



STP 35TH ANNUAL SYMPOSIUM

THE BASIS AND RELEVANCE OF VARIATION
IN TOXICOLOGIC RESPONSES

SAN DIEGO • CALIFORNIA | JUNE 26–30, 2016

Saturday, June 25

NTP Satellite Symposium: Pathology Potpourri

9:00 AM–4:30 PM

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

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 will then vote using wireless keypads and the results will be displayed on the screen. Time is allowed for discussion after each voting session.

Sunday, June 26

CE 1 (Sunday AM)

8:00 AM–12:00 Noon

The Respiratory System as a Target for Drug-Induced Toxicity: Pathology and Investigational Techniques

Co-Chairs: Nicholas Macri, DVM, MS, PhD, Envigo, East Millstone, NJ; and Kumar Changani, PhD, GlaxoSmithKline Pharmaceuticals, Stevenage, Hertfordshire, UK

Safety assessment of inhaled therapeutics and chemicals, both industrial and environmental, requires detailed evaluation of the upper respiratory tract along with other standard protocol tissues. Regulatory agencies require the assessment of specific areas of the nasal cavity, larynx, trachea, and lungs in rodent and non-rodent animal models. Although histopathological changes in these organs are well-characterized in the literature, interpretation of their adversity and relevance to man are less clear-cut. The first half of this session will focus on methodologies used to deliver drugs by inhalation and the deposition patterns of inhaled drugs. Presentations on common background and test article-associated changes in different species, and comparative sensitivities of the upper respiratory tract, will cover the histopathological aspects of inhalation studies and their relevance to man. During the second half of the session, the importance of pulmonary macrophages in respiratory health and disease and models used in inhalation studies will be addressed. The final talk will focus on the use of imaging strategies for lung function. This will include MRI, CT, SPECT, PET, and optical modalities, which are being used in the pharmaceutical industry to understand disease in a longitudinal fashion. These modalities increase our understanding of drug delivery and allow discrimination

of different aspects of lung pathology, including ventilation deficits, lung perfusion, pulmonary edema, cell migration, and fibrotic lesions.

8:00 AM–8:25 AM

An Introduction to the Inhalation Study: Methods of Exposure and Tissue Processing

Alison Rowles, BSc (Hons), BVMS (Hons), PhD, MRCVS, Envigo, Suffolk, UK

8:25 AM–9:05 AM

Common Background and Test Article-Associated Microscopic Changes in the Upper Respiratory Tract of Rodents and Dogs in Inhalation Studies

Nicholas Macri, DVM, MS, PhD, Envigo, East Millstone, NJ

9:05 AM–9:40 AM

Comparative Sensitivities of the Upper Respiratory Tract in Laboratory Animals

Vasanthi Mowat, BVSc, MVSc, MRCVS, FRCPath, Envigo, Alconbury, Cambridgeshire, UK

9:40 AM–10:15 AM

Break

10:15 AM–10:50 AM

An Overview of Pulmonary Macrophages in Health, Disease, and Medicines Development

Kristen J. Nikula, DVM, PhD, Seventh Wave Laboratories, Chesterfield, MO

10:50 AM–11:20 AM

Strategy and Methodologies for Assessing and Interpreting Respiratory Function Endpoints in Toxicology Studies

Ronald K. Wolff, PhD, DABT, RK Wolff – Safety Consulting Inc., Carbondale, CO

11:20 AM–12:00 Noon

Imaging Strategies to Discriminate and Characterize Lung Pathology and Function

Kumar Changani, PhD, GlaxoSmithKline Pharmaceuticals, Stevenage, Hertfordshire, UK

CE 2 (Sunday AM)

8:00 AM–12:00 Noon

Interpreting and Integrating Clinical and Anatomic Pathology Results: Pulling It All Together

Sponsored by the American College of Toxicology (ACT)

Co-Chairs: Mary Jane Hinrichs, PhD, MedImmune, LLC, Gaithersburg, MD; and Lila Ramaiah, DVM, PhD, DACVP, Envigo, East Millstone, NJ

