Immunotoxicology Specialty Section Newsletter

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.

Jean F. Regal, Editor
Department of Pharmacology
10 University Dr.
University of Minnesota
Duluth, Minnesota 55812
Tel. (218) 726-8950 Fax (218) 726-7906
jregal@d.umn.edu

Robert W. Luebke, Associate Editor
U.S.E.P.A.
Immunotoxicology Branch (MD 92)
Research Triangle Park, NC 27711
Tel. (919) 541-3672 Fax (919) 541-4284
luebke.robert@epa.gov

Typesetting provided by Brenda House.

President's Message

Robert V. House

As the summer of 2002 draws to a close, the Immunotoxicology Specialty Section continues to grow. Although we are currently listed as the fourth-largest Specialty Section (a statistic that I'm very proud of), we have recently learned that we must remain vigilant to ensure that we're fully credited for our paid members. I would like to ask that each of you check to make sure you're fully paid up. Moreover, if you receive a message that your dues status is in question, please take time to make sure your status is accurate. Our finances are directly tied to membership, and the Executive Committee has to make limited dollars work as efficiently as possible to provide services to the membership.

As in recent years, the Program Committee has assembled a full package of exciting submissions. However, I want to remind all of you that these programs don't just happen. In the past, we have depended on the membership to submit programs; this almost always resulted in a flurry of last-minute submissions. Although such eleventh-hour submissions have resulted in excellent programs, more often than not a great idea died on the vine for lack of careful organization. For this reason, the 2004 Program Committee is taking the novel approach of suggesting program ideas that can be further developed. Of course, they still depend on independent submissions, so please contact Robert Luebke or any member of the Program Committee. Any of these folks will be happy to help you flesh out your idea into a strong submission. In particular, they would like to receive submissions from young investigators, who can infuse the roster with fresh ideas. Please remember that successful submissions should appeal not just to the immunotoxicology community, but to the toxicology community at large.

A project that I am currently pursuing is the development of an Immunotoxicology Position Paper, something of a state-of-the-art summary of where the field is, and more importantly where we're going. I understand that immunotoxicology has grown to the point that such a task will be daunting; however, I believe that it's important that toxicologists from other sub-disciplines have a current view of where we stand vis-à-vis basic research, regulatory issues, and connection with toxicology in general. It is my plan that this Position Paper will be published within the next year.

On a more prosaic level, the Executive Committee has taken steps to work more efficiently, including evaluation of the various committees, and developing a Rule Book that should provide a measure of institutional memory, making operation of Specialty Section consistent over time.

No proper President's Message would be complete without a section asking for your help in facilitating the flow of information within our Specialty Section. Please remember to make use of the website for meeting announcements, notification of employment opportunities, and any other items of general benefit to the membership. Also, please remember to provide updated contact information in the event that one of the employment opportunities works in your favor.

Finally, I want to thank each member for the support that has made us one of the most active and interesting Specialty Sections in SOT.

Proposed reorganization of NIH Study Sections

B. Paige Lawrence and Robert V. House

As many of you may be aware, the NIH has proposed a rather extensive reorganization of integrated review groups (IRG) and study sections. Some of these proposed changes have been reviewed and accepted, while others remain open for comment. As part of the proposed reorganization, the alcohol and toxicology study sections (ALTX) would be eliminated, and toxicology grants would be farmed out to a variety of study sections. For example, immunotoxicology grant applications may be reviewed by study sections under the Immunology (IMM) IRG, or could perhaps go to a study section which reviews grants pertaining to a specific organ system (e.g., GI tract, respiratory system). Upon reading the proposed new IMM IRG (which was open for comment until July 29, 2002), we noticed that immunotoxicology research was not a clear component of any of the proposed study sections.

In response to concern that this might severely impact NIH funding of immunotoxicology research, the members of the Immunotoxicology Specialty Section Executive Committee sent the following letter to Dr. Carl Nathan, Chair of the IMM IRG review team, Dr. Robert T. Cook, outgoing chair of the ALTX-4 study section, and to Michael R. Martin, Director, Division of Physiological Systems, Center For Scientific Review. We plan to follow up on this letter, in the hope that our concern and suggestions will be incorporated into the revision of NIH study sections.

For those interested in this process, there are other on-going discussions regarding the inclusion of some of the ALTX study sections within other integrated review groups.

Carl F. Nathan, MD
Chairman, DRGAC IMM-SSB
Dept. of Microbiology and Immunology
Weill Medical College
Cornell University
New York, NY 10021

Dear Dr. Nathan and Members of the
Immunology IRG Review Team:

Upon reading about the NIH reorganization of IRGs, we are concerned about future NIH funding opportunities for immunotoxicology research and the lack of representation of this area. Specifically, we are concerned about where immunotoxicology research grants will fit into this new paradigm. Although, compared to basic immunology, this is a relatively small field, studies of the effects of chemicals on the immune system are a valid and important area for further scientific inquiry. We see no proposed IRG or study section into which immunotoxicology grants would clearly fit.

The spirit of immunotoxicology research is included in the 5th study section of the IMM IRG, which says it will include "primary and secondary immunodeficiencies including damage from exogenous agents". While this terminology clearly could encompass immunotoxicology, we believe it is important that the term immunotoxicology specifically be included in the description of topics reviewed by this study section. We believe this is important for the following three reasons:

(1) so new and currently funded investigators find a home for their grants,
(2) so the scientists who serve on this study section expect to receive immunotoxicology grants for review, and
(3) to insure the study section includes at least one reviewer with expertise in immunotoxicology.

In summary, our goal is to guarantee a place for immunotoxicology research in this new structure of NIH IRGs. We appreciate your thoughtful attention to our concern.

