SUNDAY, JUNE 19

Career Development Workshop (Sunday AM)

8:00 AM–12:00 Noon

Professional Visibility: The Toxicologic Pathologist's Guide to Getting Out There

*Co-Chairs: **Jessica Grieves, DVM, PhD, DACVP**, Ionis Pharmaceuticals, Inc., Carlsbad, CA; **Tracey L. Papenfuss, DVM, PhD, MS, DACVP**, Charles River Laboratories, Westerville, OH; **and Rebecca A. Kohnken, DVM, PhD, DACVP**, AbbVie, North Chicago, IL*

Professional visibility is inclusion and recognition within an organization and in the broader community to which a professional belongs. Visibility is critical for building a reputation and exerting influence and, as such, is an important factor for professional success and career satisfaction for toxicologic pathologists. Unfortunately, emphasis on this aspect of career development can be limited due to day-to-day job demands. In this session, attendees will receive insights from individuals who, in addition to scientific pursuits, have prioritized professional visibility. Topics including networking, leadership, publishing and speaking, and developing an area of expertise will be highlighted. The session will emphasize short and long-term steps you can take to increase visibility within your organization and beyond.

NTP Satellite Symposium: Pathology Potpourri (Sunday AM)

9:00 AM–12:10 PM

*Chair: **Erin M. Quist, DVM, MS, PhD, DACVP**, EPL, Inc., Durham, 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 using wireless keypads and the results will be displayed on the screen. Time is allowed for discussion after each voting session.

CE (Sunday PM)

1:30 PM–5:30 PM

No Bones About It: Considerations for Bone Toxicity, Healing, and Remodeling Studies

*Co-Chairs: **Kathleen A. Funk, DVM, PhD, DACVP**, EPL, Inc., Sterling, VA; **and Maralee McVean, PhD, DABT**, Loxo Oncology at Lilly, Fort Collins, CO*

This course will focus on bone toxicity as a potential off target effect based on the class of compound or an early and unexpected pathology signal rather than on drugs specifically designed to affect bone. The first presentation will cover normal anatomy and histology of the various bones which may be affected by drug administration and introduce animal models as a strategy to elucidate bone issues. A discussion of the various tools used to monitor bone toxicity, healing, and remodeling will be considered as they relate or drive the study design including model, species selection, and age followed by a discussion of regulatory requirements for bone therapeutics and a regulatory perspective on strategies to de-risk compounds with potential bone effects. Finally, a synopsis of the type of pathologic changes seen in bone together with various histopathologic techniques for processing and evaluating bone and integrating these pathologic changes with the other tools for measuring bone toxicity will be discussed. Pathology characteristic of certain drug classes will be covered.

1:30 PM–1:35 PM	**Introduction**
1:35 PM–2:20 PM	**More Than a Framework: Understanding Bone Biology and Histology** *S. Serra Ucer Ozgurel, PhD, University of Texas at Austin, Austin, TX*
2:20 PM–3:05 PM	**Considerations for Study Design and Tools Used to Evaluate Changes to Bone** *Aurore Varela, DVM, MSc, DABT, Charles River Laboratories, Senneville, Quebec, Canada*
3:05 PM–3:35 PM	Break
3:35 PM–4:20 PM	**Pathology of Bone: Changes Associated with Different Classes of Compounds** *Kathryn E. Gropp, DVM, PhD, DACVP, Pfizer Inc., Groton, CT*
4:20 PM–5:05 PM	**Regulatory Approaches to the Nonclinical Evaluation of Drug-Related Bone Toxicity** *Rogely W. Boyce, DVM, PhD, DACVP, Beechy Ridge ToxPath LLC, Clay, WV*
5:05 AM–5:30 PM	**Panel Discussion**

MONDAY, JUNE 20

STP 41st Annual Symposium Welcome

8:00 AM–8:10 AM

Keynote Address

8:10 AM–9:00 AM
Cynthia E. Dunbar, MD, NHLBI, NIH, Bethesda, MD

Session 1

9:00 AM–12:00 Noon

Bone Marrow Structure, Function, and Cell Biology—More Than Just the Basics

Co-Chairs: Gregory S. Travlos, DVM, DACVP, NIEHS/NTP, Research Triangle Park, NC; and Anne Provencher, DVM, MSc, DACVP, DECVCP, FIATP, Charles River Laboratories, Sherbrooke, Quebec, Canada

