DENVER

30th Annual Symposium
Toxicologic Pathology and the Immune System

SOCIETY OF TOXICOLOGIC PATHOLOGY

Program

Sunday, June 19

Continuing Education Credits

AAVSB RACE Provider #56

The CE Courses have been submitted (but not yet approved) for 4 hours of Continuing Education credits (per course) in jurisdictions which recognize AAVSB RACE approval; however participants should be aware that some boards have limitations on the number of hours accepted in certain categories and/or restrictions on certain methods of delivery of Continuing Education. The Scientific Sessions have been submitted but not yet approved by AAVSB RACE program for 20 hours of Continuing Education credits in jurisdictions which recognize AAVSB RACE approval. The NTP Satellite Symposium has been submitted but not yet approved by the AAVSB RACE program for five and a half hours of continuing education credits in jurisdictions which recognize AAVSB RACE approval. Certificates of attendance will be provided at the conclusion of NTP, each CE course, and on Thursday for the scientific sessions. Please contact the AAVSB RACE program if you have any comments/concerns regarding this program's validity or relevancy to the veterinary profession.

Continuing Education Courses

CE 1 (Sunday AM) 8:00 AM–12:00 NOON

Interacting with Regulatory Authorities: What to Do and What Not to Do

Co-Chairs: **Melissa Rhodes, PhD, DABT,** *GlaxoSmithKline, Research Triangle Park, NC and* **Hanan Ghantous, PhD, DABT,** *U.S. FDA, Silver Spring, MD*

During the process of drug development, a Sponsor will need to interact with regulatory authorities (RA), such as the FDA, PMDA, and the EMA. In order to effectively interact with these agencies, the Sponsor must remember that the RA are partners in the drug development process. Similar to sponsors, RA have a genuine concern about the well being of the patients. Sponsors and patients will also benefit from the considerable institutional knowledge of RA about study designs, toxicity, pharmacology, and drug disposition of other drugs. This course will discuss how to effectively interact with the RA so that Sponsors and RA can gain the greatest benefit from their meetings.

8:00 AM–8:40 AM	**Interacting with CDER Divisions of FDA** *Jeri El Hage, PhD, Aclairo PDG, Vienna, VA*
8:40 AM–9:20 AM	**Interacting with CBER Divisions of FDA** *Martin D. Green, PhD, U.S. FDA, Office of Vaccine Research and Review, Division of Vaccines and Related Product Applications, Rockville, MD*
9:20 AM–10:00 AM	**Interacting with the FDA: The "Animal Rule"** *Christopher Ellis, PhD, U.S. FDA, Center for Drug Evaluation and Research, Silver Spring, MD*
10:00 AM–10:20 AM	**Break**
10:20 AM–11:00 AM	**Interacting with EMA** *Christopher Powell, FRCPath, GlaxoSmithKline, Ware, United Kingdom*
11:00 AM–12:00 NOON	**Interacting with PMDA** *Kazuichi Nakamura, DVM, PhD, Shionogi & Co., Ltd., Tokyo, Japan*

Career Development Workshop

Sunday, June 19, 2011
8:00 AM–12:00 NOON

A Consultant's Calling Workshop: Do You Have What It Takes to Be a Consultant in Toxicologic Pathology?

(Free Event, registration required)

Co-Sponsors: *Toxicologic Pathologists in Consulting (TOPIC) Interest Group, the STP Education Committee, and the STP Career Development and Outreach Committee (CDOC)*

Co-Chairs: **JoAnn Schuh, DVM, PhD, DACVP, DABT,** *Applied Veterinary Pathobiology, Bainbridge Island, WA,* **Brad Bolon, DVM, MS, PhD, DACVP,** *GEMpath, Inc., Longmont, CO (TOPIC),* **Kevin Keane, DVM, PhD,** *Huntingdon Life Sciences, East Millstone, NJ (Education Committee),* **Mike Conner, DVM, DACVP,** *Theravance, Inc., South San Francisco, CA, and* **Larry Fisher, DVM, PhD, DACVP,** *Cicero, IN (CDOC)*

Advisor: **Jon Werner, DVM, PhD, DACVP,** *Amgen, Thousand Oaks, CA (Web-Based Education Task Force)*

Approximately 10% of members of the Society of Toxicologic Pathology now work as consultants in anatomic or clinical pathology or in preclinical program development. With merges, acquisitions and condensation within the bio/pharmaceutical industry, and the expertise available through academic and government pathologists, solo or small group consulting practices are an expanding area of part-time or full-time employment for toxicologic pathologists who want/need a second career or want to supplement their existing career. But do you have what it takes and do you know what it takes to successfully operate as a consultant? Based on the compiled results of a questionnaire answered by members of TOPIC, this workshop will present practical information about successfully setting up and maintaining a career as a consultant. A panel discussion will allow the audience to further benefit from the tips and tricks already learned by your colleagues who are practicing consultants in toxicologic pathology.

