

**Drug Metabolism and Pharmacokinetics Interest Group Report of the Interest Group Workshop
64th ASMS Conference, June 5 31 to June 9, 2016 San Antonio TX**

Metabolism of Biotherapeutics: When, Why and How.

The Drug Metabolism and Pharmacokinetics (DMPK) Interest Group Workshop was held on Tuesday June 7 from 5:45 to 7:00 pm. Coordinator Kevin Bateman and Co-Coordinator Philip Tiller led the meeting by introducing the session. Approximately 110 scientists attended the workshop demonstrating interest in drug metabolism and pharmacokinetics. An expert panel shared their perspectives to spur discussion on the workshop topic. The strong attendance and active attendee participation in the discussion provide a good endorsement for continuing the DMPK-IG in future years.

A brief business meeting was held at the beginning of the workshop to review the status of the current Oral Sessions, solicit ideas for future DMPK Oral Sessions and Workshops, as well as a call for nominees and volunteers for future DMPK-IG sessions.

1. Review of the DMPK IG Goals

The DMPK Interest Group goals of providing a discussion forum to MS practitioners in drug metabolism, pharmacokinetics, qualitative and quantitative, non-regulated bioanalysis include sharing:

- Recent advances in techniques and methodologies for metabolite identification and pharmacokinetic bioanalysis
- Interpretation of, and application of related guidance documents (i.e. MIST, ICH M3, DDI, expl. IND)
- Sharing of best practices across industry and academia
- Provide input on ASMS conference program of interest to scientists working in DMPK
- Reach out and coordinate with related groups to complement scope and broaden outreach to scientific community

2. Solicitation for nominations for 2017 and future DMPK IG Coordinators

2016: Kevin Bateman, Merck & Co (Coordinator) – kevin_bateman@merck.com
Philip Tiller, RMI Laboratories (Co-Coordinator) – philip_tiller@rmilaboratories.com

The attendees were asked to vote for future coordinators based on a list of 4 volunteers, Mark Cancilla (Merck & Co) Jeff Alberts (Lilly), Mingshe Zhu (BMS) and Jonathan Josephs (Thermo). The two who obtained the most votes were Mark Cancilla and Jonathan Josephs.

Thus the DMPK-IG future coordinators are:-

2017: Philip Tiller, RMI Laboratories (Coordinator)
Mark Cancilla, Merck & Co. (Co-Coordinator)

2018: Mark Cancilla, Merck & Co (Coordinator)
Jonathan Josephs, Thermo (Co-Coordinator)

2019: Jonathan Josephs, Thermo (Coordinator)

3. Update on the DMPK Interest Group's Impact on the 2016 ASMS Program

We thank the ASMS Program Vice President of Programs Vicki Wysocki for being receptive to our requests and proposals for a comprehensive set of DMPK oriented oral sessions for the 2016 meeting. This responsiveness was reflected in the increased number of DMPK oriented Oral sessions and the positive feedback from the Interest Group attendees. In addition the DMPK-IG workshop was returned to the Monday evening time slot (although we moved it to Tuesday night at the request of a new

workshop). The DMPK oriented oral sessions were:

- Mon AM: Ion Mobility: Small Molecules, Pharmaceuticals, and DMPK
- Mon PM: Antibodies and Anti-body Drug Conjugates
- Tues AM: HRMS for Quantitation in Drug Discovery, Development and Beyond
- Tues PM: Quantitative Analysis in Drug Discovery and Development
- Weds AM: Imaging: Pharmaceuticals and Metabolites
- Weds PM: MS in the Regulatory Environment
- Thurs AM: New Developments in Ionization and Sampling for DMPK
- Thurs PM: MS Solutions for Drug Metabolism Challenges

4. Suggestions on ASMS 2017 Oral Session Topics from DMPK-IG Attendees

The attendees agreed that the current topics were still of high interest and supported expanding on them on the 2017 program, thus suggested oral session topics for ASMS 2017 are

Session Title/ Topic	Day/ Time
Ion Mobility: Small Molecules, Pharmaceuticals, and DMPK	Mon AM
Analytical challenges of microdosing and microsampling studies	Mon PM
Data acquisition approaches for drug metabolism studies	Tues AM
MS Solutions for Drug Metabolism Challenges	Tues PM
Imaging: Pharmaceuticals and Metabolites	Wed AM
HRMS for Quantitation in Drug Discovery and Development	Wed PM
Antibody and Antibody-Drug-Conjugates	Thu AM
Intact Mass Analysis for Protein Quantitation	Thu PM

.Attendees provided many additional suggestions for additional/alternate topics such as:-

Biotransformation of non-small molecules

HRMS in regulated bioanalysis

Antibody drug conjugates and mass spectrometry, DAR analysis, characterization

Met ID of non-P450 metabolites

As an interest group we wish to continue to work with the ASMS Vice President of Programs to identify potential Oral Session topics and Oral Session Chairs. In order to support a strong DMPK focus in future ASMS meetings the DMPK IG encourages people to submit DMPK focused abstracts for oral sessions to the 2017 ASMS.

Based on feedback from Attendees and DMPK IG Members, the DMPK-IG requests returning scheduling the DMPK-IG Workshop to Monday night 5:45 to 7 pm as has been the tradition for many years in the past.

5. Discussion Topic: “Metabolism of Biotherapeutics: When, Why and How”

Biotherapeutics are a steadily growing proportion of the pharmaceutical research and development landscape. Molecules are evolving beyond traditional monoclonal antibodies and antibody-drug conjugates to include bispecifics, truncated mAbs, nanobodies, cyclic and stapled peptides, Ig

fragments, Non-Ig based scaffolds and so on. Understanding the metabolism of these new modalities is an expanding opportunity for mass spectrometry and requires that traditional small molecule scientists adapt to these new large(r) molecules. The goal of the workshop was to stimulate a discussion on the when, why and how for the metabolism of biotherapeutics in the discovery, pre-clinical and clinical arena. A panel offered opening comments on the current state and provided thoughts on where the field is going. Questions from the audience resulted in a robust discussion and a recommendation that the topic be part of the Oral program for ASMS 2017.

Based on this background the four panel speakers provided their expert perspectives:

1. Peptide Metabolite Identification – Mark Cancilla
 - Approach to peptide metabolism for active metabolites
 - Software for data processing peptide metabolites
2. MS approaches to study biotherapeutic variants in vivo – Jack Kellie
 - Biotherapeutic quant, try and understand changes in structure, glycoforms, oxidation, deamidation, etc – what's happening to the protein?
 - Why do we need to do?
3. ADC Biotransformation – Dian Su
 - Metabolites of ADCs – why we study? How the data gets used.
 - Find and Quant active metabolites of linker and payload
4. Therapeutic peptide antibody conjugates - Hongyan Li
 - Understanding biotrans of peptide payload

Following the brief presentations, the audience and Panel Members engaged in an extended discussion with additional viewpoints from the audience adding many points of discussion to the panel members' introduction. The audience interest in this discussion was evidenced by the fact that we had to curtail questions and comments in order for the workshop to finish.

Current Officers for the ASMS DMPK Interest Group:

Kevin Bateman, Ph. D. (Outgoing Coordinator)
Merck & Co.
770 Sumneytown Pike
WP75A-200
West Point, PA
19486
e-mail: kevin_bateman@merck.com

Philip Tiller, Ph. D. (Coordinator for 2017)
RMI Laboratories.
418 Industrial Drive
North Wales, PA
19454
e-mail: philip_tiller@rmilaboratories.com