

ESTP Newsletter 2017 (3)



Editor Zuhal Dincer (zuhal.dincer@covance.com)

President's column

Dear ESTP members,

Shortly before summer break, I will give you an update about our recent activities.

During the STP Meeting in Montreal, another President's Meeting took place and all representatives of the national societies gave their commitment for further intense collaboration. First ideas were discussed and will be followed up during the next meetings. The next President's Meeting will be held during the ESTP Meeting in Lyon. In Montreal, I met the President of the STP, Brad Bolon, the incoming President, Jim Fikes, as well as the President-elect, Paul Snyder, who all three promised to try to come to Lyon!



The Cutting Edge Pathology Meeting (ESTP/ECVP/SFPT Joint Meeting) in Lyon (August 30 to Sept 02) moves closer and the SOC opened a LinkedIn Group with new and relevant topics which are regularly updated by the organizers.

<https://www.linkedin.com/groups/8592864>

The publication of the last ESTP Adversity Workshop, held in Barcelona 2016, is also on its way and will be submitted soon. We will seek endorsement of this publication by all other Tox Path societies. During the STP Meeting in Montreal a poster was shown and very well received by the audience. You will also find a poster about the workshop in Lyon.

These are the most important things which happened during the last months and I hope I could inform you a little bit about the work the ESTP Board is doing.

I'm always happy to receive direct feedback from the membership and I'm glad to answer your question!

I wish you a nice summer, wonderful summer holidays and hope to see most of you in Lyon!

Best regards

Sibylle Gröters
ESTP Chairman
sibylle.groeters@basf.com

STP 36th Annual Symposium
24-29 June, 2017 Montreal, Quebec, Canada

This year, STP (Society of Toxicologic Pathology) 36th annual symposium was held in Montreal, Canada. The congress took place in the Montreal Convention Centre and was excellent week of sessions on the **“Toxicologic Pathology of the Musculoskeletal System”** with NTP (National Toxicology Program) Satellite Symposium,

“Pathology Potpourri,” poster sessions, and short seminars at lunch breaks.



Convention centre, Montreal

I have travelled to Montreal on Friday 23rd June that I could be able to join the NTP interactive satellite symposium starting on the 24th June, Saturday. The NTP symposium was all day and focused on presentations of very challenging lesions. It was chaired by Susan Elmore and we had a good time! During each talk, the speakers projected a series of images of lesions on one screen with a choice of diagnoses/answers on a separate screen. The audience voted using wireless keypads and the results was displayed on the screen. Time was allowed for great discussions after each voting session. For me, this was the best part of the congress!

On Sunday 25th June, there were four different CE (Continuous Education) courses, two in the morning and two in the afternoon. The courses were held on the following topics:

- *Impact of Age on the Stage-Aware Assessment of Reproductive Tract*
- *Current Practices and Challenges in Method Validation*
- *Tissue-Based Image Analysis*
- *What You Always Wanted to Know About Immunotoxicology in Pharmaceutical Development... but Were Afraid to Ask*

I have attended the ‘Immunotoxicology’ CE course. All the presentations were available to be downloaded in the STP congress website. The course provided an overview of some of the most important immunotoxicology drug development platforms, and reviewed ICH Guidelines and current paradigms in immunotoxicology. I enjoyed very much listening the talk titled ‘Cytokines: friend or foe’ and presented by Dr Gautham Rao from Genentech.

On Monday 26th June, the first session of the Musculoskeletal System started with the “*Toolbox for the Evaluation of the Musculoskeletal System*” session for diagnostic and experimental pathologists. Speakers gave an overview of available tools that can be used to uncover changes in bones and muscles including familiar

histopathology tools, exploring other approaches such as bone biomarkers, biomechanical testing, histomorphometry, and various imaging tools that can characterize effects at organ, tissue, and cell levels. In this session, the recently published INHAND bone and joint publication was reviewed and the rationale was given for the changes. The day continued on the “*Bone Therapeutics: Safety Considerations*”. The session also gave an overview of a major regulatory requirement in the nonclinical filing package for bone therapeutics, studies designed to assess the impact of an agent on bone quality. Town hall was held after 5.30pm and the discussion topic was “*Points to Consider in Histopathology Severity Grading*” which we clearly needed more time to discuss. Watch out for the manuscript coming soon!

