



Toxicologic Pathology of the Digestive Tract and Pancreas 32nd Annual Symposium

Portland, Oregon Oregon Convention Center June 16-20, 2013

Saturday, June 15

NTP Satellite Symposium: Pathology Potpourri 9:00 AM-4:30 PM

(Free Event, registration required)

Chair: Susan A. Elmore, MS, DVM, DACVP, DABT, FIATP, National Institute of Environmental Health Sciences, Research Triangle Park, NC

This interactive symposium on interpreting pathology slides is sponsored by NTP and has become a popular premeeting event for attendees. While it is free, registration is required due to space limitations.

The object of this interactive symposium is to provide continuing education on interpreting pathology slides, to generate lively and productive conversation, and to have a good time. During each talk, the speakers will project a series of images of lesions on one screen with a choice of diagnoses/answers on a separate screen. The members of the audience with wireless keypads will then vote and the voting results will be displayed on the screen. After each voting session, time is allowed for discussion.

9:00 AM-9:10 AM

Welcome and Introductory Remarks

Susan A. Elmore, MS, DVM, DACVP, DABT, FIATP, NTP and NIEHS, Research Triangle Park, NC

9:10 AM-9:30 AM

An Unusual Bone Lesion in Mice

Margarita M. Gruebbel, DVM, PhD, DACVP, EPL, Research Triangle Park, NC

9:30 AM-10:00 AM

Interstitial Infiltrates of the Rat Kidney

Cynthia C. Shackelford, DVM, MS, PhD, EPL, Research Triangle Park, NC

10:00 AM-10:30 AM

Interesting Background Lesions in Hamsters

Elizabeth McInnes, BVSc, PhD, FRCPATH, MRCVS, FIATP, Gribbles Healthscope, South Australia, Australia

10:30 AM-11:00 AM

Break

11:00 AM-11:30 AM

Lung Lesions in Control Rats from Gavage Studies

Torrie Crabbs, DVM, DACVP, EPL, Inc., Research Triangle Park, NC

11:30 AM-12:00 Noon

Top Shelf Quandaries

David E. Malarkey, DVM, PhD, DACVP, FIATP, NTP and NIEHS, Research Triangle Park, NC

12:00 Noon-1:30 PM

Lunch

1:30 PM-1:50 PM

Electronmicroscopy Brain Teasers

Connie Cummings, DVM, PhD, EPL, Inc., Research Triangle Park, NC

1:50 PM-2:10 PM

Cell Death: Always a Diagnostic Challenge

Susan A. Elmore, MS, DVM, DACVP, DABT, FIATP, NTP and NIEHS, Research Triangle Park, NC

2:10 PM-2:30 PM

Challenging Rat Uterine Nonneoplastic Lesions

Molly H. Boyle, DVM, MPH, DACVP, Integrated Laboratory Systems, Inc., Research Triangle Park, NC

2:30 PM-3:00 PM

Challenging Rat Uterine Neoplasms

Crystal Johnson, DVM, DACVP, Charles River Laboratories, PAI, Research Triangle Park, NC

3:00 PM-3:30 PM

Break

3:30 PM-4:00 PM

Lesions from the Gastrointestinal INHAND Organ Working Group

Thomas Nolte, DVM, MSc, FIATP, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany

4:00 PM-4:30 PM

Foreign Material in Rat Kidney

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



Sunday, June 16

Continuing Education Courses

CE 1 (Sunday AM) 8:00 AM–12:00 Noon

Role of the Pathologist in GLP Studies

Co-Chairs: Kathleen A. Funk, DVM, PhD, DACVP, EPL Inc., Sterling, VA, and Klaus Weber, PhD, DVM, MSBiol, AnaPath GmbH, Intingen, Switzerland

There are many roles that toxicologic pathologists serve in regard to toxicology and carcinogenicity studies. This session will provide a summary of the many different tasks performed by pathologists throughout differing stages of evaluations, describe expectations of each phase of pathology review, and explore their relationships with the Study Director, Sponsor, and other pathologists. Also to be discussed is the issue of what constitutes study raw data and what is to be included in the toxicology report. The roles of the Study Pathologist, Peer Review Pathologists, Pathology Working Group Chairperson and participants of Pathology Working Groups (PWGs) or Scientific Advisory Panels (SAPs) will be detailed along with the applicable GLP regulations and best practices for pathology evaluations.

