevant metals, as well as a description of the history, occurrence, and general toxicology of each metal. A series of appended Tables offers the opportunity to examine the immunotoxic effects of a single metal in a concise and efficacious manner.

### . . .And a Book That's Already Here

The International Programme on Chemical Safety (IPCS) has published an outstanding volume entitled *Principles and Methods for Assessing Direct Immunotoxicity Associated with Exposure to Chemicals* (Environmental Health Criteria 180). This book is up-to-date and information-dense. Although it would be of

particular usefulness as an introductory text for students or postdocs, it could also serve as a handy reference for researchers already active in the field.

The book is divided into seven major topics: Introduction to Immunotoxicology; Health Impacts of Selected Immunotoxic Agents; Strategies for Testing the Immunotoxicity of Chemicals in Animals; Methods of Immunotoxicology in Experimental Animals; Essentials of Immunotoxicity Assessment in Humans; Risk Assessment; and, Some Terms Used in Immunotoxicity. Numerous color photographs, drawings and tables clearly illustrate the text and clarify some difficult concepts.

Copies of this outstanding volume are available for Sw.fr. 55 from the Office of Distribution and Sales, World Health Organization, 1211 Geneva 27, Switzerland (Fax number 41-22-7914857).

**Meeting Report**

The Annual Fall Meeting of the Midwest Regional Society of Toxicology was held on October 24, 1997 at Covance Laboratories in Madison, WI. The topic of this year's meeting was *Current and Future Perspectives on Immunotoxicology*. Approximately one hundred scientists from the Midwest were on hand to learn about how immunotoxicology is used in decision-making by both government and industry.

Dr. Sheryl Reilly of the U.S. E.P.A. spoke on "Current Immunotoxicology Regulatory Issues Under TSCA and FIFRA," describing similarities and difference in current and proposed EPA regulations. Sheryl was followed by Dr. Kenneth Hastings of the U.S. F.D.A., whose presentation on "Current Issues in Immunotoxicity Evaluation in Drugs" used nucleoside analogs as an example of how immunotoxicology can play an important role in drug development, particularly of drugs for treatment of conditions with a strong immunological involvement.

Dr. Michael Holsapple of the Dow Chemical Company followed by presenting the perspective of an academician-turned industrial immunotoxicologist in the talk "The Role of Immunotoxicology in the Chemical Industry." Dr. Jeanine Bussiere of Genentech closed the meeting with the talk "Use of Immunotoxicity Testing for Safety Evaluation of Biotechnology Compounds: A Case by Case Approach."

It is gratifying to note the increasing interest in immunotoxicology, as evidenced by the proliferation of regional meeting devoted to the subject. Apparently, the word is getting out!

*The Immunotoxicology Specialty Section Newsletter* is published quarterly. Please address all questions, comments, news items or other submissions to:

Robert V. House, Editor
IIT Research Institute
10 West 35th Street
Chicago, IL 60616
312-567-4294 (T)
312-567-4296 (F)
rhouse@iitri.com (E)

Judith T. Zelikoff, Editor
Institute of Environmental Medicine
New York University Medical Center
Long Meadow Road
Tuxedo, NY 10987
914-351-5624 (T)
914-351-5472 (F)
judyz@charlotte.med.nyu.edu (E)

**MEETING ANNOUNCEMENT**
**PLEASE POST AND DISTRIBUTE**

Fourth National Health and Environmental Effects Research Laboratory Symposium
on Research Advances in Risk Assessment

EXTRAPOLATION IN HUMAN HEALTH AND ECOLOGICAL RISK ASSESSMENTS:

Wayne R. Munns, Jr., Ph.D., Chair, Organizing Committee
Robert MacPhail, Ph.D., Co-Chair, Organizing Committee

Risk-based environmental decisions are rarely based upon effects information measured directly in humans or entire ecological systems. More typically, assessments of risk are based upon extrapolations of measured endpoints to the effects of concern. Such extrapolations are a major source of uncertainty in human health and ecological risk assessments. Potential integration of health and ecological risk research to improve extrapolation approaches will be explored in the Fourth NHEERL Symposium Series on Research Advances in Risk Assessment. The Symposium will focus on the methods, models, and data employed to extrapolate across biological organization, spatial scales, and through time to highlight key health and ecological effects research issues. Presentations and discussions will identify commonalities in research approaches and methodologies for conducting extrapolations, with the fundamental goal of reducing uncertainties in human health and ecological risk assessments. The format will include invited platform presentations, panel discussions, and contributed poster presentations.

The 1998 Symposium is scheduled for April 27-30, 1998 in Cary, North Carolina. To be placed on the mailing list for the 1998 Symposium, complete the form and return by mail or fax.

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