

ESTP Newsletter 2024 (2)

Editor Amy Narewski

(ESTP contact link: <https://www.eurotoxpath.org/contact.php>)



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2024	
<u>July 19</u>	TiHo Hannover (sponsored by ESTP) Residency Programm, Toxicologic Pathology Training Program, Module "Nervous System", Virtual LINK
<u>August 26-27</u>	Davis Thompson Foundation Symposium on Dermatopathology San Lorenzo de El Escorial (Madrid), Spain LINK
<u>August 28</u>	IATP IATP Satellite Symposium, New Approach Methodologies (NAMs) for Neurotoxicity Assessment and Regulatory Perspectives Medical Device Safety Assessment: Pathology and Toxicology Perspectives, San Lorenzo de El Escorial (Madrid), Spain LINK
<u>August 28-31</u>	ESTP, ECVP/ESVP 5 th Cutting Edge Pathology Congress, Neuropathology: The vast Pink Wonderland (Spain) LINK
<u>September 12</u>	16.00-17.30 11th joint webinar of the ESTP_SFTP_BSTP and ECVP_ESVP, Digital Pathology in veterinary and toxicologic pathology, online, LINK
<u>September 18</u>	ESTP Annual General Assembly of the ESTP 16.00-18.00, Virtual
<u>October 28 – November 1</u>	Davis Thompson Foundation Pathology of Lab Animals Bern, Switzerland LINK
<u>November 14-15</u>	BSTP BSTP 39th Annual Scientific Meeting "Development Toxicology and Pathology" (York, UK) LINK
<u>November 25-27</u>	RITA Panel Meeting (online) LINK
2025	
<u>March 20-21</u>	ESTP Classic Examples in Toxicologic Pathology XXXII, Hannover, Germany

The ESTP council

<i>Chairwoman</i>	Silvia Guionaud	<i>Secretary</i>	Raffaella Capobianco
<i>Vice President</i>	Lars Mecklenburg	<i>Treasurer</i>	Kuno Würsch
<i>Past Chairman</i>	Franck Chanut	<i>Designated Chairwoman</i>	Vanessa Schumacher
<i>Congress councillor</i>	Anna-Lena Frisk	<i>Councillor digital pathology</i>	Lise Bertrand
<i>Councillor to represent University Teachers</i>	Ingo Gerhauser	<i>Councillor early career pathologists</i>	Simone Tangermann
<i>Councillor for nomenclature</i>	Ute Bach	<i>Councillor for electronic communication</i>	Rupert Kellner
<i>BSTP Representative</i>	Zuhal Dincer	<i>NTP Representative</i>	Eveline de Rijk
<i>Hungarian STP Representative</i>	György Selenyi	<i>SFPT Representative/ Toxicologic Pathology journal liaison</i>	Béatrice Gauthier
<i>STP liaison, chair of the scientific and regulatory standards committee</i>	Annette Romeike	<i>Chair, awards committee</i>	Hans Harleman
<i>Chair, Pathology 2.0 working group</i>	Dirk Schaudien	<i>Chair, clinical pathology committee</i>	Monika Keresztes
<i>Admin Assistant to the ESTP EC</i>	Amy Narewski		

President's Column

Dear ESTP members,

We are in the last stretch before our annual conference, which will this year be held in San Lorenzo de El Escorial near Madrid, and in collaboration with ESVP/ECVP. This is a fantastic opportunity to connect with our colleagues from diagnostic and experimental veterinary pathology, meet old friends and make new acquaintances. In addition, our part of the event will focus on neuropathology, a research area that has been boosted by a renewed interest therapies for neurological disorders. Hurry and register if you haven't done so yet!

Due to operational constraints, we will this year have a virtual Annual General Meeting separate from the congress in September, and I strongly urge you to attend. We will inform you about a

number of new developments concerning our official journal, Toxicologic Pathology, including plans to go paperless, as well as important updates to our constitution. Also, please take a moment to cast your vote on our new council, for which electronic elections will open shortly!

This is the last President's column coming from me. The last two years went very quickly, with a lot of momentous developments and important decisions. I was very fortunate to be supported by a fantastic council with many experienced and highly committed individuals. Serving on the ESTP executive committee is an honour and a privilege, and for me it was a pleasure also.

Hope to see you in El Escorial!