Best regards,
Robert V. House, Ph.D.
President, Immunotoxicology Specialty Section
Society of Toxicology

and the members of the
Immunotoxicology Specialty Section Executive Committee:

Tom Kawabata, Ph.D. (Vice President),
Jean Regal, Ph.D (Secretary/Treasurer),
Bob Luebke, Ph.D (Vice President elect),
Jean Meade, Ph.D (Senior Councilor),
Mary Jane Selgrade, Ph.D (Councilor/Past President),
B. Paige Lawrence, Ph.D (Councilor),
Peyton Myers (Student Representative)

Membership Committee Report

Submitted by B. Paige Lawrence

Once again, the attendance at our annual mixer and business meeting indicates that our membership is growing; however our record of dues-payment reveals that many Immunotoxicology Specialty Section members are either not paying their dues or, for some reason, their payment is not being recorded by SOT. In all honesty, it appears to be a bit of both, but poor record keeping by SOT is a small part of the problem. A larger problem is poor compliance by our membership. Therefore, I implore you to please do the following:

1. **On your annual SOT membership renewal form, remember to check the Immunotoxicology Specialty Section box.**
2. **Please remember to include the additional fees for Specialty Section membership.** SOT tells me that many people check the box but don't include the extra money. Therefore, you don't get counted by SOT as a bona fide member of the Specialty Section.
3. **Keep a record** that you paid and/or verify with SOT that they received your payment and recorded it properly.
4. **Pay your dues on time.** People who pay their dues late slip through the cracks when SOT tallies up Specialty Section members, and we therefore do not always get credit for late comers.

As a reminder, student and postdoctoral members of SOT are permitted to join one Specialty Section for free. However, their mentor/sponsor must be a member of SOT. Moreover, for students and postdocs to join a Specialty Section gratis, they still need to check the appropriate Specialty Section box on the annual dues/renewal form and return it to SOT.

Mentors: please encourage your students and postdoctoral fellows to join SOT and check the Immunotoxicology Specialty Section box.

SOT will be mailing out the 2003 annual membership renewal forms this fall. Please take the time to renew your membership in both SOT and the Immunotoxicology Specialty Section.

THANK YOU

To all the Immunotoxicologists who paid their Specialty Section dues.

230 strong and growing

If you have concerns or ideas, please feel free to share them with us. If you are moving, please send us your new email address and contact information. The current roster for the Membership Committee and our email addresses are as follows:

B. Paige Lawrence (chair)	bpl@wsu.edu
T. Scott Thurmond	Scott.Thurmond@cfsan.fda.gov
Marsha Ward	ward.marsha@epa.gov

R&D Systems Offers Training Workshops

R&D Systems is now offering training workshops for ELISA/ELISpot, and ELISA/mRNA quantitation at their Minneapolis Headquarters. These 2-2½ day workshops are designed to provide hands-on experience in these assays including assay theory, troubleshooting tips, and practical experience. These workshops focus on the use of kits (R&D kits, one would suppose) and the company points out that they are not intended to teach how to construct assays from scratch. Cost for the workshops is $650 each, which includes training, 2 nights hotel, 2 lunches, and 2 dinners. (Price excludes air and ground transportation.).

Dates for these workshops are:

ELISA/ELISpot

- September 18-20, 2002 (Full) • February 5-7, 2003 • May 7-9, 2003

mRNA

- November 7-8, 2002

More details, course outlines, and registration forms are available at: www.rndsystems.com

Program Committee Report

Submitted by Bob Luebke

Believe it or not, it is time to begin thinking about the program for the 2004 SOT meeting in Baltimore. Over the years, the Immunotoxicology Specialty Section has been fortunate to have a group of dedicated individuals that could be counted on for good program ideas. As a result, we have an excellent record of acceptance for program items submitted to the SOT Program Committee, and Immunotoxicology scientific sessions are well attended. However, to ensure that our program items are of interest to the greatest number of our members and prospective members, it is important to maintain a flow of program items from a wide range of the membership. This year the Immunotoxicology Program Committee continues the tradition of soliciting symposia, workshops, roundtable discussion and continuing education course ideas from the membership. If you have an idea for a program item, even if you are not able to chair or co-chair the session, please send it to us along with the names of potential organizers or session chairs. Co-sponsorship of program items by other Specialty Sections is encouraged, if appropriate, since a wider audience will be attracted to the session. This is not lost on members of the national Program Committee; the likelihood of approval is generally higher for co-sponsored sessions. Please send in your ideas early, to avoid the last minute rush. You can send your ideas to any member of the Program committee (see below).

The categories include Continuing Education, Symposia, Workshops, Roundtable, Innovation in Applied Toxicology and Innovation in Toxicological Sciences. A description of each category is available on the SOT web site. From the SOT homepage, click on the icon for the upcoming meeting, then select Scientific Sessions from the Scientific Program dropdown menu.

The 2002-2003 Program Committee members are:

Bob Luebke (chair)	luebke.robert@epa.gov
Don Frazier	donald_e_frazier@groton.pfizer.com
Dori Germolec	germolec@niehs.nih.gov
Ian Gilmour	gilmour.ian@epa.gov
Ian Kimber	ian.kimber@syngenta.com
Greg Ladics	gregory.s.ladics@usa.dupont.com
Jean Meade	bhm8@cdc.gov
MaryJane Selgrade	selgrade.maryjane@epa.gov
Amber Wyman	awyman@mc.rochester.edu

Regulatory Committee Report

Submitted by Ken Hastings

Well, it's summertime, so not much is happening on the regulatory front. However, there are a couple of publications of interest that have appeared recently. The first is a report of an ILSI/HESI Immunotoxicology Technical Committee Task Force working on drug allergy:

> Adkinson, N.F., Jr., Essayan, D., Gruchalla, R., Haggerty, H., Kawabata, T., Sandler, J.D., Updyke, L., Shear, N.H., and Wierda, D. (2002). "Task Force Report: Future Research Needs for the Prevention and Management of Immune-Mediated Drug Hypersensitivity Reactions." *J. Allergy Clin. Immunol.*, 109, S461-S478.