8:00 AM–8:05 AM

Introduction

8:05 AM–9:00 AM

Role of Toxicologic Pathologist

Klaus Weber, PhD, DVM, MSBiol, AnaPath GmbH, Intingen, Switzerland

9:00 AM–9:55 AM

Role of the Peer Review Pathologist

James Hailey, DVM, DACVP, GlaxoSmithKline, Research Triangle Park, NC

9:55 AM–10:15 AM

Break

10:15 AM–11:05 AM

Pathology Working Groups (PWG): Definition, Application in Toxicity and Carcinogenicity Studies, and Examples

Peter C. Mann, DVM, EPL NorthWest, Seattle, WA

11:05 AM–12:00 Noon

A Regulator's Perspective on the Process

Mark Seaton, PhD, US FDA/CDER, Silver Spring, MD

Career Development Workshop

Sunday, June 16

8:00 AM–12:00 Noon

Environmental Toxicologic Pathology

(Free Event, registration required)

Co-Chairs: Keith Nelson, DVM, PhD, DACVP, MPI Research, Mattawan, MI, and Olga Pulido, MD, MSc, ABPath, FIATP, Health Canada, Ontario, Canada

The 2013 Career Development Workshop will feature speakers on a wide range of topics in environmental toxicologic pathology. Dr. Jeff Wolf, of EPL, will present a basic overview of alternative models in environmental toxicologic pathology, including amphibians and fish, information on continuing training in alternative model species pathology, and the future of alternative model use. Dr. Tabitha Viner, from the US Fish & Wildlife Service Forensic Pathology laboratory, will present on the role of the veterinary pathologist in wildlife forensic investigations, focusing on forensic investigations of oil, lead, and other toxicities in wildlife. Dr. Charles Wood, from the US Environmental Protection Agency, will discuss the role of the veterinary pathologist in the regulatory field of environmental toxicology. The workshop will conclude with a roundtable discussion involving all of the speakers.

CE 2 (Sunday PM) 1:30 PM–5:25 PM

Inflammatory Biomarkers—Sponsored by the STP Clinical Pathology Special Interest Group (CPIG)

Co-Chairs: Lila Ramaiah, DVM, PhD, DACVP, Huntingdon Life Sciences, Princeton, NJ, and William Reagan, DVM, PhD, DACVP, Pfizer, Groton, CT

Drug-induced toxicity to the immune and inflammatory systems encompasses a wide variety of adverse effects, ranging from exaggerated pharmacology (intended immunomodulation), to immunotoxicity (unintended immunosuppression or immune stimulation), drug-induced hypersensitivity and autoimmunity. Inflammatory biomarkers are valuable tools for the identification, characterization and monitoring of effects. Inflammatory biomarkers, often themselves mediators of inflammatory and immune responses, include cytokines, acute phase proteins, complement, and hemostatic proteins. This session explores the current use of inflammatory biomarkers in preclinical safety assessment. Topics encompass the evaluation of acute phase proteins, cytokines and complement in rodent



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and large animal models of inflammation. Emphasis is on relevance, utility, application, and use of inflammatory biomarkers, as well as on their translatability and predictivity from *in vitro* to *in vivo* models and from nonclinical to clinical settings. Factors that influence study design and biomarker selection, including preanalytical and analytical considerations, technologies and platforms, and species differences will be discussed. The session also includes short case studies with opportunity for open discussion with audience members.