The bone marrow is the soft, supple, highly vascular tissue found within bone cavities. There are two types of bone marrow tissues. The yellow marrow, consisting predominantly of adipose cells, and the red marrow, where the hematopoietic stems cells reside and where blood cell production (i.e., hematopoiesis) primarily occurs. The major function of the bone marrow is to generate blood cells and, on average, bone marrow can generate billions of new blood cells daily. Bone marrow contains two main types of stem cells. Hematopoietic stem cells (HSC), found in red marrow, are responsible for the production of blood cells. Bone marrow mesenchymal stem cells (multipotent stromal cells) produce the non-blood cell components of marrow, including fat, cartilage, fibrous connective tissue, stromal cells that support blood formation, and bone cells. This morning session is planned to examine certain functions of the bone marrow, hematopoietic stem cells and hematopoiesis. First, an introductory presentation will provide an expanded description of bone marrow structure and function. The second presentation delves into an exploration of the hematopoietic process outside the confines of the bone marrow (e.g., extramedullary hematopoiesis). Following a brief break, the third presentation will focus on the role of pyruvate kinase activation in the treatment of hereditary hemolytic anemia. The talk will discuss the potential activation of the marrow isoform (PKM2) and erythrocyte isoform (PKR) to improve hematopoiesis and control hemolysis in a variety of disease conditions (e.g., pyruvate kinase deficiency, α and β-thalassemia, and sickle cell disease). Further, the potential use of PKR activators to increase cellular ATP, reduce 2-3 diphosphoglycerate, and improve the antioxidant function of erythrocytes will be explored. Finally, focusing on stem cell niche interactions in skeletal muscle and bone marrow in the context of exercise and obesity, this session will end with a presentation looking at the external cues that regulate the cellular composition of the stem cell niche and how the changes in cellular composition of the stem cell niche regulate stem cell function. .

9:00 AM–9:05 AM	**Introduction**
9:05 AM–9:25 AM	**Inside the Vault: Bone Marrow Structure and Function** *Cynthia Willard-Mack, VMD, PhD, Labcorp, East Millstone, NJ*
9:25 AM–10:10 AM	**Outside the Vault: EMH** *Cynthia Willard-Mack, VMD, PhD, Labcorp, East Millstone, NJ*
10:10 AM–10:40 AM	Break
10:40 AM–11:20 AM	**Ineffective Hematopoiesis and Hemolytic Anemias: Gene Therapy, Marrow Energetics, and Combination Strategies** *Bruce D. Car, BVSc, PhD, Agios Pharmaceuticals, Cambridge, MA*
11:20 AM–12:00 Noon	**How Does Lifestyle Influence the Bone Marrow Microenvironment?** *Michael DeLisio, PhD, University of Ottawa, Ottawa, Ontario, Canada*

Session 2

1:30 PM–5:00 PM

Methodologies and Emerging Technologies for the Evaluation of the Hematopoietic Systems

***Co-Chairs: Allison Vitsky, DVM, DACVP**, Pfizer Inc., San Diego, CA; and **Florence Poitout-Belissent, DVM, DACVP, DECVP**, Charles River Laboratories, Senneville, Quebec, Canada*

Hematology and bone marrow analysis is central to our understanding of the hematopoietic system and how it responds to insults, and this session will provide a review of current and novel approaches for the evaluation of the hematopoietic system in the context of nonclinical investigations. The session will begin with a discussion on histological and cytological bone marrow evaluations, providing information around their similarities and differences as well as guidance on what types of interpretations, correlations, and attributions can be made using each method. This will be followed by information on novel approaches for evaluation of the hematopoietic system using automated hematology analyzers, including details around the quantitative assessment of bone marrow cell suspensions as well as introducing several newly available hematology parameters. Several exciting emerging technologies will also be covered, beginning with the application of *in vitro* screening assays to detect hematopoietic cytotoxicity and elucidate certain mechanisms of toxicity. This will be followed by a discussion on intravital microscopy and live cell imaging and how these methods can assist with de-risking hematopoiesis-associated safety concerns, and a presentation on the application of cellular barcoding to hematopoietic stem and progenitor cells in nonhuman primate models. This session will conclude with a review of recent assays using artificial intelligence for the evaluation of bone marrow.