Silvia Guionaud

ESTP Chairwoman

Classic Examples in Toxicologic Pathology XXXI, March 14 and 15, 2024

author: Smitha Pillai

This was my first Classic Examples in Toxicologic Pathology meeting, as an attendee and a speaker. When I was presented with this opportunity, I was excited to present on dysgeusia (an entity we rarely hear about in toxicologic pathology, but relevant clinically), and visit Germany for the first time! It turned out to be an incredible event combining science and pathology, a venue to meet wonderful people, make a couple of lifelong friends, re-connect with a childhood friend who lived in Munich, and tour the Bavarian paradise!

Drs. Thomas Nolte and Charlotte Lempp were great organizers and moderators. They met with the speakers in advance at a 'preparatory meeting' that included clear guidelines on timelines, submission of slide scans, case material handouts, seminar style and schedule. All slides were submitted and presented digitally. The handouts and digital slides of presented cases were available for the registrants, for pre-read before the meeting! It was great to see many veterinary pathology residents and PhD students volunteering to organize, take the reins of technical help during the seminar, and get involved in discussions.

The speakers did an excellent job of presenting their cases. There was a diverse mixture of presentations covering multiple therapeutic modalities and organ systems including the

reproductive tract, liver, kidney, and even taste buds! The seminars were not only limited to demonstrating lesions on slides; these were invaluable lessons in understanding the physiology and pathology of organ systems, and many covered investigative efforts that delved into the mechanisms of toxicity. Kudos to the speakers for the very well written handouts as well, and these are treasures for future references!

Dr. Krystyna Siudak was the first presenter. She demonstrated interesting female reproductive tract lesions following administration of progesterone receptor agonist, and their translational relevance. Dr. Sebastien Laurent presented on selective estrogen receptor degrader, demonstrated a few classic liver lesions, supplemented with results of investigative studies to understand the mechanisms of liver toxicity. Dr. Robert Johnson presented on GalNAc mRNA-related liver findings, with an excellent discussion on mechanisms of toxicity associated with class effect of GalNAc-siRNA conjugates. Dr. Mark Cesta presented virtually and showed very interesting histopathological examples of cholangiofibrosis. Dr. Enrico Vezzali presented on multiorgan lesions (liver, pituitary, thyroid gland, gall bladder) related to orexin antagonists that are used to treat insomnia, in dogs and rats. Dr. Thomas Nolte had to step in last minute and gave an excellent presentation on liver findings and reactive metabolites. Dr. Kuno Wuersch covered multiorgan lesions following administration of Gq/11 inhibitor. He discussed the G protein coupled receptors (GPCRs) and their signaling pathways in detail and set the stage for my talk on taste perception that are also

mediated by GPCRs. Drs. Emmanuelle Balme and Arno Kalkuhl discussed GPR40 agonists and their related toxicity including diabetes and liver lesions. We also had an MD renal pathologist, Dr. Jan Hinrich Braesen, who presented a few classic cases of cholemic nephropathy. I had the opportunity to present on physiology and pathology of taste perception (dysgeusia) resulting from an oncology small molecule agent, and it was well received.



I thoroughly enjoyed the conference, especially the in-person interactions and cultural experience. I would vote for this seminar to be on-site every year. In addition to pathology discussions, I enjoyed meeting many fellow colleagues from different countries. During my visit, transportation strikes were ongoing in Germany, with many trains and flights delayed or canceled. I specially want to thank Drs. His-Yu Yen and Alexa, who brought train tickets for me in advance, walked me to the train station and reserved a spot for me at the security check point, to make my journey as comfortable as possible. I would forever be grateful for your help! I also enjoyed the bite sized snacks and desserts at seminar break, and water from refillable glass bottles. USA, take note!

Visiting Germany was a fun, cultural experience. I enjoyed commuting by train and the hospitality of the people there. Many people were happy to help when I could not understand the signs in German, and one person even carried my heavy suitcase over a flight of stairs when the elevator was broken. On my return trip, I spent a day at Munich, toured the Marienplatz, English Garden, food markets and tried some of the famous beer, Weißwurst, sweet pretzels and pork knuckle.

Overall, it was a great experience that enriched my heart and mind. I would love to attend this conference again in the future!

Quo vadis? Is there a future for the “*Guess What*” Section?