This paper contains an extensive analysis of immune-mediated drug hypersensitivity reactions and makes numerous recommendations concerning research needs. Of particular importance is the call for more funding of research in drug allergy.

The second is the report of a Drug Information Association meeting that was held in Noordwijk, The Netherlands, in November, 2001. This paper is particularly important for understanding the European Agency for the Evaluation of Medicinal Products/Committee for Proprietary Medicinal Products (EMEA/CPMP) position on the immunotoxicity evaluation of new drugs:

> Putman, E., Van Loveren, H., Bode, G., Dean, J., Hastings, K., Nakamura, K., Verdier, F., and Van der Laan, J.-W. (2002). "Assessment of the Immunotoxic Potential of Human Pharmaceuticals: A Workshop Report." *Drug Info. J.*, 36, 417-427.

Mark your calendar for the following:

The Society of Toxicology is pleased to announce its Continuing Concepts in Toxicology Workshop: *Non-clinical Safety Evaluation of Preventive Vaccines: Recent Advances and Regulatory Considerations*. Under the auspices of the CBER, FDA and the SOT, this workshop will be held December 2-3, 2002 at the Crystal City Marriott at Reagan National Airport, Arlington, VA with the sponsorship of the FDA Office of Women's Health.

Finally, the FDA Center for Drug Evaluation and Research (CDER) *Guidance for Industry: Immunotoxicology Evaluation of Investigational New Drugs* should be appearing on the FDA website soon. This is the final version. (I know: we've heard this before. Really, this time it's going to happen).

Communications Committee Report

Submitted by Peyton Myers

Work is already underway to get the next directory for the Immunotoxicology Specialty Section ready for 2003. We are attempting to clarify who is, or is not, an Immunotoxicology Specialty Section member before querying the membership for updates/changes to their directory information. Once we clarify the correct membership, we will begin the process of updating everyone's directory information. Also, the next Immunotoxicology Specialty Section directory will not be in bound format as the previous versions (i.e., a hard copy). This version will be an electronic directory in a PDF format (the same format as this newsletter). This should cut costs on many fronts for both individual members and the Immunotoxicology Specialty Section.

Several updates have been made to the Immunotoxicology Specialty Section webpage. Since the last update, we have had one more job posting for an immunotoxicologist. If anyone has any job offerings, please forward them to LMyers@LSUHSC.edu in order to get them posted to the website. Also, a change has been made to the website. We now have a link for Important Announcements which are pertinent to the Immunotoxicology Specialty Section. Please check the website for updated announcements.

http://www.toxicology.org/MemberServices/SpecSection/immunotox/Index.html

Meeting Report

Andrij Holian

New Directions and Needs in Asbestos Research
Conference organizers: Andrij Holian and Elizabeth Putnam
University of Montana-Missoula
June 24-25, 2002

Asbestos minerals which have been used commercially.

The Center for Environmental Health Sciences Conference, entitled "New Directions and Needs in Asbestos Research", was held at the University of Montana-Missoula on June 24 and 25, 2002. The mission of the conference was to bring together international experts to identify new investigative avenues that will allow the research needs of emerging asbestos-exposed populations to be addressed. A serious health situation was identified due to the exposure of Libby, Montana residents to asbestos-contaminated vermiculite mined and processed in the local area from 1923 to 1990. While these exposures have primarily affected residents of Libby, exposures have also occurred in a much larger community through the worldwide distribution of the contaminated vermiculite. With the identification of asbestos-related diseases (ARD) in inhabitants of areas around the vermiculite expansion plant in Minneapolis, as well as in vermiculite workers from Ohio and California, the potential national impact of asbestos-contaminated vermiculite exposure is becoming more evident.

Session summaries

The theme of the first session was asbestos exposure effects on human health, using Libby, Montana as an example. The message of the session was that the health effects from years of continuous asbestos exposure in Libby are still being uncovered, and that the disease course as a result of these exposures is different in many ways from previously described ARD. These differences may be in part due to the qualitatively different fibers, and the high number of short and thin fibers, as well as the extensive exposures in the Libby valley. In his keynote address, Dr. Henry Falk suggested that researchers view the 15-30 years between diagnosis and disease progression as a "window of opportunity" for the development of therapeutic interventions.

Discussion of chronic disease development mechanisms began with a presentation on the damage induced by iron-derived free radicals. It was demonstrated that the mitochondrial death pathway regulated asbestos-induced apoptosis, mediated in part by iron-derived reactive oxygen species. In addition, studies indicated that crocidolite-induced DNA damage was dependent upon the release of iron from the fibers and production of NO by the inducible form of nitric oxide synthase (NOS-2). Additional studies

suggested that the induction of NOS-2 resulted from activation of signaling pathways caused by a change in the intracellular redox environment due to a decrease in glutathione and the presence of iron from asbestos fibers. These mechanisms may be important in the induction of both pulmonary fibrosis and cancer.

It has long been demonstrated that short fibers are generally non-pathogenic, while long fibers can cause "frustrated phagocytosis". Data were presented demonstrating that TNFα was induced to a much greater extent by long fibers than by shorter ones. Longer fibers also induced NFκB to bind to DNA much more readily than short fibers, and long fibers increased phosphorylation of MAP kinase p38 and ERK. Thus fiber length played an important role in the potential pathogenicity of fibrous particles with effects magnified when fibers were too long to be completely phagocytized.

The role of immune mechanisms in the development of ARD was investigated in both humans and animal models. The roles of the alveolar macrophage in antigen presentation and thus the chronic stimulation of the Th2 pathway were examined. All forms of asbestos tested caused alveolar macrophage apoptosis and necrosis as well as lung fibrosis in mice. An examination of autoimmune disease indices in asbestos-exposed Libby volunteers indicated that there was a significant increase in these parameters in the Libby cohort compared to an age and sex-matched cohort. These results suggested that further assessment of autoimmune responses in this cohort was warranted.