1:30 PM–1:35 PM	**Introduction**
1:35 PM–2:05 PM	**Bone Marrow Cytological and Histological Evaluations** *Dina Andrews, DVM, PhD, DACVP, Amgen, Inc., Camarillo, CA*
2:05 PM–2:35 PM	**Novel Methods for the Evaluation of Hematopoiesis and Circulating Blood Cells: New, Better, or Both?** *Allison Vitsky, DVM, DACVP, Pfizer Inc., San Diego, CA; and Florence Poitout-Belissent, DVM, DACVP, DECVP, Charles River Laboratories, Senneville, Quebec, Canada*
2:35 PM–3:10 PM	***In Vitro* Hematopoietic Cells Toxicity Assays** *Wendy Hu, PhD, Pfizer Inc., San Diego, CA*
3:10 PM–3:40 PM	Break
3:40 PM–4:10 PM	**Intra Vital Microscopic and Live Cell Imaging—Neutrophils, Extracellular Traps, and Cellular Toxicity** *Madhu Sirivelu, BVSc, PhD, DACVP, Pfizer Inc., Andover, MA*
4:10 PM–4:40 PM	**Hematopoietic Stem and Progenitor Cells Barcoding** *Cynthia E. Dunbar, MD, NHLBI, NIH, Bethesda, MD*
4:40 PM–5:00 PM	**Artificial Intelligence for Bone Marrow Evaluation** *Mark A. Smith, DVM, DACVP, Charles River Laboratories, Reno, NV*

Annual Business Meeting and Town Hall: Disruption in NHP Supply: Catalyst for Progress or Crisis for Patients?

5:30 PM–7:00 PM

Mystery Slide Session: Hematopoietic Pathology

7:30 PM–9:30 PM

***Co-Chairs: Tara P. Arndt, DVM, DACVP**, Labcorp, Madison, WI; and **Kyathanahalli Janardhan, BVSc, MVSc, PhD, DACVP**, AbbVie, North Chicago, IL*

This year's Mystery Slide Session will focus on the hematopoietic system and submissions are open to all attendees. This will be an educational and fun session composed of 8–10-minute engaging cases in several formats. If you have an interesting cytology, blood smear, hematopoietic histopathology case, or clinical pathology data set, please watch for the call for cases!

TUESDAY, JUNE 29

Session 3

8:00 AM–12:00 Noon

Mechanisms of Decreased Erythropoiesis and Erythroid Cell Injury

***Co-Chairs: Lila Ramaiah, DVM, PhD, DACVP**, Pfizer Inc., Pearl City, NJ; and **A. Eric Schultze, DVM, PhD, DACVP, FIATP**, Eli Lilly and Company, Indianapolis, IN*

Deleterious effects on erythrocytes are among the most commonly observed in preclinical animal toxicity studies. Despite their apparent simplicity and ease of analysis, there is more to erythrocytes than meets the eye. Mechanisms of erythrotoxicity extend beyond blood loss and cytotoxicity and are discerned using a complex array of endpoints beyond hematocrit and bone marrow histopathology.

This session will delve into the mechanisms of erythrotoxicity, with emphasis on decreased erythropoiesis and erythroid cell injury. An introductory description of erythropoiesis will be followed by an example of deep transcriptomics and chromatin profiling to characterize erythrocyte differentiation using functional studies of GATA1, a specific master regulator. The second presentation will discuss investigations characterizing p38 MAP kinase inhibitor-induced disruption of erythroid maturation. Immediately prior to the break, we welcome a guest presentation by a student member/trainee. We hope that all meeting attendees will participate and provide an attentive audience for our potential future colleagues. Immediately after the preplanned break, the fourth presentation will discuss mechanisms and detection of erythrocyte injury, with focus on osmotic fragility due to dyslipidemia. The session will conclude with a case presentation of morphologic, numeric and functional erythrocyte abnormalities caused by the dietary supplement, black cohosh.

8:00 AM–8:10 AM	**Introduction** *Lila Ramaiah, DVM, PhD, DACVP, Pfizer Inc., Pearl City, NJ; and A. Eric Schultze, DVM, PhD, DACVP, FIATP, Eli Lilly and Company, Indianapolis, IN*
8:10 AM–9:00 AM	**Mechanisms of Physiologic and Pathologic Erythropoiesis and Functional Studies of GATA1** *Leif Ludwig, MD, PhD, Berlin Institute of Health at Charité–Universitätsmedizin Berlin and Berlin Institute for Medical Systems Biology (BIMSB), Berlin, Germany*
9:00 AM–9:45 AM	**Effects of p38 MAP Kinase Inhibitors on the Differentiation and Maturation of Erythroid Progenitors** *Deidre A. Dalmas, MS, PhD, GlaxoSmithKline, Collegeville, PA*
9:45 AM–10:00 AM	**Student Speaker**
10:00 AM–10:30 AM	Break
10:30 AM–11:15 AM	**Erythroid Injury—Mechanisms, Detection, and Adversity** *Erica Behling-Kelly, DVM, PhD, DACVP, Cornell University College of Veterinary Medicine, Ithaca NY*
11:15 AM–12:00 Noon	**Black Cohosh Herbal Extract and Hematologic Alterations in B6C3F1/N Mice** *Michelle C. Cora, DVM, DACVP, NIEHS/NTP, Research Triangle Park, NC*

