Immunotoxicology Specialty Section Newsletter

The Immunotoxicology Specialty Section Newsletter is published 3 times/year (January, June and November) in both printed and electronic formats. 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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Typesetting courtesy of Lexicon Services

President's Message

by Judith Zelikoff

This year is rapidly coming to a close and Y2K is only "minutes away". We have gotten a number of things off the ground and look forward to an exciting meeting in Philadelphia.

Our Specialty Section (SS) Reception will be held on Monday evening at 6:15, so mark your calenders. We will be changing pace a bit by having Dr. Jack Dean welcome the new millennium by presenting an upbeat discussion on the past, present, and future of immunotoxicology. Dr. Dean is well-known to all of us in this field as one of the founding fathers of immunotoxicology. We are also trying to arrange for some sort of entertainment that will go well with our chicken fingers and nachos. This year it appears that SOT decided to reduce the time for SS receptions to only one hour. We have a lot on the agenda this year so please plan to stay a bit longer.

I want to thank all of you who have submitted nominations for our three new awards. Nominations will be accepted up until November 29th. Also, many of our members have responded to our plea for recommendations for Specialty Section officers that will serve in the upcoming year. Let me assure you that each recommendation will be given full consideration by the Immunotoxicology Nominating Committee when they meet before the end of the year.

Deciding upon a new Student Representative was a difficult decision since we had so many really good candidates, but we have elected Susan Carol Mckarns to serve as the liaison between the students and Immunotoxicology Executive Council. Be sure to touch base with her to make your particular interests/concerns known. She has already been working on a number of issues with me which will hopefully enhance connections between the students and full/associate members of our SS. She may be contacting our student members in regards to the student sub-section of the updated Immunotoxicology SS membership directory which Drs. Mitchell Cohen (Chairperson, Education Committee) and Michael McCabe (Chairperson, Membership Committee) are working on. I thank Susan for all of her help. Also, please remember that the Awards Committee (chaired by Dr. John Barnett) are anxiously awaiting student and post-doc submissions of their poster/platform presentations. The deadline for these submissions is

continued on page 2 . . .

President's Message

. . . continued from page 1

January 31, 2000. Please direct your questions to Dr. Barnett or refer to your previous SOT Communique or June SS newsletter for additional details. A copy of the newsletter can be found on our website.

I would like to congratulate Drs. Norbert Kaminski and Michael McCabe for their imminent appointment to the NIH ALTX-4 Study Section. It is my pleasure to be serving with them on Study Section and it is clear that our scientific discipline is well-represented. In this same regard, a piece of news that some of you might find of interest concerns the proposed restructuring of the NIH Division of Research Grants and the establishing of new Special Emphasis Panels, none of which appear to directly consider Immunotoxicology. This could be disastrous for those of us in academia or those entering the academic environment and seeking grant funding. However, thanks to the early heads-up from Dr. Scott Burchiel many of us were able to send off letters to the NIH voicing our concerns. We'll just have to wait to see how this turns out.

Thanks for a pleasant half-year and I look forward to seeing all of you in March. Before then, however, please feel free to contact me if you have any concerns or new ideas that might help to strengthen our SS.

Committee Reports

REGULATORY COMMITTEE

submitted by Kenneth Hastings

ICCVAM

As we reported in the last issue of the Newsletter, the Murine Local Lymph Node Assay (LLNA), the first test method to undergo peer review by the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), was endorsed by the Peer Review Panel and ICCVAM as a stand-alone alternative to traditional guinea pig assays (e.g. the guinea pig maximization test, the Buehler assay) for identifying test chemicals that could produce allergic contact dermatitis. Early in the year, this recommendation of ICCVAM was forwarded to the various ICCVAM agencies with a request that a response and comments on implementation be formulated.

