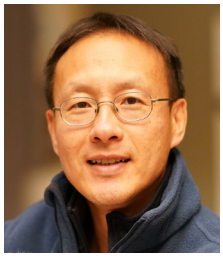
TWO-DAY COURSE, Saturday and Sunday
DMPK: Experimentation and Data Interpretation

Instructors

Naidong Weng
GSK

Mingshe Zhu
Mass Defect Technologies



Wilson Shou
BMS

Mass spectrometry has become the dominant analytical tool throughout the DMPK and bioanalytical research areas in drug discovery and development continuum. This short course will provide thesis on mass spectrometry in DMPK and bioanalysis in support of R&D and the registration process. The course will use case studies to focus on the "why" and "how" knowledge base regarding the use of mass spectrometry to measure small molecule drugs, biologics, and their conjugates in the discovery and development phases. Contents will include an introduction to the concepts / principles of DMPK, an overview of drug discovery / development processes, and common practices in drug metabolism and bioanalytical studies. Current mass spectrometry technologies applied in ADME screening in lead optimization, drug quantification in PK studies, drug metabolite identification in animals and humans, as well as GLP bioanalysis quantification in clinical and toxicology studies will be discussed along with updated industry practices for experimental design, data interpretation, and data reporting. Case studies to solve common drug metabolism and bioanalytical issues will be given to reinforce concepts and analysis techniques learned in class.

Major topics covered in this course

Basic DMPK concepts applied in pharmaceutical research: This portion will include basic principles of drug metabolism and pharmacokinetics, introduction of PK concepts and parameters as well as common metabolic reactions, metabolizing enzymes and metabolism research models.

Role of DMPK in drug discovery and development: This portion will provide an overview of various types of drug metabolism and bioanalytical studies throughout the life time of a drug candidate.

Drug metabolite profiling and identification in drug discovery and development: This portion will cover basic concepts of drug metabolite identification (Met ID) using LC-HRMS technologies. Typical Met ID experiments will be discussed in detailed such as metabolic soft-spot identification and reactive metabolite screening in drug discovery, and metabolite identification and radiolabeled ADME studies in humans in drug development. Focus will be given on applications of a variety of LC-HRMS based data acquisition and data mining techniques to metabolite detection and characterization of small molecule drugs.

Quantitative analysis of drug candidates and their metabolites in vitro and in vivo by LC/MS: This portion will cover science, technique, regulation and compliance of bioanalysis, sample preparation, and LC/MS/MS technologies for quantification in preclinical and clinical studies. Quantification of protein and conjugate drugs by LC/MS also will be discussed. Focus will be placed on LC and MS technology and technique.

High-throughput bioanalysis with LC/MS: This portion will cover the evolution of high-throughput MS techniques for bioanalysis, and discuss the suitability of these HTMS techniques in DMPK studies at different stages of drug discovery and development.

In vitro ADME screening enabled by software/automation and LC/MS: This portion will cover the rationale and conduct of early in vitro ADME screening to optimize ADME and other drug-like properties for lead optimization in drug discovery. Commonly used software and automation technologies to facilitate the high-throughput, high-capacity and fast-turnaround ADME screening workflows will be discussed.

Application of LC/MS technologies in conducting special drug metabolism and ADME studies. This

position will cover evaluating in vitro drug interaction potentials and radiolabeled ADME studies in support drug development, including concept, assay, analytical method and case studies. In addition, strategy and method for studying release and metabolism of payload-containing components from ADCs as well as analytical strategy for studying in vitro metabolism of oligoneucides will be discussed.

Applications of LC/MS in analysis of biologics and biomarkers: This portion will cover recent applications of LC/MS in quantification of protein therapeutics and biomarkers as well as study of biotransformation / disposition of antibody-drug conjugates for characterization of ADME / PK of biologics and PK/PD of small molecule drugs.

Course materials: Electronic copies of PowerPoint presentations and a reference book (M. Lee and M. Zhu. Mass Spectrometry in Drug Metabolism and Disposition: Basic Principles and Applications. John Wiley & Sons, May, 2011) will be provided.

Introduction to Course Instructors

Naidong Weng, Ph.D.
GSK (Naidong.x.weng@gsk.com)

Dr. Weng is Senior Director and Head of LC-MS Bioanalysis and Biomarkers within Bioanalysis, Biomarkers, and Immunogenicity (BIB) at GSK. His global teams are responsible for method development, validation, sample analysis and CRO study monitoring for preclinical and clinical non-GLP, GLP and GCP studies. He also has responsibilities for the protein MS group in BIB supporting project teams across GSK includes target engagement and target turnovers to inform PK/PD modeling and monitoring in vivo structural integrity of biopharm molecules.

Dr. Weng has extensive experiences in broad analytical and DMPK disciplines for both science and compliance. He made numerous contributions to NDA/ANDA/IND submissions of multiple programs including IMBRUVICA. Since 2007, he built strong internal teams and external CRO teams to support JNJ portfolios. He is the DMPK discovery data integrity (DDI) champion and laboratory safety champion. In additional to manage teams of diversified culture and education to support end-to-end bioanalysis or analysis for multiple programs in his career, he is always a hands-on manager. Currently he also has personal responsibilities for bioanalysis of four important programs at clinical stages as the study monitor and bioanalytical representative at the project teams.