1:30 PM–1:40 PM

Introduction

*Lila Ramaiah, DVM, PhD, DACVP,
Huntingdon Life Sciences, Princeton,
NJ*

1:40 PM–2:30 PM

**The Challenges for
Preclinical to Clinical
Translation of the Systemic
Inflammatory Response
Syndrome**

*Calvert Loudon, DVM, PhD, Johnson
& Johnson Pharmaceuticals, Raritan,
NJ*

2:30 PM–2:45 PM

**Case Studies: Acute Phase
Proteins**

*Niraj K. Tripathi, BVSc, MVSc,
PhD, DACVP, Covance Laboratories,
Inc., Madison, WI*

2:45 PM–3:35 PM

**Considerations for the
Use of Cytokines as Safety
Biomarkers *In Vivo***

*Jacqueline Tarrant, BVSc, PhD,
DACVP, Genentech, San Francisco,
CA*

3:35 PM–3:50 PM

**Detection of Circulating
Cytokines in Cynomolgus
Macaques with Multiplex
Array (Luminex)**

**Technology: A Case Study
Using Staphylococcal
enterotoxin B (SEB) and
Lipopolysaccharide (LPS)**
*Madeline M. Fort, PhD, DABT,
Amgen Inc., Seattle, WA*

3:50 PM–4:20 PM

Break

4:20 PM–5:10 PM

**Analysis and Interpretation
of Complement Activation
from *In Vivo* Data**

*Patricia C. Giclas, PhD, National
Jewish Health, Denver, CO*

5:10 PM–5:25 PM

**Case Study: Increased
Complement Fractions
in Cynomolgus Monkeys
Administered a Monoclonal
Antibody**

*Nancy E. Everds, DVM, DACVP,
Amgen Inc., Seattle, WA*

CE 3 (Sunday PM) 1:00 PM–5:00 PM

**Juvenile Animal Studies in Pediatric Drug
Development—Sponsored by the American College
of Toxicology (ACT)**

*Co-Chairs: LaRonda Morford, PhD, Covance Laboratories,
Greenfield, IN, and Kok Wah Hew, PhD, DABT, Takeda
Global R&D Center, Inc., Deerfield, IL*

This course will provide guidance on the current US and EU nonclinical regulatory requirements and toxicity study considerations when preparing for pediatric clinical trials, as well as the timing of juvenile toxicity studies. Regulatory presentations will include current pediatric regulations in US and EU as well as Paediatric Investigation Plan (PIP) evaluation procedures by the Nonclinical Working Group of the Paediatric Committee (PDCA) in EMA. Speakers from the industries will share their experience in designing and conducting juvenile animal studies, and scientific considerations when designing a nonclinical program to support pediatric drug development. Both small molecule and large molecule (biologics) pharmaceuticals will be discussed. The speakers will also discuss results of surveys for juvenile animal studies conducted across the pharmaceutical industry with both new chemical entities and new biological entities. The course will end with a panel discussion where speakers will address questions or comments from attendees.

1:00 PM–1:05 PM

Introduction

*Kok Wah Hew, PhD, DABT, Takeda
Global R&D Center, Inc., Deerfield,
IL*

1:05 PM–1:45 PM

**Juvenile Animal Studies
In Pediatric Drug
Development—US
Regulatory Perspective**

*Ikram Elayan, PhD, Senior
Pharmacology/Toxicology Reviewer,
US FDA, Silver Spring, MD*



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1:45 PM-2:30 PM

Juvenile Animal Studies In Pediatric Drug Development—EU Regulatory Perspective

Jacqueline Carleer, DVM, Chair, Nonclinical Working Group of Paediatric Committee (PDCO), EMA, Brussels, Belgium

1:30 PM-1:35 PM

Introduction

Michael W. Leach, DVM, PhD, DACVP, Pfizer, Andover, MA

1:35 PM-2:15 PM

Hypersensitivity Reactions: A Review of Mechanisms

James B. Rottman, DVM, PhD, DACVP, Amgen, Cambridge, MA

2:30 PM-3:00 PM

Break

2:15 PM-2:50 PM

Assessment of Anti-Drug Antibodies in Toxicology Studies

Daniel T. Mytych, PhD, Amgen, Thousand Oaks, CA

3:00 PM-3:40 PM

Juvenile Animal Studies for New Chemical Entities

Graham P. Bailey, Senior Scientific Director, Janssen Pharmaceutical N.V., Beerse, Belgium

