Toxicologic Pathology and the Immune System

Scientific Sessions

Co-Chairs:
Susan Elmore, DVM, MS, DACVP, DABT, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC
Patrick J. Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE, and Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

The Society of Toxicologic Pathology (STP) will host a symposium on the fundamentals and recent innovations in the field of toxicologic pathology and the immune system. The focus of this international meeting is to correlate advances in the morphologic evaluation and interpretation of immunopathology findings with functional, cellular, and molecular knowledge in a series of plenary and poster sessions.

The major goal of the meeting is to provide an interactive program that allows for discussion of the current state of knowledge of immunopathology evaluations in conventional toxicology and specialized immunopathology studies. Foundational sessions will include fundamentals of Immune System Biology, including Basic Immunology, Functional Tests and Toxicologic Immunopathology; Innate Immunity; Acquired Immunity; Developmental Immunology; Challenges of Therapeutic Immunomodulation; and Issues and Observations Concerning Environmental Exposure to Immunotoxictants.

The presentations will focus on a mix of standardized and contemporary pathology methods for immunopathology investigations. The meeting will also provide a unique forum to review the progress in the application of best practices for routine and specialized pathology evaluations of the immune system across the pharmaceutical, chemical, and academic worlds of pathology. An interactive panel discussion will explore the issues associated with differentiation of stress effects and immunotoxicity.

The traditional NTP Satellite Symposium, entitled Pathology Potpourri, in advance of the symposium will focus on the customary presentations of challenging lesions but will also include a presentation on proposed INHAND lymphoid nomenclature. Four continuing education sessions will be held on Sunday before the general sessions begin; Interacting with Regulatory Authorities: What to Do and What Not to Do; Novel Biomarker Discovery, Qualification, and Application in Drug Development: What’s New, What’s Used, and What’s New, Used and Successful; Ultrastructural Analysis and Toxicologic Pathology; and Histopathology of the Rodent Lymphoid and Hematopoietic Systems. A half-day Career Development Workshop: “A Consultant’s Calling Workshop: Do You Have What It Takes to Be a Consultant in Toxicologic Pathology?” will also be held on Sunday and the Career Development Lunchtime Series Monday will provide guidance on the use of professional networking in career development.

The immune system and its responses is one of the more complex and challenging arenas of toxicologic inquiry and regulatory concern, and this congress promises to be an opportunity to review and expand your knowledge in this important field. We hope you will join us for this exciting program in Denver.

Monday Morning

8:10 AM–9:10 AM
Keynote Address:
TCDD: An Environmental Immunotoxicant Reveals a Novel Pathway of Immunoregulation
Nancy Kerkvliet, PhD, Oregon State University, Corvallis, OR

Session 1

9:10 AM–12:00 NOON
Immune System Biology: Immunology, Functional Tests and Toxicologic Pathology

Co-Chairs:
Susan Elmore, DVM, MS, DACVP, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC and Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

Various aspects of the normal anatomy, histology, immunology, and general toxicologic pathology of the immune system will be reviewed. The overview will include basic immunology, tests of immune function, and enhanced histopathology of the immune system. Subsequent Symposium sessions will delve into more detail of these aspects of the immune system.

9:10 AM–9:15 AM
Introduction
Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

9:15 AM–10:00 AM
Immunology for the Toxicologic Pathologist
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

10:00 AM–10:40 AM
Break
Career Development Lunchtime Series
12:30 PM–1:30 PM
Professional Networking Using New Technologies
Co-Chairs: Julie Johnson, DVM, PhD, DACVP, Abbott Laboratories, Abbott Park, IL, Elizabeth Galbreath, DVM, PhD, DACVP, Lilly Research Laboratories, Indianapolis, IN, Kevin Keane, DVM, PhD, Huntington Life Sciences, East Millstone, NJ, and Alric Lopez, DVM, PhD, DACVP, Huntington Life Sciences, East Millstone, NJ

Presented by the STP Career Development and Outreach Committee, Education Committee, and Internet Committee

(Free Event, registration required)

STP Web Site Technology
Using the new STP collaboration tool—ToxPathNet
- Common interest groups for discussions and publicity for events/topics of interest
- Committee work and business of STP
- Access to resources, previous Career Development/Continuing Education Workshop presentations
- Much, much more

