SUNDAY, JUNE 25

CE1 (AM)

8:00 AM–12:00 Noon

Development of Gene Therapies for Ocular Indications: From Concepts to Risk Assessment

Co-Chairs: ***Helen S. Booler, BSc (Hons), BVetMed, DECVP, PhD, MRCVS,*** *Novartis, Basel, Switzerland;* ***Jacqueline Brassard, DVM, PhD, DACVP,*** *Brassard Toxicologic Pathology Consultancy, Tustin, CA; and* ***Meg Ferrell Ramos, DVM, PhD, DACVP,*** *AbbVie, Irvine, CA*

Gene therapy in general has emerged as a research topic of choice in recent years. There has been a resurgence of interest and investment in the field of ocular gene therapy, driven by improved understanding of the genetic basis of ocular disease, advances in viral vector technology and unique anatomic and immunologic properties of the eye. The approval in 2017 of the first ocular gene therapy, indicated for patients with RPE65-associated retinal dystrophies, has provided hope for patients with many previously untreatable inherited retinal dystrophies, and has shifted the way we think about the treatment of ocular diseases more widely. With more ocular gene therapeutics in the pipeline, it is a good time to review the design and development of gene therapy products, with an emphasis on the nonclinical development, common in-life and histopathologic findings, risk assessment and a discussion of the translatability of nonclinical findings and the relevance to patients.

8:00 AM–8:05 AM	**Introduction**
8:05 AM–8:45 AM	**An Overview of Gene Therapies both General and Specific to Ocular Indications** *Jacqueline Brassard, DVM, PhD, DACVP, Brassard Toxicologic Pathology Consultancy, Tustin, CA*
8:45 AM–9:25 AM	**Toxicology, Study Design, Emerging Safety Trends, and Regulatory Considerations in the Development of Ocular Gene Therapies** *Ingrid M. Pruimboom-Brees, DVM, PhD, DACVP, Novartis AG, Basel, Switzerland*
9:25 AM–9:45 AM	**Immunological Considerations and Immune-Mediated Pathology in the Development of Ocular Gene Therapies** *Meg Ferrell Ramos, DVM, PhD, DACVP, AbbVie, Irvine, CA*
9:45 AM–10:15 AM	**Break**
10:15 AM–11:00 AM	**In-Life Observations and Pathology of AAV-Based Gene Therapies** *Helen S. Booler, BSc (Hons), BVetMed, DECVP, PhD, MRCVS, Novartis, Basel, Switzerland*
11:00 AM–11:45 AM	**An Introduction to Ocular Oligonucleotide Therapies, In-Life Observations, and Associated Pathology** *Krishna Yekkala, BVSc, PhD, DACVP, Janssen Research and Development of Johnson & Johnson, Spring House, PA*
11:45 AM–12:00 Noon	**Panel Discussion**

Division of Translational Toxicology (DTT) Satellite Symposium: Pathology Potpourri (Sunday AM)

9:00 AM–12:00 Noon

Co-Chairs: ***Mark F. Cesta, DVM, PhD, DACVP,*** *NIEHS, Research Triangle Park, NC;* ***Erin M. Quist, DVM, MS, PhD, DACVP,*** *Charles River Laboratories, Durham, NC; and* ***Robert Sills, DVM, PhD, DACVP,*** *NIEHS, Research Triangle Park, NC*

The objective of this interactive symposium is to provide continuing education on interpreting pathology slides and data, 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, and the results will be displayed on the screen. Time is allowed for discussion after each voting session.

Career Development Workshop (Sunday PM)

1:30 PM–5:30 PM

Communicate to Advocate: Utilizing Power Skills for All Stages of Your Career

Co-Chairs: ***Vimala Vemireddi, BVSc, MS, DABT, DACVP,*** *Labcorp, Ashburn, VA; and* ***Rebecca A. Kohnken, DVM, PhD, DACVP,*** *AbbVie, North Chicago, IL*

The Career Development and Outreach Committee, in collaboration with the Diversity, Inclusion, and Belonging Committee and Women in Tox Path Subcommittee, brings this session to you. Self-advocacy is crucial to success in all aspects of life, especially one's career. Whether you're an entry-level professional or renowned expert, it's vital to articulate your accomplishments and the value you bring to your organization. In this session, attendees will learn tips and strategies from professionals who have successfully advocated for themselves and others, including overcoming challenges associated with bias and discrimination. Topics include how to leverage power skills in the job search, how to communicate and negotiate during the job interview, and how to advocate for yourself, and others.