Dear Colleagues,

Case presentations are without doubt of invaluable value for a pathologist. Lesions, once observed, usually burn themselves into our memories. The presentation of cases was the highly appreciated centerpiece of the former annual German ToxPath meetings. Other Societies (e.g. BSTP) sent series of slides for evaluation and later discussion rounds or Organizations (e.g. AFIP) presented cases for active contribution.

Since the very beginning of the ESTP we have provided you on our homepage with interesting cases from the field of toxicopathology. The purpose was not only to make you aware of rare findings but also to be in contact with the community to come to new ideas in case of unknown explanations. A similar approach to use the homepage has been undertaken from the STP.

A total of 31 cases have been prepared over the last years for your continuous education – the first diagnosis was received on Oct. 11, 2002. Already then, the number of received solutions was quite low. However, all cases are still available on the homepage and can be looked up in the “solution overview”. They ranged from easy ones to such where a diagnosis was difficult to make or was even impossible, and covered lesions from mainly rats, but also from mice, NHPs, rabbits, hamsters, and even fish. Are you aware of this?

It was never easy to find a suitable case but a number of colleagues finally helped out. Nevertheless, the initial goal to present four cases per year was not to fulfill. Still today, your support is welcome and moreover, highly needed. So, if you have an interesting case, please contact the *Guess What* Team: <https://www.eurotoxpath.org/guesswhat/index.php>

For the preparation of the solution, the focus was set to implement the opinions of the participating audience to provide an extensive collection of differential diagnoses. However, to do so a suitable number of answers from the community is essential.

At the annual meetings and in the committee reports we have frequently complained about the low number of submissions to our cases, ranging from 3 (Case 30) to 28 (Cases 14, 15), and we have asked ourselves what the reason may be. From the number of hits on the homepage it became clear that there was an, even international, interest – but why the shyness to send in a diagnosis, even if it is possible to do it anonymously. Our desperate final call in the 2nd ESTP Newsletter of 2019 remained unanswered by the membership.

Interestingly, we receive a high number of suggestions for a solution from participants outside of our Society, indicating the high interest in the international community. For example, for the current case 31 (open until September 5, 2024) we have received clearly more answers from non-ESTP members - mainly from the Asia-Pacific region - than from our own members.

We therefore have thought to initiate a survey to hear the opinion of YOU, OUR MEMBERSHIP, how you feel about continuation of the *Guess What* section. A respective [questionnaire is available here](#). Please, pay attention on its announcement on our homepage and have a look on it and please, take a few minutes of your precious time to fill out the survey. Thanks in advance!

Your *Guess What* Team: Matthias Rinke, Susanne Rittinghausen, Dirk Schaudien

[LINK to Guess What Current Case](#)

The current case:
Testis lesion of a 22 months old Wistar rat

posted: 05-Mar-2024 closing: 05-Sep-2024



Pathology session organized by the ESTP&STP working group “Complex in vitro models & Pathology” @ the 3rd MPS World Summit 2024 in Seattle, USA, on June 10th to 14th

The ESTP/STP Working Group on CIVM & Pathology contributed for the third year with a session titled “Filling the Translational Gap: Pathophysiological Considerations Enhance CIVM,” organized by Lindsay Tomlinson (Pfizer, Co-lead ESTP&STP working group) and moderated by Julia Kühnlenz (Bayer) and Deidre Dalmas (fGSK). This pivotal global conference on complex in vitro models (CIVM), also known as microphysiological systems (MPS), brought together platform developers, academia, industry, and governmental institutions to discuss advancements in 3D organoids and organ-chips.

Lindsay Tomlinson presented insights from the working groups recent publication: emphasizing the importance of understanding pathophysiology in CIVM development. The session included three use cases: Eliah Shamir (Genentech) discussed an improved FFPE processing approach for combining organoids, Akhmetzada Kargazhanov (PhD student, University of Central Florida) recreated neuromuscular pathology in Alzheimer’s

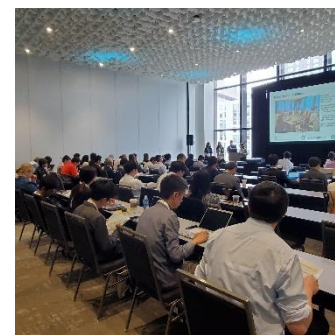
Speakers and Session Chairs: Julia K., Lindsay T., Maggie Q., Eliah S., Akhmetzda K. and Deidre D.



disease using a human iPSC-derived model, and Maggie Qi (Professor, Massachusetts Institute of Technology) presented a Retina-on-a-Chip for glaucoma research. The session was well-received and fostered numerous discussions with the speakers afterward.

