



ISSX

International Society for the Study of Xenobiotics

Volume 46

Issue 1, 2022

ISSX President's Message

By Scott Obach,
ISSX President

Greetings fellow ISSX members and welcome to 2022. We are all truly hopeful that the challenges of 2020-2021 are behind us and we can look to 2022 with optimism. I must admit that I've really missed seeing my many science friends from around the world and am hopeful we will be able to meet again to talk about our science and life in general at the 2022 joint ISSX and MDO meeting in Seattle this September 11-14.

Before looking to what we hope to do in 2022, I want to first give sincere thanks to Ann Daly who very successfully navigated ISSX through the two most difficult years we have ever faced. As an organization that has in-person meetings as a main focus, not being able to do that posed a significant threat to its viability. She, with help from our Association Management Company, Smithbucklin, really came through for us. In fact, one of the crowning successes driven by the challenges

of a global pandemic was the enhancement of a robust webinar series. Thanks to Ann and the Continuing Education Committee for establishing that forum and we have every intention of it continuing as a benefit to ISSX members post-pandemic. If you have an idea for a webinar and/or would like an opportunity to share your research with the ISSX community, please contact us. In particular, this can be a great opportunity for some of our younger members to showcase their latest research and gain valuable visibility. I will state that I have really enjoyed taking an hour from the daily grind to sit back and learn something new from these webinars.

At the forefront of goals for ISSX for the next two years is continuing to address challenges of diversity and inclusion. For centuries, science has been the almost exclusive domain of white males in western cultures and it is astounding to think of how much better the world would be

today if all people in the past had an opportunity to bring their brilliance, creativity, and innovation to humankind, irrespective of their gender, race, nationality, religion, or any other characteristic not aligned with the historical hegemony. There were and are, of course, exceptions but these individuals had to surpass extra hurdles to realize their potential and achieve their success. We won't reverse centuries of the status quo overnight, but we can make strides now so that the future of our science will be one of opportunity, diversity, and equity. To that end, over the past year ISSX has been formulating two new awards to recognize achievement in our field



Scott Obach
ISSX President

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Book Review

CONTEMPORARY ACCOUNTS IN DRUG DISCOVERY AND DEVELOPMENT

Editors; Xianhai Huang, Robert Asanian, Wayne Tang.
John Wiley & Sons Inc.
528 pp. ISBN; 978-1-119-62771-5 (2022).

For those not intimately involved in the pharmaceutical industry, it is sometimes difficult to appreciate the monumental effort that is required to place a drug on the market. The process is lengthy, complex, and costly, and opportunities are sought continually that may shorten this journey without introducing any problems or compromise safety and efficacy. The drug discovery and development processes are explained in detail for several drugs and potential candidates under investigation. The combined aspects of biology and chemistry, together with their application to structure-activity knowledge and relationships, pharmacokinetic and pharmacodynamic features, and clinical investigation are discussed. The case histories presented provide a complete and “wholesome” approach integrating the complex picture involved in the procurement of a medicinal agent.

Thirty authors have come together to write fifteen extensive chapters, the titles of which are as follows. “Current drug discovery: Great challenges and great opportunity. (An introduction to contemporary accounts in drug discovery and development)”; “Advanced computational modelling accelerating small molecule discovery: A growing track record of success”; “Discovery and development of the soluble guanylate cyclase (sGC) stimulator Vericiguat for the treatment of chronic heart failure”; “Finding cures for Alzheimer’s disease: From gamma secretase inhibitors to gamma secretase modulators and beta secretase inhibitors”; “Discovery of novel antiviral agents enabled by structural biology, compact modules and phenotypic screening”; “Discovery of subtype selective agonists of the group II metabotropic glutamate receptors”; “Discovery of Taselisib (GDC-0032): An inhibitor of PI3K α with selectivity over PI3K”; “Drug discovery with DNA-encoded library technology: Inhibitor of soluble epoxide hydrolase to clinical candidate”; “Discovery of HTL26119: Family B GPCR structure-based drug design is now a reality”; “Discovery and potential application of

[¹¹C]MK-6884: A positron emission tomography (PET) imaging agent for the study of M₄ muscarinic receptor positive allosteric modulators (PAMs) in neurodegenerative disease”; “Targeted protein degradation by proteolysis targeting chimeras (PROTACs): A revolution in small molecule drug discovery”; “Entrepreneurial drug hunter: Macrocyclic peptide modalities”; “Application of pyrrolbenzodiazepine (PBD) in antibody drug conjugates”; “Combination therapy case studies in anticancer and anti-infectious disease drug discovery and development”; “Accelerating drug discovery and development: Translational medicine in combating the Covid-19 pandemic.”

This volume contains a wealth of information and will be of interest to a wide range of individuals engaged in the drug discovery, drug development, and medicinal chemistry arenas. It also provides an insight into the lengthy processes involved and shows how different aspects integrate together to provide a fruitful and desired outcome. As such, students whose studies impinge upon this area, should find it of relevance and helpful in their endeavours.

NOTE: For those interested in the above book, another entitled, “Case Studies in Modern Drug Discovery and Development” (Huang X, Asanian R, Eds) [ISBN: 9780470601815: Wiley & Sons], is available containing fifteen chapters concerning the discovery and development of several other therapeutic agents.

Book Alert

Steve Mitchell, Imperial College London, UK

Book Ordering Information

John Wiley & Sons Inc.
9600 Garsington Road
Oxford OX4 2DQ, UK
Tel: +44.1865.776868

111River Street
Hoboken, NJ 07030-5774, USA
Tel: 201.748.6000

Physiologically-based Pharmacokinetic (PBPK) Modeling

An ISSX Virtual Workshop Event • June 7–9, 2022

INVITATION TO ATTEND

Please join us for an exciting virtual workshop, "Physiologically-based Pharmacokinetic (PBPK) Modeling," which has been organized through the efforts of the **ISSX Modeling and Simulation Focus Group** under the leadership of the Focus Group Chairs, Manthena Varma and Yuan Chen.