Tuesday Afternoon

Free time

WEDNESDAY, JUNE 22

Session 4

8:00 AM–12:00 Noon

To Clot or Not to Clot: Deepening Our Understanding of Alterations in the Hemostatic Systemy

***Co-Chairs: Karrie A. Brenneman, DVM, PhD, DACVP**, Pfizer Inc., Cambridge, MA; and **William J. Reagan, PhD, DACVP**, Pfizer Inc., Groton, CT*

In response to vascular injury, there is a delicate balance between the formation of clots that keep hemorrhage in check and fibrinolysis that prevents deleterious formation of thrombi/emboli. Administration of proposed therapeutic or toxic substances can disrupt this homeostatic equilibrium directly or indirectly resulting in hemorrhage, thrombosis, or both. Evaluation of these perturbations and understanding their mechanism of toxicity can be challenging for the clinical and anatomic pathologist alike. This session discusses these challenges in the context of development of lipogenesis inhibitors, gene therapies for hemophilia B, and antibody-drug conjugates as well as recent advances in platelet biology and preclinical biomarkers of hypercoagulable states..

8:00 AM–8:05 AM	**Introduction** *Karrie A. Brenneman, DVM, PhD, DACVP, Pfizer Inc., Cambridge, MA*
8:05 AM–8:40 AM	**Coagulation Pathways: Fluid Phase, Cell-Based, and Vascular Bed Hemostasis** *Marjory Brooks, DVM, DACVIM, Cornell University, Ithaca, NY*

8:40 AM–9:20 AM	**The Sweet Side of Platelet Clearance** *Renata Grozovsky, PhD, University of Miami, Miami, FL*
9:20 AM–9:50 AM	**The Effects of Lipogenesis Inhibitors on Platelet Production in Humans and Nonclinical Species** *William J. Reagan, PhD, DACVP, Pfizer Inc., Groton, CT*
9:50 AM–10:20 AM	Break
10:20 AM–10:50 AM	**A Post-Marketing Investigation of Thrombocytopenia and Hemorrhagic Events in Patients Administered Mylotarg** *Allison Vitsky, DVM, DACVP, Pfizer Inc., San Diego, CA*
10:50 AM–11:30 AM	**Gene Therapy for Hemophilia: Learnings from Hemophilia B** *Debra Pittman, PhD, Pfizer, Inc., Cambridge, MA*
11:30 AM–12:00 Noon	**Preclinical Markers of Hypercoagulability: Practical Predictors or Pipe Dream?** *Marjory Brooks, DVM, DACVIM, Cornell University, Ithaca, NY*

Career Development Roundtable

12:30 PM–1:30 PM

Mentoring with Intention: A Panel Discussion on Mentorship and Coaching

*Chair: **Alexandria D. Byas, DVM, DACVP**, Merck, Philadelphia, PA*

Session 5

1:30 PM–5:00 PM

Understanding Off-Target and Idiosyncratic Hematologic Effects in Toxicology Studies

***Co-Chairs: Adam Aulbach, DVM, DACVP**, Inotiv, Galesburg, MI; and **Laura Cregar, DVM, DACVP**, Charles River Laboratories, Mattawan, MI*

A variety of therapeutic modalities have the potential for off-target/unanticipated adverse effects on blood cell counts and/or hematologic function in nonclinical species and in humans. These effects are often indirectly related to the therapeutic agent and can be the result of aberrant cell activation, autoimmunity/immunogenicity, drug-dependent and independent immune responses, and/or downstream sequela of cytokine and complement activation. This session will review key concepts related to the pathophysiology of off-target hematotoxicity including contemporary investigational approaches using case examples to emphasize key concepts.