With more evidence accumulating to indicate the involvement of growth factors in ARD, model systems have become important tools for these investigations. Studies demonstrating the utility of genetically manipulated mice as model systems for the analysis of asbestos response pathways were presented.

The second keynote address, by Dr. Kenneth Olden, presented the use of genomics as a research tool for studies of many environmentally caused diseases. Genomics has the potential for great impact on the development of new and more informative test systems, and thus, the application of toxicogenomics allows hypothesis-driven research to develop. In this session, data were presented on the contribution of genetic variation to ARD development in humans. The importance of exposure data was emphasized. Microarray analysis of mesothelioma cell line RNA demonstrated differentially expressed genes implicating potential new pathways of investigation. Microarray analysis of lung RNA from asbestos-exposed mice demonstrated specific gene expression signatures for individual fiber types, suggesting the potential for using biological methods to type fibers by toxic signatures, as contrasted to purely mineralogical means of classification.

Recommendations

The consensus of the participants was that asbestos research had been somewhat neglected in the last twenty years: previous studies had not been repeated with new analytical and toxicological methods. Because of ongoing asbestos exposures at many sites, including the natural outcroppings of tremolite asbestos in California, ARD will continue to be a national health issue. The development of better diagnostic methods, a more thorough delineation of the natural history of ARD, and an understanding of the cellular and molecular mechanisms of disease development are all necessary for the development of effective therapeutics to prevent disease progression. Achieving these goals will require the allocation of additional money to support ongoing research as well as to recruit new researchers from broad disciplines. In addition, the contribution of the exposed community to the research effort cannot be ignored. Education of the community and transmission of newly gained information has to remain a priority. Because of the proliferation in the use of fibrous material, both natural and manmade, the information gained by these studies may have much broader implications for patient care than being limited to asbestos-exposed patients.

The panel discussions raised questions of the validity of exposure estimates, and the difficulty in extrapolating from animal model studies to human studies. The animal models, while not perfect, remain an important tool in the dissection of asbestos exposure pathways. These animal models need to be validated with data from human studies. The development of specific biological indices may prove to be a more accurate estimate of exposure than the attempt to reconstruct exposures that occurred in the past. The importance of including significant numbers of individuals in a cohort was also emphasized. Discussion of the utility of having "pure" forms of asbestos for these experiments brought up the point that human exposures tend to occur by "dirty" mixtures. The value of having standardized samples with which to work in the laboratory was endorsed by all of the participants.

Meeting Announcements

September 2002

Chemical Mixtures

The Society of Toxicology is co-sponsoring the International Conference on Chemical Mixtures 2002 (ICCM 2002), which is scheduled for September 10-12, 2002 at the Crowne Plaza Ravinia Hotel, Atlanta, Georgia. The meeting is sponsored by the Agency for Toxic Substances and Disease Registry (ATSDR), with co-sponsorship from the National Institute for Environmental Health Science (NIEHS), U.S. Environmental Protection Agency (EPA), U.S. Food and Drug Administration (FDA), Health Council of the Netherlands (Gr), National Institute for Occupational Safety and Health (NIOSH), and the International Joint Commission (IJC), as well as the SOT.

The conference will include plenary sessions, breakout sessions, and poster papers that focus on mixtures research, mixtures health risk assessment, and computational methodologies. For more information visit the conference web page at http://www.erg.com/iccm.

December 2002

Safety Evaluation of Vaccines

Workshop on Non-clinical Safety Evaluation of Preventive Vaccines: Recent Advances and Regulatory Considerations. Under the auspices of the CBER, FDA and the SOT, this workshop will be held at the Crystal City Marriott at Reagan National Airport, Arlington, VA with the sponsorship of the FDA Office of Women's Health.

The objective of this meeting is to determine the most appropriate non-clinical methods for vaccine safety testing of investigational new vaccine products. Specifically, discussion will be focused on issues concerning methodologies that can be used to determine the potential adverse effects of new vaccines and adjuvants, appropriate animal models for these evaluations, and the utility of these data for the design and conduct of clinical trials. In addition, the meeting will offer an opportunity for participants to discuss potential approaches to developmental toxicity studies as addressed in the new guidance on reproductive toxicity evaluation of vaccines www.fda.gov/cber/vaccine/vacpubs.htm

This will be an interactive seminar intended for experts in the area of vaccines and preclinical development especially from the disciplines of Regulatory evaluation, Toxicology and Immunology. Due to the space limitations at the seminar facility and the meeting format, registrations will be limited to 150 participants and will be processed as received, with consideration given to the number of representatives per company.

For more information:
http://www.toxicology.org/MemberServices/Meetings/cct-vaccines.html

November 2003

Chemical Allergy: Models and Mechanisms

ITCASS is organizing its meeting in Paris on November 8th and 9th 2003. The topic will be "chemical allergy: models and mechanisms" as usual. The program is based on the presentations sent by members or people who want to attend, so as to keep the meeting in an informal setting. If you need more information contact: Marc Pallardy, INSERM U461, Faculté de Pharmacie Paris XI, rue JB Clément, 92296 Châtenay-Malabry, France

e-mail: marc.pallardy@cep.u-psud.fr
fax: 00-33-1-46 83 54 96

Useful URLs

Submitted by Bob Luebke

The National Center for Environmental Research, part of the U.S. Environmental Protection Agency's Office of Research and Development, provides a list and description of open and upcoming grant RFAs on their web site(http://es.epa.gov/ncer/rfa/). There are 4 solicitations per year, in January, April, August and October. The site provides access to archives of previously funded grants, final reports, and progress reports from current grants. It is possible to sign up for email updates on current grants, and to personalize the page to reflect your interests. One caveat: when this piece was written in early August, several upcoming RFAs on the page were listed as opening in August of 2002, and one in July of 2002, but no link was available for more information. These include:

Opens July 2002

- Exploratory/Futures Research

Opens August 2002

- Aggregate and Cumulative Risk Assessment for Pesticides
- Drinking Water (microbial and chemical)
- NAAQS Implementation Research
- Novel Analysis of Data on Human Exposure to Toxic Chemicals in the Environment

Opens October 2002

- Feasibility of Using Human Health and Exposure Information to Evaluate Environmental Decision-Making

According to the NCER office, final details are still being worked out and October is a more likely opening date for all of the above.