ABOUT THE WORKSHOP

This virtual workshop will be focused on the advancements in the application of PBPK as a mechanistic tool in the discovery and development setting. The workshop has been structured into three sessions with emphasis on emerging trends such as special population, biomarker-informed DDI modeling, and diverse drug development applications. Each session will include lectures and short presentations, the latter will be selected from the pool of abstracts from the students and industry attendees. Additionally, interactive virtual poster sessions will be planned throughout the course of the workshop. This format will be conducive for scientists from around the world to join, learn, and share their research.

The objectives of these sessions are to provide education on the scope and utility of PBPK modeling, to highlight emerging areas and recent direction, and to share success stories and learnings in drug development and regulatory findings.

WORKSHOP ORGANIZERS

WORKSHOP ORGANIZING COMMITTEE CHAIRS:

Manthena Varma, Pfizer Inc. and Yuan Chen, Genentech Inc.

WORKSHOP ORGANIZING COMMITTEE MEMBERS:

Oliver Hatley, Certara UK Limited, Simcyp Division
Peter Kilford, Labcorp
Yurong Lai, Gilead Sciences
Nita Patel, Eli Lilly and Company
Venkatesh Pilla Reddy, AstraZeneca
Maria Posada, Eli Lilly and Company
Jaydeep Yadav, Merck Research Laboratories
Ping Zhao, Bill and Melinda Gates Foundation

CALL FOR ABSTRACTS

This workshop will feature daily abstract presentations in virtual poster sessions. Additionally, selected abstract authors will have an opportunity to present in the daily lectures and panel discussions with invited speakers. Student and postdoc abstract authors will have an opportunity to compete for best poster presentations as well.

Don't delay! **Submit an abstract** by Monday, April 4, 2022.

WORKSHOP REGISTRATION FEES

	Early Through May 6	Regular May 7–Jun 9
ISSX Member	\$425	\$495
Nonmember	\$565	\$615
Student/Postdoc Member	\$99	\$99
Student/Postdoc Nonmember	\$125	\$125

Register today!

WORKSHOP PROGRAM*

Tuesday, June 7, 2022 | 10:00 am–2:00 pm ET (US)

Session 1: Mechanistic Modeling of PK in Special Population

Chairs: Yuan Chen, Genentech, and Oliver Hatley, Certara UK Limited, Simcyp Division

10:00 am–10:05 am | Welcome and Introduction

10:05 am–10:35 am | Keynote Lecture: Special Populations of Organ Impairment, Pediatrics & Others
To be determined

10:35 am–10:55 am | Organ Impairment PBPK
Tycho Heimbach

10:55 am–11:05 am | Break

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Physiologically-based Pharmacokinetic (PBPK) Modeling

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11:05 am–11:25 am | IQ Ped PBPK Work
James Yates

11:25 am–11:45 am | Regulatory Perspective on PBPK
Modeling of Special Population
Ying-hong Wang, US FDA

11:45 am–11:55 am | Student or Selected Presentation
To be determined

11:55 am–12:05 pm | Student or Selected
Presentation
To be determined

12:05 pm–12:10 pm | Session Closing Remarks

12:10 pm–1:00 pm | Break

1:00 pm–2:00 pm | Poster Session 1

WEDNESDAY, JUNE 8, 2022

10:00 AM–2:00 PM ET (US)

Session 2: Current State of Biomarker-informed PBPK Modeling to Predict DDIs

*Chairs: Nita Patel, Eli Lilly and Company, and Yurong Lai,
Gilead Sciences*

10:00 am–10:05 am | Welcome and Introduction

10:05 am–10:35 am | Keynote Lecture: Utility of
Biomarkers and EVs (Hepatic and Renal) in Assessing
PK Variability
A. David Rodrigues, Pfizer Inc.

10:35 am–10:55 am | Biomarker Informed Prediction
of OATP1B DDIs
Aleksandra Galetin, University of Manchester

10:55 am–11:05 am | Break

11:05 am–11:25 am | Regulatory Perspective on
Transporter and CYP Biomarkers
Xinning Yang, US FDA

11:25 am–11:35 am | Selected Presentation
Emi Kimoto

11:35 am–11:45 am | Selected Presentation
Kenta Yoshida

11:45 pm–12:25 pm | Roundtable Discussion with
Speakers

12:25 pm–12:30 pm | Session Closing Remarks

12:30 pm–1:00 pm | Break

1:00 pm–2:00 pm | Poster Session 2

THURSDAY, JUNE 9, 2022 | 10:00 AM–2:00 PM ET (US)

Session 3: Successful Drug Development Stories and Learnings

*Chairs: Venkatesh Pilla Reddy, AstraZeneca, and Jaydeep
Yadav, Merck Research Laboratories*

10:00 am–10:05 am | Welcome and Introduction

10:05 am–10:25 am | Recent Examples of PBPK
from FDA and Implementation of Verification/validation
in Reviewing PBPK Submissions
Yuching Yang, US FDA

10:25 am–10:45 am | PBPK Joins PMX in Fight
of COVID-19 Therapeutics
Venkatesh Pilla Reddy, AstraZeneca

10:45 am–10:55 am | Break

10:55 am–11:15 am | PBPK Case Studies for
Regulatory Submissions Including Consultant Examples
Karen Yeo, Certara

11:15 am–11:35 am | Recent IQ PBPK Induction Survey
Outcome and Current Status
Tammie Cabalu, Merck

11:35 pm–12:25 pm | Roundtable Discussion with
Speakers

12:25 pm–12:30 pm | Session Closing Remarks

12:30 pm–1:00 pm | Break

1:00 pm–2:00 pm | Poster Session 3

*Program subject to change.

Renew Your ISSX Membership for 2022

Thank you for your membership and support of ISSX!

If you haven't yet renewed, we urge you to remain a part of the premier international association that advances research and education on the interplay of living systems with medicines and chemicals for the benefit of society worldwide by renewing your ISSX membership today.

