

MEET the EXPERTS

TRANSPORTER CONFERENCE

SEOUL '19
NOVEMBER 14



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SOLVO[®]
BIOTECHNOLOGY
A CHARLES RIVER COMPANY

About SOLVO Biotechnology



SOLVO[®]
BIOTECHNOLOGY
A CHARLES RIVER COMPANY

1999

- The first transporter CRO

2005

- Second laboratory site opened

2012

- SOLVO USA subsidiary opened

2018

- Joined Citoxlab Group; Moved Budapest laboratory site

2019

- Joined Charles River Laboratories

1999 - 2005

- VT and ATPase assays developed for efflux transporters

2005-2012

- Uptake transporter assays (OATs, OCTs, OATPs, PEPTs, NTCP, MATEs) developed

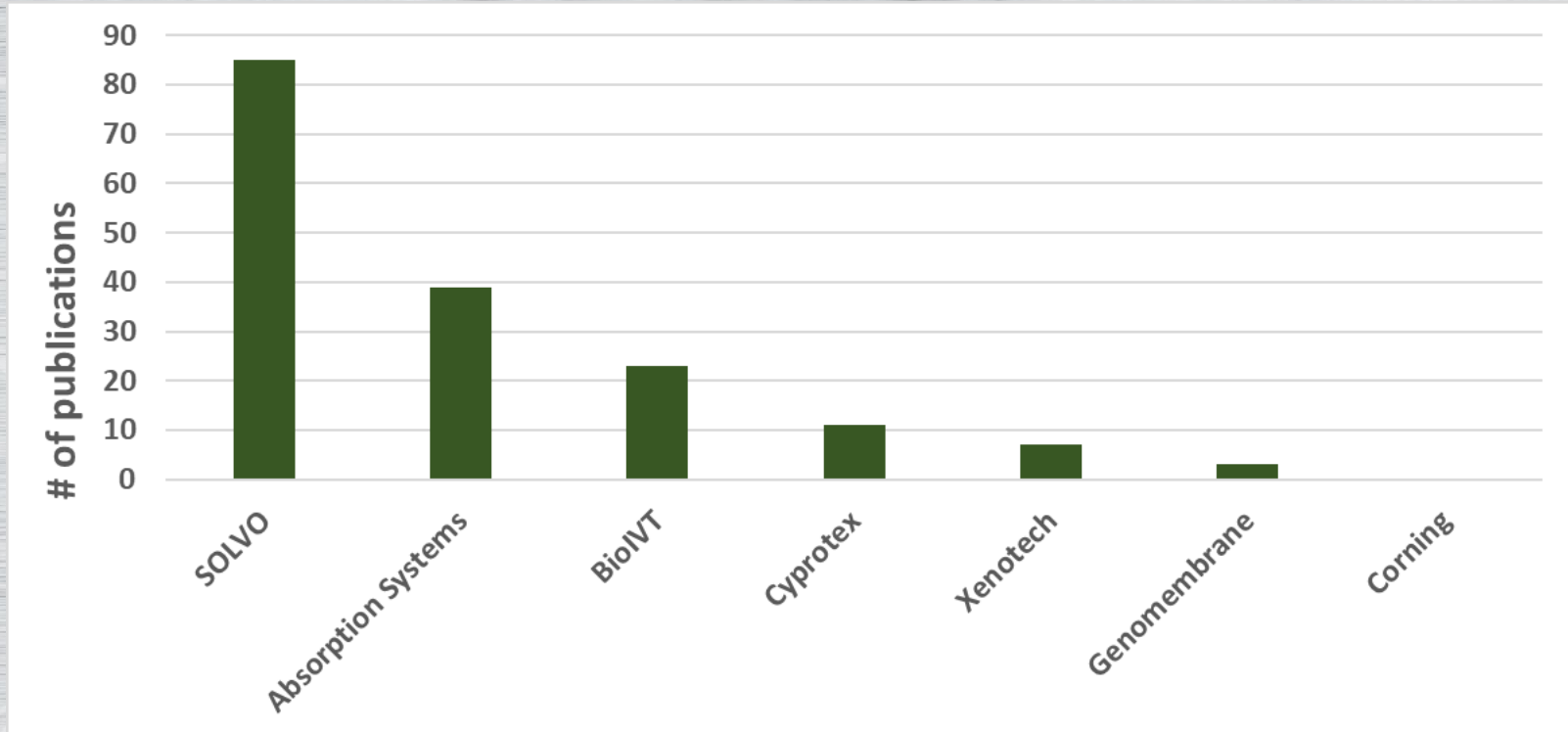
