ISSX Newsletter from the Bioanalysis in ADME Science and Biotransformation, Mechanisms, & Pathways Focus Groups

FEBRUARY 2023

The chairs of the ISSX Bioanalysis in ADME Science Focus Group (BASFG) and the Biotransformation, Mechanisms, and Pathways Focus Group (BMPFG) are pleased to jointly disseminate this newsletter to introduce the new leadership for each group, provide a few updates regarding the ISSX/MDO meeting that occurred in September and the future of the focus groups which evolved out of conversations held at the most recent ISSX meeting, and to put out a call for applications for the steering committees for both groups for the 2023-2024 term.

International Society for the Study of Xenobiotics (ISSX)

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Bioanalysis in ADME Science Focus Group Leadership

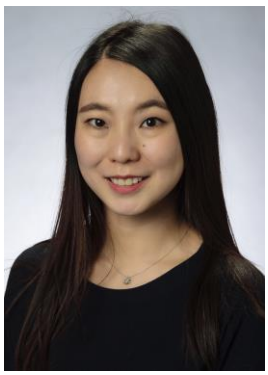
Dear Esteemed Colleagues and Friends,

Bingming Chen and I would like to introduce ourselves as the new ISSX Bioanalysis in ADME Science Focus Group chairs and humbly thank Lucinda Hittle and Mike Reilly for their service as previous chairs. Lucinda and Mike did an amazing job building a solid foundation for this focus group.

NEW CHAIRS – MATT ALBERTOLLE AND BINGMING CHEN

Matt Albertolle, Ph.D.

Matt Albertolle has worked at Takeda for the past two years and has extensive expertise in oligonucleotide, peptide, and small molecule analysis. He earned his PhD in the laboratory of Fred Guengerich at Vanderbilt University focusing mostly on P450 inhibition via posttranslational modifications. His repertoire of expertise includes proteomics, metabolomics, bioanalysis, and enzymology.



Bingming Chen, Ph.D.

Bingming Chen has worked at Merck for the past five years in the area of preclinical development focusing on biotransformation and tissue distribution. Prior to Merck, she earned both her BS and PhD from University of Wisconsin-Madison and MBA from University of Illinois-Urbana Champaign. She has extensive expertise in label-free mass spectrometry imaging, quantitative glycomics and LC-MS biomolecule characterization.

Biotransformation, Mechanism, and Pathways Membership, Leadership, & Steering Committee Updates

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 to hearing from you on proposals & ideas for the BMPFG to focus on (e.g., meetings/webinars & potential publication topics for the group to consider).

Thank you to everyone who has participated in this group through the BMPFG LinkedIn page. We continue to encourage members to use this space for discussions 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. 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!

Since its inception, Amit Kalgutkar has chaired the BMPFG, initiating many new ideas that furthered the science within this community. We would like to thank him for the passion and ideas that led this group to create meeting content, publications, and other activities that contributed to the biotransformation community. As he is stepping down as co-chair of this focus group, Amit will be chairing the 25th North American ISSX Meeting in Boston this September and we look forward to the content of that meeting! Valerie Kramlinger will become chair of the BMPFG and Aaron Teitelbaum will become co-chair. In addition to Amit, we would like to thank Rheem Totah, Deepak Dalvie, Dian Su, and James O'Neil for their service on the BMPFG steering committee in 2021 and 2022. Carley Heck will remain on the steering committee, with the **remaining 5 positions open for new members**. Information on joining the BMPFG steering committee can be found on page 7.

BMPFG Membership, Leadership, & Steering Committee Updates

Valerie Kramlinger, Ph.D.

Valerie Kramlinger is a research professor in the department of Pharmacology at Vanderbilt University, serving as director of DMPK within the Warren Center for Neuroscience Drug Discovery. Prior to this role, she spent eight years working within the pharmaceutical industry focusing on small-molecule ADME, including biotransformation, to support drug discovery and development. She earned her BS and PhD at the University of Minnesota in chemistry and biochemistry, respectively, and carried out postdoctoral research in the laboratory of Fred Guengerich at Vanderbilt University focusing on cytochrome P450-mediated metabolism of endogenous substrates.

Aaron Teitelbaum, Ph.D.

Dr. Aaron M. Teitelbaum is currently the Associate Director of In Vitro ADME at Boehringer Ingelheim Pharmaceuticals GmbH. His main responsibility is leading the in vitro ADME team, specifically focusing on the DMPK characterization of small molecules within the hit-to-lead, lead optimization, and candidate selection stages of drug discovery programs. Dr. Teitelbaum's research interests include investigating in silico approaches for predicting ADME and biotransformation, characterizing the in vitro drug metabolism enzyme and transporter function within specific disease states, evaluating intestinal organoids and organ-on-a-chip technologies as novel in vitro preclinical models, and optimizing internal workflow efficiencies for high-throughput ADME assays. Prior to joining Boehringer Ingelheim in 2016, Dr. Teitelbaum earned his Ph.D. in Medicinal Chemistry in 2012 from the University of Minnesota and completed two post-doctoral fellowships at the University of Washington and Washington University in St. Louis, respectively.