The interpretation of safety findings in toxicology studies requires an integrative weight of evidence approach that



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takes into account all collected data sets. Data must be evaluated in its entirety, as neither clinical nor anatomic pathology can be relied upon in isolation to fully understand the relationship between study findings and the test article. Basic principles for correlating anatomic pathology and clinical pathology findings and for integrating these with other study endpoints will be reviewed. A series of case examples, presented jointly by a clinical pathologist and an anatomic pathologist, will be used to illustrate the collaborative effort required between clinical and anatomic pathologists. In addition, the diagnostic utility of kidney and liver biomarkers will be discussed, based on data from meta-analyses of preclinical qualification and other studies. Examples of traditional and novel biomarker data implementation in nonclinical toxicology studies will also be presented to illustrate the relationship between discrete changes in biochemistry and tissue morphology in the real world drug development space.

8:00 AM–8:05 AM

Introduction

Mary Jane Hinrichs, PhD, MedImmune, LLC, Gaithersburg, MD

8:05 AM–8:55 AM

Principles for Correlating Anatomic Pathology and Clinical Pathology Findings in Toxicology Studies—Teasing Out Cause and Effect

Lila Ramaiah, DVM, PhD, DACVP, Envigo, East Millstone, NJ

8:55 AM–9:45 AM

Interpretation of Toxicity Findings through the Combination of Clinical and Anatomic Pathology Data (Part 1)

Elizabeth V. Skuba, DVM, MVSc, DACVP, Novartis Pharmaceuticals, East Hanover, NJ

9:45 AM–10:15 AM

Break

10:15 AM–11:05 AM

Interpretation of Toxicity Findings through the Combination of Clinical and Anatomic Pathology Data (Part 2)

William O. Iverson, DVM, MedImmune, LLC, Faber, VA

11:05 AM–11:55 AM

Evaluation and Implementation of Traditional and Non-traditional Biomarkers of Kidney and Liver Injury

Daniela Ennulat, DVM, PhD, GlaxoSmithKline, King of Prussia, PA

11:55 AM–12:00 Noon

Questions and Discussion

CE 3 (Sunday PM)

1:30 PM–5:30 PM

Hematotoxicity and Immunotoxicity Assessment: Essential Principles and Emerging Modalities

Co-Chairs: Bill Siska, DVM, MS, DACVP, Charles River Laboratories, Reno, NV; and Denise Boumou, DVM, PhD, DACVP, Bristol-Myers Squibb Company, Princeton, NJ

Toxicity involving the hematopoietic system and lymphoid organs is frequently encountered in nonclinical safety studies and represents an important regulatory focus. Clinical pathology and anatomic pathology endpoints have traditionally been used for a first-line assessment of hematotoxicity and immunotoxicity, with additional specialized testing generally performed on a case-by-case basis consequent to study findings or in light of recognized drug class effects. As more specialized techniques including flow cytometry, functional assays, and other novel in vitro evaluations are increasingly utilized, it is important to understand the relationships between these modalities and traditional endpoints, and to be familiar with their advantages and limitations. This session will present comprehensive approaches to the evaluation of hematopoietic and lymphoid organ toxicity and will highlight correlations between non-traditional testing and routine endpoints through didactic presentations and integrated case examples.

1:30 PM–2:15 PM

Correlation Among Bone Marrow Cytology, Histopathology, and Hematology Data in the Assessment of Hematotoxicity in Nonclinical Studies: Principles and Case Examples

Anne Provencher, DVM, MSc, DACVP, DECVCP, FIATP, Charles River Laboratories, Sherbrooke, Quebec, Canada

2:15 PM–2:55 PM

Application of Flow Cytometry for Hematotoxicity Evaluation of Rodent Bone Marrow