2012-2018

- Preclinical animal transporter models, holistic cell models (B-CLEAR, HepatoPac, aProximate)

2019 Onwards

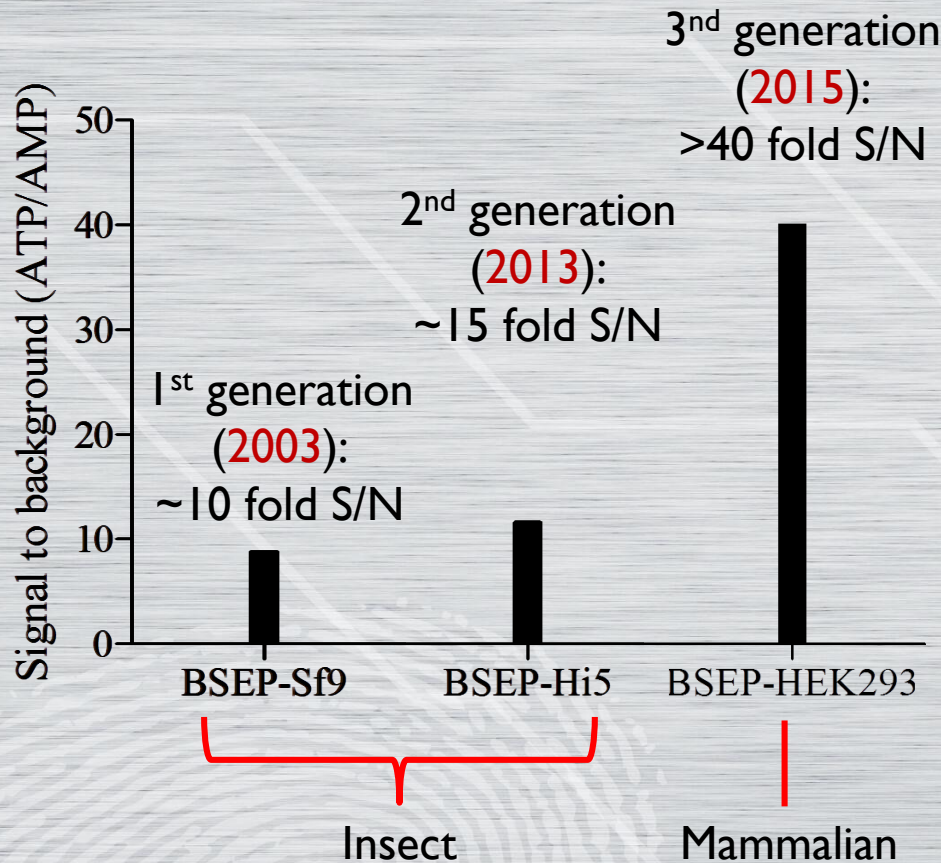
- Expansion of bioanalytical capabilities, automated transporter screening, drug metabolism services

Strong Track Record of Research and Development



- Established reputation for scientific excellence within the field of drug transporters

Driving Innovation in Transporter Research



SOLVO Biotechnology first to market mammalian membrane vesicles

Superior assay performance
>40-fold dynamic range using BSEP-HEK293 vesicles, compared to ~10-fold using traditional Sf9 insect membranes