The **ISSX Webinar Series** is one of our most popular benefits of membership and provides members with the opportunity to learn about a variety of topics presented by leaders in the field. The **ISSX Focus Groups** provide an excellent forum for scientific discourse and members are encouraged to join one or all four groups. In addition, the **New Investigators Group** is very active and this group provides an excellent way to connect with fellow early career scientists to share experiences and tips. Another point of connection for members is the **ISSX Mentorship Program**, which links early career scientists with experienced colleagues to provide career advice and discuss career options. Finally, ISSX members benefit from steep discounts to our highly-rated scientific meetings where they learn about the latest research developments, network with leaders in the field, and present their research in multiple forums. Please make plans to attend the ISSX/MDO 2022 Meeting this September 11-14.

Mark Your Calendar for These Upcoming Events

2022 will be an exciting year to expand your connections. We look forward to greeting you at our virtual and in-person educational events. ISSX members enjoy steeply discounted registration for workshops and meetings. Please save the dates and make plans to join us!

- **April 11-13:** The ISSX Transporters Focus Group is cosponsoring virtual workshop, *Drug Transporters in ADME: From the Bench to the Bedside*, with the American Association of Pharmaceutical Scientists (AAPS). ISSX members will be sent a code to receive the AAPS member rate for registration!
- **April 25:** The American Society for Clinical Pharmacology & Therapeutics (ASCPT) will host a virtual Satellite Session, *DDI Risk Assessment* –

Approaching Global Convergence and Understanding Emerging Innovation. ISSX members will be sent a code to receive the ASCPT member rate for registration!

- **June 7-9:** The ISSX Modeling and Simulation Focus Group is also organizing a virtual workshop, Physiologically-based Pharmacokinetic (PBPK) Modeling. **Registration is now open** and additional details will be announced soon!
- **September 11-14:** ISSX is planning a joint meeting with the Microsomes and Drug Oxidations (MDO) which will be held in person in Seattle, Washington.

More information about these events will be shared soon. Be sure to renew your membership to access the ISSX member discounts to attend!

Please follow the steps below to complete your renewal:

1. Visit issx.org/renew.
2. On the right-hand side of the page, log in with your ISSX username and password. If you do not know your username or password, you may re-set it by visiting issx.org/password.
3. Click "RENEW YOUR MEMBERSHIP NOW" in the blue box at the top of your profile page.
4. On the next screen, review and update your contact information to ensure uninterrupted communication from ISSX.
5. Once you verify your contact information, you will be directed to the payment screen, where you may view your renewal options, including instant payment online via credit card.
 - If you would like to pay by check, select "Bill Me" under Payment. You can access your invoice on the subsequent page and it will be automatically sent to you via email. Please print the invoice and submit it with your check to: **ISSX
8652 Solution Center
Chicago, IL 60677-8006**

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Renew Your ISSX Membership for 2022

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If you have questions about renewing your membership or membership benefits, please contact ISSX by phone at +1-202-367-1160 or by email at information@issx.org.

DONATIONS

ISSX relies on assistance from members and other individuals as well as corporate entities to advance our mission. If you would like to make a gift to ISSX, please visit www.issx.org/donations to learn about the various funds you can support.

ISSX is a 501 (c)(3) organization incorporated in the United States. As such, your contribution may qualify for a tax deduction. Consult your tax advisor for full information. Our federal tax identification number is 22-2432063. If you need a copy of our federal W-9 form, simply email information@issx.org and we will promptly reply.

ISSX President's Message

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in a spirit of diversity and inclusiveness. First, as an international organization, we are starting an award of recognition for Outstanding Achievement by a Xenobiotic Scientist from an Underrepresented Nation. This will be given at the ISSX international meetings and the recipient must be one from a country where it is considerably more challenging to carry out a successful research program. (A list of the eligible nations is derived from a 2020 United Nations assessment of technological readiness of nations and will be made available to members at request.) The upcoming meeting in Seattle is an international one so we hope to make our first award there. Please consider nominating a worthy colleague. The second award is still in the development stage and will be for outstanding scientific achievement by an underrepresented minority in our field. This award will be focused on North America where racial and ethnic groups (specifically Black, Latinx, Pacific Islander, and Native American groups) are grossly underrepresented in STEM careers. An *ad hoc* committee led by Prof. Jose Manautou is developing this award—stay tuned for more on that as it progresses. Awards are just one way to help promote diversity and we look to our membership for thoughts and ideas on how we can strive to achieve this goal.

Please mark your calendars for the upcoming April 11–13 AAPS in-person workshop which is co-sponsored by ISSX and the ISSX Transporters Focus Group: Drug Transporters in ADME: From the Bench to the Bedside.

As part of the co-sponsorship, ISSX members will receive the AAPS member rate to attend. Additionally, the ISSX Modeling and Simulation Focus Group has partnered with the ASCPT for an online Satellite Session of their 2022 Online Annual Meeting on Monday, April 25: *DDI Risk Assessment—Approaching Global Convergence and Understanding Emerging Innovation*. ISSX members will receive the ASCPT member rate to attend – please keep an eye on your email for a special code to receive the discounted rate! The Modeling and Simulation Focus Group is also putting together a virtual workshop to be held June 7–9. More information about the workshop focus and program is included in this newsletter.

Finally, I look forward to the September 11–14 meeting in Seattle. Mike Zientek and his co-chair from Microsomes and Drug Oxidations, Xiaobo Zhong, are assembling what will be an excellent meeting. I am truly hopeful we will be able to assemble (sans masks!) for a reinvigorating exchange of knowledge and ideas. But rest assured that if the global pandemic is not under control by that point we will adjust and adapt either with extra precautions to keep attendees safe at the venue or in a worst-case scenario with another virtual conference.

I look forward to a successful year for ISSX in 2022. See you soon!

Enroll in the ISSX Mentorship Program for 2022!

CALLING ALL ISSX MEMBERS!

The ISSX Mentorship Program pairs young investigators with senior scientists within and across career pathways to discuss career options, review competencies for success, consider challenges and problems, and receive practical advice from experienced scientists. This program is an exclusive member benefit that has seen great success since its inception.