2:50 PM-3:15 PM

Immunogenicity/Hypersensitivity and Other Immune Endpoints in Toxicity Studies with Protein Therapeutics

Deborah Finco, BS, MS, Pfizer, Groton, CT

3:40 PM-4:20 PM

Juvenile Toxicity Studies with Biopharmaceuticals: Considerations and Current Practices

LaRonda Morford, PhD, Covance Laboratories, Greenfield, IN

3:15 PM-3:45 PM

Break

4:20 PM-5:00 PM

Panel Discussion

All Speakers

3:45 PM-4:15 PM

Specialized Techniques for Detecting Immunogenicity and Hypersensitivity Reactions in Tissues

Jennifer L. Rojko, DVM, PhD, DACVP, Pathology Associates, CRL, Frederick, MD

CE 4 (Sunday PM) 1:30 PM-5:15 PM

Immunogenicity/Hypersensitivity of Biologics

Co-Chairs: Michael W. Leach, DVM, PhD, DACVP, Pfizer, Andover, MA, and Marque Todd, DVM, PhD, Pfizer, San Diego, CA

4:15 PM-5:00 PM

Pathology of Hypersensitivity Reactions

Joseph Beyer, DVM, PhD, DACVP, Genentech, South San Francisco, CA

Biologics are becoming more common in the pharmaceutical industry, have shown significant therapeutic benefit in many indications, and hold great promise in many other indications that are currently being studied. However, administration of biologics to animals or humans can be immunogenic, which in some cases may result in hypersensitivity reactions. These reactions can be minimal to severe, and quite variable between individuals. It can sometimes be challenging to differentiate on-target, pharmacologically-mediated effects from hypersensitivity, thus confounding study interpretation. However, such differentiation is often critical, because immunogenicity and hypersensitivity reactions in animals are generally not considered predictive of what will occur in humans, and thus associated findings are usually not considered relevant to humans (in contrast to on-target pharmacologic effects which often are relevant). This session will review different types of hypersensitivity reactions, methods of assessing immunogenicity and hypersensitivity reactions, and cover the changes that pathologists might observe in studies where these reactions are occurring.

5:00 PM-5:15 PM

Practical Applications in Case Studies

Michael W. Leach, DVM, PhD, DACVP, Pfizer, Andover, MA



Toxicologic Pathology of the Digestive Tract and Pancreas

Scientific Co-Chairs: Dimitry M. Danilenko, DVM, PhD, DACVP, Genentech, Inc., South San Francisco, CA, Mark F. Cesta, DVM, PhD, DACVP, National Institute of Environmental Health Sciences, Research Triangle Park, NC, and Prashant R. Nambiar, BVSc&AH, MS, PhD, DACVP, DABT, Pfizer Inc., Groton, CT

The 2013 STP Scientific Symposium will cover fundamental biology and recent innovations in the toxicologic pathology of the digestive tract and pancreas.

The focus of this international meeting is to correlate advances in the morphologic evaluation and integration of findings in the digestive tract and pancreas with functional, cellular, and molecular knowledge in a series of plenary and poster sessions. The meeting will provide a venue for interactive discussion of the current state of knowledge in both conventional and specialized nonclinical safety studies of the digestive tract and pancreas. Core sessions will include Normal Digestive Tract Functional Anatomy and Physiology, Inflammatory Bowel Disease, Digestive Tract Toxicity and Risk Assessment, Digestive Tract Carcinogenesis, Biomarkers of Digestive Tract and Pancreatic Injury and Disease, and Pancreatic Toxicity and Carcinogenesis. The symposium keynote address will focus on the gut microbiome and its critical interactions with the digestive tract epithelium and the mucosal immune system during health and disease.

Individual presentations will focus on a mix of traditional and contemporary strategies for the pathophysiologic and toxicologic evaluation of the digestive tract and pancreas. The meeting will also provide a unique forum for reviewing recent progress in developing and optimizing best practices for routine and specialized toxicologic pathology evaluation of digestive tract and pancreas across academia and the pharmaceutical and chemical industries. The symposium will also feature practical case study presentations as part of two scientific sessions: the session on Digestive Tract Toxicity and Risk Assessment and the session on Pancreatic Toxicity and Carcinogenesis.