Over 200 Transporter Products and Services

- Efflux transporter services
 - Vesicular Transport Assays
 - MDCKII Monolayer Assays
 - LLC-PK1 Monolayer Assays
 - ATPase Assays
- Uptake transporter assays
- Custom assay development
- LC/MS-MS quantification of transporter proteins
- qPCR gene expression analysis
- Drug metabolism services
- LC/MS-MS analytics
- Aqueous solubility services
- Protein binding/Non-specific binding
- Rat brain endothelial cell monolayer assay
- Caco-2 and KO monolayer assay
- Hepatocyte uptake , sandwich-culture (B-CLEAR™), and micropatterned co-culture (HepatoPac™) assays
- aProximate™ renal proximal tubule cell assay
 - Human, rodent, dog, cyno *in vitro* predictive & mechanistic tox
 - Bidirectional transport/accumulation assessment

SOLVO Advantage

- **Deep understanding of transporters**
 - 20 years of experience
 - First company to commercialize transporter assays
 - Dedicated R&D team, over 85 transporter publications
 - Flexibility in experimental set-up, from initial screening, through regulatory study design, to detailed kinetic characterization
- **In-house reagent generation and assay development**
 - Not dependent on external reagent suppliers
 - Thorough understanding of assays and experimental variables
 - Experience with custom assay development in multiple assay formats
 - Widest range of transporter products and services on market

13 Years of Regulatory Change

Guidance for Industry

2006: FDA Draft Guidance (P-gp)

Drug Interaction Studies — Study Design, Data Analysis, and Implications for Dosing and Labeling

2007: Formation of International Transporter Consortium (ITC)

REVIEWS

2010: ITC Transporter White Paper (P-gp, BCRP, OATPIBI, OATPIB3, OCT2, OAT1, OAT3)

2010: EMA Draft Guidance (P-gp, BCRP, OATPIBI, OATPIB3, OCT2, OAT1, OAT3, BSEP, OCT1)

2012: Revised FDA Draft Guidance (P-gp, BCRP, OATPIBI, OATPIB3, OCT2, OAT1, OAT3, BSEP, MATEs, MRPs)

2013: Seven ITC Whitepapers Published

2013: Final EMA Guidance (more detailed)

2014: PMDA Guidance published

2017: PMDA Draft Guidance Updated;
FDA Draft Guidance Updated
EMA Concept Paper on Guidance Update
Released (Update expected!)

Guidance for Industry Drug Interaction Studies — Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations



23 June 2012
CHMP/CHMP/560/10/Rev. 1
Committee for Human Medicinal Products (CHMP)

Guideline on the Investigation of Drug Interactions Final

Discussion in the Efficacy Working Party (EWP)	June/October 1996
Transmission to the CHMP	February 1997
Transmission to interested parties	March 1997
Deadline for comments	September 1997
Re-submission to the EWP	December 1997
Approval by the CHMP	December 1997
Date for coming into operation	June 1998
Draft Rev. 1 Agreed by the EWP	April 2010
Adoption Rev. 1 by CHMP for release for consultation	22 April 2010
End of consultation Rev. 1 (deadline for comments)	31 October 2010
Agreed by Pharmacokinetics Working Party	February 2012
Adopted by CHMP	21 June 2012
Date for coming into effect	1 January 2013

This guideline replaces guideline CHMP/CHMP/560/95.

Keywords Interaction, guideline, metabolism, inhibition, induction, transport, enzyme, transport protein, transporter, absorption, food, distribution, PK/PD, PKC, JmC.

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SOLVO Webinars

Leveraging relationships with key opinion leaders, including:

- Caroline Lee
- Jash Unadkat
- Les Benet
- Gerry Kenna
- Maciej Zamek-Gliszczynski
- David Rodrigues
- Dhiren Thakker
- Oliver Langer
- Colin Brown
- Salman Khetani
- Birk Poller
- Mary Paine
- Ken Brouwer

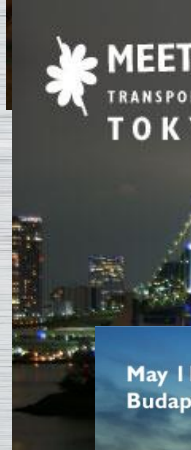
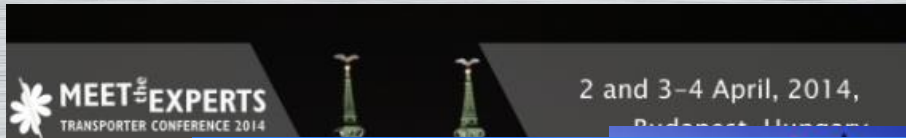


Transporter Book



- Why are transporters important?
- What are the expectations of regulatory agencies?
- How to study transporters?
- Where do transporter interactions occur?
- Which transporters to study?

