Dear Drug Discovery Toxicology Specialty Section members and friends,

While my 10 year old daughter Natalia is out for pumpkin carving and trick or treating with her papa, I am staying home with a nice cup of coffee to finally get this fall newsletter of to you.

I am always amazed how fast a year goes by. From year beginning goal planning, to preparing SOT posters, to submitting proposals for next year's SOT, to a busy summer with camps and heat and bugs, before you know it, you get this huge to do list of what still needs to be done before the end of the year.

I wish cloning efforts would be more advanced so at times I could simply quadruple my efforts. Joking aside, I am happy to write to you today to share a few things with you.

We had great attendance during our annual SOT specialty section meeting and were pleased to see students and postdoc members produce such outstanding science that we honored during our reception. The top three DDTSS Emil Pfitzer Student Awards for students were presented by Erik Harstad, and Stefan Ruepp presented Pfitzer awards for the top three postdoctoral fellows. This year's winners were:

Graduate Student winners

First place ($1000): Arya Sobhakumari (University of Iowa)

Second Place ($400): Monica Langley (Iowa State)

Third Place ($150): Kazuhisa Miyakawa (Michigan State)

Postdoc winners

First place ($1000): Durga Tripathi (Texas A&M)

Second Place ($400): Rachel Church (The Hamner)

Third Place ($150): Mili Mandal (Rutgers)

At next year's reception, we are hoping to have a talk/discussion that will be solving some myths about careers in academia versus industry, which we hope to be of interest to our student and post doc members.

Again, members of this specialty section came forward with some fine proposals for 2014 and we are happy to spill the secret that we will be sponsoring the following:

2014 Proposals:

"**Use of Stem Cells in Toxicity Testing—From Basic Research to Personalized Toxicology**" by Stephane Dhalluin and Yvonne Will

"Beyond hERG: Novel Cardiovascular De-Risking Strategies and Their Regulatory Acceptance" by John Davis and Tiffany Brabham

"**The Use of Dogs and Minipigs As an Alternative to the Nonhuman Primate in Nonclinical Safety Assessment of Biopharmaceuticals"** by John Wisler and J Bluemel

"**Science-Based Preclinical Safety Assessment: Decision Making to Enhance Regulatory Success"** by Ruth Roberts and M Hinrichs

"**Does This Chemical Make My Liver Look Fat? (Environmental Exposures and Steatosis" by** Charleen Mcqueen and Cherrington.

"**Clinical Evaluation of Emerging Biomarkers of Drug-Induced Liver Injury"** by Jiri Aubrecht and Alisson Harril

Members also have been prolific with publications and so I am attaching some at the end of this document for your reading pleasure and of course in hopes that we can foster some more conversations between members of the drug discovery toxicology specialty section. While reading the title I thought that maybe I should pose a question for the members to engage into some discussion and maybe, who knows, perhaps could lead to a topic for a CCT conference. CCT stands for Contemporary Concepts in Toxicology, which are meetings on a specific topic of interest. These are one- to two-day focused, open registration, scientific meetings in contemporary and rapidly progressing areas of toxicological sciences. CCT meetings may be held as satellites to the SOT Annual Meeting, specialty or regional meetings, or may be held independently. Meetings may also be held virtually. The intent of the CCT meetings is to provide a forum for dissemination and discussion of those developments that are likely to have the greatest importance for advancing the science of toxicology. In order to maintain the quality standards of the Society, only meetings in which SOT maintains scientific and administrative control will be considered as CCT meetings. Over the years, a wide range of topics have been discussed. Please take a moment to visit the CCT webpage at http://www.toxicology.org/ai/meet/CCT_Guidelines.asp. Also Eric Harstad would be delighted to provide you with even more detail.

So my question today is the following: I have noted that most in vitro assays or screening paradigms leave a large false negative space (regardless of the sensitivity values some folks' like to claim). I am wondering if we think that 3D models and co-cultures will close this gap. How would we model such an important component such as genetics, sex, multiple drug use, environmental exposures and of course age. I would love to hear from all of you.

As a reminder to you as well, below please find the current DDTSS officers. If you would like to get involved and would like to be nominated in the future for any of these positions, please let me know.

President:	Yvonne Will
Vice President:	Andrew Olaharski
Vice President-elect:	Dan Kemp

Secretary/Treasurer:	Brandon Jeffy
Councilors:	Eric Harstad Robert Dunn
Past-President	John Wisler
SAC Representative:	Monica Langley
PDA Representative:	Durga Tripathi

I hope you enjoyed this update and please let me know if there is anything I should be doing for you as the member of this section. Kind regards,

Yvonne Will on behalf of all the officers

Member Publications in 2013

Glenn H Cantor and Evan B Janovitz. 2013. Discovery Toxicology and Pathology. In: Haschek and Rousseaux's Handbook of Toxicologic Pathology. 3rd edition (W.M. Haschek-Hoch, C.G. Rousseaux, M.A. Wallig, eds.), Elsevier Inc., Academic Press, pp. 703-724

Matthew A Wallig, Evan B Janovitz. 2013. Morphologic manifestations of toxic cell injury. In: Haschek and Rousseaux's Handbook of Toxicologic Pathology. 3rd edition (W.M. Haschek-Hoch, C.G. Rousseaux, M.A. Wallig, eds.), Elsevier Inc., Academic Press, pp. 77-106

Poulin P, Dambach DM, Hartley DH, Ford K, Theil FP, Harstad E, Halladay J, Choo E, Boggs J, Liederer BM, Dean B, Diaz D. An algorithm for evaluating potential tissue drug distribution in toxicology studies from readily available pharmacokinetic parameters.