To date, the ICCVAM Agencies (regulatory and non-regulatory) have responded in writing and/or at a public meeting of the National Toxicology Program (NTP) Advisory Committee for ICCVAM on October 14, 1999. Agency responses have been overwhelmingly favorable. Both the US Food and Drug Administration (FDA) and the US Environmental Protection Agency (EPA) have provided written responses, along with presentations at the Oct. 14 meeting, indicating acceptance of the LLNA ICCVAM Peer Review Report. Additionally, these two major regulatory agencies intend to adopt the LLNA for regulatory purposes. Specifically, the FDA has indicated that the LLNA would be acceptable to support the safety of clinical trials and marketing applications for drugs, medical devices, food additives, and cosmetic ingredients where guinea pig assays would have been used. The EPA indicated that the LLNA is an acceptable free standing test in the pesticide and toxic substances programs and, in addition, would be considered the preferred method for testing where there are no reservations concerning its use.

While there has been broad acceptance of the LLNA, the process of modifying guidelines, guidance documents, and the like to reflect this remains an area for attention. However, progress is being made. In fact, test results with the LLNA have already been accepted by the FDA to support the safety of clinical trials with topical drug products. Although the situation with respect to cosmetics is less clear, this should be worked out in the near future. It is also important to note that while non-regulatory agency acceptance of the ICCVAM report will have no direct regulatory impact, it is nevertheless important in its scientific implication. The Oct. 14 meeting provided an opportunity for public dissemination of the status of the LLNA within ICCVAM agencies: each agency is formulating their own announcement mechanism of the implementation of this test method. (Thanks to Denise Sailstad, US EPA, for help in preparing this report).

ECETOC

The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) has established a Task Force to consider aspects of skin sensitization testing, which is chaired by Dr. Ian Kimber. At this point, Dr. Kimber reports that the Task Force will address two remits: (1) in the context of animal welfare considerations, make recommendations for the conduct of current and proposed OECD skin sensitization test methods with respect to (a) appropriate test configuration (protocol) for the purposes of hazard identification and labeling and (b) the requirement for positive controls; and (2) make recommendations for the use of relevant skin sensitization test methods for the purposes of (a) determination of relative potency and the threshold dose necessary for the induction of skin sensitization and (b) risk assessment. The first report is in final stages of completion.

OECD

The situation with OECD guideline 407 (essentially, one month repeat-dose toxicology studies in rodents) is that, as adopted 27th July, 1995, the following immune-related end-points should be evaluated: weight and histopathology of thymus and spleen, and histopathology of draining and distant lymph nodes, Peyer's patches, and bone marrow, along with standard hematology with differential cell counting. According to Dr. Josephus Vos, inclusion of some form of functional assay (the plaque assay or the ELISA equivalent) is still under consideration.

ILSI

The International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) Immunotoxicology Technical Committee has established a Drug Hypersensitivity Project Committee, which is chaired by Dr. Thomas Kawabata. The Committee includes clinical allergists, pharmacologists, and toxicologists from academia, industry, and government, and has the stated purpose of drafting a white paper on the state of the art in drug allergy testing. The Committee does not have any regulatory authority; rather, the intent is to identify areas of concern in drug allergy and to make recommendations that would stimulate research in this area. Specifically, the Committee is addressing the issue of systemic drug hypersensitivity, especially drug allergies observed following oral or parenteral administration. The Committee is not considering issues related to dermal or respiratory hypersensitivity: these appear to be special concern areas that are being adequately addressed by current research. The Committee anticipates having a completed product sometime in the next year.

SPECIALTY SECTION PROGRAM COMMITTEE REPORT

submitted by Don Fraser and Dori Germolec

I am proud to report that of the ten proposals generated this past year from the Immunotoxicology Specialty Section, seven have been accepted for presentation at the upcoming 2000 SOT Annual Meeting in Philadelphia. The 2000 Program includes: three Symposia entitled: 1) *Immunotoxicity of Ethanol: Lessons from a Structurally Simple, but Functionally Complex Immunotoxicant*; 2) *Values and Limitations of Transgenic Animals in Immunotoxicity*; and, 3) *Dendritic Cells: Targets for and Mediators of Immunotoxicity and Allergy*; two Workshop Sessions entitled: 1) *Human Immunotoxicity: Examples and Strategies for Determining Risk*; and, 2) *Latex Allergy in the Workplace*; one Roundtable Session entitled *Autoimmune Consequences of Toxicant Exposure in Human Populations: Fact or Fiction?*; and, one Continuing Education Course entitled *Pulmonary Immunotoxicology*. I would like to thank all those responsible for an exciting line-up of programs, particularly Judith Zelikoff and Kathleen Rodgers for all their guidance, and the Immunotoxicology Program Committee. Finally, I would like to congratulate Dori Germolec on the birth of her son Iain, as his impending delivery at the time of this past year's SOT, provided me an opportunity to serve as Co-chair (with Judy Zelikoff) of the Program Committee. Congratulations to Dori and her family, and thanks again to all. - D.F.