The digestive tract and pancreas are rapidly growing areas of toxicologic inquiry and regulatory concern, and this symposium promises to be a great opportunity to review and expand your knowledge in this important field.

Monday, June 17

Scientific Sessions

Monday Morning

8:00 AM–8:05 AM

Symposium Welcome

8:05 AM–8:10 AM

Introduction

8:10 AM–9:00 AM

Keynote Address:

**Gut Microbiota, Low-grade
Inflammation and the
Metabolic Syndrome**

*Andrew Gewirtz, PhD, Georgia State
University, Atlanta, GA*

Session 1

9:00 AM–12:00 Noon

Normal Digestive Tract Functional Anatomy and Physiology

*Co-Chairs: Arlin Rogers, DVM, PhD, DACVP,
University of North Carolina at Chapel Hill, Chapel Hill, NC,
and Piper Treuting, DVM, MS, DACVP, University of
Washington, Seattle, WA*

Meaningful interpretation and translation of results from animal models of digestive disease must be rooted in an understanding of the similarities and differences of normal structure and function of the gastrointestinal tract in different species. The esophagus, stomach, and small intestine are critical sites of food transport, enzymatic digestion, and nutrient absorption. Disruption of one of these compartments often has effects on adjacent ones (i.e., acid reflux and Barrett's esophagus). An overview of the comparative morphology and physiology of each segment in small and large animals will be presented in order to provide meaningful context for the translation of experimental outcomes to human health. The role of the colon in physiology goes well beyond simple absorption of salt and water from ingesta prior to excretion from the body. The colon also has a systemic effect on energy homeostasis, lipid processing, and immune function. Because xenobiotics can alter mucosal signaling pathways, microfloral composition and immune responses, a review of the complex activities of the colon in health and disease will be presented to aid comparative pathologists engaged in drug development. Regenerative medicine is an emerging industry requiring understanding by toxicologic pathologists. The ability to regenerate tubular organs, including the digestive tract, requires an ability to distinguish tissue changes associated with regeneration from those that may be interpreted as abnormal or of a safety concern. Morphological changes associated with tubular organ (e.g. intestine) regeneration, and native-like tissue structures, will



be discussed along with mechanisms of the regenerative process.

9:00 AM–9:05 AM

9:05 AM–10:00 AM

Introduction

Comparative Anatomy, Physiology and Mechanisms of Disease Production of the Esophagus, Stomach, and Small Intestine

Howard Gelberg, DVM, PhD, DACVP, Oregon State University, Corvallis, OR

10:00 AM–10:30 AM

10:30 AM–11:15 AM

Break

The Colon: From Banal to Brilliant

Rani Sellers, DVM, PhD, DACVP, Albert Einstein College of Medicine, Bronx, NY

11:15 AM–12:00 Noon

Regenerative Medicine of the Gastrointestinal Tract

Timothy A. Bertram, DVM, PhD, DACVP, Tengion Labs, Winston-Salem, NC

Career Development Lunchtime Series

12:30 PM–1:30 PM

Transitioning to Management

Presented by the STP Career Development and Outreach Committee

(Free Event, registration required)

Panelists and audience members will discuss transitioning from “Bench Pathology” to a career with expanded roles in management. This session will allow attendees to become more familiar with tools that have helped pathologists make a successful transition to management as well as discuss some of the challenges that come with the role.