THE 2022 MENTORSHIP CYCLE WILL RUN THROUGH DECEMBER AND ISSX BEGAN MAKING MATCHES IN FEBRUARY 2022

The program matches mentors and mentees based on an award-winning algorithm. From there, the pairs have the flexibility to define their conversation topics to best suit the needs of their relationship. Past participants noted their focus was individual and career development, collaboration, and leadership. Milestones are set along the way for participants to review their desired outcomes of the mentorship, set goals, and provide progress updates.

WHAT DID PREVIOUS ISSX MENTORSHIP PROGRAM PARTICIPANTS SAY?

"I have learned a lot about alternate career paths and different ways that people can get to their current position. Talking with [my mentor] has also given me a lot of insight into how things are run at a larger company. During COVID19, I have felt really lucky to have a professional connection to discuss science and career paths with."

"It is an enriching opportunity to be mentored by [my mentor] in the framework of the ISSX Mentorship Program. I learned what areas of my technical expertise should be strengthened, she gave me the heads up on literature to look at and helped me enhance my organizational and leadership skills. The mentor encouraged me to engage proactively in my personal development and performance."



ISSX
MENTORSHIP
PROGRAM

"I was at a cross section of taking two completely different career paths when I started the program. [My mentor] helped me navigate through this process with thorough introspection and strength identification. Not only did I find my career direction but also who I am. She boosted my confidence and inspired me to reach my greatest potential. I feel so lucky to be her mentee!"

ISSX thanks past participants for their work and dedication to this initiative and we invite you to re-enroll in the program so that you may continue growing personally and professionally.

SIGN UP TODAY!

If you are interested in joining as a mentor or a mentee, please visit www.issx.org/ISSXMentorship to learn more.

ISSX will provide resources to help you launch and sustain effective mentoring relationships. Mentoring is a personal and professional development experience that challenges one to reflect on their own actions and behaviors over time. For those who have benefited from a helpful mentor in their lives or careers, there is often a strong drive to pay this forward to others by serving in the same role.

Finding a true mentor is not always easy. The ISSX Mentorship Program can help and we are proud to offer this valuable resource and opportunity for new relationships, skills, and conversations to develop.

The ISSX Webinar Series

ABOUT THE ISSX WEBINAR SERIES

The ISSX Webinar Series is an engaging and innovative way to hear from and interact with speakers from around the world on a range of topics related to the metabolism and disposition of xenobiotics. Members can participate for free in regularly scheduled live webinars with an exciting range of speakers, as well as watch previous webinars on your own schedule.

ISSX webinars are presented by internationally recognized scientists on a variety of subjects relevant to the field. The ISSX Continuing Education Committee is charged with the responsibility for reviewing these educational offerings and setting the webinar schedule.

MARK YOUR CALENDAR FOR THESE UPCOMING ISSX WEBINARS

April 2022

April 19, 2022 at 11:00 AM ET US (15:00 UTC)

ISSX New Investigator Group Fireside Chat

A Conversation with Sonia de Morais, Ph.D., SdM Biopharma Consultants LLC

About the ISSX New Investigator Group Fireside Chats:

The ISSX New Investigator Group will present a series of Fireside Chats with influential senior scientists in our field. Each chat session will be moderated by a member of the group and the discussion will include wide-ranging topics such as current scientific trends, leveraging your network, and thinking strategically about your career in industry, academia, and/or government.

Questions:

If you would like to submit questions in advance of the session, please submit them to information@issx.org by Monday, April 18, 2022.

About the Speaker:

Dr. Sonia de Morais has an extensive career in research in pharmaceutical sciences both in academia and industry. Following a Bachelor of Science degree in Pharmacy from the University of Sao Paulo state in Araraquara, Brazil, Dr. de Morais gained a Master of Science degree from the University of Bath in England. She then moved to Canada where she conducted doctoral studies at the Faculty of Pharmacy at University of Toronto characterizing the impact of deficiencies in glucuronidation pathways on acetaminophen bioactivation and hepatotoxicity. Dr. de Morais continued her career with a postdoctoral research at the Medical

School of the University of Toronto, in Canada, in the Department of Pharmacology and a postdoctoral fellowship at the National Institutes of Environmental Health Sciences (NIEHS) in North Carolina. Following her research at NIEHS, Dr. de Morais worked as a Research Fellow at Yale University with Dr. Jennifer Doudna, who recently won the Nobel Prize for the discovery of CRISPR. Dr. de Morais started her career in the pharmaceutical industry at Boehringer Ingelheim in Ridgefield, Connecticut in 1995. She led a team of scientists involved in in vitro drug metabolism assays and in vivo PK, in support of project teams in the Discovery and Development phases. She moved to Pfizer in 1999 and started a laboratory focused on drug transporter technology. Her role expanded beyond transporters, to include in vitro drug metabolism and safety assays as well as the development of in silico tools to support hit-to-lead projects. Dr. de Morais moved to Abbott/AbbVie laboratories in 2008 and worked in a lead DMPK role until mid-2016. Her role involved leading all DMPK functions in the North Chicago site, including in vitro high throughput and definitive assays for regulatory filings for drug metabolizing enzymes and transporters, biotransformation, bioanalysis and in vivo pharmacokinetics. Dr. de Morais has been invited to speak at many national and international events and has an extensive publication record. In July 2016, she chaired a session on drug transporters at the Drug Metabolism Gordon conference. She was also part of the International Society for the Study of Xenobiotics (ISSX) council in the role of treasurer, and Head of the Finance Committee. She departed AbbVie in 2016 and is currently working as an independent consultant for the biopharmaceutical industry.

May 2022

May 3, 2022 at 11:00 AM ET US (15:00 UTC)

ISSX New Investigator Group Fireside Chat

A Conversation with Ken Korzekwa, Ph.D., Temple University

About the ISSX New Investigator Group Fireside Chats:

The ISSX New Investigator Group will present a series of Fireside Chats with influential senior scientists in our field. Each chat session will be moderated by a member of the group and the discussion will include wide-ranging topics such as current scientific trends, leveraging your network, and thinking strategically about your career in industry, academia, and/or government.