LinkedIn and Other Professional Networks
Panelists will include Dr. Brad Bolon, Dr. Alric Lopez, Dr. Ken Schafer, and Mr. Terry Leyden

Session 2
1:30 PM–5:00 PM
Innate Immunity
Co-Chairs: Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN and Peter Ward, MD, University of Michigan, Ann Arbor, MI

This session will focus on aspects of innate (non-specific) immunity relevant to pathogenesis of disease, including recognition molecules, cells and effector mechanisms. Specific topics to be covered include: protective and harmful innate immune responses in sepsis mediated by IL-17A; evidence for crosstalk between the complement system and toll-like receptors (TLR) during inflammation; and the role of dendritic cells at the interface between non-specific immunity and specific immunity. In each presentation, morphological and functional aspects of the innate immune responses will be covered.

1:30 PM–1:35 PM
Introduction
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

1:35 PM–2:15 PM
Anatomy of Innate Immunity
Braedon McDonald, MD, PhD, University of Calgary, Calgary, AB, Canada

2:15 PM–2:55 PM
Role of IL-17A in Sepsis
Peter Ward, MD, University of Michigan, Ann Arbor, MI

2:55 PM–3:25 PM
Break

3:25 PM–3:40 PM
Student Speaker

3:40 PM–4:20 PM
Crosstalk between Complement and TLRs
Wenchao Song, PhD, University of Pennsylvania School of Medicine, Philadelphia, PA

4:20 PM–5:00 PM
Cellular Regulation of the Inflammatory Response
Peter Henson, PhD, University of Colorado Health Sciences Center, Denver, CO
5:30 PM–6:30 PM  
**Town Hall Meeting**

**Best Practices on Recovery Studies: The Role of the Pathologist**

The Town Hall Meeting this year will be dedicated as an opportunity to provide member feedback to the SRPC Working Group that is preparing a guidance document on the recovery potential of histomorphologic changes observed in species routinely used in nonclinical toxicology studies. The group is working to review regulatory guidelines and make recommendations regarding why do recovery, when to have a study with a recovery, how to design a recovery arm, the potential outcomes of recovery and their interpretations, and a review of vaccine guidelines and concerns regarding delayed toxicity.

You are encouraged to attend this session and take the opportunity to provide your thought and concerns regarding this important topic.

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**Tuesday Morning**

**Session 3**

**8:00 AM–12:00 NOON**

**Acquired Immunity**

Co-Chairs: JoAnn Schuh, DVM, PhD, DACVP, Applied Veterinary Pathobiology, Bainbridge Island, WA and Gail Pearse, BVM&S, DACVP, GlaxoSmithKline, Ware, UK

Acquired immunity goes beyond innate immunity to provide controlled recognition and memory for specific antigenic challenges. Predominately involving activation of T and B cells, the resulting cellular- and secretory-mediated activity provides immediate and long-term host defenses. This session will highlight the biological advances in control of acquired immunity through T regulatory cells, the pathophysiology of effector cells and regulatory molecules in immunosuppression and hypersensitivity and allergy, and dysregulation that leads to loss of tolerance and autoimmune diseases.

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**8:05 AM–8:40 AM**

**Introduction**

JoAnn Schuh, DVM, PhD, DACVP, Applied Veterinary Pathobiology, Bainbridge Island, WA

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**8:40 AM–9:15 AM**

**Regulatory T-cells: Diverse Phenotypes Integral to Immune Homeostasis and Suppression**

Rich Peterson, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC

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**9:15 AM–9:50 AM**

**Immunosuppression: Upsetting the Balance**

Curtis Maier, PhD, GlaxoSmithKline, Research Triangle Park, NC

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**9:50 AM–10:05 AM**

**Cytokine Pathways in Allergic Inflammatory Disease**

Cara M. M. Williams, PhD, Wyeth Discovery Research, Cambridge, MA

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**10:05 AM–10:40 AM**

**Student Speaker**

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**10:40 AM–11:15 AM**

**Pyrrhic Victory through Total War: Immune Responses in Autoimmune Disease**

Brad Bolon, DVM, MS, PhD, DACVP, GEMpath, Inc., Longmont, CO

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**11:15 AM–12:00 NOON**

**Panel Discussion: Stress Effects vs. Immunotoxicity**

Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

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**Tuesday Afternoon**

**Free Time**

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**Wednesday, June 22**

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**Wednesday Morning**

**Session 4**

**8:00 AM–12:00 NOON**

**The Immune System throughout Life**

Co-Chairs: George Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH and Frieke Kuper, PhD, TNO, Zeist, Netherlands

The immune system is not a fixed entity, but instead goes through a progression of anatomical and functional changes starting with the fetus and newborn, progressing through adolescence and adulthood, and culminating in senescence. The basic anatomy and physiology of the immune system are genetically determined and depend
heavily on endocrine and neural functioning. For example, life changes such as pregnancy and lactation have a significant impact on the immune system. Therefore, the effects of environmental factors and the efficacy of drugs differ with age/life stage and condition.