12:00 Noon–1:30 PM

Exhibitor Sponsored Lunch

For Registered Attendees

Monday Afternoon

Session 2

1:30 PM–5:00 PM

Inflammatory Bowel Disease

Co-Chairs: Lauri Diehl, DVM, PhD, DACVP, Genentech, South San Francisco, CA, and Brad Bolon, DVM, MS, PhD, DACVP, DABT, FATS, FIATP, The Ohio State University, Columbus, OH

Inflammatory bowel disease (IBD) afflicts as many as 1 in every 200 people in Europe and as many as 1 in every 300 in North America. The underlying pathogenesis is a complex mix of genetic and environmental factors which result in the loss of tolerance to commensal gut flora and poorly-controlled mucosal inflammation. The mechanisms influencing whether or not IBD is limited to the colon (e.g., ulcerative colitis) or has a broader distribution (e.g., Crohn’s disease, which can affect any part of the gastrointestinal tract) have yet to be defined. One major paradigm of growing importance to IBD is the interaction between immune cells, the mucosal epithelium, and the intestinal microbiome. This session will begin with a discussion of pathogenesis, current treatments and unmet medical needs for IBD. The next two talks will examine the innate immune system and its role in gastrointestinal health, particularly its relationship with the gut commensal organisms. The final speaker will explore animal models of IBD, emphasizing their biology and pathology as they apply to the discovery and development of new anti-IBD therapies.

1:30 PM–1:35 PM

Introduction

1:35 PM–2:15 PM

Overview of IBD and Evolving T Cell-based Therapy: An Old Player in the Current Understanding and Treatment of IBD

Zili Zhang, MD, PhD, Case Western Reserve University, Cleveland, OH

2:15 PM–3:05 PM

Intestinal Fungal Communities and their Role in Inflammation

David Underhill, PhD, Cedars Sinai, Los Angeles, CA

3:05 PM–3:35 PM

Break

3:35 PM–4:20 PM

Leukocyte-Epithelial Interactions and Mucosal Homeostasis

Charles A. Parkos, MD, PhD, Emory University, Atlanta, GA



4:20 PM-5:00 PM

Animal Models of Inflammatory Bowel Disease: Challenges of Modeling Human Disease

Lauri Diehl, DVM, PhD, DACVP, Genentech, South San Francisco, CA

8:50 AM-9:35 AM

Derisking Small Molecule Kinase Inhibitor Intestinal Toxicities

Richard A. Westhouse, DVM, PhD, DACVP, Bristol-Myers Squibb, Princeton, NJ

5:30 PM-6:30 PM

Town Hall Meeting

9:35 AM-9:55 AM

Student Speaker (TBD)

9:55 AM-10:25 AM

Break

10:25 AM-11:10 AM

Digestive Tract Neuroimmune Interactions in Health and Disease

Alan E. Lomax, PhD, Gastrointestinal Diseases Research Unit, Queen's University, Ontario, Canada

Tuesday, June 18

Tuesday Morning

Session 3

8:00 AM-12:00 Noon

Digestive Tract Toxicity and Risk Assessment

Co-Chairs: Zaher A. Radi, DVM, MBA, PhD, DABT, DACVP, Pfizer Worldwide R&D, Cambridge, MA, and Mehrdad Ameri, DVM, MS, PhD, DACVP, Amgen, Thousand Oaks, CA

11:10 AM-12:00 Noon

Case Studies of Digestive Tract Toxicity

Zaher A. Radi, DVM, MBA, PhD, DABT, DACVP, Pfizer Worldwide R&D, Cambridge, MA, Mehrdad Ameri, DVM, MS, PhD, DACVP, Amgen, Thousand Oaks, CA, and Prashant R. Nambiar, BVSc&AH, MS, PhD, DACVP, DABT, Pfizer, Groton, CT

Drug toxicity is one of the major causes of costly late-stage development failures and market withdrawals. Xenobiotics-induced toxic effects on the gastrointestinal (GI) tract can be one of the liabilities associated with novel therapeutics. GI toxicity, preclinical to clinical translation, in vitro derisking strategies, and sympathetic neuroimmune interactions will be discussed in this session. Appropriate preclinical toxicology approaches to detect adverse GI events and to evaluate the relevance of preclinical findings to the clinical setting is critical to reduce attrition due to GI toxicity. Speakers from academia and pharmaceutical industries will review the GI system in health and disease, GI neural circuits, neurotransmitters, and receptors involved in the sympathetic regulation of GI tract pathophysiology, derisking small molecule receptor targets, and GI tract risk assessment strategies. The session will conclude with practical case studies and pertinent examples of drug-induced GI tract toxicities encountered in drug development of novel therapeutics.