Cindy Zhang, BS, MS, Bristol Myers-Squibb Company, Princeton, NJ

2:55 PM–3:25 PM

Break

3:25 PM–4:05 PM

Case Study of the Megakaryocyte Colony Forming Cell Assay as an *In Vitro* Model of Drug-Induced Thrombocytopenia, *In Vitro* to *In Vivo* Translatability, Cross-Species Translatability, and Use in Risk Mitigation

Jacqueline Tarrant, BVSc, PhD, DACVP, Genentech, Inc., South San Francisco, CA



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4:05 PM–4:45 PM

Immunotoxicity that the TDAR May Not Address

Florence G. Burlison, PhD, Burlison Research Technologies, Inc., Morrisville, NC

4:45 PM–5:30 PM

Immunotoxicity Assessment: One Size Does Not Fit All

Ellen W. Evans, DVM, PhD, DACVP, Pfizer, Inc., Groton, CT

CE 4 (Sunday PM)

1:30 PM–5:30 PM

Is It Adverse, Adaptive, Artifact?

Co-Chairs: Thomas Steinbach, DVM, DACVP, DABT, EPL, Inc., Durham, NC; and Arun Pandiri, BVSc&AH, MS, PhD, DACVP, DABT, National Toxicology Program, NIEHS, Research Triangle Park, NC

One of the principal challenges of a toxicologic pathologist is to determine and differentiate a true adverse effect from an adaptive response. A number of factors can interfere with a clear, reasoned determination of adversity starting with the lack of consensus on the definition of adversity. In addition, the introduction of artifact, both in poor study design and in histopathology and other data sets can lead to an improper determination of adversity. This CE course will attempt to address these challenges in determining if a finding is adverse or not. The course begins with an overview and position statement from the STP committee on adverse versus adaptive effects and is followed by a discussion on how artifacts and spurious findings can complicate adversity determination. In addition, lectures with case examples will be provided from clinical pathology and anatomic pathology to determine adverse versus adaptive effects. The course will close with a regulatory perspective on interpreting adverse versus adaptive effects. This CE course is designed to provide practical knowledge with numerous relevant case examples in toxicologic pathology and would be useful to the practicing toxicologic pathologist.

1:30 PM–2:10 PM

What is an Adverse Response in Toxicologic Pathology?

Roy L. Kerlin, BVSc, PhD, DACVP, Pfizer, Inc., Groton, CT

2:10 PM–2:50 PM

Adverse or Adaptive? No, It Is an Artifact

Peter Mann, DVM, PhD, EPL NorthWest, Seattle, WA

2:50 PM–3:20 PM

Break

3:20 PM–4:00 PM

Adaptive versus Adverse Responses in Clinical Toxicologic Pathology

Nancy Eoerds, DVM, DACVP, Amgen, Inc., South San Francisco, CA

4:00 PM–4:40 PM

Adverse versus Adaptive Lesions in Anatomic Toxicologic Pathology

Alok K. Sharma, BVSc, MVSc, MS, PhD, DACVP, DABT, Covance Laboratories, Inc., Madison, WI

4:40 PM–5:20 PM

Regulatory Perspective on Adverse versus Adaptive Responses in Toxicologic Pathology

Peyton Myers, PhD, US FDA, Silver Spring, MD

5:20 PM–5:30 PM

Questions and Discussion

Monday, June 27

8:00 AM–8:10 AM

Symposium Welcome

8:10 AM–9:00 AM

Keynote Address: Cornerstones of Toxicology

A. Wallace Hayes, PhD, DABT, FATS, FIBiol, FACFE, ERT, Harvard School of Public Health, Boston, MA and Michigan State University Institute for Integrative Toxicology, East Lansing, MI

Session 1

9:00 AM–12:00 Noon

Real World Toxicology Outcomes: Impact of Species and Strain Selection on Drug Development Programs

Co-Chairs: Diane Gunson, BVSc, PhD, DACVP, Novartis Pharmaceuticals Corporation, East Hanover, NJ; and Emily Meseck, DVM, DACVP, DABT, Novartis Pharmaceuticals Corporation, East Hanover, NJ

Selection of a rodent strain and non-rodent species for pharmacologic and toxicity testing has far ranging implications for drug development programs. Variation in toxicologic responses due to species or strain selection in drug safety programs will be explored through three detailed case studies and a comparison of neoplastic findings in toxicology studies between two common outbred rat strains. The impact of species and strain selection on variation in biologic and toxicologic responses and the impact of that variation on drug development programs, including program outcomes and mitigation strategies, will be discussed in the context of the case studies.