Coming: Fall 2003

Encyclopedic Reference of Immunotoxicology

Submitted by H.-W. Vohr

A year ago I was asked by Springer-Verlag to edit a book about immunotoxicology. The book is intended to fit into a new collection of comprehensive encyclopedic reference books that will provide rapid and selective information about the fast-growing and complex field of immunotoxicology. The objective of this publication is not to replace textbooks on immunology, but rather to provide a useful complement to the textbooks. Entries will consist of short keynotes as well as in-depth essays. The simple A-Z format will provide easy access to relevant information in the field of immunotoxicology. Extensive cross-references between keywords and related articles will enable efficient searches in a user-friendly manner. Outstanding colleagues have joined the Editorial Board, i.e. J. Dean, M. Holsapple, R. House, M. I. Luster, P. Ulrich, H. Van Loveren, and K. L. White Jr., and will help to make this project a success.

For many years, discussions centered around identifying a battery of tests which would easily and reliably identify the immunotoxic potential of a substance. Requirements became more specific only after extensive experience was gained by some industrial laboratories as well as through national and international collaborative studies on immunotoxicity. The first guidelines with the title "Immunotoxicity" were enforced by the American Environmental Protection Agency (EPA) in 1998. The "Encyclopedic Reference of Immuntoxicology" also considers the relevant regulatory requirements.

Of course, immunotoxicology covers not only knowledge of the basic immuntoxic methods required by the guidelines or basic mechanisms of immunotoxic action, but also application of this basic information for human health. This is why plausible, well-founded risk assessment, based on both the full toxicology profile of a substance and the benefits for the patient and consumer is also just as much a part of this field. "Encyclopedic Reference of Immunotoxicology" is thus aimed not only at scientists, clinicians or project managers who are involved with immunotoxicology in some way but also at lecturers, students and the well-informed lay-person.

Publication of the "Encyclopedic Reference of Immunotoxicology" is planned for autumn 2003. You are invited to have a first look at this project on the Internet:

http://encref.springer.de/itox/

Students and Postdocs for Immunotoxicology

If anyone has new students or post docs that were not active in the Immunotoxicology Specialty Section last year, please email Peyton at LMyers@LSUHSC.edu with his/her name and address. This will help update the list of active students and post docs who are interested in activities for the SOT annual meeting in Salt Lake City.

Employment Opportunity

Immunotoxicologist: US Army CHPPM

US Army Center for Health Promotion and Preventive Medicine is looking for a Ph.D. with experience in immunotoxicology. Job duties will include setting up a panel of immunotoxicity screening assays, as well as consultations on human health issues. Background in immunology, toxicology and biochemistry required. For further information contact:

Dr. Michael Major
Health Effects Research Program
US Army CHPPM
michael.major@apg.amedd.army.mil
410-436-7159

Deadlines for Awards Nominations

Consider submitting a nomination.

November 29, 2002

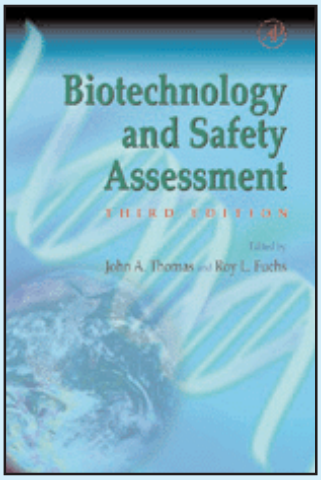
- **Career Achievement**
- **Best SOT Journal Paper of the Year**
- **Outstanding Young Immunotoxicologist**

February 7, 2003

- **Best Presentations by a Student and by a Post-doctoral Trainee**

Watch for more details in the November Newsletter

Book Announcement *by Robert House*



Biotechnology and Safety Assessment, Third Edition

Edited by John A. Thomas and Roy L. Fuchs
Academic Press, 2002

ISBN: 0126887217

$99.95 from Academic Press
(www.academicpress.com)

Since I contributed a chapter, it would be unethical in the extreme for me to write a review of this excellent book. Instead, I have provided verbatim a copy of Academic Press' announcement:

"A comprehensive treatise on new developments in biotechnology, the authors of ***Biotechnology and Safety Assessment, 3e****, bring readers an up-to-date review of food safety issues, pre-clinical safety and development of new foods and drugs, plant biotechnology, food allergies and safety assessment, and consumer benefits with regard to genetically modified food.*

Tomorrow's foods will be obtained from genetically modified crops, offering consumers higher nutritional value and more of it. Our medications will be obtained through a variety of biotechnological procedures yielding more potent and specific medications for diseases and vaccines. In order to make this view of the future come to light, John A. Thomas and Roy L. Fuchs have updated their classic in order to keep readers one step ahead. Written by internationally recognized molecular biologists, plant agronomists, microbiologists, toxicologists, nutritionists, and regulatory authorities, this third edition is an excellent and authoritative resource, making it a valuable resource to any biomedical library or scientific bookshelf."

In comparison to previous editions, the third edition of ***Biotechnology and Safety Assessment*** concentrates rather heavily on biotech-derived plants, making it a good resource for anyone interested in learning more about genetically modified food.

Compiled by Helen Ratajczak

ANYTIME you have a new publication to report, please send it to hratajcz@rdg.boehringer-ingelheim.com It will be included in the next newsletter.