8:00 AM-8:05 AM

Introduction

8:05 AM-8:50 AM

Digestive Tract Toxicity: Adverse Events and Preclinical to Clinical Translation

Judit E. Markovits, DVM, PhD, DACVP, Novartis Institutes for Biomedical Research, Cambridge, MA

Tuesday Afternoon

Free Time



Wednesday, June 19

Wednesday Morning

Session 4

8:00 AM-12:00 Noon

Digestive Tract Carcinogenesis

Co-Chairs: Jerrold M. Ward, DVM, PhD, DACVP, Global Vet Pathology, Montgomery Village, MD, and Kishore Guda, DVM, PhD, Case Western Comprehensive Cancer Center, Cleveland, OH

The session covers comprehensive aspects of digestive tract carcinogenesis in humans and laboratory animals. The pathology and molecular aspects of carcinogenesis in the esophagus, stomach, and colon will be reviewed with the aim of targeting key molecular pathways for cancer chemoprevention, and developing novel molecular biomarkers for early detection of cancer. Since both genetics and environment play an equally important role in gastrointestinal cancer predisposition, the effect of diet in modulating cancer risk will be discussed. Furthermore, preclinical animal models to study the etiology, pathogenesis, methods of prevention and therapy with goals of applications to humans will be presented.

8:00 AM-8:05 AM

Introduction

8:05 AM-8:50 AM

Biomarkers and the Pathogenesis of Gastrointestinal Cancer

William M. Grady, MD, Fred Hutchinson Cancer Center, Seattle, WA

8:50 AM-9:35 AM

Targeting Mutated Pathways for Colon Cancer Therapy

Zhenghe John Wang, PhD, Case Western Comprehensive Cancer Center, Cleveland, OH

9:35 AM-10:10 AM

Rodent Intestinal Carcinogenesis: Pathology and Evaluation Methods for Nonclinical Models

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

10:10 AM-10:30 AM

Break

10:30 AM-11:15 AM

Animal Models of Helicobacter-Associated Gastric Cancer

11:15 AM-12:00 Noon

James G. Fox, DVM, DACLAM, Massachusetts Institute of Technology, Cambridge, MA

Diet, Genes, and Microbes: Complexities of Colon Cancer Prevention

Diane F. Birt, PhD, Iowa State University Department of Food Science and Human Nutrition, Ames, IA

Wednesday Afternoon

Practical Application of MRI Histology in Toxicologic Pathology

12:00 Noon-1:30 PM

Sponsored by IATP and STP

(Free Event, advance registration required*)

Isotropic 3-D in vivo MRI images of rats and mice as well as images of formalin-fixed whole tissue specimens are possible with compact scanners that can now be safely used in an animal room, a histology laboratory, or a pathologist's office. Compact MRI in vivo imaging provides an opportunity for longitudinal evaluation of tissue changes and tumor development in experimental animal models. Imaging of whole fixed tissue samples permits a thorough examination of multiple digital slices with subsequent volumetric measurement of 3-dimensional structures while leaving the specimen intact for subsequent conventional H&E histology. This session will provide examples of major organ system pathologies encountered in rodent toxicity and carcinogenicity studies with emphasis on how MRI imaging technology can serve as an important adjunct to conventional pathology evaluation. The objective will be to use rodent animal models and show live animal images followed by images of the fixed specimens from the same animal model and comparison with conventional H&E-stained sections.

*Session is limited to the first 75 attendees who preregister. Lunch will be provided.



Session 5

1:30 PM-5:00 PM

Biomarkers of Digestive Tract and Pancreatic Injury and Disease

Co-Chairs: Allison Vitsky, DVM, DACVP, Pfizer, San Diego, CA, and Florence Poitout, DVM, DACVP, DECVCP, Charles River Laboratories, Senneville, Quebec, Canada

Reliable, noninvasive biomarkers of toxicity are a crucial part of both preclinical and clinical studies, enhancing compound screening and dose selection and allowing for the development of novel drugs with optimal safety profiles. Recent advances in technology, including genomic and proteomic approaches, have improved the throughput and sensitivity of existing biomarker assays and have also helped to expand the biomarker toolkit. This session will commence with a review of commonly utilized digestive biomarkers in clinical veterinary settings, then progress to discussions of the ways that these and other novel biomarkers are being utilized to successfully detect and evaluate compound-associated gastrointestinal and pancreatic lesions in exploratory toxicity studies.