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9:00 AM–9:15 AM

Introduction

Diane Gunson, BVSc, PhD, DACVP, Novartis Pharmaceuticals Corporation, East Hanover, NJ

9:15 AM–10:00 AM

Differences in Types and Incidence of Neoplasms in Wistar Han and Sprague Dawley Rats

Klaus Weber, DVM, MSBiol, PhD, Anapath GmbH, Oberbuchsitzen, Switzerland

10:00 AM–10:30 AM

Break

10:30 AM–11:00 AM

Differences in Sensitivity between Cynomolgus Monkeys of Mauritian or Asian Origin

Peter K. Hoffmann, MD, PhD, Novartis Pharmaceuticals Corporation, East Hanover, NJ

11:00 AM–11:20 AM

Examples of the Impact of Species and Strain on Immunotoxicology Assessment

Ellen W. Evans, DVM, PhD, DACVP, Pfizer, Inc., Groton, CT

11:20 AM–12:00 Noon

Management of Pseudoallergic Responses in Beagle Dogs

John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories, Maryland Heights, MO

Session 2

1:30 PM–5:00 PM

Deciphering Sources of Variability in Clinical Pathology—It's Not Just About the Numbers

Co-Chairs: Adam Aulbach, DVM, DACVP, MPI Research, Mattawan, MI; Anne Provencher, DVM, MSc, DACVP, DECVP, FIATP, Charles River Laboratories, Sherbrooke, Quebec, Canada; and Niraj Tripathi, BVSc, MVSc, PhD, DACVP, Covance Laboratories, Inc., Madison, WI

This session will explore variability in Clinical Pathology data and its impact on the overall interpretation of the data and determination of toxicity and/or effect of experimental procedures. The presentations will discuss potential effects of many variables on clinical pathology parameters, from animal physiology to the collection process, specimen handling and analysis, from study design to the use of statistics, and how to manage those variables to ensure accurate interpretation of clinical pathology data in research and drug development. The first two presentations will focus on preanalytical and analytical variables that can influence clinical pathology data, and the third presentation will cover the influence of study design on clinical pathology results. After the break,

a presentation on the use of statistics and reference intervals for data interpretation, as well as approach to qualifiers to describe a magnitude of changes in clinical pathology reports. The session will end with an interactive session of case reports/panel discussions where invited speakers will present cases/data on the different topics to generate discussion between the panel (speakers and co-chairs) and participants.

1:30 PM–1:35 PM

Introduction

Adam Aulbach, DVM, DACVP, MPI Research, Mattawan, MI; Anne Provencher, DVM, MSc, DACVP, DECVP, FIATP, Charles River Laboratories, Sherbrooke, Quebec, Canada; and Niraj Tripathi, BVSc, MVSc, PhD, DACVP, Covance Laboratories, Inc., Madison, WI

1:35 PM–2:10 PM

Preanalytical Considerations

Nancy Everds, DVM, DACVP, Amgen, Inc., South San Francisco, CA

2:10 PM–2:45 PM

Analytical Considerations

A. Eric Schultze, DVM, PhD, DACVP, FIATP, Eli Lilly and Company, Indianapolis, IN

2:45 PM–3:20 PM

Study Design

Adam Aulbach, DVM, DACVP, MPI Research, Mattawan, MI; Anne Provencher, DVM, MSc, DACVP, DECVP, FIATP, Charles River Laboratories, Sherbrooke, Quebec, Canada; and Niraj Tripathi, BVSc, MVSc, PhD, DACVP, Covance Laboratories, Inc., Madison, WI