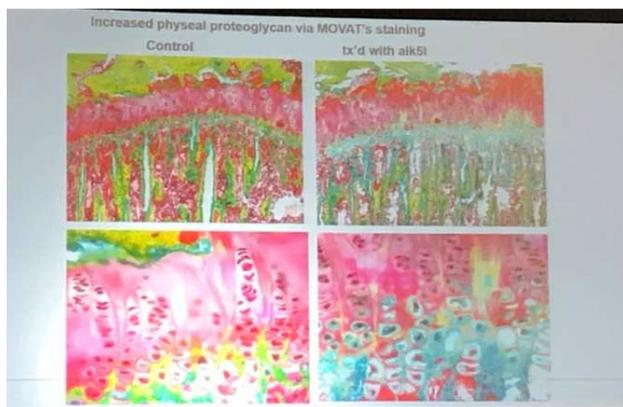
On Tuesday 27th June, morning session started on the topic titled “*Unintended Pharmacologic Effects on Bone*”. Examples of molecular pathways (WNT, SHH, VEGF) and bone findings was presented with emphasis on describing the pathogenesis and how the basic biology was altered in the growth plate, metaphysis, trabecular bone, and bone marrow. The impact of the findings along with de-risking strategies was also discussed.

As STP congress tradition, we had a free afternoon to do our own activities. After a very nice lunch, some of us went to see the Notre-Dame Basilica (The church Canadian singer Celine Dion was married in).



On Wednesday 28th June, speakers reviewed developments in the evolving role of the skeleton as an endocrine organ, and its relevance in toxicology evaluations as part of a whole-body, systems biology approach to drug safety assessment. The topic was “*Structural Approaches to Bone and Joint Repair*” for the afternoon session. This session covered methods and models used to evaluate novel approaches for repairing bones and joints: an overview of bone and joint devices, with an emphasis on preclinical and clinical evaluations of implant sites; an example of *ex vivo* tissue engineering as a therapeutic option for arthritis; comparing the benefits and limitations of different animal models of

joint damage and repair; and an overview of the unique standards and guidance that steer approval of novel bone and joint treatments.



The last day, Thursday 29th June, focused on the skeletal muscle and began with a review of the basic toolbox for evaluating skeletal muscle in toxicology studies including specimen collection and orientation, species differences, and common background findings. Commonly used histochemical stains and other specialized approaches utilized in the evaluation of skeletal muscle was also discussed. The second presentation provided an overview of the classic skeletal muscle biomarkers and current commercially available assays and concluded with an update on the status of the US FDA working groups' qualification efforts and discussion of case studies analyzing the performance of biomarker assays in drug development. The session continued focusing on sarcopenia and highlighted the importance of health issues associated with aging in the worldwide population. Key mechanisms currently implicated in the pathophysiology and progression of this condition was discussed, as well as the current controversies and future directions in the field of Sarcopenia research. The final presentation included a review of several animal models of muscular dystrophy and utilized Duchenne's muscular dystrophy to illustrate some emerging image analysis tools being employed to mitigate the challenge of providing quantitative clinical biomarker data in patients.

Lastly, I would like to mention Dr Gordon Hard receiving his **2017 STP Lifetime Achievement Award**. Dr Hard has been instrumental in shaping and developing the global field of toxicological pathology through his research and participation in a wide range of international pathology related activities as well as through his leadership within the Toxicologic Pathology world. Congratulations Dr Hard!

Catching up with friends and colleagues during breaks, lunch times, evening meals and welcome & farewell receptions was the highlight of the meeting for me and many. Before taking my flight back home, I took the

Montreal bus tour to complete the picture of this productive meeting.

A big thank you to everyone for this great symposium!

With best regards

Zuhail Dincer
zuhail.dincer@covance.com

What is the role of the STP Regulatory Forum committee?

The Regulatory Forum committee wants to initiate and stimulate discussion and debate and encourages ESTP and STP members to contribute to the Forum by submitting manuscripts of interest to the readership and well-reasoned opinions.