Agenda

8:00 AM–8:05 AM	**Introduction**
8:05 AM–8:35 AM	**"So You Wanna Be a Consultant..."** *Brad Bolon, DVM, MS, PhD, DACVP, GEMpath, Inc., Longmont, CO*
8:35 AM–8:50 AM	**...And Just What Type of Consultant Are You Going to Be?** *JoAnn C.L. Schuh, DVM, PhD, DACVP, DABT, Applied Veterinary Pathobiology, Bainbridge Island, WA*
8:50 AM–9:20 AM	**Setting up Your Worldwide Headquarters** *Michael Tomlinson, DVM, PhD, DACVP, Nova Pathology, PC, Bellingham, WA*
9:20 AM–9:50 AM	**Legal, Monetary, and Administrative Aspects** *Graham Smith, BVMs, MRCVS, MSc, DACVP, CanBioPharma Consulting Inc., Rockwood, ON, Canada*
9:50 AM–10:20 AM	**Break**
10:20 AM–10:50 AM	**Networking and Advertising Your Services** *JoAnn C.L. Schuh, DVM, PhD, DACVP, DABT, Applied Veterinary Pathobiology, Bainbridge Island, WA*
10:50 AM–11:20 AM	**Professional Groups and Lateral Consultants to Assist You** *D. Reid Patterson, DVM, PhD, DACVP, Reid Patterson Consulting, Inc., Bonita Springs, FL*
11:20 AM–12:00 NOON	**Panel Discussion**

CE 2 (Sunday AM) 8:00 AM–12:00 NOON

Biomarker Discovery, Qualification, and Application in Drug Development: What's New, and What You Need to Know

Co-Chairs: **Jacqueline Tarrant, BVSc, PhD, DACVP,** *Genentech, San Francisco, CA,* **Dina Andrews-Cleavenger, DVM, PhD, DACVP,** *Amgen, Inc., Thousand Oaks, CA, and* **Dominique Brees, DVM, PhD,** *Pfizer R&D, Sandwich, United Kingdom*

Staying abreast of the biomarker field is no longer a pursuit of interest only to early drug discovery and safety scientists. The success of consortium driven biomarker discovery efforts and their recent approval by regulatory agencies has thrust the biomarker field to the forefront across all facets of drug development. Remaining up to date on the most promising novel biomarker discoveries, being alert to biomarkers currently seeking regulatory approval and understanding the utility and translational impact of newly approved preclinical safety biomarkers is a daunting task that falls primarily on the shoulders of safety pathologists. The first part of this course is aimed to highlight novel biomarker discovery efforts in carcinogenicity and genomics; two fields poised to revolutionize safety biomarkers in their respective fields. The second part of the course is devoted to revisiting recent advances, new regulatory submissions and examining the real world impact and utility of the more familiar renal and cardiac toxicity biomarkers. Practical aspects of study design, sample collection, techniques, analysis and interpretation will also be addressed to provide the participant with a well rounded and applicable session.

8:00 AM–8:05 AM	**Introduction**
8:10 AM–8:55 AM	**Overview of the Novel Biomarkers of Carcinogenicity** *Jiri Aubrecht, PharmD, PhD, Pfizer, Groton, CT*

Genomics biomarker, DNA methylation, discrimination between genotoxic drug and Non-Genotoxic drugs.

9:00 AM–9:45 AM **Genomics Biomarkers: miRNA and mRNA Biomarkers**
Igor Mikaelian, DVM, MSc, DACVP, Hoffman La Roche, Nutley, NJ

9:45 AM–10:00 AM **Break**

10:00 AM–10:45 AM **New Urine Biomarkers of Renal Injury on the Horizon-What's Next and How are They Superior?**
Denise Bounous, DVM, PhD, DACVP, Bristol-Myers Squibb Company, Princeton, NJ

New performance data on renal toxicity biomarkers previously qualified with the FDA/EMEA and the next wave of novel renal biomarkers being prepared for submission to regulators.

10:50 AM–11:35 AM **Cardiotoxicity Now: Existing and Emerging Biomarkers of Injury and Dysfunction**
Brian Berridge, DVM, PhD, DACVP, GlaxoSmithKline, Research Triangle Park, NC

New markers of injury and dysfunction including post-qualification complexities of structure-function relationships and application.