3:20 PM–3:50 PM

Break

3:50 PM–4:25 PM

Statistics/Reference Intervals/Magnitude and Qualifiers

Robert Hall, DVM, PhD, DACVP, Covance Laboratories, Inc., Madison, WI

4:25 PM–5:00 PM

Panel Discussion

Tuesday, June 28

Session 3

8:00 AM–12:00 Noon

Influence of Experimental Design and Environmental Conditions

Co-Chairs: Theresa Boulineau, DVM, MS, DACVP, Novartis Institutes for Biomedical Research, East Hanover, NJ; and Sherry J. Morgan, DVM, PhD, DACVP, DABT, DABVT, AbbVie, Inc., North Chicago, IL



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Careful planning of studies is paramount to optimizing the probability of a successful study – one in which the results can be clearly interpreted and decisions can be made. Understanding the potential ramifications of experimental design on study interpretation is one of the major facets of study planning. Session 3 will cover some of the aspects of experimental design and potential associated environmental conditions that may affect the outcome of toxicology studies. The first two presentations will provide specific examples of how selection of species and strains (Cynomolgus monkey or rodents) can affect clinical or anatomic pathology results and interpretation. This will be followed by an in-depth discussion of the potential effect of vehicles/formulations on general toxicology studies (both clinical and anatomic pathology) as well as specific considerations for developmental/reproductive toxicology studies. An additional presentation will cover facets of study design (other than vehicles/formulations) on the outcome of developmental/reproductive toxicology studies. The session will conclude with a presentation on how bioinformatics may be utilized to optimize study design and interpretation.

8:00 AM–8:10 AM

Introduction

Theresa Boulineau, DVM, MS, DACVP, Novartis Institutes for Biomedical Research, East Hanover, NJ; and Sherry J. Morgan, DVM, PhD, DACVP, DABT, DABVT, AbbVie, Inc., North Chicago, IL

8:10 AM–8:45 AM

Species/Strain Differences and How they Affect Study Designs and Outcomes–Anatomic Pathology

Karyn Colman, BVetMed, MRCVS, Novartis Institutes for Biomedical Research, East Hanover, NJ

8:45 AM–9:20 AM

Species/Strain Differences and How They Affect Study Designs and Outcomes–Clinical Pathology

Kirstin Barnhart, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL

9:20 AM–10:00 AM

Break

10:00 AM–10:40 AM

Multi-functional Approach to Topic of Vehicles/Formulations and Their Effect on Study Outcomes

Brian Enright, PhD, DABT, AbbVie, Inc., North Chicago, IL; Michael Logan, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL; and Katharine Whitney, DVM, PhD, DACVP, AbbVie, Inc., North Chicago, IL

10:40 AM–11:20 AM

Influence of Study Design on Developmental/Reproductive Toxicology Study Outcomes

Paul M.D. Foster, PhD, ATS, Division of the National Toxicology Program (NTP), National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC

11:20 AM–12:00 Noon

Modern Data Analysis–Bioinformatics and How It Can Be Used in Study Design/ Interpretation

Elizabeth V. Skuba, DVM, MVSc, DACVP, Novartis Pharmaceuticals, East Hanover, NJ

Afternoon

Free Time

Wednesday, June 29

Session 4A

8:00 AM–12:00 Noon

Influence of Epigenetics, Genetics, and Immunology

Co-Chairs: Robert Johnson, DVM, PhD, Novartis, East Hanover, NJ; and Michael Leach, DVM, PhD, Pfizer, Inc., Andover, MA