I'd like to add my thanks, especially to Don, Judy and Kathy for bailing me out and shepherding the Y2K program. Thanks to their efforts and your excellent proposals, the Immunotoxicology Specialty Section is well represented and our sessions will

continued on page 4 . . .

. . . continued from page 4

make an outstanding contribution to the meeting. See you in Philadelphia. - D.G.

SOT PROGRAM COMMITTEE REPORT

submitted by Mary Jane Selgrade

2001 is closer than you think. As unbelievable as this may seem, it's time to think about potential Symposia, Workshops, Round tables, and Continuing Ed courses for SOT 2001 to be held in San Francisco. This is a nice place, which should help to attract speakers. The Immunotoxicology Specialty Section has always done a very good job putting together programs and this makes the meeting interesting for all of us. In part we've been successful getting our submissions accepted by the Program Committee because we have gotten our act together early and been organized. If you have an idea for any of the program types described below, it works best if you come to the 2000 meeting with a proposal in hand. (We have also been known to prevail upon people who have not this to put a program together before April 1).

The proposal description should include a 150-200 word description of the proposed program, a list of potential speakers, their addresses and affiliations (by April 1 these speakers should have been contacted and agreed to participate), and names of the chairpersons. If you have an idea for a program and can think of a couple speakers, but can't think of others, float the idea over the immunotoxicology list server and ask if there is anyone who has ideas to add and would like to co-chair. SOT really likes to have co-chairs from different organizations, and it provides an excellent way for you to get to know other investigators and explore common interests. If you have an idea that may interest another specialty section contact the president of that section (they are listed in the directory) or a colleague in that section and ask who might be available to work with you on it. The program committee likes to see jointly sponsored programs. I really encourage people who have not done this before to give it a try. You do not have to be on the specialty section program committee. You don't have to be an old and venerated toxicologist (none of us would admit to that). You just need to be interested, enthusiastic, and willing to do a little work.

SOT defines the different program types as follows: Symposia present "cutting edge" science, new areas, concept, or data. Workshops emphasis accepted state-of-the-art knowledge or methods with emphasis on interactive presentations and discussion. Both are 3 hours or less (maximum 5 speakers). Round tables present controversial issues in a 1 ½ hour format that includes a moderator and 2-3 speakers. Each speaker makes a 3-5 minute statement and the balance of time is for questions and discussion. Continuing Ed presents generally accepted, state-of-the-art knowledge with the goal of education. There are 4-5 speakers and a syllabus with all the overheads. In general, SOT will pay for no more than 1 non-member speaker/symposium. The specialty section can usually pick up a second non-member speaker. Remember this is a Toxicology meeting. Don't stray too far from that topic. The Immunotoxicology Specialty Section program committee will need program descriptions by April 1 so that we can prioritize them and send them on to SOT by April 15. The Specialty Section's priorities carry a lot of weight with the SOT program committee, so it's important that we see the program. If I can answer any questions or help anyone in putting together a program please call (919-541-1821) or email selgrade.maryjane@EPAmail.EPA.Gov). We need your help to make the 2001 meeting the best ever.

AWARDS COMMITTEE REPORT

submitted by John Barnett

Members are reminded that nominations for the Achievement Award, Paper of the Year Award and Young Investigator Award are due soon. The criteria for these nominations were recently sent to all members on the Immunotoxicology List Server and were also discussed in the last newsletter. If you have discarded the last newsletter it is available on our web site. ▩

Meeting Reports

We're all aware of the growing importance of immunotoxicology to the scientific and regulatory communities. One way to track the professional recognition of our discipline is by the number of scientific meetings that include immunotoxicology on the program. If you have organized or participated in a local, national or international meeting in which immunotoxicology was a focus, please let us know, and it will be included in the next newsletter.