With this scientific session and the recent publication by the working group: **Stokar-Regenscheit et al. Complex In Vitro Model**

Characterization for Context of Use in Toxicologic Pathology: Use Cases by



Collaborative Teams of Biologists, Bioengineers, and Pathologists. Toxicologic Pathology. 2024;0(0).

doi:10.1177/01926233241253811, the working group aims to raise awareness among different expert fields towards a collaborative effort in characterizing and validating novel complex in vitro models for the context of use in Toxicologic Pathology.

07/02/2024, Julia Kuehnlentz, Deidre Dalmas, Lindsay Tomlinson and Nadine Stokar on behalf of the ESTP & STP working group “Complex in vitro models & Pathology”

Servier's Saclay site focused on Pathology and the 3Rs.



On May 23 and 24, the Paris-Saclay Servier site had the honor of hosting the [Annual Meeting of the French Society of Toxicological Pathology](#) which was dedicated to the practical, strategic, and emerging role of the pathologist in the progression of the 3 R's.

This meeting brought together renowned international and national private/public speakers (including pathologists and 3R's specialists) and was the opportunity to show that

the pathologists and nonclinical teams' commitment to the 3Rs is continuous and effective.

The veterinary pathologist is a key player in this field given his multiple expertise and the communication between the different players is essential to achieve the objectives set. For example, histopathological changes due to stress may move forward changes in sampling methods or husbandry conditions, or abnormal histopathological results may permit to identify/anticipate a risk of a health problem.

Another major part of the pathologist's activity was highlighted as his involvement in the development/validation of new in vitro methods and the contribution to other 3R approaches: justification of studies, refinement of study

designs, endpoint determination, biobanking creation and potential impact on regulatory policy.

Digital pathology, artificial intelligence and virtual controls were also topics discussed at the meeting in order to find

a way to minimize the use of animals.

These 2 days were an opportunity to recall the improvements already made, to brainstorm about progress and possible future achievements on the 3Rs and 4Rs and all of it with interesting people, sharing science and making new friends. It was a wonderful and fruitful time.

Flavia, on behalf of the SOC

2024 STP Annual Symposium

Well situated in the inner harbor of Baltimore [this year's STP meeting](#) took place June 16 – 19. The topic of the 43rd annual symposium was “Innovative Therapeutics: Biology, Toxicologic Pathology, and Regulatory Perspectives”. On a first glance the topic seems to be a repetition of the last year's ESTP meeting “Emerging Therapeutic Modalities”. However, in detail new information and other details were presented. The STP meeting started Sunday morning with the CE course “Immunotoxicology from a Pathology Perspective” with another CE course in the afternoon “Nonclinical Safety Evaluation of Long-Acting Injectables in Animal Models”. Concurrently, there was the DTT Satellite Symposium “Pathology Potpourri” in the morning and the Career Development Workshop “US FDA Modernization Act 2.0”. In the next days the session topics were “AAV-Based Therapies”, “Adoptive Cell Therapies”, “Targeted Delivery of siRNA and ASO-Based Therapies”, “mRNA and Self-Amplifying RNA (saRNA): Opportunities for Disease Prevention and Therapy”, “Protein Degradation”, and “LNP and Other Delivery Systems”. Further, on Monday night, there was an interesting Town Hall “Adversity 2.0” discussion. Sixty-three quite interesting posters were displayed.



In summary, the STP meeting was quite interesting and did not represent a repetition of last year's ESTP meeting but was complementary and has been worth to attend. It was also great to socialize and interact with the US based colleagues, which was possible during the breaks, poster sessions, and especially during the welcome reception on Sunday night and the president's reception Wednesday night.

Another personal highlight was the 2024 Toxicologic Pathology Best Paper Award for the best review of the ESTP Pathology 2.0 Molecular Pathology Special Interest Group about “Review of In Situ Hybridization Techniques for Drug Research and Development” in 2023. I'd like to express my gratitude to all co-authors and especially to the first author for this great review.

Dirk Schaudien