Carley Heck, Ph.D.

Carley Heck completed her PhD in 2019, where she studied drug metabolism and toxicity of NNRTIs with Namandjé Bumpus at Johns Hopkins School of Medicine. Carley currently works as a Principal Scientist in Biotransformation at Pfizer (Groton, CT), where she employs biotransformation science to support both drug discovery and development programs. Her current research interests include bioactivation and drug toxicity, with a specific focus on acyl conjugations. Since 2021, she has served as a steering committee member of the ISSX Biotransformation Mechanism and Pathways Focus Group

Highlights from the joint ISSX/MDO 2022 Meeting

Short Courses

September's ISSX/MDO short course offerings were a great success.

The short course sponsored by the BASFG had a number of people who attended and gained an overview of four unique dimensions of bioanalysis for proteins, cell and gene therapy, including: 1) Ligand Binding Assays, 2) Liquid Chromatography/Mass Spectrometry for Large Molecules, 3) PCR including digital droplet techniques, and 4) Immunogenicity. Each section was taught by an experienced industrial scientist in this discipline and included relevant case studies and applications.
Speakers included:

- Fundamentals and Applications of LC/MS and CE/MS for Large Molecules Bioanalysis
    - Mei Han, Amgen, Inc., South San Francisco, CA, USA
- Impact of Novel Ligand Binding Assay Technologies on Bioanalysis
    - Sally Fischer, Genentech, South San Francisco, California, USA
- Fundamentals of Immunogenicity
    - Marina Li, Merck, West Point, PA, USA
- Fundamentals of PCR Including Digital Droplet Techniques
    - Matthew Albertolle, Takeda Pharmaceuticals, San Diego, California, USA

Focus Group Discussions

FOCUS GROUP DISCUSSION RESULTS

Bioanalytical Focus Group

The Bioanalytical Focus Group Discussion hour was sparsely attended this year indicating the need to pivot the focus of the group to topics more relevant to the ISSX members. After some key discussions, it was decided to shift the topics to a more macromolecular ADME focus which will encompass the following topics:

1. Methods of analysis and catabolism of biologics and data interpretation in drug discovery and development.
2. New technologies and approaches for the bioanalysis of intact protein therapies and their catabolic products.
3. Bioanalytical and ADME assessment of peptide, oligonucleotide, and biologic therapies.
4. Identification of new analytical tools for improving in vitro models.
5. DMPK approaches to optimizing exposures with limited resources.
6. Strategies and methods for early identification of issues associated with potentially toxic metabolites in drug discovery.

Biotransformation Focus Group

The BMPFG Discussion hour was well attended this year, indicating a strong ongoing interest in the topics the group is promoting. We recapped the activities that were promoted by the focus group over the last year and opened the floor for members to propose ideas for future efforts.

Generally, most interest was focused on the biotransformation of small molecules, so together with the Bioanalysis focus group, we ‘rebranded’ our group focus to strictly small molecules. Larger modality topics will now be under the BASFG.

Ideas for potential future efforts included the following:

1. Continued efforts to promote the increase of drug metabolism/biotransformation within the academic community.
2. Generating materials (short videos or publications) discussing principles of biotransformation, how one uses biotransformation data
3. Continued use of our social media or other platforms to share recent publications, job opportunities, and other relevant information in the field

Upcoming ISSX Activities in 2023

Small Molecule Metabolites in Drug Discovery and Development Workshop

Virtual Workshop
March 1- 3, 2023
Workshop Chairs: Carley Heck, Ph.D., and Valerie Kramlinger, Ph.D.

This workshop is designed to discuss small-molecule drug metabolites including how we identify and quantify them, as well as discussion around what information is needed regarding metabolites in the discovery and development phases of drug discovery. The round table sessions with the speakers should lead to some lively discussion! See the complete program here and register here.

25th North American ISSX Meeting

Westin Boston Waterfront Hotel
Boston, Massachusetts, USA
September 10 - 13, 2023
Meeting Chairs: Amit Kalgutkar, Ph.D. and Fatemeh Akhlaghi, Ph.D.

The agenda and registration for this meeting will be available soon, so stay tuned!

Call for Steering Committee Member Applications

BASFG Steering Committee

The BASFG would like to extend a call for applications for a newly formed steering committee that will assist in design of short courses, webinars, and symposia over the next year. Please send application emails to bingming.chen@merck.com and matthew.albertolle@takeda.com. **Please apply by Monday, March 20, 2023.**

BMPFG Steering Committee

As mentioned on page 2, **we are looking for new members of the BMPFG steering committee, and currently have five open slots.** This group meets virtually once a month to help plan content for the greater BMPFG membership. Last year the group published a position paper on the "Future of Biotransformation Science in the Pharmaceutical Industry" and assisted in planning content for both the ISSX North American 2022 meeting and the upcoming March 2023 workshop (see page 6). We are looking to continue our efforts in educating the scientific community in the importance biotransformation science, as well as inspire and inform the next generation of biotransformation experts through highlighting important tools and work in our field. Please apply here to join the steering committee. **Please apply by Monday, March 20, 2023.**