CE2 (Sunday PM)

1:30 PM–5:30 PM

Toxicologic Neuropathology of Novel Therapeutics

*Co-Chairs: **Dinesh Bangari, BVSc, MVSc, MS, PhD, DACVP**, Sanofi, Framingham, MA; and **Lisa Lanigan, DVM, PhD, DACVP**, Charles River Laboratories, Ashland, OH*

The goal of this session is to provide a well-rounded overview of the rapidly emerging biopharmaceutical research that is focused on developing novel therapeutics for the treatment of nervous system disorders and neuromuscular diseases. These modalities include vector-based therapies such as lentiviral and adeno-associated viral vectors (AAVs), cell-based therapies such as stem cells and CAR-T cells, nucleic acid-based therapies such as antisense oligonucleotides (ASOs) and mRNAs, and novel antibody-based therapeutics. The session will begin with an overview of the mechanisms of action for each of these therapeutics, how they can specifically target the nervous system and the unique aspects of safety risk assessment for these novel biotherapeutics. Additionally, there will be a presentation on the methods for investigating biodistribution, pharmacokinetics and pharmacodynamics to enable clinical/human dose prediction of these novel therapeutics. Finally, several short case studies will be presented to demonstrate the importance of an informed safety assessment for novel biotherapeutics that target the nervous system.

1:30 PM–2:10 PM	**Vector-Based and Cell-Based Therapies: How Do They Work, What Do They Target?** *Sarah Cramer, DVM, PhD, DACVP, StageBio, Frederick, MD*
2:10 PM–2:50 PM	**Nucleic Acid-Based Therapies (ASO/mRNA): How Do They Work, What Do They Target?** *Jessica Grieves, DVM, PhD, DACVP, Ionis Pharmaceuticals, Carlsbad, CA*
2:50 PM–3:15 PM	**Case Studies and Open Discussion**
3:15 PM–3:45 PM	**Break**
3:45 PM–4:25 PM	**Nonconventional Antibodies for Neurodegenerative Diseases: How Do They Work and What Do They Target?** *Rene Meisner, DVM, DACVP, DABT, Denali Therapeutics, South San Francisco, CA*
4:25 PM–5:10 PM	**Pharmacokinetics and Biodistribution: How Do You Know You've Hit Your Target?** *Arlin Rogers, DVM, PhD, Alnylam Pharmaceuticals, Cambridge, MA*
5:10 PM–5:30 PM	**Case Studies and Open Discussion**

Welcome Reception

5:30 PM–7:00 PM

MONDAY, JUNE 26

STP 42nd Annual Symposium Welcome

8:00 AM–8:10 AM

Keynote Presentation: Humans with Comorbidities—A Susceptible Population for Drug-Induced Liver Injury

8:10 AM–9:00 AM

Anna Mae Diehl, MD, Duke University, Durham, NC

Session 1

9:00 AM–12:00 Noon

Considerations to Evaluate Toxicities in the Hepatic and Biliary System

*Co-Chairs: **Russell Cattley, VMD, PhD, DACVP, FIATP**, Auburn University, Auburn, AL; and **Bhanu P. Singh, BVSc, MS, DACVP, DABT, FIATP**, Gilead Sciences, Inc., Foster City, CA*

A variety of emerging therapeutic modalities have the potential for hepatobiliary toxicity in nonclinical species and in humans. Understanding mechanisms of the liver toxicity is a key step in improving drug safety testing by providing the basis for mechanism-based risk assessments. This session will review key considerations in evaluating hepatoxicities related to kinase inhibitors, RNAi and gene therapy.

9:00 AM–9:05 AM	**Introduction**
9:05 AM–9:45 AM	**Transporter-Mediated DILI in the Liver** *Kim Brouwer, PharmD, PhD, University of North Carolina at Chapel Hill, Chapel Hill, NC*

9:45 AM–10:15 AM	**Effect of RNAi and LNP in the Liver** *Nicholas A. Robinson, BVSc, PhD, DACVP, Alnylam Pharmaceuticals, Cambridge, MA*
10:15 AM–10:45 AM	**Break**
10:45 AM–11:15 AM	**Effect of Gene Therapy in the Liver** *Laurence O. Whiteley, DVM, PhD, Pfizer, Inc., Cambridge, MA*
11:15 AM–11:45 AM	**Kinase Inhibitor-Related Hepatotoxicity** *Kim Brouwer, PharmD, PhD, University of North Carolina at Chapel Hill, Chapel Hill, NC*
11:45 AM–12:00 Noon	**Panel Discussion**