1:30 PM-1:35 PM

Introduction

1:35 PM-2:15 PM

Review of Commonly Used Clinical Pathology Parameters for General Gastrointestinal Disease

Jörg Steiner, DVM, PhD, DACVIM, DECVIM-CA, Texas A&M University, College Station, TX

2:15 PM-2:35 PM

Student Speaker (TBD)

2:35 PM-3:00 PM

Break

3:00 PM-3:40 PM

Evaluation of Potential Biomarkers of Gastrointestinal Toxicity in Preclinical Studies

Allison Vitsky, DVM, DACVP, Pfizer, San Diego, CA

3:40 PM-4:20 PM

MicroRNA Biomarkers of Gastrointestinal Toxicity in Tissues and Biofluids

Amy H. Yang, PhD, DABT, Pfizer, San Diego, CA

4:20 PM-5:00 PM

Biomarkers of Exocrine Pancreatic Injury

Jennie L. Walgren, PhD, Lilly, Indianapolis, IN

5:30 PM-5:50 PM

Awards Ceremony

5:50 PM-6:30 PM

Annual Business Meeting

7:00 PM-9:00 PM

President's Reception

Thursday, June 20

Thursday Morning

Session 6

8:00 AM-12:00 Noon

Pancreatic Toxicity and Carcinogenesis

Co-Chairs: Arun R. Pandiri, BVSc&AH, MS, PhD, DACVP, Experimental Pathology Laboratories, Inc., Durham, NC, and A. Eric Schultze, DVM, PhD, DACVP, FIATP, Eli Lilly and Company, Indianapolis, IN

The goals of this session are to provide an update on pancreatic toxicological pathology, to present novel information on responses of the pancreas to xenobiotics, and to provide a current understanding on pancreatic tumorigenesis. The session will begin with an overview of anatomy and physiology of the pancreas as well as pancreatic responses to xenobiotics. The session will highlight various rodent models used to study nonneoplastic pancreatic diseases and the molecular pathogenesis of pancreatic tumorigenesis. In addition, real case studies emphasizing associated liabilities and derisking activities will be used to illustrate the practical aspects of pancreatic toxicity. By the end of the session, the audience will develop a better appreciation for the pancreas as a target organ in toxicological studies.

8:00 AM-8:05 AM

Introduction

8:05 AM-8:45 AM

Overview of Exocrine Pancreatic Pathobiology with Respect to Pharmacology and Toxicology

Arun R. Pandiri, BVSc&AH, MS, PhD, DACVP, Experimental Pathology Laboratories, Inc., Durham, NC



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**Pathogenesis of Pancreatic
Cancer: Lessons Learnt from
Animal Models**

*L. Charles Murtaugh, PhD,
University of Utah, Salt Lake City,
UT*

9:25 AM–10:05 AM

**Pancreatic Toxicity at the
Exocrine-Endocrine Interface**

*Karrie A. Brenneman, DVM, PhD,
DACVP, Pfizer, Andover, MA*

10:05 AM–10:35 AM

Break

10:35 AM–11:15 AM

**Animal Models of
Nonneoplastic Pancreatic
Diseases**

*John R. Foster, BSc, PhD, FRCPath,
FIATP, HonFBTS, AstraZeneca,
Macclesfield, Cheshire, UK*

11:15 AM–12:00 Noon

**Species- and Dose-Specific
Pancreatic Responses and
Progression in Repeat-Dose
Studies with G1181771X,
a Novel Cholecystokinin-1
Receptor Agonist in Mice,
Rats and Monkeys**

*Chandikumar S. Elangbam, BVSc,
PhD, DACVP, GlaxoSmithKline,
Research Triangle Park, NC*

12:00 Noon

Meeting Adjourned