11:40 AM–12:00 NOON **Wrap Up Questions**

CE 3 (Sunday PM) 1:30 PM–5:00 PM

Histopathology of the Rodent Lymphoid and Hematopoietic Systems

Co-Chairs: **Cynthia L. Willard-Mack, VMD, PhD,** *Huntingdon Life Sciences, East Millstone, NJ, and* **Jerrold M. Ward, DVM, PhD, DACVP,** *Global VetPathology, Montgomery Village, MD*

This continuing education session will set the stage for the general meeting by providing a broad overview of histopathology of the lymphoid and hematopoietic organs and tissues. The first lecture is designed to provide attendees with a comprehensive review of normal morphology of bone marrow, thymus, spleen, lymph nodes and MALT as a basis for appreciating material in subsequent sessions. The use of specialized techniques important for the identification and observation of hematopoietic cells and tissues will be explored. Immunohistochemistry enables pathologists to study normal antigen expression in hematopoietic cells, identify cell populations in inflammatory lesions and diagnose hematopoietic disorders. *In vivo* intravital microscopy is an exciting recent modality that allows the activities of fluorescently labeled living cells to be observed in intact tissues in real time. Some of the more challenging aspects of diagnostic immunopathology will be discussed, including the differentiation of reactive and neoplastic lesions and the diagnosis of hematopoietic neoplasia in CD-1 mice.

1:30 PM–1:35 PM **Introduction**

1:35 PM–2:20 PM **An Integrated Overview of the Structure and Function of Lymphoid and Hematopoietic Organs**
Cynthia L. Willard Mack, VMD, PhD, Huntingdon Life Sciences, East Millstone, NJ

The histology of normal hematopoietic and lymphoid organs will be reviewed to provide the basis for recognizing and interpreting lesions in the immune system. The important role of fibroblastic reticular cells will be emphasized. The vascular and lymphatic elements that link these organs together into an integrated system will be discussed.

2:20 PM–2:50 PM **The Utility of IHC in the Identification of Lymphoid and Hematopoietic Cells in Normal Tissues and Interpretation of Inflammatory, Toxic and Proliferative Lesions**
Jerold E. Rehg, DVM, DACVP, St. Jude Children's Research Hospital, Memphis, TN

Immunophenotyping plays a key role in diagnosis and classification of hematolymphoid toxicity and proliferations. The immunologic profile of hematolymphoid proliferations may be assessed by flow cytometry or immunohistochemistry. Unfortunately, pathologists often have only paraffin embedded tissue with which to work. Cases of various hematolymphoid proliferations will be used to illustrate normal IHC markers for rodent hematopoietic cells and how IHC can help solve morphologic conundrums.

2:50 PM–3:15 PM **Break**

3:15 PM–4:00 PM **The Role of Bone Marrow as a Hematopoietic and Secondary Lymphoid Organ**
Irina Mazo, MD, PhD, Harvard Medical School, Boston, MA

Intravital microscopy (IVM) is a powerful ***in vivo*** tool to visualize and analyze cell behavior in both intra- and extravascular spaces during various physiological and pathological conditions. The talk will use the murine cranial bone marrow (BM) IVM model to characterize BM organization and topography and the marrow's role as a hematopoietic and secondary lymphoid organ.

4:00 PM–4:30 PM **Differentiation of Hematopoietic and Immune System Reactive Lesions (Hyperplasias) from Neoplasias**

Jerrold M. Ward, DVM, PhD, DACVP, Global VetPathology, Montgomery Village, MD

The immune system of rodents and other species provides a protective network of tissues and cells against endogenous and exogenous stimuli including toxins. This lecture will review the types of reactive lesions in spleen, lymph node, thymus and other tissues including hyperplasias. Differentiation of reactive lesions from early and full blown neoplasias will be illustrated and discussed.

4:30 PM–5:00 PM **CD1 Mouse Immune System Pathology**

Alys E. Bradley, BSc, BVSc, MAnimSc, DipRCPath, FRIPH, MRCVS, FRCPath, Charles River Laboratories, Tranent, Edinburgh, Scotland

This talk will outline the common spontaneous background lesions seen in CD-1 mouse hematopoietic and lymphoid system organs in short-term, chronic and life-time studies. Lesions such as lymphocytic infiltrations, thymic lymphoid hyperplasia and lymphomas are common spontaneous background findings in Charles River CD-1 mice, yet may be unusual in other mouse strains.