Career Development Roundtable

Advocacy from Above: Tools for Managers to Empower Others

12:30 PM–1:30 PM

Co-Chairs: ***Laura Hoon-Hanks, DVM, PhD, DACVP****, Inotiv, Boulder, CO; and* ***Alex D. Byas, DVM, PhD, DACVP****, Merck & Co., Inc., West Point, PA*

This multi-person panel on advocacy from the perspective of management and other high-level leadership positions, hosted by the Career Development and Outreach Committee, is part of a continuing series in collaboration with the STP Women in Tox Path subcommittee (STP Diversity, Inclusion, and Belonging Committee), ACVP Women in Pathology Special Interest Group, and ACVP Lifelong Learning Committee. The goal of this roundtable is for panelists to share experiences related to advocacy while providing tools for audience members to advocate for others from a place of allyship in support of diversity and inclusion. The intended discussion is meant to transcend workplace interactions and broadly encompass a range of relationship types. Topics include expanding your talent pool, engagement, and participation in professional organizations for students and trainees of all levels, hiring practices, promotion opportunities, and other support strategies.

Session 2

1:30 PM–5:00 PM

Translational Relevance of Rodent Models to Predict Human Liver Disease

Co-Chairs: ***Robert R. Maronpot, DVM, MS, MPH****, Maronpot Consulting, LLC, Raleigh, NC; and* ***Debabrata Mahapatra, BVSc, MVSc, MS, PhD, DACVP, DABT****, Inotiv, Research Triangle Park, NC*

Animal models are essential to understand the complex pathobiology of human diseases. George Box's aphorism based on statistics, "All models are wrong, but some are useful," certainly applies to animal models of disease. This session will explore the translational relevance of various animal models to human liver disease beginning with a historic overview of the rodent cancer bioassay with emphasis on hepatocarcinogenesis from early work at the National Cancer Institute, refinement by the National Toxicology Program and contemporary efforts to identify potential mechanisms and their relevance to human cancer risk. This will be followed by a presentation of recently elucidated understanding of the molecular drivers and signaling mechanisms of liver pathophysiology and liver cancer, including factors associated with liver regeneration and metabolic hepatocellular zonation, and how these drivers dictate tumor metabolism and immune microenvironment. Next a presentation on our contemporary understanding of the role of nuclear receptors in hepatic homeostasis and drug response will highlight nuclear receptor activation and crosstalk in modulating biological responses associated with liver damage and neoplastic response. The final presentation will close with an overview and translational relevance of different DILI rodent model systems focused on pathology and mechanisms with commentary on current relevant US FDA perspective.

1:30 PM–2:15 PM	**Rodent Liver Tumors: NCI/NTP Historic Perspective** *Robert R. Maronpot, DVM, MS, MPH, Maronpot Consulting, LLC, Raleigh, NC*
2:15 PM–3:00 PM	**Recapitulating Human HCC Subsets in Mice for Understanding Biology and Precision Therapy** *Paul Monga, MD, Pittsburgh Liver Research Center, Pittsburgh, PA*
3:00 PM–3:30 PM	**Break**
3:30 PM–4:15 PM	**Nuclear Receptor MOA-Induced Hepatocarcinogenesis: Human Relevance** *James E. Klaunig, PhD, ATS, FIATP, AAAS, Indiana University, Zionsville, IN*
4:15 PM–5:00 PM	**Model Systems to Study DILI** *Frederic Moulin, DVM, PhD, DABT, US FDA/CDER, Silver Spring, MD*

Annual Business Meeting and Town Hall

5:30 PM–7:00 PM

TUESDAY, JUNE 27

Keynote Presentation: The State of the Science—Application of Microphysiological Systems to Identify Hepatobiliary Toxicities

8:00 AM–9:00 AM

D. Lansing Taylor, PhD, University of Pittsburgh, Pittsburgh, PA

Session 3

9:00 AM–12:00 Noon

Novel Experimental Model Systems to Understand Toxicity and Carcinogenicity in the Liver

*Co-Chairs: **Magali Guffroy, DVM, DACVP**, AbbVie, North Chicago, IL; and **James E. Klaunig, PhD, ATS, FIATP, AAAS**, Indiana University, Zionsville, IN*

This session will examine several novel and emerging experimental model systems developed to help understand and predict drug-associated hepatobiliary toxicities and carcinogenicity. In the first part of the session, emerging complex *in vitro* models (including static and flow-based spheroid models and microphysiological systems) will be reviewed and discussed. The second part of the session will examine the application and use of cell painting techniques to identify potential hepatic toxicants. The session will conclude with an update of our current use of next generational sequencing approaches to identify hepatic toxicity. Overall, the session will emphasize the key challenges in implementation of these models in the safety testing paradigm during early discovery/development, lessons learned/strategies for minimizing hepatotoxicity risk of drug candidates, and potential to enhance prediction of DILI liability.