ASTHMA, ALLERGY AND HYPERSENSITIVITY

Cohen MD, Sisco M, Baker K, Li Y, Lawrence D, Van Loveren H, Zelikoff JT, Schlesinger RB. Effects of inhaled ozone on pulmonary immune cells critical to antibacterial responses in situ. Inhalation Toxicology 14:599-619, 2002.

Crosby JR, Cieslewicz G, Borchers M, Hines E, Carrigan P, Lee JJ, Lee NA. Early phase bronchoconstriction in the mouse requires allergen-specific IgG. J Immunol 168:4050-4054, 2002.

Dearman RJ, Caddick H, Stone S, Kenna JG, Basketter DA, Kimber I. Immunogenic properties of rapidly digested food proteins following gavage exposure of mice: a comparison of ovalbumin with a potato acid phosphatase preparation. Food Chem Toxicol 40: 625-633, 2002.

De Jong WH, Van Och FMM, Hartog Jager CF den, Spiekstra SW, Slob W, Vandebriel RJ, Van Loveren H. Ranking of allergenic potency of rubber chemicals in a modified local lymph node assay. Toxicological Sciences 66:226-232, 2002.

Fakhrzadeh L, Laskin JD, Laskin DL. Deficiency in inducible nitric oxide synthase (NOSII) protects mice from ozone induced-lung injury. American Journal of Respiratory and Cell Biology 26:413-419, 2002.

Fischer PH, Steerenberg PA, Snelder JD, Van Loveren H, Van Amsterdam LGC. Association between exhaled nitric oxide, ambient air pollution and respiratory health in school children. Int Arch Occup Environ Health 75:348-353, 2002.

Kimber I, Basketter DA, Gerberick GF, Dearman RJ. Allergic contact dermatitis. Int Immunopharmacol 2: 201-11, 2002.

Kimber I, Dearman RJ. Approaches to assessment of the allergenic potential of novel proteins in food from genetically modified crops. Toxicol Sc 68: 4-8, 2002.

Lee YC, Kwak Y-G, Song CH. Contribution of vascular endothelial growth factor to airway hyperresponsiveness and inflammation in a murine model of toluene diisocyanate-induced asthma. J Immunol 168:3595-3600, 2002.

Redegeld FA, Heijden MW van der, Kool M, Heijdra BM, Garssen J, Kraneveld AD, Van Loveren H, Rhoholl P, Saito T, Verbeek S, Claassens J, Koster AS, Nijkamp FP. Immunoglobulin-free light chains elicit immediate hypersensitivity-like responses. Nature Medicine 8:694-701, 2002.

Wagner JG, Hotchkiss JA, Harkema JR. Enhancement of nasal inflammatory and epithelial responses after ozone and allergen coexposure in brown Norway rats. Toxicol Sc 67:284-294, 2002.

Warbrick EV, Dearman RJ, Kimber I. IgG and IgE antibody responses following exposure of Brown Norway rats to trimellitic anhydride: comparison of inhalation and topical exposure. Toxicology 172: 157-168, 2002.

Warbrick EV, Dearman RJ, Kimber I. Induced changes in total serum IgE concentration in the Brown Norway rat: potential for identification of chemical respiratory allergens. J Appl Toxicol 22: 1-11, 2002.

Reviews

Atherton KT, Dearman RJ, Kimber I. Protein allergenicity in mice: a potential approach for hazard identification. Ann N Y Acad Sci 964: 163-171, 2002.

Kimber I, Dearman RJ. Allergic contact dermatitis: the cellular effectors. Contact Dermatitis 46: 1-5, 2002.

AUTISM

Alarcon M, Cantor RM, Liu J, Gilliam TC, Geschwind DH. Autism Genetic Research Exchange Consortium. Evidence for a language quantitative trait locus on chromosome 7q in multiplex autism families. American Journal of Human Genetics 70:60-71, 2002.

Bartolo PA. Communicating a diagnosis of developmental disability to parents: multiprofessional negotiation frameworks. Child: Care, Health & Development 28:65-71, 2002.

Bolte S, Ozkara N, Poustka F. Autism spectrum disorders and low body weight: is there really a systematic association? International Journal of Eating Disorders 31:349-51, 2002.

Casanova MF, Buxhoeveden DP, Switala AE, Roy E. Minicolumnar pathology in autism. Neurology 58:428-32, 2002.

Christie B. Scottish expert group finds no link between MMR and autism. BMJ 324:1118, 2002.

Eaton L. New research on autism and measles "proves nothing". BMJ 324:315, 2002.

Kemner C, Oranje B, Verbaten MN, van EH. Normal P50 gating in children with autism. Journal of Clinical Psychiatry 63:214-7, 2002.

Morton R, Sharma V, Nicholson J, Broderick M, Poyser J. Disability in children from different ethnic populations. Child: Care, Health & Development 28:87-93, 2002.

Nash JM. The secrets of autism. Time 159:46-56, 2002.

O'Callaghan FJ. Autism—what is it and where does it come from? QJM 95:263-5, 2002.

Shao Y, Raiford KL, Wolpert CM, Cope HA, Ravan SA, Ashley-Koch AA, Abramson RK, Wright HH, DeLong RG, Gilbert JR, Cuccaro ML, Pericak-Vance MA. Phenotypic homogeneity provides increased support for linkage on chromosome 2 in autistic disorder. American Journal of Human Genetics 70:1058-61, 2002.

Siegal M, Varley R. Neural systems involved in "theory of mind". Nature Reviews Neuroscience 3:463-71, 2002.

Wakefield J. New centers to focus on autism and other developmental disorders. Environmental Health Perspectives 110:A20-1, 2002.

Reviews

Andres C. Molecular genetics and animal models in autistic disorder. Brain Research Bulletin 57:109-19, 2002.