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The ISSX Webinar Series

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Questions:

If you would like to submit questions in advance of the session, please submit them to information@issx.org by Monday, April 18, 2022.

About the Speaker:

Dr. Ken Korzekwa is Professor of Pharmaceutical Sciences at Temple University School of Pharmacy. He received his Ph.D. in Medicinal Chemistry from the University of Washington and was a PRAT fellow, Staff Fellow, and Senior Staff Fellow at the NIH. Prior to joining Temple University, he has been an Associate Professor at the University of Pittsburgh, was involved in two startup companies, and was Director and Distinguished Senior Investigator at Merck. His research interests are developing predictive models for drug metabolism and pharmacokinetics.

June 2022

June 14, 2022 at 11:00 AM ET US (15:00 UTC)

Predicting Drug-drug Interactions—How do we handle atypical kinetics and time-dependent inactivation?

Presented by Swati Nagar, Ph.D., Temple University School of Pharmacy

Educational Needs Statement:

This webinar is intended to highlight the importance of using numerical method for analysis of in-vitro TDI assays. This webinar will be helpful to folks who are interested in learning about Numerical method and how it is used to improve clinical DDI predictions.

Abstract:

Predicting drug-drug interactions is critical for drug safety especially with patients increasingly being prescribed multiple medications. The presentation will focus on in vitro methods to estimate enzyme kinetics for small molecule metabolism, and use of these kinetic parameters to build predictive models for drug interactions. Atypical (non-Michaelis-Menten) kinetics and time-dependent inactivation will be discussed.

About the Speaker:

Swati Nagar is a Professor in the Department of Pharmaceutical Sciences at Temple University School of Pharmacy. She obtained her Ph.D. in Pharmaceutics at the University of Minnesota in 2003. She completed a postdoctoral fellowship in Pharmacology at Fox Chase Cancer Center in 2005. Swati joined Temple University School of Pharmacy, Department of Pharmaceutical

Sciences in 2005 as Assistant Professor, and was promoted to the rank of Associate Professor with tenure in 2011, and Professor in 2018. She teaches Pharm D and graduate pharmacokinetics.

Swati's lab has a long-standing interest in understanding the disposition of conjugated metabolites, specifically the pharmacokinetics of metabolites with respect to their formation and transport. Further, in collaboration with Dr. Ken Korzekwa, she is developing methods to better understand complex kinetics of time-dependent inhibition. Another key collaborative area of research with the Korzekwa lab is developing models to predict intracellular concentrations in the presence of drug transporters.

Swati has co-authored several peer-reviewed research and review articles, and she co-edited a book titled 'Enzyme Kinetics in Drug Metabolism: Fundamentals and Applications' (Springer/Humana Press; 1st edition 2014; 2nd edition 2021). Swati is a past Chair of the Delaware Valley Drug Metabolism Discussion Group, a past Chair of the AAPS PPDM Drug Metabolism Focus Group, Chair of the 2018 Gordon Research Conference on Drug Metabolism, past member of the steering committee of the International Transporter Consortium, and a member of several professional organizations including ISSX. She currently serves on the editorial board of *Drug Metabolism and Disposition and Xenobiotica*.

Additional webinars will be announced soon! Check the **ISSX webinar schedule** to stay in the know on upcoming scientific lectures and discussions.

Did you miss a recent webinar? Sign into your ISSX membership account and view all past webinars [here](#).

Do you have an idea for a webinar? Submit a Proposal to Present for the ISSX Webinar Series

We want to hear from you! Complete a brief form online to **submit your proposal today**. The information presented in the ISSX Webinar must be balanced and provide the attendee with an objective viewpoint. Proposals for the ISSX Webinar will be evaluated for the ability to provide educational content to ISSX members. The scientific content (merit) of the webinar is subject to review and prior approval by the ISSX Continuing Education Committee (CEC) is needed before proceeding.

Save the Date: ISSX/MDO 2022: The 24th International Symposium on Microsomes and Drug Oxidations and 13th International ISSX Meeting

September 11–14, 2022 | Seattle, Washington

JOIN US IN SEATTLE, WASHINGTON THIS SEPTEMBER!

On behalf of the Meeting Organizing Committee, it is our pleasure to invite you to the 24th International Symposium on Microsomes and Drug Oxidations (MDO) and 13th International Meeting of the International Society for the Study of Xenobiotics (ISSX). This meeting will convene at the Westin Seattle, September 11–14, 2022.

This is the second co-organized meeting for MDO and ISSX and it provides an extremely valuable and truly unique opportunity for researchers to gather and exchange ideas and expertise. In addition to an outstanding scientific program, the meeting provides you with access to state-of-the-art exhibits and ample opportunities to present your work during our poster presentation sessions.

MEETING ORGANIZING COMMITTEE

Meeting Organizing Committee Chairs: Mike Zientek, Takeda, USA, ISSX, and Xiaobo Zhong, University of Connecticut, USA, MDO

Meeting Organizing Committee Members:

MDO:

Huichang Bi, Sun Yat-Sen University, China
Xinxin Ding, University of Arizona, USA
Emily Scott, University of Michigan, USA
Miki Nakajima, Kanazawa University, Japan
Damjana Rozman, University of Ljubljana, Slovenia
Aiming Yu, University of California at Davis, USA

ISSX:

Namandjé Bumpus, Johns Hopkins, USA
Mike Coughtrie, UBC, Canada
Barry Jones, Pharmaron, United Kingdom
Scott Obach, ISSX President, Pfizer, USA
Masayo Oishi, Astellas Pharma, Japan
Allan Rettie, University of Washington, USA



PRELIMINARY PROGRAM*

Sunday, September 11, 2022

Short Course 1: Bioanalytical Short Course

Chairs: Lucinda Hittle, Merck, Rahway, New Jersey, USA and Matthew Albertolle, Takeda Pharmaceuticals, San Diego, California, USA