The Pacific Northwest Association of Toxicologists (PANWAT)

The PANWAT meeting was held at "The Resort at the Mountain" near Mt. Hood, Oregon on Oct. 1-2. As President this year, I was in charge of the program. Since the topic of the symposium can influence how many people attend the regional meeting, and since we have few immunotoxicologists in our area, I looked to blend immunology with other subdisciplines. The title of the symposium was "Cytokines in Target Organ Toxicity". The speakers were:

- Nancy Kerkvliet, Oregon State University: *Introduction to cytokines;*
- Debra Laskin, Rutgers University: *Cytokines and tissue injury;*
- Kevin Driscoll, Procter and Gamble: *Cytokines and regulation of pulmonary inflammation;*
- Paige Lawrence, Wash. State University: *The role of cytokines in immunotoxicity. TCDD and influenza A infection;*
- Dori Germolec, NIEHS: *The role of cytokines in dermal toxicity;*
- Curt Omiecinski, U of W: *Cytokines and regulation of P450 activity.*

The symposium was very well-received, turnout was great (86 people registered), and the weather was perfect. For further information, contact Nancy Kerkvliet.

The New York Academy of Sciences

NYAC sponsored a meeting entitled *Toxicology for the Next Millennium*, held at the Airlie House in Warrenton, VA, September 20-23, 1999. The conference featured talks on advances in toxicology, including cancer, neurotoxicology, developmental toxicology and immunotoxicology. The immunotoxicology session was chaired by Mike Luster of NIOSH. The speakers included:

- Akira Takashima, University of Texas Southwest Medical Center: *New technologies to prevent and treat contact hypersensitivity responses;*
- Mike Luster, NIOSH: *Use of molecular biology in immunotoxicology research;*
- Bob Luebke, EPA: *Aging and resistance to infection following xenobiotic exposure;*
- MaryJane Selgrade, EPA: *Development of animal models to assess the effects of air pollutants on allergic lung disease;*
- Mike Holsapple, Dow Chemical; *Systemic approach to assess xenobiotic-induced immunosuppression.*

For further information, contact Bob Luebke.

The 26th Annual Aquatic Toxicology Workshop (ATW)

This meeting was held October 4-8, 1999 in Edmonton, Alberta. The meeting was attended by about 300 people, primarily consultants, and representatives from industry and government. This year, however, academics also made a notable showing at the meeting.

The ATW, also known as SETAC-Canada, is held on an annual basis; the meeting focuses primarily on aquatic issues, with a particular emphasis upon those most relevant to the Canadian environment. The 1999 program included sessions on endocrine disruption, health impacts of mining, legal implications of investigative toxicology, and environmental effects of pulp and paper mill processing. This year, in collaboration with Judith Zelikoff, the ATW Organizers tried something unique for this group by including a full day symposium session on Immunotoxicology, co-chaired by Judith Zelikoff and Peter Thomas. The purpose of the symposium was to communicate the basic concepts of immunotoxicology to non-immunotoxicologists and to inform the regulators and government agencies that immunotoxicology has been, and would continue to be, a useful system for predicting the impact of

continued on page 6 . . .

. . . continued from page 5

contaminated aquatic environments on directly and indirectly-exposed species.

The Symposium was entitled *Profiling Immunotoxicology*. The session began with Peter Thomas (Covance Laboratories, USA) discussing historic and current approaches used in immunotoxicology testing, followed by Jeff Vos (RIVM, Bilthoven, The Netherlands) discussing the comparative sensitivity of different fish species to pollutant-induced immunotoxicity. Vickie Blazer (U.S. Geological Survey, USA) and Judith Zelikoff (New York University School of Medicine, USA) discussed the usefulness of fish immune parameters as biomarkers of exposure and effects, respectively. Tracy Collier (NOAA, USA) presented data on the usefulness of host resistance studies in fish for predicting adverse health outcomes in feral populations. The symposium then moved up the evolutionary ladder with Keith Grasman (Wright State University, USA) discussing immunosuppression in fish-eating birds of the Great Lakes and Peter Ross (Institute of Ocean Sciences, Canada) discussing the role of immunotoxicity in disease-related mass mortalities in marine mammals. Bob Luebke (Environmental Protection Agency, USA) discussed the potential immunotoxic effects of pesticide exposure in humans. Marshall Adams (Oak Ridge National Laboratories, USA), the final speaker, brought the issues home and discussed the utility of immunotoxicological studies in ecological and human risk assessment. Following the formal presentations, Dr. Thomas moderated an hour-long panel discussion which included issues that ranged from "immunotoxicology in the new millennium" to the utility of immunotoxicology in "real-world" situations.