Controversial topics, topics of regulatory importance, and other informative topics will be published as follows:

- Full or short papers that provide reviews (including technical reviews), opinions and perspectives on regulatory issues and strategies related to nonclinical toxicology testing and risk assessment
- Commentary on draft and final regulatory guidance
- Announcements and reviews of meetings and activities related to regulatory issues of interest to toxicologic pathologists
- Letters from readers that address controversial topics related to regulatory perspective

The *Regulatory Forum* manuscripts will be available in the OnlineFirst section of the *Toxicology Pathology* website. The following are the last published pieces of opinion:

- Imaging Applications in Toxicologic Pathology – Recommendations for Use in Regulated Nonclinical Toxicity Studies (Maronpot et al.)
- Utility of *in Vitro* Secondary Pharmacology Data to Assess Risk of Drug-induced Valvular Heart Disease in Humans: Regulatory Considerations (Papoian et al.)
- Use and Utility of Animal Models of Disease for Nonclinical Safety Assessment: A Pharmaceutical Industry Survey (Morgan et al.)

We look forward to your submissions this year from all parts of the world! And thank you in advance for investing time in crafting your manuscripts, informing and educating colleagues.

Please contact any member of the committee with questions. The *Regulatory Forum* Committee:
Armando R. Irizarry (Chair; USA)
Cecilia Parrula (Co-Chair; USA)
Karyn Colman (USA)
Shayne Gad (USA)
Chris Houle (USA)
Zaher Radi (USA)
Mike Ringenberg (USA)
Bindu Bennet (*Tox Path* Editorial Board Liaison, USA)
Karen Regan (EC Liaison; USA)
Frank Geoly (SRPC Liaison, USA)
Beatrice Sacre-Salem (Europe, ESTP member).

With best regards,

Beatrice Sacre-Salem
beatrice_sacresalem@merck.com

**Announcement & Invitation to ESTP
Annual General Assembly in Lyon
30th August 2017**

Dear ESTP Members,

On behalf of the ESTP Executive Committee and ESTP Chair, Sibylle Gröters, I would like to cordially invite you to our next Annual General Assembly which will take place during our annual meeting, in Lyon (France), on 30th August 2017 (17.15 – 19.00 pm local time).

If you have not yet registered for the meeting, we cordially invite you to find the necessary information on our website and register as soon as possible. The agenda for the AGA has been sent to all members by e-mail. Besides general topics and administrative topics, the Executive Committee and other Committees will update you with recent activities of our Society, such as society journal, Classic Examples, the INHAND initiative, International Expert Workshops on "Adversity", and more.

In preparation of the AGA we will make sure that you receive the annual reports from the various councillors, committees and working groups prior to the Assembly by separate e-mail(s).

We are very much looking forward to welcoming you in Lyon, France

Best regards,

Gabriele Pohlmeier-Esch
ESTP Secretary
(On behalf of the present ESTP Executive Committee)
gabriele.pohlmeier-esch@boehringer-ingelheim.com

**ESTP International Expert Workshops
- Update -**

Dear ESTP Members,

Our 5th workshop, entitled "**Adversity of Lysosomal Accumulation**" is coming to a successful end. You will find a poster with the workshop results at our upcoming congress in Lyon, France. The paper with workshop results is in its final draft stage and will be submitted for publication in *Toxicologic Pathology*, within the next couple of weeks. We would like to thank all workshop participants for their active participation, valuable discussions and endurance!

In the meantime, the kick-off teleconference for our 6th workshop took place beginning of July: "**Adversity of thyroid follicular epithelial hypertrophy/hyperplasia, differentiation between direct and indirect mechanisms and their implication for risk assessment**". About one half of the 26 participants of this workshop (toxicopathologists, clinical pathologists, endocrinologists, investigative and regulatory toxicologists) are new members. The group will now have monthly teleconferences until the face-to-face expert discussion in Berlin, 16-17 May, 2018. We are very grateful to Bayer AG who kindly offered to host the meeting at their Berlin site.

Further information will be given at the ESTP annual general assembly in Lyon, or can be obtained from one of the organizers at any time.

Wolfgang Kaufmann
wolfkauf@gmail.com
Barbara Lenz
barbara.lenz@roche.com
Xavier Palazzi
xavier.palazzi@pfizer.com
Gabriele Pohlmeier-Esch
gabriele.pohlmeier-esch@boehringer-ingelheim.com