Short Course 2: Biotransformation Short Course

Chairs: Rheem Totah, University of Washington, Seattle, Washington, USA, and Deepak Dalvie, Crinetics Pharmaceuticals, San Diego, California, USA

Short Course 3: Modeling and Simulation Short Course

Chairs: Manthena Varma, Pfizer, Groton, Connecticut, USA, and Ping Zhao, Bill & Melinda Gates Foundation, Seattle, Washington, USA

Short Course 4: Transporters Short Course

Chairs: Xiaoyan Chu, Department of ADME and Discovery Toxicology, Merck & Co. Inc., Kenilworth, NJ, USA, and Xinning Yang, Office of Clinical Pharmacology, US Food and Drug Administration, Silver Spring, Maryland, USA

New Investigator Meet-up and Concurrent Focus Group Meetings

Opening Keynote Presentation and Panel: Perspectives on Long-held Clearance Concepts

Leslie Z. Benet, UCSF School of Pharmacy, San Francisco, California, USA and K. Sandy Pang, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada

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Opening Welcome Reception with Exhibitors and Posters

Monday, September 12, 2022

Concurrent Focus Group Meetings

Plenary Lecture 1: Cytochrome P450 Interactions with their Redox Partners

Emily Scott, University of Michigan, Ann Arbor, Michigan, USA

Concurrent Symposia 1 & 2

Symposium 1: Advances in in silico ADME and Structure-based Modeling Prediction

Chairs: Christopher Keefer, Pfizer, Groton, Connecticut, USA and Emily Scott, University of Michigan, Ann Arbor, Michigan, USA

Symposium 2: Organization of P450 System and Related Proteins in Biological Membranes

Chairs: Wayne L. Backes, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA and Michal Otyepka, Palacký University Olomouc, Olomouc, Czechia

Concurrent Symposia 3 & 4

Symposium 3: Cryo-EM to Advance Functional and Mechanistic Insights of Enzymes and Transporters

Chair: Yoichi Osawa, University of Michigan, Ann Arbor, Michigan, USA

Symposium 4: 3-D culture, Organ-on-chip, and Microphysical Systems in ADME Studies

Chairs: Baitang Ning, National Center for Toxicological Research of the U.S. FDA, Jefferson, Arkansas, USA and Nina Isoherranen, University of Washington, Seattle, Washington, USA

A Tribute to Michael Waterman

ISSX Awards Presentations

The 2022 R.T. Williams Distinguished Scientific Achievement Award

Award finalist to be determined.

The 2022 Frederick J. Di Carlo Distinguished Service Award

Award finalist to be determined.



Tuesday, September 13, 2022

Plenary Lecture 2: Gut Microbiome and Drug Metabolism

Kiran Patel, College of Osteopathic Medicine, Davie, Florida, USA

Concurrent Symposia 5 & 6

Symposium 5: Clinical Development Impact Stories of Micro Dosing and Microtracer Studies

Chairs: Marie Croft, Pharmaron ABS, Inc, Germantown, Maryland, USA and Graeme Young, GSK, Ware, Hertfordshire, United Kingdom

Symposium 6: Role of Non-coding RNAs in Xenobiotic Metabolism and Regulation

Chairs: David J. Waxman, Boston University, Boston, Massachusetts, USA and Kyoungyun Kim, University of Cincinnati, Cincinnati, Ohio, USA

ISSX Awards Presentations

ISSX Poster Award Finalist Competition Podium Presentations

Award finalists to be determined.

NEW: 2022 Award for Outstanding Achievement in Xenobiotic Research by a Scientist from an Underrepresented Nation

Award finalist to be determined.

2022 Distinguished Accomplishments in Drug Discovery and Development Award

Award finalist to be determined.

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ISSX New Investigators Group Session: Advancement and Influencers in the Prediction of Drug Interactions and Human Exposure

Chairs: Jaydeep Yadav, Merck, Boston, Massachusetts, USA and Katrina Claw, University of Colorado, Aurora, Colorado, USA

Attendee Networking Event

Wednesday, September 14, 2021

Plenary Lecture 3: Structure-Metabolism-Toxicity Evaluation of Bioactive Molecules in Drug Discovery

Klarissa Jackson, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Concurrent Symposia 7 & 8

Symposium 7: ADME and Toxicity of Nanocarriers for Drug Delivery

Symposium 8: Clinical Importance of Drug Transporters

Chairs: Aiming Yu, University of California Davis, Sacramento, California, USA and Lauren Aleksunes, Rutgers University, Piscataway, New Jersey, USA



Plenary Session: Drug Discovery from the Trenches

Chairs: Masayo Oishi, Astellas Pharma Inc., Tsukuba, Ibaraki, Japan and Karim Azer, Axcella Therapeutics, Cambridge, Massachusetts, USA

*Program subject to change.

ABSTRACT SUBMISSIONS AND REGISTRATION

Poster presentations are an integral component of ISSX meetings.

We encourage all those involved in the fields of metabolism, pharmacology, toxicology, molecular biology and other related disciplines to consider submitting an abstract for a poster presentation at the ISSX/MDO 2022 Meeting. The abstract submissions and registration site opens soon! Be sure you're signed up to get the latest emails from ISSX by visiting www.issx.org/subscribe

Welcome New Members

The International Society for the Study of Xenobiotics proudly welcomes the following new members. We greatly appreciate their support and hope that each remains aligned and affiliated with ISSX for many years to come.