Overall, the symposium was a huge success and will be published in *Human and Ecological Risk Assessment*. Moreover, based upon the overwhelming interest, the chairs are planning to submit a modified version of the symposium as a Continuing Education Course for SOT.

For further information, contact Judith Zelikoff or Bob Luebke.

8th Summer School in Immunotoxicology

submitted by Jacques Descotes

The 8th school organized by the nonprofit association "Summer School in Immunotoxicology" was devoted to preclinical methods for detecting the potential hypersensitivity of pharmaceuticals. It was held in Divonne-les-Bains (France) on 4-6 October 1999 and attended by over 80 participants and speakers from Europe, the US, Japan and South Africa.

Traditionally, summer schools begin with a medical approach of the immunotoxicological issue being considered. E. Van Ganse (Lyon Poison Center, France) overviewed the pharmaco-epidemiology of drug allergies and G. Choquet-Kastylevsky (Lyon Poison Center and INSERM U503) current procedures for the diagnosis of drug allergies in humans. Both presentations demonstrated the difficulties of addressing drug allergies from a medical point of view that are reminiscent of the difficulties when predicting the potential of pharmaceuticals to induce hypersensitivity preclinically.

Prior metabolic activation of the offending drug is often required for allergic reactions to develop. K. Parke (Liverpool University, UK) reviewed the most illustrative examples. One major recent advance in our understanding of the mechanisms of drug allergies is the identification of the role of T lymphocytes and the Th1/Th2 balance (H. Lebrec, Paris University, France). Interestingly, drugs can also interact directly with T lymphocytes, and the concept of non-covalent drug recognition by T cells was overviewed by W. Pichler (University of Bern, Switzerland).

The Gell and Coombs classification of drug allergies, although still widely used, is hardly valid today and cannot be considered as a helpful tool, particularly in the context of preclinical safety evaluation (J. Descotes, Lyon Poison Center and INSERM U503). The question why a molecule is a sensitizer remains a difficult one even though some progress has been made in the structure-activity relationships of contact sensitizers (J.P. Lepoittevin, University of Strasbourg, France). Due to the pivotal role of cytokines in the regulation and development of drug allergies, techniques to measure cytokines are critical to

assess hypersensitivity as reviewed by R. House (Covance Laboratories, USA).

Few models are available to predict the potential hypersensitivity of pharmaceuticals. The Local Lymph Node Assay (LLNA) is promising, especially with the addition of cytokine fingerprinting (I. Kimber, AstraZeneca, UK), as is the Popliteal Lymph Node Assay (PLNA), either the primary ('classical') or the modified PLNA (R. Pieters, Utrecht University, The Netherlands). Transgenic animals are potentially useful models although their application in the field of drug allergies is still in its infancy (B. Ryffel, Cape Town University, South Africa). Finally, testing for the immunogenicity of macromolecules in laboratory animals raises specific questions addressed by D. Wierda (Eli Lilly and Co, USA).