He and his team at JNJ is being recognized in the industry for various types of innovation; biomarker bioanalysis and HRMS for simultaneous intact protein bioanalysis and catabolite identification are just two recent research focus areas. He is also an early pioneer of using HILIC-MS/MS for bioanalysis. He co-edited two books on bioanalysis (Eliminating bottlenecks for efficient bioanalysis: practices and applications in drug discovery and development, Future Science, 2014; Targeted biomarker quantitation by LC-MS, Wiley, 2017) and one Special Focus Issue of Bioanalysis on Bioanalytical Laboratory Structure and Management (Bioanalysis, 2014). Dr. Weng has published over 110 peer reviewed scientific papers and organized/presented at various scientific symposiums including AAPS, ASMS, Pittcon, APA, EAS, CPSA etc. He has reviewed well over 170 submitted manuscripts.

Dr. Weng is the US regional editor for Biomedical Chromatography (Wiley). He is on the leadership team for AAPS Bioanalytical Chromatography Working Group. He is the current President for Chinese American Chromatography Association (CACA) and is the President-elect for Chinese American Mass Spectrometry Society (CASMS).

Mingshe Zhu, Ph.D.
MassDefect Technologies, Princeton, NJ, USA (mingshe.zhu@yahoo.com)

Dr. Zhu is an independent drug metabolism and LC-HRMS technology consultant (2017-present). He currently serves as the CSO of MassDefect Technologies that develops and applies new LC-HRMS technology for profiling and identifying metabolites of small molecule drugs and new drug modalities. He also has responsibilities in managing biotransformation projects of Keystone Bioanalytical and XenoFinder. In the last several years, Dr. Zhu has provided drug metabolism consultations to pharma, biotech and CRO companies in USA and China, which include developing new strategies and methods in ADME studies, managing various biotransformation, radiolabeled ADME and DDI studies, and solving drug metabolism issues faced in drug discovery and development. His consulting work has supported IND and NDA filings of many clinical and drug candidates, respectively, and helped the marketing approval of five new drugs (Anlotin, Ensartinib Hydrochloride, Fospropofol Disodium, Donafenib, Olverembatinib) in China. Dr. Zhu previously worked in Dept of Biotransformation, Bristol-Myers Squibb (BMS) (1998-2016), where he and his team supported over 10 discovery programs, more than 15 development drug candidates, and worldwide approvals of ABILIFY (Aripiprazole) and FORXIGA (Dapagliflozin). Dr. Zhu and his collaborators at BMS developed several innovative LC-MS workflows and data-mining technologies such as mass defect filter, background subtraction and multiple ion monitoring for drug metabolite detection and identification, which now are routinely used in drug metabolism research worldwide. Recently, his research interests

have been expanded to ADME studies of unconventional drug modalities, such as ADC, oligonucleotides, peptides, herbal medicines, covalent drugs, and stable isotope labeled drugs. He received Ph.D. in chemical toxicology at SUNY Albany and completed post-doctoral fellowship in drug metabolism at University of Washington. Dr. Zhu served as the chair of the ISSX focus group of “Bioanalysis in ADME Science” (2016-2018) and taught drug metabolism and mass spectrometry short courses at ASMS (2011-present), EAS (2002-2010) and ACS (2006, 2008). He co-edited two books, Drug Metabolism in Drug Design and Development and Mass Spectrometry in Drug Metabolism and Disposition, and co-authored over 100 research articles and reviews. (Selected publications: https://pubmed.ncbi.nlm.nih.gov/?term=Mingshe+Zhu&sort=date&size=100) .

Wilson Shou, Ph.D.
BMS (wilson.shou@bms.com)

Dr. Shou is Scientific Senior Director in the Lead Discovery and Optimization department at BMS. Since joining BMS in 2007, he has been leading a team responsible for centralized high-throughput in vitro ADME (HT-ADME) screening effort for small molecule discovery programs across the entire research portfolio. His team has contributed to the optimization of ADME properties for compounds from several hundred discovery programs, enabling the progression of more than 50 candidates to clinical development. Many of these development candidates have since become marketed drugs, including apixaban (Eliquis), dapagliflozin (Farxiga), asunaprevir (Sunvepra), daclatasvir (Daklinza), rimegepant (Nurtec) and deucravacitinib (Sotyktu), Recently, he also took on additional responsibilities overseeing the MS-based high-throughput screening (HTS) and affinity selection by mass spectrometry (AS/MS) efforts for hit identification and triaging in the lead discovery space.

Dr. Shou is a recognized expert in high-throughput mass spectrometry (HTMS), and has implemented many innovative HTMS approaches, including multiplexed LC/MS, RapidFire-MS, laser diode thermal desorption/MS (LDTD/MS) and most recently acoustic ejection mass spectrometry (AEMS), to increase MS analysis speed and make it compatible with label-free screening applications in HT-ADME and HTS. In addition to HTMS, he also has extensive experience in lab automation, software-assisted MS data interpretation, ML/AI model building, and process improvement & optimization. He received his Ph.D. in analytical chemistry from Georgia Tech, and has authored/co-authored more than 60 peer-reviewed papers, 5 book chapters, and more than 100 podium & poster presentations. Dr. Shou is the co-editor of a book in bioanalysis (Eliminating bottlenecks for efficient bioanalysis, Future Science, 2014), and is currently on the editorial board of Biomedical Chromatography. He has served on the organizing committees for numerous international conferences, and chaired multiple oral sessions at ASMS, SLAS, EAS, CASMS and PITTCON. He has been a committee member of the annual HT-ADME conference since its inception in 2011 and served as the conference chair in 2013. He has been a member of ASMS since 1997 and served on the ASMS Nominating Committee from 2020-2021.