2022 NEW MEMBERS

Vikram Arya, Food and Drug Administration, Silver Spring, Maryland, United States

James Cali, Promega Corporation, Verona, Wisconsin, United States

Lisa Cheng, the University of British Columbia, Vancouver, British Columbia, Canada

Tongyi Dou, NIH, Bethesda, Maryland, United States

Charlotte Gabel-Jensen, Novo Nordisk, Maaloev, Denmark, Denmark

Ulrike Gradhand, EMD Serono, Darmstadt, Germany

Murugesh Kandasamy, Indiana University, Indianapolis, Indiana, United States

Prajwala Karnati, Dr. Reddys Laboratory, IPDO, Bachupally, Hyderabad, India

Eva Klásková, Masaryk University, Brno, Czech Republic

Niyanta Kumar, Merck, West Point, Pennsylvania, United States

Parusharamulu Molgara, Suven Life Sciences Ltd, Hyderabad, Telangana, India

Donnia Robins, Merck KGaA, Darmstadt, Germany

Roz Southall, Certara UK, Sheffield, South Yorkshire, United Kingdom

Sandhya Subash, Washington State University Spokane, Washington, United States

Masahiro Utoh, Shin Nippon Biomedical Laboratories, Ltd., Tokyo, Tokyo Head Office, Japan

Gautam Vijaywargi, Dr. Reddy's Laboratories Ltd, Hyderabad, Telangana, India

James Yates, GSK, Stevenage, Hertfordshire, United Kingdom

ISSX Focus Groups

ISSX Focus Groups provide ISSX members with a great opportunity to network with your colleagues while discussing topics relevant to the day. Your participation in the ISSX Focus Groups help us to enhance the exchange of the most current scientific research information and open doors to endless opportunities for collaboration and career advancement. View the latest from the ISSX Focus Groups and join today!

BIOANALYSIS IN ADME SCIENCE

The aims of this group include: (a) to promote state-of-the-art analytical technologies to solve challenging issues faced in ADME studies and bioanalysis, (b) to enable industrial scientists to actively contribute to and participate at ISSX meetings and associated activities, and (c) to enhance synergy between industrial scientists and academic researchers.

BIOTRANSFORMATION, MECHANISMS, AND PATHWAYS

Points for discussion include: (a) metabolism-directed drug design (e.g., incorporation of D to reduce metabolic liability), (b) mechanisms underlying biotransformations that yield “unusual” metabolites and characterization of the metabolizing enzymes responsible for their formation, and (c) idiosyncratic immune-mediated toxicity via metabolism (e.g., reactive metabolites).

MODELING AND SIMULATION

This group focuses on the role of modeling and simulation in drug development in all stages, including topics such as (a) translational extrapolations from preclinical data to clinical expectations, (b) drug-drug interactions, (c) extrapolations of PK/PD data to special populations, (d) early dose optimization, and (e) selection of doses for clinical testing.

TRANSPORTERS

The goals of this focus group are to disseminate and promote state-of-the-art research and foster collaborations among ISSX members on the role of transporters in drug disposition, drug interactions, efficacy, and toxicity, and their impact on drug discovery, development, and regulatory decision making.

UPCOMING EVENTS

The ISSX Transporters Focus Group is cosponsoring virtual workshop, **Drug Transporters in ADME: From the Bench to the Bedside**, with the American Association of Pharmaceutical Scientists (AAPS) to be held April 11–13. ISSX members will be sent a code to receive the AAPS member rate for registration!

The ISSX Modeling and Simulation Focus Group is organizing a virtual workshop, Physiologically-based Pharmacokinetic (PBPK) Modeling from June 7–9. **Registration is now open** and additional details will be announced soon!

In Memoriam, Tsuneo Omura

July 29, 1930–January 29, 2022

Adapted from a piece originally published in ASBMB Today.



The biochemical community, especially his colleagues in the field of cytochrome P450, lost one of its true pioneers with the death of Professor Tsuneo Omura on 29 January 2022. He discovered cytochrome P450 in his work with the late Prof. Ryo Sato at Osaka University, and a Clarivate search

indicates that a JBC paper (J. Biol. Chem. 239, 2370-2378, 1964) describing the work has been cited at least 12,700 times. Tsuneo Omura was an Honorary Member of the ASBMB, a distinct honor.

Tsuneo Omura was born 29 July 1930 in Shizuoka Prefecture, Japan. He graduated from the University of Tokyo with a B.S. in Chemistry and then worked as an Instructor and Lecturer in Chemistry at Shizuoka University. The course of his doctoral work and advancement was rather unique compared to our current systems, but in 1960 he joined Prof. Ryo Sato's laboratory at the Osaka University Institute for Protein Research as an Associate Professor. In 1961 he was awarded a D. Sc. in Biochemistry from the University of Tokyo, based on the work he had performed at Shizuoka University. It was during the early 1960s in Osaka that Omura and Sato published three major papers about the discovery of P450 (including the very highly cited one in the JBC), plus seven others in related areas. From 1964-1966, Omura was a visiting scientist at the Johnson Foundation of the University of Pennsylvania (with Ronald W. Estabrook) and then Rockefeller University (with Philip Siekevitz). He returned to the Osaka Institute for Protein Research and then moved in 1970 to the position of Professor of Biology and Molecular Biology at Kyushu University, a position he held throughout his career until he assumed Emeritus status in 1994. From 1995-1997 he was a Visiting Professor of Biochemistry at Vanderbilt University (with Michael R. Waterman and others).

Prof. Omura made many contributions to the field of P450 research throughout his career. These include studies on the regulation of P450s and, in particular, trafficking of P450s in both the endoplasmic reticulum

and mitochondria. His studies with mitochondrial P450s, specifically the cholesterol side chain cleavage enzyme, led to an enhanced understanding of the regulation of these P450s by proteins such as Ad4BP/SF-1, a steroidogenic transcription factor.

Not surprisingly, Prof. Omura was a leading figure in Biochemistry in Japan, and many of his students went on to very productive careers. Along with Honorary ASBMB Membership, Omura received the first R. T. Williams Award from the International Society for the Study of Xenobiotics in 2001, and he was also honored at the 1994 International Microsomes and Drug Oxidations (MDO) meeting. Omura continued to attend and actively participate in meetings many years after his retirement. He presented a plenary lecture at the 2018 MDO meeting in Kanazawa. Tributes were also made to him at a special 2012 meeting in Fukuoka, commemorating 50 years since his discovery of cytochrome P450.