9:00 AM–9:05 AM	**Introduction**
9:05 AM–9:40 AM	**Novel *In Vitro* Liver Models, Cross-Species Comparisons and Predictive Values of the Models** *Leah Norona, PhD, Genentech, South San Francisco, CA*
9:40 AM–10:15 AM	**Cell Painting and High-Content Imaging to Identify Potential Hepatotoxicants** *Joshua A. Harrill, PhD, US EPA, Research Triangle Park, NC*
10:15 AM–10:45 AM	**Break**
10:45 AM–11:25 AM	**Are We There Yet? Application of Microphysiological Systems to Detect Hepatic Toxicity** *Prathap K.S. Mahalingaiah, DVM, MS, PhD, DABT, AbbVie, North Chicago, IL*
11:25 AM–12:00 Noon	**Next Generation Sequencing Approaches to Identify Potential Hepatocarcinogens** *Arun K. Pandiri, BVSc&AH, MS, PhD, DACVP, DABT, NIEHS, Research Triangle Park, NC*

Session 4

1:30 PM–5:00 PM

Toxicogenomics Approaches to Address Toxicity and Carcinogenicity in the Liver

*Co-Chairs: **Eric Blomme, DVM, PhD**, AbbVie, North Chicago, IL; and **Arun K. Pandiri, BVSc&AH, MS, PhD, DACVP, DABT**, NIEHS, Research Triangle Park, NC*

Over the past two decades, toxicogenomics technologies have been applied for various purposes in toxicology including generating hypotheses, addressing mechanisms, establishing translational relevance of changes, and predicting treatment outcomes. Although in principle toxicogenomics encompasses all -omics approaches (measuring DNA, RNA, protein, metabolites and epigenetic factors), much of the field has been mainly focused on transcriptomics due to cost and practical considerations. The transcriptomics technologies range from array-based approaches to next generation sequencing methods. This session will focus on the practical applications of toxicogenomics technologies to address toxicity and carcinogenicity in the liver. The introductory talk will provide a broad overview of these technologies and introduce some of the concepts related to these applications in toxicologic pathology. The second talk will introduce a systems biology concept of weighted gene co-expression network analysis (WGCNA) that identifies clusters (modules) of highly correlated genes that correspond to a specific biological function and will discuss examples demonstrating the integration of these co-expressed gene modules with defined physiology/pathology outcomes. The last two presentations will discuss the unique applications of these technologies in the areas of environmental toxicology/carcinogenicity and pharmaceutical development, respectively. In the end, all the speakers will engage the audience in a round table discussion.

1:30 PM–2:10 PM	**A Practical Primer to Toxicogenomic Technologies and Approaches** *Arun K. Pandiri, BVSc&AH, MS, PhD, DACVP, DABT, NIEHS, Research Triangle Park, NC*
2:10 PM–2:50 PM	**Integration of Pathology and Weighted Gene Co-Expression Network Analysis to Study Hepatotoxicity** *James L. Stevens, PhD, Paradox Found Consulting Services, LLC, Apex, NC*
2:50 PM–3:20 PM	**Break**
3:20 PM–4:00 PM	**Transcriptomic Approaches to Predict Environmental Hepatocarcinogens** *Scott S. Auerbach, PhD, NIEHS, Research Triangle Park, NC*

4:00 PM–4:40 PM **Integration of Toxicogenomic Data into Pharmaceutical Risk Assessment**
Eric Blomme, DVM, PhD, AbbVie, North Chicago, IL

4:40 PM–5:00 PM **Panel Discussion**

WEDNESDAY, JUNE 28

Session 5

8:00 AM–12:00 Noon

Hepatic Biomarkers and Clinical Pathology

*Co-Chairs: **Paula Katavolos, DVM, PhD**, Bristol Myers Squibb, New Brunswick, NJ; and **Adam Aulbach, DVM, DACVP**, Inotiv, Galesburg, MI*