Boddaert N, Zilbovicius M. Functional neuroimaging and childhood autism. Pediatric Radiology 32:1-7, 2002.

Horvath K, Perman JA. Autism and gastrointestinal symptoms. Current Gastroenterology Reports 4:251-8, 2002.

Korvatska E, Van de Water J, Anders TF, Gershwin ME. Genetic and immunologic considerations in autism. Neurobiology of Disease 9:107-25, 2002.

Rourke BP, Ahmad SA, Collins DW, Hayman-Abello BA, Hayman-Abello SE, Warriner EM. Child clinical/pediatric neuropsychology: some recent advances. Annual Review of Psychology 53:309-39, 2002.

Sweeten TL, Posey DJ, Shekhar A, McDougle CJ. The amygdala and related structures in the pathophysiology of autism. Pharmacology, Biochemistry & Behavior 71:449-55, 2002.

AUTOIMMUNITY, HYPERSENSITIVITY

Bertry-Coussot L, Lucas B, Danel C, Halbwachs-Mecarelli L, Bach J-F, Chatenoud L, Lemarchand P. Long-term reversal of established autoimmunity upon transient blockade of the LFA-1/intercellular adhesion molecule-1 pathway. J Immunol 168:3641-3648, 2002.

De Jong WH de, Tentij M, Spiekstra SW, Vandebriel RJ, Van Loveren H. Determination of the sensitising activity of the rubber contact sensitisers TMTD, ZDMC, MBT and DEA in a modified local lymph node assay and the effect of sodium dodecyl sulfate pretreatment on local lymph node responses. Toxicology 176: 123-134, 2002.

Garred P, Voss A, Madsen HO, Junker P. Association of mannose-binding lectin gene variation with disease severity and infections in a population-based cohort of systemic lupus erythematosus patients. Genes and Immunity 2:433-441, 2002.

Kimber I, Dearman RJ. Immunologic basis for autoimmunity and the potential influences of xenobiotics. Toxicol Lett 127: 77-81, 2002.

Whitekus M J, Li N, Zhang M, Wang M, Horwitz M A, Nelson S K, Horwitz L D, Brechun N, Diaz-Sanchez D, Nel A E. Thiol antioxidants inhibit the adjuvant effects of aerosolized diesel exhaust particles in a murine model for ovalbumin sensitization, J Immunol 168:2560-2567, 2002.

CYTOKINES AND CHEMOKINES

Asokananthan N, Graham PT, Fink J, Knight DA, Bakker AJ, McWilliam AS, Thompson PJ, Stewart GA. Activation of protease-activated receptor (PAR)-1 PAR-2, and PAR-4 stimulates IL-6, IL-8, and prostaglandin E2 release from human respiratory epithelial cells. J Immunol 168:3577-3585, 2002.

Beger E, Deocharan B, Edelman M, Erblich B, Gu Y, Putterman C. A peptide DNA surrogate accelerates autoimmune manifestations and nephritis in lupus-prone mice. J Immunol 168:3617-3626, 2002.

Bhushan M, Cumberbatch M, Dearman RJ, Andrew SM, Kimber I, Griffiths CE. Tumour necrosis factor-alpha-induced migration of human Langerhans cells: the influence of ageing. Br J Dermatol 146: 32-40, 2002.

Corbaz A, ten Hove T, Herren S, Graber P, Schwartsburd B, Belzer I, Harrison J, Plitz T, Kosco-Vilbois MH, Kim S-H, Dinarello CA, Novick D, van Deventer S, Chvatchko Y. IL-18-binding protein expression by endothelial cells and macrophages is up-regulated during active Crohn's disease. J Immunol 168:3608-3616, 2002.

Cumberbatch M, Dearman RJ, Kimber I. Influence of ageing on Langerhans cell migration in mice: identification of a putative deficiency of epidermal interleukin-1beta. Immunology 105: 466-477, 2002.

Ryan LK, Copeland LR, Daniels MJ, Costa ER, Selgrade MJK. Proinflammatory and Th1 cytokine alterations following ultraviolet radiation enhancement of disease due to influenza infection in mice. Toxicol Sc 67:88-97, 2002.

Stankova J, Turcotte S, Harris J, Rola-Pleszczynski M. Modulation of leukotriene B4 receptor-1 expression by dexamethasone: potential mechanism for enhanced neutrophil survival. J Immunol 168:3570-3576, 2002.

EFFECTS: COMPOUNDS

Ahmad N, Laskin JD, Laskin DL. Regulation of cyclooxygenase-2 expression in hepatic macrophages by nitric oxide during acute endotoxemia. Journal of Leukocyte Biology 71: 1005-1011, 2002.

Dambach DM, Watson LM, Gray KR, Durham SK, Laskin DL. Role of CCR2 in macrophage recruitment and cytokine expression in the liver during acetaminophen induced hepatotoxicity. Hepatology 35:1093-1103, 2002.

De Jong WH, Goldhoorn CA, Kallewaard M, Geertsma RE, Van Loveren H, Bijlsma JWJ, Schouten JSAG. Study to determine the presence of antipolymer antibodies in a group of Dutch women with a silicone breast implant. Clinical and Experimental Rheumatology 20: 151-160, 2002.

Jeon YJ, Youk ES, Lee SH, Suh J, Na YJ, Kim HM. Polychlorinated biphenyl-induced apoptosis of murine spleen cells is aryl hydrocarbon receptor independent but caspases dependent. Toxicol Appl Pharmacol 181:69-78, 2002.

Kimber I, Cumberbatch M, Dearman RJ, Headon DR, Bhushan M, Griffiths CE. Lactoferrin: influence on langerhans cells, epidermal cytokines, and cutaneous inflammation. Biochem Cell Biol 80: 103-107, 2002.

Putman E, Van Loveren H, Bode G, Dean J, Hastings K, Nakamura K, Verdier F, Van Der Laan JW. Assessment of the immunotoxic potential of human pharmaceuticals: a workshop report. Drug Information Journal 36:417-427, 2002.