At the end of this two-day school, that much more had to be known and done before one can reliably predict the potential of pharmaceuticals for hypersensitivity was a widely shared conclusion, particularly from a regulatory perspective (K. Hastings, US FDA). The final roundtable chaired by J. Dean (Sanofi-Synthelabo, USA) and J. Descotes addressed a set of key issues. Drug hypersensitivity is certainly a major problem for the industry. Causative or risk factors to be considered include the daily dose (to be as small as possible), bioactivation of the mother compound (that can lead to reactive metabolites and unwanted covalent binding), and patient's factors, such as (immuno)genetic predisposition, lifestyle, age, stress, underlying disease... Models, the predictive value of which was discussed, include expert systems, biomarkers in clinical trials, the PLNA and LLNA, and *in vitro* exposure of human T cells. "Data mining" to expand structure-activity relationship database (including input from failed compounds) and improved rules are required to refine existing expert systems. The PLNA was considered the first choice assay, but a large interlaboratory validation study was deemed absolutely necessary. That useful information can also be obtained from the human experience was stressed, including immunological endpoints in clinical studies and the definition of individuals at risk of hypersensitivity.

The full text of all presentations and the final recommendations will be published as a special issue of the journal *Toxicology*, expected to be published by mid-2000.

Safety Evaluation of Immunomodulatory Biopharmaceuticals: Can We Improve the Predictive Value of Preclinical Studies?

submitted by Joan Rener

This conference, organized and sponsored by Biogen, Covance Laboratories, and the USFDA, was held on September 23 and 24 at the Bethesda Marriott, Bethesda, MD. The purpose of this meeting was to address the difficult issues of designing appropriate preclinical testing strategies for compounds intended to treat non-life-threatening diseases of the immune system. Speakers from industry, academia and US and European regulatory agencies discussed the strengths and limitations of current testing strategies and new methods and technologies. Specific topics included:

- The human immune system as a target for drug development
- Comparison of rodent, primate, and human immune responses
- Summaries of animal and clinical trial data
- Regulator agencies' approaches to risk/benefit assessment
- Improving preclinical approaches to risk assessment

The scientific presentations were followed by four roundtable sessions in which the audience and speakers addressed the following issues:

- Methods for predicting tumorigenicity
- Methods for assessing immunocompetence in vivo
- Methods for assessing immunocompetence in vitro
- Methods for assessing reproductive effects and the immunocompetence of offspring

The proceedings will be published in early 2000 in *Human and Experimental Toxicology*.

Upcoming Meetings

One of our own immunotoxicology members, Judith Zelikoff will be attending and presenting a paper on *Immune System Biomarkers of Environmental Pollution* at the fourth Princess Chulabhorn International Science Congress which will meet from November 28 - December 2, 1999 in Bagkok, Thailand to discuss *Chemicals in the 21st Century*. The aims of the Congress is to interrelate the key areas of health, environment and technology by bringing together experts and practitioners from a wide range of specializations all of which involve the use and control of chemicals. Through the sharing of expertise and the exchange of knowledge, new directions for the beneficial and safe use of chemicals will be sought as a benchmark for developments in the next century.

Speakers from at least 11 different countries will meet and discuss such areas as:

- Biomarkers of Human Exposure to Environmental Toxicants
- Environmental Carcinogenesis
- Cancer Chemoprevention
- Endocrine Disruptors
- Indoor Air Quality
- Environmental Biomarkers
- Metals in health and disease.

The meeting offers a unique setting for toxicologists from all over the world to come together and discuss the negative and positive impact of chemicals on our life quality of life. For further information, contact Judith Zelikoff.

Environmental Health Perspectives Monograph on Autoimmunity Available

Volume 107, Supplement 5 of *EHP* was recently published, and is recommended reading for anyone interested in the possible role that environmental chemicals may play in the development of autoimmune disease. The monograph is based on a workshop entitled *Linking Environmental Agents and Autoimmune Diseases*, held at the National Institute of Environmental Health Sciences (Research Triangle Park, NC) on September 1-3, 1998. The monograph is subdivided into sections on Susceptibility, Systemic Diseases, Organ-Specific Diseases, and Specific Exposures and Mechanisms. These topics are book-ended by an overview of the topic and workshop summary/research agenda. There's a lot of information here, and none of it is light reading. Still, this volume provides a good single resource on an important topic. Check it out. ▣

Committee Membership: 1999-2000

Awards Committee
Chair: John Barnett
Members: Jeanine Bussiere, Mitch Cohen, Don Frazier, Ian Kimber, Mike McCabe, Leigh Ann Naas, Jean Regal, Kathy Rodgers, Larry Updyke, Michael Whitekus, Judith Zelikoff