Meet The Experts Symposia



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NOVEMBER 14

May 1
Budapest



Agenda - AM

Chair: Joe Zolnerciks, PhD, Vice President of Business Development, SOLVO Biotechnology

TIMING	DURATION (min)	TOPIC	SPEAKER
09:15-09:45	30	Registration and Coffee	
09:45-10:00	15	Opening	Joe Zolnerciks, PhD, Vice President of Business Development, SOLVO Biotechnology
		Drug Discovery and Development	
10:00-10:40	40	Keynote: The Next Frontier in ADME Science: Predicting and Verifying Tissue Drug Exposure	Jashvant Unadkat, PhD, Professor of Pharmaceutics in the School of Pharmacy, University of Washington, Seattle, US
10:40-11:10	30	Contribution of Xenobiotic Transporters to Drug Disposition	Jasminder Sahi, PhD, Senior Director, Department of Translational Medicine and Exploratory Development, Sanofi-Aventis (China), Shanghai, China
11:10-11:40	30	<i>In Vitro</i> Platforms for De-risking Nephrotoxicity	Colin Brown, PhD, Institute for Cell & Molecular Biosciences, Newcastle University, Director of ADMET Technology, Newcells Biotech, Newcastle, UK
11:40-12:40	60	Lunch Seminar: Solutions by SOLVO to support your ADME-Tox research: Beáta Kovács, M, PhD, Account Manager, SOLVO Biotechnology	

Agenda - PM

Chair: Roelof de Wilde, Director of Sales, SOLVO Biotechnology

		Barriers and Transporters	
12:40-13:20	40	Keynote: Regulation Mechanism of P-gp in the Blood-Brain Barrier	Tetsuya Terasaki, PhD, Professor, Division of Membrane Transport and Drug Targeting, Department of Biochemical Pharmacology and Therapeutics, Tohoku University Graduate School of Pharmaceutical Sciences, Tohoku, Japan
13:20-13:50	30	Long-lasting Inhibition of OATPs: Update on the Mechanisms and Impact	Woojin Lee, PhD, Associate Professor, College of Pharmacy, Seoul National University, Seoul, Korea
13:50-14:20	30	OATP2A1/SLCO2A1 Determines Prostaglandins' Action by Distributing Them to the Required Place at the Right Time	Takeo Nakanishi, PhD, Professor, Takasaki University of Health and Welfare Faculty of Pharmacy, Takasaki, Japan
14:20 - 14:50	30	Coffee Break	
		Transport and Metabolism	
14:50-15:30	40	Keynote: Food Effect on Intestinal Transporters ASBT and OATP2B1	Ikumi Tamai, PhD, Professor, Institute of Medical, Pharmaceutical and Health Sciences, Faculty of Pharmaceutical Sciences, Kanazawa University, Japan
15:30-16:00	30	Integrated In Vitro and In Vivo Approaches to Drug Metabolism Investigations - a Study Case	Massimiliano Fonsi, PhD, DMPK Director, Citoxlab, a Charles River Company, France
16:00-16:30	30	Nasal Route for CNS Drug Repurposing and Novel Delivery to the Brain	Joan Z Zuo, PhD, Professor and Director of the School of Pharmacy at the Chinese University of Hong Kong, China
16:30-16:50	20	Closing remarks	Roelof de Wilde, Director of Sales, SOLVO Biotechnology
16:50-18:00	70	Reception	

Thank you to our sponsor!