EFFECTS: ENVIRONMENT

Dorger M, Allmeling A-M, Kiefmann R, Munzing S, Messmer K, Krombach F. Early inflammatory response to asbestos exposure in rat and hamster lungs: role of inducible nitric oxide synthase. Toxicol Appl Pharmacol 181:93-105, 2002.

Rankouhi TR, van Holsteijn I, Letcher R, Giesy JP, van den Berg M. Effects of primary exposure to environmental and natural estrogens on vitellogenin production in carp (Cyprinus carpio) hepatocytes. Toxicol Sc 67:75-80, 2002.

Reviews

Friedman EM, Lawrence DA. Environmental stress mediates changes in neuroimmunological interactions. Toxicol Sc 67:4-10, 2002.

GENETICS AND IMMUNOLOGY

Endlich B, Armstrong D, Brodsky J, Novotny M, Hamilton TA. Distinct temporal patterns of macrophage-inflammatory protein-2 and KC chemokine gene expression in surgical injury. J Immunol 168:3586-3594, 2002.

Locati M, Deuschle U, Massardi ML, Martinez FO, Sironi M, Sozzani S, Bartfai T, Mantovani A. Analysis of gene expression profile activated by the CC chemokine ligand 5/RANTES and by lipopolysaccharide in human monocytes. J Immunol 168:3557-3562, 2002.

Miyamasu M, Sekiya T, Ohta K, Ra C, Yoshie O, Yamamoto K, Tsuchiya N, Tokunga K, Hirai K. Variations in the human CC chemokine eotaxin gene. Genes and Immunity 2:461-463, 2002.

Pennie WD, Kimber I. Toxicogenomics: transcript profiling and potential application to chemical allergy. Toxicol In Vitro 16: 319-326, 2002.

Vockerodt M, Tesch H, Kube D. Epstein-Barr virus latent membrane protein-1 activates CD25 expression in lymphoma cells involving the NFkB pathway. Genes and Immunity 2:433-441, 2002.

MODELS AND METHODS

Freund YR, Dabbs J, Creek MR, Phillips SJ, Tyson CA, MacGregor JT. Synergistic bone marrow toxicity of pyrimethamine and zidovudine in murine in vivo and in vitro models: mechanism of toxicity. Toxicol Appl Pharmacol 181:16-26, 2002.

Walmod PS, Berezin A, Gallagher HC, Gravemann U, Lepekhin EA, Belman V, Bacon CL, Nau H, Regan CM, Berezin V, Bock E. Automated in vitro screening of teratogens. Toxicol Appl Pharmacol 181:1-15, 2002.

Reviews

Basketter DA, Evans P, Fielder RJ, Gerberick GF, Dearman RJ, Kimber I. Local lymph node assay - validation, conduct and use in practice. Food Chem Toxicol 40: 593-598, 2002.

REPRODUCTION AND DEVELOPMENT

Ankley GT, Kahl MD, Jensen KM, Hornung MW, Korte JJ, Makynen EA, Leino RL. Evaluation of the aromatase inhibitor fadrozole in a short-term reproduction assay with the fathead minnow (Pimephales promelas). Toxicol Sc 67:121-130, 2002.

Hanley TR Jr, Breslin WJ, Quast JF, Carney EW. Evaluation of spinosad in a two-generation dietary reproduction study using Sprague-Dawley rats. Toxicol Sc 67:144-152, 2002.

Kim, HS, Shin J-H, Moon HJ, Kim TS, Kang IH, Seok J-H, Kim IY, Park KL, Han SY. Evaluation of the 20-day pubertal female assay in Sprague-Dawley rats treated with DES, tamoxifen, testosterone, and flutamide. Toxicol Sc 67:52-62, 2002.

Little SA, Mirkes PE. Teratogen-induced activation of caspase-9 and the mitochondrial apoptotic pathway in early postimplantation mouse embryos. Toxicol Appl Pharmacol 181:142-151, 2002.

GENERAL IMMUNOTOXICOLOGY

Kimber I, Dearman RJ. Immune responses: adverse versus non-adverse effects. Toxicol Pathol 30: 54-58, 2002.

Piersma AH, Verhoef A, Sweep CGJ, Jong WH de, Van Loveren H. Developmental toxicity but no immunotoxicity in the rat after prenatal exposure to diethylstilbestrol. Toxicology 174:173-181, 2002.

Rojas M, Rugeles MT, Gil DP, Patino P. Differential modulation of apoptosis and necrosis by antioxidants in immunosuppressed human lymphocytes. Toxicol Appl Pharmacol 180:67-73, 2002.

Sleijffers A, Garssen J, Gruijl FR de, Boland GJ, Van Hattum J, Van Vloten WA, Van Loveren H. UVB exposure impairs immune responses after hepatitis B vaccination in two different mouse strains. Photochemistry and Photobiology 75:541-546, 2002.

Termorshuizen F, Wijga A, Garssen J, Outer PN den, Slaper H, Van Loveren H. Exposure to solar ultraviolet radiation in young Dutch children: Assessment by means of a 6-week retrospective questionnaire. Journal of Exposure Analysis and Environmental Epidemiology 12: 204-213, 2002.

Termorshuizen F, Garssen J, Norval M, Koulu L, Laihia J, Leino L, Jansen CT, Gruijl F de, Gibbs NK, Simone C De, Van Loveren H. A review of studies on the effects of ultraviolet irradiation on the resistance to infections: evidence from rodent infection models and verification by experimental and observational human studies. International Immunopharmacology 2:263-275, 2002.

Reviews

Kuper CF, Heer E. de, Van Loveren H, Vos JG. Immune System. In: Handbook of Toxicologic Pathology, Second Edition, Volume 2. Academic Press 585-646, 2002.