ISSX Biotransformation, Mechanisms, and Pathways Focus Group Newsletter

AUGUST 2021

The ISSX Biotransformation, Mechanisms, and Pathways Focus Group (BMPFG) is led by chair Amit Kalgutkar, co-chair Valerie Kramlinger, and the steering members Deepak Dalvie, Carley Heck, James O'Neill, Dian Su, Aaron Teitelbaum, and Rheem Totah. The goals of this group are to disseminate and promote state-of-the-art research and foster discussion and collaboration among ISSX members on the role of biotransformation in drug design, drug-drug interactions, drug safety, and beyond. In addition to providing a discussion forum, this group will also aim to generate and publish position papers on new vistas in biotransformation science in relation to drug discovery/development. The focus group will engage members throughout the year via webinars, workshops, and by contributing to ISSX meeting planning.

International Society for the Study of Xenobiotics (ISSX)

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BMPFG Related Activities at the 24th North American ISSX Meeting

The 24th North American ISSX meeting has a stimulating program that is sure to foster scientific exchange, networking, and collaborative discovery. Below, the members of the BMPFG steering committee highlight some sessions that are likely to be of particular interest to those in the biotransformation community.

Monday, September 13th 9:00 - 12:00 EST

Short Course 1: Drug Metabolism in Pharmaceutical Drug Discovery and Development

Co-chairs: Valerie Kramlinger, Novartis, Cambridge, Massachusetts, USA and Ana Vergara, Merck, West Point, PA, USA

Sponsored by BMPFG, this course is designed to include a number of topics that both cover and branch out from our traditional liver and small-molecule focused mindset. It will cover basics of drug metabolism, how drug metabolism is applied in drug discovery and development, and how drug metabolism concepts do (or do not) translate to newer modalities. The unifying focus through each topic will be to discuss how biotransformation work directly influences drug discovery and development in industry.

Tuesday, September 14th 1:20 - 3:10 EST

Symposium 3: Identifying Biotransformations of Next Generation Biologics

Co-chairs: Mark Cancilla, Merck & Co., Inc., West Point, Pennsylvania, USA and Brooke Rock, Amgen, South San Francisco, California, USA

The increased complexity of biologic drug modalities has changed our understanding of their pharmacokinetic and metabolic assessment. The overall stability of a chemically modified or engineered proteins upon administration has been demonstrated to be linked to its efficacy. This session will focus on identifying biotransformations of complex biologics to further understand their metabolic fate as well as to aid in their design for the assessment of their therapeutic potential

BMPFG Related Activities at the 24th North American ISSX Meeting

Wednesday, September 15th 10:30 - 12:30 EST

Symposium 5: Driving Innovation in Qualitative and Quantitative Bioanalysis

Co-chairs: Lucinda Hittle, Merck & Co., Inc., Rahway, New Jersey, USA and Valerie Kramlinger, Novartis, Cambridge, Massachusetts, USA

As a partnership between the ISSX Bioanalysis in ADME Science and Biotransformation focus group, the BMPFG sponsored session will present various aspects of quantitative and qualitative analysis. Topics include novel informatics, instrumentation and imaging; approaches will be presented with an emphasis on application to both small and large molecules. The objective of this session is to highlight state-of-the-art methodologies that are being applied to continuously improve bioanalytical and biotransformation capabilities for xenobiotics.

Friday, September 17th 2:00 - 3:50 EST

Plenary Session: Predicting the Unpredictable – Idiosyncratic Drug Toxicity

Co-chairs: Amit S. Kalgutkar, Pfizer Inc., Cambridge, Massachusetts, USA and Kaushik Mitra, Janssen Pharmaceutica

Sponsored by the BMPFG, this session will discuss how cumulative research over several decades has implicated the involvement of bioactivation (formation of electrophilic reactive species) in idiosyncratic drug toxicity. Consequently, “avoidance” strategies have been inserted into drug discovery paradigms, which include the exclusion of structural alerts and possible termination of reactive metabolite-positive compounds. The symposium will focus on the recent progress on the limitations of the structural alert avoidance strategy and novel strategies to assess idiosyncratic toxicity in preclinical/clinical drug discovery paradigm.

You can find more information regarding the lectures that comprise each of these symposia at www.issx2021.org

Because this event is online, attendees will have access to the presentations and recordings even after the meeting ends. Don’t miss out on this amazing learning opportunity!

Highlight of an Upcoming Position Paper

The BMPFG steering committee is excited to announce our upcoming position paper that discusses the current state and future prospects of biotransformation research.

More specifically, over the past decades, the number of scientists trained in departments dedicated to traditional medicinal chemistry, biotransformation, and/or chemical toxicology have seemingly declined. Yet, there remains a strong demand for such specialized skills in the pharmaceutical industry, particularly within drug metabolism/pharmacokinetics (DMPK) departments. In this position paper, the members of the BMPFG steering committee reflect on the current and diverse roles and responsibilities of scientists trained in the biotransformation field in pharmaceutical companies and contract research organizations. The ability of scientists with a biotransformation/organic chemistry background to solve complex drug metabolism problems encountered during research and development efforts on both small molecule or large molecular modalities is exemplified in six relevant case studies. Finally, the authors stress the importance and continued commitment to training the next generation of biotransformation scientists who are not only experienced in the metabolism of conventional small molecule therapeutics, but are also equipped to tackle emerging challenges associated with new drug discovery modalities including peptides, protein degraders and antibodies.

Look for this upcoming publication in Drug Metabolism and Disposition. We look forward to further discussion on this topic!

Ongoing ISSX BMPFG Activities

ISSX BMPFG LinkedIn Group

After our last newsletter, have had great engagement on our ISSX BMPFG LinkedIn page. This space was created to allow for discussions between BMPFG members on scientific topics, dissemination of recent publications of interest to the group, advertisement of biotransformation-related seminars and job opportunities, and connection with other members within our scientific community. Thank you for the active participation on this page- your involvement is what drives the success of this effort! If you haven't yet, we invite you to join the group. To do so, look us up "ISSX Biotransformation Mechanisms and Pathways Focus Group" on LinkedIn!

The Members of the ISSX BMPFG

As of now, we have > 350 members in the ISSX BMPFG. We would like to extend our warmest welcome to all existing and new members! We appreciate your support and hope you enjoy the programming, discussion, and networking opportunities! Please sign up on the ISSX Website if you are interested in joining the focus group. We look forward towards hearing from you on proposals & ideas for the BMPFG to focus on (e.g., meetings/webinars & potential publication topics for the group to consider). To join, please visit www.issx.org/page/fg1.

Engagement and Programming

The ISSX BMPFG steering committee is working to increase programming and engagement opportunities, including webinars and discussion content for the LinkedIn group. If you have a proposal for a seminar or a discussion topic, please reach out to Amit or Valerie at BMPFG@issx.org.

Call for Ideas

If you would like to start a discussion on a topic on the LinkedIn page, join the ISSX BMPFG LinkedIn group. If you have a paper summary to submit for the next BMPFG newsletter, email Valerie and Amit at BMPFG@issx.org.