Tsuneo Omura will be remembered as a humble and very thoughtful man. He was very friendly, communicative, and always very anxious to help young scientists and lend his advice. His laboratory was always open to visitors from abroad, and he was very happy to help people throughout the 91-plus years of his life. Many visitors recall his joy in driving his guests all around Kyushu with many stops at pottery-making artisans and notable sites, including the active volcano, Mt. Aso. Due to his warm personality and erudite knowledge, many students were attracted to him. During 24 years of his tenure in Kyushu University, 112 undergraduate students and 42 graduate students joined his laboratory, and 33 of them took Ph. D. degrees under his thoughtful and persistent guidance. All the students spent meaningful and valuable time in his laboratory, and he created an atmosphere of camaraderie and mutual respect. He was a true sensei in every sense of this Japanese title of honor.

Prof. Omura was preceded in death by his wife, Yone (9 December 2000), and is survived by their three children. Obviously, he was loved by many scientists in the field, and he will be missed.

Written by F. Peter Guengerich, Bettie Sue S. Masters, Ken-Ichirou Morohashi, Masahiko Negishi, & Hiroshi Yamazaki

In Memoriam, Brian Kevin Park

June 24, 1951–January 27, 2022



Kevin Park's outstanding career at the University of Liverpool spanned nearly 50 years, and centred on the disciplines of pharmacology, toxicology, and medicinal chemistry. His contributions to improving drug safety nationally and internationally made

major impact in terms of benefiting individual patients, public health, Government policy and the pharmaceutical industry.

Kevin graduated with a BSc in Chemistry from the University of Liverpool in 1971, followed by a PhD in Organic Chemistry in 1975. He then spent 2 years as a postdoctoral fellow in the Department of Biochemistry, before accepting a lectureship in the Department of Pharmacology and Therapeutics. Kevin's appointment was transformational for the Department, where he established new areas of research, developed one of the largest research groups in the University, and progressed rapidly through the academic ranks, becoming Wellcome Senior Lecturer in 1983 and, in 1989, a Wellcome Principal Research Fellow (the most prestigious of the Wellcome Trust's personal awards). In recognition of his excellence in research and teaching, Kevin was promoted to Professor of Pharmacology and Therapeutics in 1989. He then succeeded Professor Sir Alasdair Breckenridge to become Head of Department for Molecular and Clinical Pharmacology in 1999. Kevin was the Founding Director of the MRC Centre for Drug Safety Sciences, established in 2008 as one of the first centres in the world to focus on drug safety. "Human to Molecule and Back Again," the title of a Festschrift held in his honour in 2019, reflected the foundational principles of his outstanding research success. In fact, Kevin's vision was that, "It is all pharmacology..." referring collectively to the fields of conventional pharmacology, toxicology, and drug metabolism that are usually treated as separate disciplines, yet are all about the interactions of drugs from small molecules to macromolecules with the proteins of the body.

The lifelong quest for Kevin was to understand and predict adverse drug reactions based on the chemical structure of the drug and to be able to identify susceptible individuals. What amazed those who knew him or heard his lectures was how Kevin was able to understand chemistry, immunology, and cell biology in such complex detail. Moreover, his group was always at the forefront of technological innovation to link these disciplines together. Kevin's research contributions were extensive, with more than 700 full scientific publications in the top Pharmacology and Medical journals. He was frequently on the speaker list of major national and international conferences highlighting the reach of his work. These included numerous European and International ISSX meetings, where he was either an invited speaker or session chair. Kevin's wealth of scholarship over the years in a difficult research area led to many prestigious prizes and awards including the Pfizer Medal for Innovative Science (2000), the Barnes Prize from the British Toxicology Society (2017), and an Honorary Fellowship from the British Pharmacological Society (2016), the highest award from the BPS. Additional recognition came from the Royal Society of Chemistry and from ISSX, from which he received the European Scientific Achievement Award in 2012. Kevin's contribution was instrumental in the Department of Molecular and Clinical Pharmacology at the University of Liverpool being awarded the Queen's Anniversary Prize for Further and Higher Education in 2018; this prize, which is the highest accolade for any academic institution in the UK, was awarded by the Prince of Wales and Duchess of Cornwall at Buckingham Palace. In addition, Kevin made enormous contributions to public service through his work with the Medicine and Healthcare Products Regulatory Agency (MHRA)—he sat on various advisory committees including the Committee on Safety of Medicines (1993–2005) and the Commission on Human Medicines (2005–2015). Kevin also gave of his time to ISSX, where he served on the Scientific Affairs Committee and the Awards Committee in the early 2000s, and was a member of ISSX Council (2006–2009).

Kevin was a great teacher and developed the Chemistry-Pharmacology honours course at the University of Liverpool. He supervised a staggering 135 PhD students and numerous postdoctoral fellows throughout his career—he knew all their work thoroughly, and

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In Memoriam, Brian Kevin Park

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interacted frequently with them. He operated an open-door policy, where he was always ready to meet up and discuss data. Where research was not advancing, he would think of possible solutions; he was always interested, and always one step ahead of most of us. He did not suffer fools gladly, yet he was the first to support and mentor his students and colleagues who had work or personal problems with a friendly arm around the shoulder, a supportive comment, probably with a humorous observation thrown in to cheer people up. He recognised that the research endeavour can be very frustrating and stressful, and requires a sprinkling of good fortune as well as dedication and inspiration.

Kevin had an extraordinary drive and scientific intellect, and he was held in the highest esteem for his sharp mind, his wit, his genuine interest, and his scientific rigour and integrity. The world of pharmacology has lost

one of its greatest original thinkers and scientists. His parting leaves us saddened, but honoured to have had the privilege to have known and worked with a true great. He leaves a remarkable legacy with very many of his PhD students holding professorial positions in universities and senior positions in industry. Yet, behind all the honours and glittering career was a humble, shy man. Kevin liked nothing better than to chat about the latest research, what his colleagues were finding, and probably bemoan the latest piece of bureaucracy. Then, over a beer or two and a Chinese meal, it was his other passions: cycling and Manchester United!

Kevin is survived by his wife, Caryl, his children Cathryn and Gareth, and his three grandchildren.

Written by Munir Pirmohamed, Dennis Smith, and Tom Baillie.

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