DENVER

30th Annual Symposium
Toxicologic Pathology and the Immune System

SOCIETY OF TOXICOLOGIC PATHOLOGY

Program

June 19–23, 2011

Monday, June 20

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 Immunotoxicants*.

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; Biomarker Discovery, Qualification, and Application in Drug Development: What's New, and What You Need to Know; Ultrastructural Analysis and Toxicologic Pathology; and Histopathology of the Rodent Lymphoid and Hematopoietic Systems. A half-day Career Development Workshop: "Leaving the Rat Race: Consulting as a Career Choice 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* **Jerry 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**

10:40 AM–10:55 AM **Student Speaker**

10:55 AM–11:15 AM **Functional Testing/Clinical Pathology Evaluation of the Immune System**
Denise Bounous, DVM, PhD, DACVP, Bristol Meyers Squibb, Princeton, NJ

11:15 AM–12:00 NOON **Enhanced Histopathology of the Immune System**
Susan Elmore, DVM, MS, DACVP, DABT, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC

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,*** *Huntingdon 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***

Monday Afternoon

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 cross talk 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**

Reversibility in Toxicity Studies

Tuesday, June 21

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.

8:00 AM–8:05 AM **Introduction**
JoAnn Schuh, DVM, PhD, DACVP, Applied Veterinary Pathobiology, Bainbridge Island, WA

8:05 AM–8:40 AM **Regulatory T-cells: Diverse Phenotypes Integral to Immune Homeostasis and Suppression**
Rich Peterson, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC

8:40 AM–9:15 AM **Immunosuppression: Upsetting the Balance**
Curtis Maier, PhD, GlaxoSmithKline, Research Triangle Park, NC

9:15 AM–9:50 AM **Cytokine Pathways in Allergic Inflammatory Disease**
Cara M. M. Williams, PhD, Wyeth Discovery Research, Cambridge, MA

9:50 AM–10:05 AM **Student Speaker**

10:05 AM–10:40 AM **Break**

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

11:15 AM–12:00 NOON **Panel Discussion: Stress Effects vs. Immunotoxicity**
Paul Snyder, DVM, PhD, DACVP, Purdue University, West Lafayette, IN

Tuesday Afternoon **Free Time**

Wednesday, June 22

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.

8:00 AM–8:10 AM **Introduction**
George Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH

8:10 AM–9:00 AM	**Development and Aging of Lymphoid Organs** *Reina Mebius, PhD, VU Medical Center, Amsterdam, Netherlands*
9:00 AM–9:40 AM	**Macrophages and Neurodegeneration of the Brain** *Christine Dijkstra, PhD, VU Medical Center, Amsterdam, Netherlands*
9:40 AM–10:20 AM	**Break**
10:20 AM–10:50 AM	**Immune Functioning in Non-lymphoid Organs: The Liver** *George Parker, DVM, PhD, DACVP, WIL Research Laboratories, Ashland, OH*
10:50 AM–11:30 AM	**Juvenile Immunotoxicity** *Michael P. Holsapple, PhD, ILSI Health and Environmental Sciences Institute, Washington, DC*
11:30 AM–12:00 NOON	**Sensitive Periods during Adult Life: Pregnancy, Lactation** *Frieke Kuper, PhD, PhD, TNO, Zeist, Netherlands*
12:30 PM–1:30 PM	**Spanish/Portuguese Session**

Wednesday Afternoon

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?** *Thomas T. Kawabata, 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**
3:40 PM–4:20 PM	**Establishing the Carcinogenic Risk of Immunomodulatory Drugs** *James Weaver, PhD, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD*
4:20 PM–5:00 PM	**Challenges and Approaches for Balancing Efficacy with Toxicity** *Christopher Horvath, DVM, MS, DACVP, Taligen Therapeutics, Cambridge, MA*

5:30 PM–6:30 PM	**Awards Ceremony and Annual Business Meeting**
7:00 PM–9:00 PM	**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*

This session 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 Immunotoxcity 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*