In nonclinical studies, variability in responses often occurs both within studies (inter-animal variability), as well as between studies using the same species. Potential causes of this variability include genetic and epigenetic variants. This is especially true for studies with nonhuman primates, which have genetic variability similar to that observed in the human population. However, examination of the role of genetics and epigenetics in variability in nonclinical studies has generally been limited. The objective of this session is to provide attendees with a basic understanding of both genetics and epigenetics, and the potential impact that genetic and epigenetic variants can have in nonclinical studies. In this session, a population analysis of cynomolgus monkey genetic variability, with a comparison to the human exome, will be presented, as well as case studies evaluating the functional impact of identified variants, and potential variants associated with toxic phenotypes such as drug-induced fulminant liver failure. This will provide the roadmap for a general strategy of assessing the impact of genetic variation of different phenotypes. This approach overall introduces a paradigm shift in using genetic characterization of species used in toxicity studies to understand the genetic basis of drug-associated toxicity signals. Although rodents used in toxicity studies are generally inbred and genetically identical, or outbred with limited genetic diversity, a diversity



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outbred (DO) population of mice was recently established with the aim of improving the prediction of human safety risk. As an example, DO mice have been used to model idiosyncratic liver injury caused by pharmaceutical drugs and herbal supplements. DO mice can also be used for whole genome association analyses to identify translational pharmacogenetic risk factors for toxicity, and examples of this will be presented. In addition, the utility of integrated genome-wide epigenomic and transcriptomic profiling of tissues from animal models will be discussed with particular emphasis on the mechanistic basis for species-specific differences in non-genotoxic hepatocarcinogenesis and implications for human cancer risk assessment. The session will conclude with a presentation discussing the role of epigenetic regulation of endothelial cell (EC) function. Endothelial dysfunction is directly or indirectly involved in >70% of all cases of human death, most notably due to their central role in cardiovascular disease and tumors. Recent advances in whole genome analyses have shed unexpected light into the contribution of epigenetic modifications as regulator of EC phenotype and function. The presentation will prototypically present the role of epigenetic EC changes during adolescent vessel maturation.

8:00 AM–8:05 AM

Introduction

Robert Johnson, DVM, PhD, Novartis, East Hanover, NJ; and Michael Leach, DVM, PhD, Pfizer, Inc., Andover, MA

8:05 AM–8:40 AM

Genetic Variation in Non-human Primates and Impact for Toxicology Programs

Olivier Grenet, PhD, Novartis Institutes for Biomedical Research, Basel, Switzerland

8:40 AM–9:15 AM

Genetics, a Factor to Consider in Drug Safety Assessment Studies using Cynomolgus Monkeys

Karissa Adkins, PhD, Pfizer, Inc., Groton, CT

9:15 AM–9:50 AM

Low Frequency Clinical Adverse Drug Reactions Can Be Predicted and Studied by Using Genetically Diverse Mouse Populations

Alison Harrill, PhD, University of Arkansas for Medical Sciences, Little Rock, AR

9:50 AM–10:05 AM

Student Speaker

TBD

10:05 AM–10:40 AM

Break

10:40 AM–11:15 AM

Epigenetics in Toxicology

Jonathan Moggs, PhD, Novartis Institutes for Biomedical Research, Basel, Switzerland

11:15 AM–12:00 Noon

Epigenetics and Angiogenesis

Hellmut Augustin, ProfDrMedVet, PhD, Deutsches Krebsforschungszentrum (DKNZ), Heidelberg, Germany

Postnatal Organ Development as a Complicating Factor in Juvenile Toxicity Studies

Sponsored by IATP and STP

12:00 Noon–1:30 PM

Co-Chairs: George A. Parker, DVM, PhD, DACVP, DABT, WIL Research, Hillsborough, NC; and Catherine Picut, VMD, JD, DABT, DAVCP, WIL Research, Hillsborough, NC

In this practical approach to evaluating juvenile toxicity studies in rodent models, speakers will present a spectrum of histological changes not commonly seen in conventional toxicity studies.