Program Committee
Chair: Dori Germolec
Members: Mitch Cohen, Don Fraser, Brian Freed, Ian Kimber, David Lawrence, Paige Lawrence, Greg Ladics, Mike Lynes, Mike McCabe, Kathy Rodgers, Kathy Sarlo

Methods Committee
Chair: G. Frank Gerberick
Members: Jeanine Bussiere, Kenneth Hastings, Robert House, Deborah Keil, Greg Ladics, Robert Luebke, Craig Zwicki

Regulatory Committee
Chair: Kenneth Hastings
Members: Don Frazier, Joe Griffin

Membership Committee
Chair: Michael McCabe
Members: Mitchell Cohen, Tai Liang Guo, Craig Zwicki

Education Committee
Chair: Mitchell Cohen
Members: Brian Freed, Steve Holladay, Niel Karrow, David Lawrence, Neil Pumford

Communications Committee
Chair: Robert House
Members: Bob Luebke, Linda Thurmond

Clip this list and use it as a handy check-sheet when shopping at your local library

Recent Immunotoxicology Publications

DATA ANALYSIS

Keil, D. et al. (1999). Evaluation of multivariate statistical methods for analysis and modeling of immunotoxicology data. Toxicol. Sci. 51:245-258.

Selgrade, M.K. (1999). Use of immunotoxicity data in health risk assessments: uncertainties and research to improve the process. Toxicology 133(1):59-72.

AUTOIMMUNITY

Environmental Health Perspectives, volume 107, Supplement 5. (1999). Entire volume.

Pieters, R. et al. (1999). Assessment of autoimmunogenic potential of xenobiotics using the popliteal lymph node assay. Methods 19(1):71-77.

METHODS

Burchiel, S.W. et al. (1999). Uses and future applications of flow cytometry in immunotoxicity testing. Methods 19(1):28-35.

Gaspard, I. et al. (1999). Quantitation of cytokine mRNA expression as an endpoint for prediction and diagnosis of xenobiotic-induced hypersensitivity reactions. Methods 19(1):64-70.

House, R.V. (1999). Theory and practice of cytokine assessment in immunotoxicology. Methods 19(1):17-27.

Pallardy, M. et al. (1999). Assessment of apoptosis in xenobiotic-induced immunotoxicity. Methods 19(1):36-47.

PESTICIDES

Colosio, C. et al. (1999). Immune parameters in biological monitoring of pesticide exposure: current knowledge and perspectives. Toxicol. Lett. 108(2-3):285-95.

Voccia, I. et al. (1999). Immunotoxicity of pesticides: a review. Toxicol. Ind. Health 15(1-2):119-32.

HOST RESISTANCE

de Waal, E.J. et al. (1999). Effects of salmeterol on host resistance to *Trichinella spiralis* in rats. Int. J. Immunopharmacol. 21(8):523-9.

Fischer, W.H. et al. (1999). Function and dysfunction of CD4(+) T cells in the immune response to melanoma. Cancer Immunol. Immunother. 48(7):363-370.

Luebke, R.W. et al. (1999). Effects of aging on resistance to *Trichinella spiralis* infection in rodents exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Toxicology 136(1):15-26.

VARIOUS CHEMICALS AND DRUGS

Albano, E. et al. (1999). Hydroxyethyl radicals in ethanol hepatotoxicity. Front. Biosci. 4:D533-40.

Bruder, M.C. et al. (1999). Intestinal T lymphocytes of different rat strains in immunotoxicity. Toxicol. Pathol. 27(2):171-9.

Chen, S. et al. (1999). Persistent effect of in utero meso-2,3-dimercaptosuccinic acid (DMSA) on immune function and lead-induced immunotoxicity. Toxicology 132(1):67-79.

Dastych, J. et al. (1999). Murine mast cells exposed to mercuric chloride release granule-associated N-acetyl-beta-D-hexosaminidase and secrete IL-4 and TNF-alpha. J. Allergy Clin. Immunol. 103(6):1108-14.

De Jong, W.H. et al. (1999). Detection of immunotoxicity of benzo[a]pyrene in a subacute toxicity study after oral exposure in rats. Toxicol. Sci. 50(2):214-20.