Claire N. Medine, Baltasar Lucendo-Villarin, Christopher Storck, Faye Wang, Dagmara Szkolnicka, Ferdous Khan, Salvatore, Pernagallo, James R. Black, Howard M. Marriage, James A. Ross, Mark Bradley, John P. Iredale, Oliver Flint, David C. Hay. (2013). Developing High-Fidelity Hepatotoxicity Models From Pluripotent Stem Cells. Stem Cells Translational Medicine 2, 505-509.

Dagmara Szkolnicka, Sarah Farnworth, Balta Lucendo–Villarin, Christopher Storck, Wenli Zhou, John P. Iredale, Oliver Flint, David C. Hay. Accurate Prediction of Potential Liver Injury Using Stem Cell Derived Populations. Stem Cells Translational Medicine (Accepted for publication)

Faye Wang and Oliver Flint. (2013). BMS-986001, an HIV nucleoside reverse transcriptase inhibitor, does not degrade mitochondrial DNA in long-term primary cultures of cells isolated from human kidney, muscle and adipose tissue. Antimicrobial Agennts and Chemotherapy (Accepted for Publication).

Julieta M. Panzica-Kelly, Kimberly C. Brannen, Yan Ma, Cindy X. Zhang, Oliver P. Flint, Lois Lehman-McKeeman, Karen A. Augustine-Rauch. (2013).Establishment of a Molecular Embryonic Stem Cell Developmental Toxicity Assay. Toxicological Sciences, 131(2): 447–457

Guo, L., Coyle, L., Abrams, R., Kemper, R.A., Chiao, E.T., and Kolaja K.L. (2013, in press) Refining the Human iPSC-Cardiomyocyte Arrhythmic Risk Assessment Model. *Toxicological Sciences*, Advance Access publication September 18th, 2013.

Morelli, James, Ciaccio Paul J. Differential Cytotoxicity Responses by Dog and Rat Hepatocytes to Phospholipogenic Treatments. Journal of Toxicology. (2013): Article ID 956404

Borders, et al. (2013). "Effects of tyrosine kinase inhibitors on rat isolated heart function and protein biomarkers indicative of toxicity." Journal of Pharmacological and Toxicological Methods 68(1): 150-159.

Persson M, Løye AF, Mow T, Hornberg JJ. A high content screening assay to predict human drug-induced liver injury during drug discovery. Department of Exploratory Toxicology, Non-Clinical Safety Research, H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark. Electronic address: mpss@lundbeck.com.

Laifenfeld D, Luing Q, Swiss R, Park J, Macoritto M, Will Y, Younis H, Lawton M. Utilization of Reverse Causal Reasoning of Hepatic Gene Expression in Rats to Identify Molecular Pathways of Idiosyncratic Drug-Induced Liver Injury. Toxicol Sci. 2013 Oct 17. [Epub ahead of print]

Nadanaciva S, Aleo MD, Strock CJ, Stedman DB, Wang H, Will Y. Toxicity assessments of nonsteroidal anti-inflammatory drugs in isolated mitochondria, rat hepatocytes, and zebrafish show good concordance across chemical classes. Toxicol Appl Pharmacol. 2013 Oct 15;272(2):272-80. doi: 10.1016/j.taap.2013.06.019. Epub 2013 Jun 26.

Swiss R, Niles A, Cali JJ, Nadanaciva S, Will Y. Validation of a HTS-amenable assay to detect drug-induced mitochondrial toxicity in the absence and presence of cell death. Toxicol In Vitro. 2013 Sep;27(6):1789-97. doi: 10.1016/j.tiv.2013.05.007. Epub 2013 May 29.

Khetani SR, Kanchagar C, Ukairo O, Krzyzewski S, Moore A, Shi J, Aoyama S, Aleo M, Will Y. Use of micropatterned cocultures to detect compounds that cause drug-induced liver injury in humans. Toxicol Sci. 2013 Mar;132(1):107-17. doi: 10.1093/toxsci/kfs326. Epub 2012 Nov 14.

Hynes J, Nadanaciva S, Swiss R, Carey C, Kirwan S, Will Y. A high-throughput dual parameter assay for assessing drug-induced mitochondrial dysfunction provides additional predictivity over

two established mitochondrial toxicity assays. Toxicol In Vitro. 2013 Mar;27(2):560-9. doi: 10.1016/j.tiv.2012.11.002. Epub 2012 Nov 10.

Naven RT, Swiss R, Klug-McLeod J, Will Y, Greene N. The development of structure-activity relationships for mitochondrial dysfunction: uncoupling of oxidative phosphorylation. Toxicol Sci. 2013 Jan;131(1):271-8. doi: 10.1093/toxsci/kfs279. Epub 2012 Sep 13

Leucine-rich repeat kinase 2 (LRRK2)-deficient rats exhibit renal tubule injury and perturbations in metabolic and immunological homeostasis. PLoS One. 2013 Jun 14;8(6):e66164. doi: 10.1371/journal.pone.0066164. Print 2013.

Pharmacological inhibition of polo like kinase 2 (PLK2) does not cause chromosomal damage or result in the formation of micronuclei. Toxicol Appl Pharmacol. 2013 May 15;269(1):1-7. doi: 10.1016/j.taap.2013.02.012. Epub 2013 Mar 1.