1:30 PM–1:35 PM	**Introduction** *Adam Aulbach, DVM, DACVP, Inotiv, Galesburg, MI*
1:35 PM–2:05 PM	**Overview of Pathophysiologic Mechanisms Involved in Off-Target Hematologic Effects** *Jacqueline Tarrant, DVM, PhD, DACVP, CSL Behring, King of Prussia, PA*
2:05 PM–2:55 PM	**Idiosyncratic Drug-Induced Immune-Mediated Cytopenias** *Brian R. Curtis, PhD, DABMLI, MT(ASCP) SBB, Versiti Blood Research Institute, Milwaukee, WI*
2:55 PM–3:10 PM	**Student Speaker**
3:10 PM–3:40 PM	Break
3:40 PM–4:00 PM	**Immunohematological Changes Associated with Antisense Oligonucleotide-Associated Thrombocytopenia in Monkeys** *Padma K. Narayanan, DVM, MS, PhD, Wave Life Sciences, Lexington, MA*
4:00 PM–4:40 PM	**Hematologic Changes as Secondary Effects: Iron-ing Out the Impact of Inflammation, Stress, and Other Factors** *William Siska, DVM, MS, DACVP, Charles River Laboratories, Reno, NV*
4:40 PM–5:00 PM	**Recovery from Myelosuppressive Doses of Radiation in the Rhesus Monkeys** *Dina Andrews, DVM, PhD, DACVP, Amgen, Inc., Thousand Oaks, CA*

Awards and Recognition Ceremony

5:30 PM–6:30 PM

President's Reception

7:00 PM–10:00 PM

THURSDAY, JUNE 23

Session 6

8:00 AM–12:00 Noon

Current Topics in Hematopoietic Neoplasms and Clonal Diseases

*Co-Chairs: **Michelle L. Lepherd, BVSc, PhD, DACVP**, Genentech, South San Francisco, CA; and **Dana B. Walker, DVM, DACVP, MS, PhD**, Novartis Institute of Biomedical Research, Cambridge, MA*

Hematopoietic neoplasia and clonal hematopoiesis are human disorders that have a high degree of unmet medical need. Research and drug development in these areas is rapidly evolving and becoming increasingly complicated as more is understood about the genomics and molecular biology of these conditions. This session will focus on hematolymphoid clonal conditions with emphasis on myeloproliferative and myelodysplastic disorders. The session will cover comparative classification of hematolymphoid neoplasia and dysplasia in laboratory animals and humans, including aspects of clinical pathology, anatomic pathology, molecular pathology, and genetics, as well as the prevalence of and a practical approach to evaluation and interpretation of hematopoietic neoplasia in aging rodents in non-clinical carcinogenicity studies. Invited speakers will cover topics ranging from the epigenetic mechanisms and role of X-chromosome inactivation (XCI) maintenance in regulation of transcription and chromatin structure in hematopoietic cells and causal role of XCI loss in myeloproliferative neoplasia and myelodysplastic syndromes; the role of inflammation in pathogenesis of myeloproliferative neoplasia; and the role of immunomodulatory drugs in promoting tumorigenesis, particularly hematological malignancies with consideration of immunologic components implicated, and for future drug development.

8:00 AM–8:05 AM	**Introduction**
8:05 AM–8:40 AM	**Tumors of the Hematolymphoid System** *EJ Ehrhart, DVM, PhD, DACVP, Charles River Laboratories, Fort Collins, CO*
8:40 AM–9:15 AM	**Perspectives on Hematopoietic Neoplasia in Carcinogenicity Toxicology Studies** *Aaron M. Sargeant, DVM, PhD, DACVP, Charles River Laboratories, Spencerville, OH*
9:15 AM–10:00 AM	**Balancing X-Chromosome Dosage in Hematopoietic Cells: Mechanistic Insights and Impact on Cancer** *Eda Yildirim, PhD, Duke University School of Medicine, Durham, NC*
10:00 AM–10:30 AM	Break
10:30 AM–11:15 AM	**Key Role of Inflammation in Myeloproliferative Neoplasms: Instigator of Disease Initiation, Progression, and Symptoms** *Angela Fleischman, MD, PhD, University of California Irvine, Irvine, CA*
11:15 AM–12:00 Noon	**Immunomodulators and Cancer Risk** *Hervé N. Lebrec, PharmD, PhD, DABT, Sonoma Biotherapeutics South San Francisco, CA*

Meeting Adjourned

12:00 Noon