Gasiorowski, K. et al. (1999). Evaluation of genotoxic and immunotoxic activities of potential glucose biosensor components: ferrocenes. Biometals 12(1):19-26.

Graziano, M.J. et al. (1999). Immunotoxicity of the anticancer drug CI-994 in rats: effects on lymphoid tissue. Arch. Toxicol. 73(3):168-74.

Kamath, A.B. et al. (1999). Role of Fas-Fas ligand interactions in 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced immunotoxicity: increased resistance of thymocytes from Fas-deficient (lpr) and Fas ligand-defective (gld) mice to TCDD-induced toxicity. Toxicol. Appl. Pharmacol. 160(2):141-155.

Kim, J.H. et al. (1999). Effect of biphenyl dimethyl dicarboxylate on the cellular and nonspecific immunosuppressions by ketoconazole in mice. Arch. Pharm. Res. 22(3):255-61.

Klykken, P. C. et al. (1999). Toxicology and humoral immunity assessment of octamethylcyclotetrasil-oxane (D.4) following a 28-day whole body vapor inhalation exposure in Fischer 344 rats. Drug Chem. Toxicol. 22(4); 655-678

Lall, S.B. et al. (1999). Role of corticosteroids in cadmium induced immunotoxicity. Drug Chem. Toxicol. 22(2):401-9.

Li, Q. et al. (1999). Acute immunotoxicity of p-chloronitrobenzene in mice: II. Effect of p-chloronitrobenzene on the immunophenotype of murine splenocytes determined by flow cytometry. Toxicology 137(1):35-45.

Michielsen, C.C. et al. (1999). The role of the immune system in hexachlorobenzene-induced toxicity. Environ. Health Perspect. 107(Suppl 5):783-792.

Nilsen, A. et al. (1999). Short-term exposure of rodents to diesel exhausts: usefulness for studies of genotoxic and immunotoxic effects. Chem. Biol. Interact. 118(1):19-38.

Vandebriel, R.J. et al. (1999). In vitro exposure effects of cyclosporin A and bis(tri-n-butyltin)oxide on lymphocyte proliferation, cytokine (receptor) mRNA expression, and cell surface marker expression in rat thymocytes and splenocytes. Toxicology 135(1):49-66.

Whalen, M.M. et al. (1999). Immunotoxicity of environmentally relevant concentrations of butyltins on human natural killer cells in vitro. Environ. Res. 81(2):108-16.

Yucesoy, B. et al. (1999). In vitro effects of various metals on natural killer cell activity in cultured human lymphocytes. Immunopharmacol. Immunotoxicol. 21(3):599-607.

NON-MAMMALIAN MODELS

Beaman, J.R. et al. (1999). Mammalian immunoassays for predicting the toxicity of malathion in a laboratory fish model. J. Toxicol. Environ. Health 56(8):523-42.

Gogal, R.M. Jr. et al. (1999). Mandates to develop non-mammalian models for chemical immunotoxicity evaluation: are fish a viable alternate to rodents? Toxicol. Lett. 106(2-3):89-92.

REVIEWS/OVERVIEWS

Bernstein, I.A. et al. (1999). Cultured keratinocytes in in vitro dermatotoxicological investigation: a review. J. Toxicol. Environ. Health B Crit. Rev. 2(1):1-30.

Cohen, M.D. (1999). Symposium overview: alterations in cytokine receptors by xenobiotics. Toxicol. Sci. 48(2):163-9.

Kiecolt-Glaser, J.K., et al. (1999). Psychoneuroimmunology and immunotoxicology: implications for carcinogenesis. Psychosom. Med. 61(3):271-2.

Karol, M.H. and Stolkier, D. (1999). Immunotoxicology: past, present and future. Inhal. Toxicol. 11:523-534.

Luster, M.I. et al. (1999). Tumor necrosis factor and toxicology. Crit. Rev. Toxicol. 29 (5): 491-511.

Rudmann, D.G. et al. (1999). Utilization of genetically altered animals in the pharmaceutical industry. Toxicol. Pathol. 27(1):111-4.

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