Session 4B

1:30 PM–5:00 PM

Influence of Epigenetics, Genetics, and Immunology

Co-Chairs: Cory Brayton, DVM, Johns Hopkins University School of Medicine, Baltimore, MD; and Paul W. Snyder, DVM, PhD, EPL, Inc., West Lafayette, IN

Between and within species used to model human conditions, variation in responses to experimental interventions has often confounded results and made interpretation to humans difficult. The limitations to models include confounding, disparate, or otherwise problematic research outcomes; and for poor reproducibility and poor predictivity of translational studies. Examples of even a few immune relevant genotypes predict divergent immune and disease phenotypes, and illustrate that model animals must be assessed critically for their suitability for a particular disease. Accurate and broad-based genotype and phenotype data should be applied to model selection in an attempt to explain unexpected or disparate findings, or poor reproducibility. In the final talk of this session, the presenter will highlight some interactions with environmental factors, using examples of mouse strain-related differences in allergy induced responses to common environmental or novel allergens, and the implications for public and precision health. Mice and macaque are emphasized in this session.

1:30 PM–1:35 PM

Introduction

Cory Brayton, DVM, Johns Hopkins University School of Medicine, Baltimore, MD; and Paul W. Snyder, DVM, PhD, EPL, Inc., West Lafayette, IN



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1:35 PM–2:15 PM

Translating Rodent Models—Immune Variation and Efficacy Testing

Rani Sellers, DVM, PhD, DACVP, Pfizer, Inc., Pearl River, NY

2:15 PM–2:55 PM

Immunological Variation, Including Inflammatory SNPs and Influenza Studies

Gary R. Burleson, PhD, Burleson Research Technologies, Inc., Morrisville, NC

2:55 PM–3:25 PM

Break

3:25 PM–3:40 PM

Student Speaker

TBD

3:40 PM–4:20 PM

Immunologic Variation Attributable to MHC Differences in Macaques

David O'Connor, PhD, University of Wisconsin School of Medicine and Public Health, Madison, WI

4:20 PM–5:00 PM

Strain- and Environment-Related Factors in Murine Models of Allergic Airway Disease

Jack R. Harkema, DVM, PhD, DACVP, Michigan State University, East Lansing, MI

Thursday, June 30

Session 5

8:00 AM–12:00 Noon

Influence of Age, Hormones, and the Microbiome

Co-Chairs: Dinesh J. Stanislaus, PhD, GlaxoSmithKline, King of Prussia, PA; and Justin D. Vidal, DVM, PhD, Vet Path Services, Inc., Blue Bell, PA

The objective of this session is to discuss and elaborate on how age, hormones, and microbiome can influence toxicologic response in animals. The first presentation will provide an overview of variability in toxicology testing and discuss how underlying hormonal differences between sexes affect drug metabolism and resulting toxicologic responses. The session will next focus on the new emerging field of the microbiome and present current knowledge on how the microbiome acts as a gatekeeper to control access to chemicals and how that affects toxicologic responses. The third presentation will explore the impact of age and timing of dosing on toxicologic response. The last two presentations will be changing the direction of the discussion to more practical applications and will go into detail on how age-related changes affect the interpretation of male and female reproductive tract pathology.

8:00 AM–8:05 AM

Introduction

Dinesh J. Stanislaus, PhD, GlaxoSmithKline, King of Prussia, PA; and Justin D. Vidal, DVM, PhD, Vet Path Services, Inc., Blue Bell, PA

8:05 AM–8:45 AM

Gender Differences in Human and Animal Toxicology

Michael Gochfeld, MD, PhD, Rutgers University, Piscataway, NJ

8:45 AM–9:25 AM

Variability in Toxicologic Responses Due to the Microbiome

Ellen Kovner Silbergeld, PhD, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

9:25 AM–10:05 AM

Timing of Exposure and Windows of Sensitivity in Toxicity Testing

Paul M.D. Foster, PhD, ATIS, Division of the National Toxicology Program (NTP), National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC

10:05 AM–10:40 AM

Break

10:40 AM–11:20 AM

Impact of Age on the Male Reproductive System from the Pathologist's Perspective

Amera Remick, DVM, DACVP, DABT, WIL Research, Hillsborough, NC

11:20 AM–12:00 Noon

Impact of Age on the Female Reproductive System from the Pathologist's Perspective

Justin D. Vidal, DVM, PhD, Vet Path Services, Inc., Blue Bell, PA

12:00 Noon

Meeting Adjourned