Drug-induced liver injury (DILI) has been the most frequent single cause of safety-related marketing withdrawals for the past 50 years (US FDA) and therefore, rigorous preclinical characterization of drugs under development utilizing a combination of *in vivo* studies and *in vitro* assays is crucial to interrogate potential liabilities. Each approach comes with strengths and limitations and this session will focus on clarifying these aspects as they pertain to traditional and evolving DILI biomarkers. The first speaker, Dr. Laura Boone, will share an overview of our understanding of the biology and performance of "traditional" liver injury biomarkers across a range of species which will be followed by a talk by Dr. Daniela Ennulat, who will extend and build upon this topic with an overview of the integration of liver clinical and morphological pathology. Following invited talks by two student speakers, Dr. Alison Harrill and Dr. Jon Maher will explore and provide insights on new and emerging molecular and mass spectrometry-based liver injury biomarkers.

8:00 AM–8:05 AM **Introduction**

8:05 AM–8:45 AM **Revisiting Traditional Liver Biomarkers in Nonclinical Studies**
Laura Boone, DVM, PhD, DACVP, DABT, Labcorp, Fredericksburg, TX

8:45 AM–9:30 AM **Integration of Liver Clinical and Morphological Pathology Findings—A Data-Driven Perspective**
Daniela Ennulat, DVM, PhD, Cochranville, PA

9:30 AM–9:45 AM **Student Speaker**

9:45 AM–10:15 AM **Break**

10:15 AM–10:30 AM **Student Speaker**

10:30 AM–11:15 AM **Emerging Biomarkers of Hepatic Injury**
Alison Harrill, PhD, US EPA, Research Triangle Park, NC

11:15 AM–11:50 AM **Something Old and Something New: Speciated Bile Acids as Mechanistic Markers of Hepatobiliary Health**
Jonathan M. Maher, PhD, DABT, ATS, Pliant Therapeutics, South San Francisco, CA

11:55 AM–12:00 Noon **Panel Discussion**

Session 6

1:30 PM–5:00 PM

Classic Diagnostic Dilemmas and Case Studies on the Toxicologic Pathology of the Liver and Biliary System

*Co-Chairs: **Allison C. Boone, DVM, DACVP**, EPL, Inc., Morrisville, NC; **John M. Cullen, VMD, PhD, DACVP**, North Carolina State University, Raleigh, NC; and **David E. Malarkey, DVM, PhD, MS, DACVP, FIATP**, Cary, NC*

This final session will provide a great opportunity to review and update the knowledge on hepatic and biliary toxicologic pathology. Attendees will be introduced to several talks discussing classic and contemporary issues in hepatic and biliary toxicologic pathology via lectures and case studies from rodent and non-rodent species. The session will begin with talks that focus on classic toxicologic pathology observed in the liver and biliary system and corresponding de-risking strategies. This will be followed by case studies highlighting potential hepatic and biliary toxicity liabilities where presenters will provide case signalment, anatomic/clinical pathology data, diagnoses, and discuss potential pathogeneses.

1:30 PM–2:00 PM **Classic Toxicologic Pathology of the Liver**
Richard T. Miller, DVM, PhD, DACVP, Apex Drug Discovery and Innovation Strategies, LLC, Apex, NC

2:00 PM–2:30 PM **Classic Toxicologic Pathology of the Biliary System**
John M. Cullen, VMD, PhD, DACVP, North Carolina State University, Raleigh, NC

2:30 PM–3:00 PM **Risk Assessment for Hepatobiliary Toxicity Liabilities in Drug Development**
Richard T. Miller, DVM, PhD, DACVP, Apex Drug Discovery and Innovation Strategies, LLC, Apex, NC

3:00 PM–3:30 PM **Break**

3:30 PM–5:00 PM **Case Studies**

- Copper Toxicosis in Female Boston Terrier—Shakirat Adentunji
- Case Study on ADC-Associated Liver/Sinusoidal Injury/SOS in Monkeys—Rebecca Kohnken
- Bile Duct Lesion in a Chronic Tox Monkey Study: How Did It Happen?—Bhanu Singh
- Hepatocellular Alterations in Subchronic NTP Studies —Allison Boone
- Drug-Induced Liver Injury: Learnings from a Small Molecule Program—Kyathanahalli Janardhan
- Drug-Induced Kupffer Cell/Macrophage Lesions Associated with Microcrystal Accumulation in the Liver of Sprague-Dawley Rat—Kenji Koyama

Awards and Recognition Ceremony

5:30 PM–6:30 PM

President's Reception

7:00 PM–9:00 PM

Meeting Adjournment