**Wednesday Afternoon**

**Responsible Authorship and Publication Practices**
12:15 PM–1:30 PM

**An IATP & STP Sponsored Workshop & Panel Discussion**
A 15-minute PowerPoint presentation will highlight issues related to authorship, order of authorship, what constitutes plagiarism and self-plagiarism, ethical issues, and conflict of interest related to manuscript preparation and submission. This session will include pointers on how to get your manuscript published, how to deal with reviewers’ comments, what constitutes a least publishable unit, and responsibilities of editors and associate editors. To stimulate audience discussion and to challenge the panel members, there will be practical and realistic case presentations, including when it is appropriate to include the pathologist as an author and how best to determine the order of authorship for publications produced by a committee or working group, such as INHAND documents. A box lunch will be provided by IATP for attendees who pre-register for the session. (Please register early. Space is limited to 78 attendees.)
Talk in Portuguese
12:30 PM–1:00 PM

Pathology Assessment of Embryo-Fetal Development Effects of Immunomodulatory Drugs in Cynomolgus Monkeys

Evelyne Polack, DVM, MS, PhD, DACVP, Biogen Idec Inc., Cambridge, MA, USA

The cynomolgus monkey has become an increasingly important animal model for preclinical studies of biotechnology-derived therapeutics. This presentation will address the evaluation of potential effects of immunomodulatory human proteins on embryo-fetal development in cynomolgus monkey.

Talk in Spanish
1:00 PM–1:30 PM

A Panoramic View on the Education and Training in Veterinary and Toxicologic pathology in Brazil: the Role of the Latin American Society of Toxicologic Pathology, LASTP.

Maria Lucia Zaidan Dagli, DVM, MS, PhD, Full Professor, School of Veterinary Medicine and Animal Science, University of Sao Paulo, SP, Brazil

The aim of the presentation is to show a panoramic view of education and training in veterinary and toxicologic pathology in Brazil. Brazil has over 140 veterinary schools, distributed in practically all of its states; most of them are private schools. Disciplines of general pathology, animal pathology, pharmacology and toxicology make part of all educational programs; however, pathology of laboratory animals make part of the education program of only a few veterinary schools. Opportunities for training in veterinary pathology occur through animal pathology residence programs, or with post-graduation programs, which are nevertheless focused in educating for scientific research. The Latin American Society of Toxicologic Pathology, LASTP, has an important role in organizing training programs for professionals interested to work in this specific and important area of pathology.

Una Visión Panorámica Sobre la Educación y Entrenamiento en Patología Veterinaria y Toxicológica en Brasil: el Papel de la Asociación Latinoamericana de Patología Toxicológica, LASTP.

Maria Lucia Zaidan Dagli, DVM, MS, PhD, Full Professor, School of Veterinary Medicine and Animal Science, University of Sao Paulo, SP, Brazil

El objetivo de la presentación es mostrar una visión panorámica de la educación y entrenamiento en patología veterinaria y toxicológica en Brasil. Brasil tiene más de 140 escuelas de veterinaria, distribuidas en prácticamente todos los estados; la mayoría de ellas son escuelas privadas. Disciplinas de la patología general, patología animal, farmacología y toxicología hacen parte de todos los programas educativos, sin embargo, la patología de los animales de laboratorio hacen parte del programa de educación de sólo una pocas escuelas de veterinaria.
Oportunidades de formación en patología veterinaria ocurren a través de los programas de residencia en patología animal, o con programas de posgrado, que, no obstante se centran en la educación para la investigación científica. La Sociedad Latinoamericana de Patología Toxicológica, LASTP, tiene un papel importante en la organización de programas de formación para los profesionales interesados en trabajar en esta área específica e importante de la patología.