CE 4 (Sunday PM) 1:30 PM–5:00 PM

Ultrastructural Analysis and Toxicologic Pathology

Co-Chairs: **Karamjeet Pandher, BVSc, PhD, DACVP,** *Pfizer Inc., Groton, CT, and* **Henry Wall, DVM, PhD, DACVP,** *EPL, Inc., Research Triangle Park, NC*

Electron microscopy is a powerful technique that can help illustrate the subcellular localization of toxic injury. It can serve to provide useful insights into the nature of the toxicologic insult, its mechanism, and may even help in risk assessment. As such electron microscopy can effectively compliment other molecular techniques in developing a comprehensive toxicologic assessment of a molecule. This continuing education course aims to re-enforce the technique for practicing toxicologic pathologists and to fill knowledge gaps vis a vis the latest advances in the field of electron microscopy. Following an introduction in ultrastructural landmarks, the speakers will attempt to highlight the role of ultrastrucutral investigations in variety of toxicologic processes. By drawing on specific case studies the speakers will attempt to elucidate the techniques, proper interpretation of electron microscopy data, and its synergies with various other investigative molecular techniques. Finally, latest advances in the field such as dual beam tomography and role in nanoparticle research will be discussed.

1:30 PM–1:35 PM **Introduction**

1:35 PM–2:20 PM **Introduction to Cellular Ultrastructure**

Karamjeet Pandher, BVSc, PhD, DACVP, Pfizer Inc., Groton, CT

This short introductory presentation will focus on review of the commonly encountered subcellular organelles and structures that help navigation through the cell and identification of specific cell types.

2:20 PM–2:50 PM **Role of Ultrastructure Analysis in Preclinical Safety Evaluation: Interesting Case Studies**

Jane Fagerland, PhD, DABT, Abbott Laboratories, Abbott Park, IL

Ultrastructural pathology data, while often considered merely "nice-to-have" information, can provide clear answers to toxicologic questions, and even point to underlying mechanisms such as mitochondrial toxicity that can be confirmed with further testing. Ultrastructural evaluation intersects with other imaging methods and related technologies, such as laser capture microdissection or MALDI-mass spectrometry imaging, to correlate chemical information with morphologic findings. Case studies in which applications of transmission electron microscopy and associated imaging technologies were used to resolve preclinical safety issues will be presented.

2:50 PM–3:15 PM **Break**

3:15 PM–4:00 PM **Transmission Electron Microscopy Support of Preclinical Safety Studies: Planning and Impact of Methods on Evaluation and Interpretation**

Henry Wall, DVM, PhD, DACVP, DABT, EPL, Inc., Research Triangle Park, NC

This presentation reviews planning considerations for

transmission electron microscopy (TEM) evaluations in support of toxicity studies. It will include relevant information that may facilitate the evaluation or interpretation of ultrastructural changes. Limitations on sample quality imposed by necropsy workflow procedures, and practical sampling procedures will be discussed. Common techniques to optimize sample quality for TEM and use of semi-thin sections to focus the ultra-thin section evaluation will be highlighted. Examples and brief discussion of the potential influence of artifacts on the interpretation of ultrastructural changes and the importance of clear consistent morphological criteria to aid the interpretation of test article-induced effects will be stressed.

4:00 PM–4:30 PM **Ultrastructural Evaluation of Semen to Assess Effects of Exposure to Environmental Toxicants**
D.N. Rao Veeramachaneni, PhD, Colorado State University, Fort Collins, CO

Following toxicant exposures, seminal ejaculates may contain, in addition to sperm, somatic cells sloughed from testis, excurrent ducts, and accessory glands. Routine methods of semen evaluation do not permit characterization of subtle defects in sperm or definitive identification of denuded cells. Methods to process semen samples as biopsy material and evaluate them vis-à-vis corresponding tissue samples utilizing various light and transmission electron microscopic techniques will be presented.

4:30 PM–5:00 PM **New Information from Large Tissues Volumes to the Smallest Structures of the Cell: What New Methods in Electron Microscopy Can Do for Your Research**
Richard Gursky, FEI Company, Hillsboro, OR

Looking at new techniques previously not associated with histology or toxicology this presentation will demonstrate how and why the techniques of Duelbeam tomography and STEM tomography can be used to find nanoparticles and other labeled materials in large volumes of tissue at very low concentrations. These techniques are also useful in visualizing, sometimes for the first time, the interaction of metals and polymers with cells and tissues and for examining the relationships of cells and organelles in new ways, with the help of newly developed instrument automation. Bringing these new and exciting methodologies to everyone will help shed light on some of our most commonly asked questions.

CE 5 (Sunday PM) 1:30 PM–5:30 PM

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Christopher Powell, FRCPath, GlaxoSmithKline, Ware, United Kingdom

4:30 PM–5:30 PM **Interacting with PMDA**
Kazuichi Nakamura, DVM, PhD, Shionogi & Co., Ltd., Tokyo, Japan