Session 5
1:30 PM–5:00 PM
Immunomodulation: How Much is Too Much?

Co-Chairs: Michael W. Leach, DVM, PhD, DACVP, Pfizer Inc., Andover, MA and Patrick Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE

This session will focus on a particularly challenging question in the world of emerging therapies. As targeting of specific receptor-mediated immunological and inflammatory pathways becomes more precise and selective modulation of immune mechanisms occurs, it becomes essential to ask the question “How much immunomodulation is too much?” Another question is “How much is enough?” How can we safely dial up intentional up-regulation of prophylactic drugs and adjuvants? The key challenge is identifying that level of immunomodulation, typically immunosuppression, which will result in a beneficial outcome. To meet this challenge a heightened understanding of the complex molecular relationships that exist for immune and inflammation pathways is required, as are more astute and contemporary methods for detecting and measuring changes to those pathways. The speakers in this session will attempt to define the risks and benefits of targeted immunomodulation as they apply to both large protein biologics and small molecules and how regulatory guidances may serve to guide researchers in the decision process.

1:30 PM–1:35 PM
Introduction
Michael W. Leach, DVM, PhD, DACVP, Pfizer Inc., Andover, MA

1:35 PM–2:20 PM
How Do We Apply Regulatory Guidances for Immunotoxicity to Immunomodulatory Drugs?
Ellen W. Evens, PhD, Pfizer Inc., Groton, CT

2:20 PM–3:00 PM
Small Molecule Immunomodulatory Drugs: Challenges and Approaches for Balancing Efficacy with Toxicity
Patrick Haley, DVM, PhD, DACVP, Incyte Corporation, Wilmington, DE

3:00 PM–3:40 PM
Break
Establishing the Carcinogenic Risk of Immunomodulatory Drugs
James Weaver, PhD, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD

Challenges and Approaches for Balancing Efficacy with Toxicity
Christopher Horvath, DVM, MS, DACVP, Taligen Therapeutics, Cambridge, MA

Awards Ceremony and Annual Business Meeting

President’s Reception

Thursday, June 23

Thursday Morning

Session 6
8:00 AM–12:00 NOON
Environmental Toxicologic Pathology
Chair: Douglas C. Wolf, DVM, PhD, FIATP, ATS, U.S. Environmental Protection Agency, Research Triangle Park, NC

Environmental toxicologic pathology will focus on the impacts of environmental contaminants on the immune system and how they can affect public health and ecological systems. The first talk will overview the development and implementation of alternative cell-based, high throughput, evaluation systems for hazard identification and testing prioritization. The second talk will examine perfluorinated chemicals (PFCs), which are persistent in the environment and have been found in ground and surface waters. Epidemiologic studies suggest immune effects in humans and animal studies indicate PFCs target immune function and inflammatory responses. The third presentation will describe how air pollutants such as diesel exhaust particles, residual oil fly ash or its constitutive metals, can cause lung injury, inflammation, and potentiate allergic airway responses. The final presentation will describe the Deep Water Horizon spill, the largest oil spill and response action in U.S. history, with over 200 million gallons of crude oil released, and nearly 2 million gallons of dispersants applied. A diversity of biota were exposed, from deep ocean communities to coastal wildlife. A summary of the events of the spill, exposure pathways, and effects on wildlife including immune, endocrine, and population impacts will be presented.

8:00 AM–8:10 AM
Introduction
Douglas C. Wolf, DVM, PhD, FIATP, ATS, U.S. Environmental Protection Agency, Research Triangle Park, NC

8:10 AM–8:55 AM
Immunotoxicant Screening and Prioritization in the 21st Century
Robert Luebke, PhD, U.S. Environmental Protection Agency, Research Triangle Park, NC

8:55 AM–9:40 AM
The Immunotoxicity of Perfluorinated Compounds
Dori Germolec, PhD, National Institute of Environmental Health Sciences, Research Triangle Park, NC

9:40 AM–10:20 AM
Break

10:20 AM–11:10 AM
Lung Immunotoxicity and Health Effects of Particulate Matter
Ian Gilmour, PhD, U.S. Environmental Protection Agency, Research Triangle Park, NC

11:10 AM–12:00 NOON
Ecotoxicology of the Gulf Oil Spill
Mace Barron, PhD, U.S. Environmental Protection Agency, Gulf Breeze, FL