Tentative Outline
Special Issue for Current Drug Metabolism (CDM)

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TITLE: *In Silico* Meets *In Vitro* Techniques in ADMET profiling of Drug Discovery

Aims & Scope:

In order to improve speed, informed decision making, cost effective progression and importantly humane methods of drug discovery the scientific world is decreasing use of *in vivo* works and increasing use of *in silico* and in vitro methodologies. The effective integration of biorelevant *in vitro* models and data generated from those systems to simulate and predict the human conditions is norm of the day. Increasing recognition of Physiology based pharmacokinetics (PBPK) models by different regulatory authorities' in understanding drug-drug interaction, human dose projection is a prime example of the global trend. Computer aided identification of metabolic soft spots, using structural properties of drug metabolizing enzymes have helped medicinal chemists to tackle cytochrome P450-mediated drug disposition and associated risks. Pharmacokinetics and pharamacodynamics models (PK-PD) have helped understanding in the large molecules area, where obtaining tissue concentrations is a challenge.

The improvement of molecular biology techniques over the years have helped scientists to express human proteins in different systems, thus providing tools to understand importance of either single enzyme or transporter in overall disposition of a compound. Similarly, the advancement in microphysiological systems (MPS) provided scientists with *in vitro* tools that holistically represent either an organ or a system. These have improved understanding in complex phenomena and diseases such as drug-induced liver injury (DILI), non-alcoholic steatohepatitis (NASH), Cancer, in addition to assist in identifying different disease related biomarkers. Providing in vitro tools also necessitate exploration of biorelevant, easy to use probe substrates to understand interaction of compounds with different enzymes or transporters. Endogenous probe substrates have the additional advantage of feasibility of being used as biomarker. Integration of in vitro data from each enzyme or transporters necessitates modelling and simulation works. Finally, prediction to human conditions involves use of the models refined by using data from relevant preclinical species, with data from human enzymes or transporters.

6-8 Keywords:

ADMET, Biodistribution, In silico, In vivo, PBPK, PK-PD, MPS

Subtopics: (Paper titles along with the Contributors complete name, affiliation and emails)

1. Impact of drug-target complex accumulation on target inhibition: A case study of a biologic targeting a soluble protein. Devang Shah[1] and Anjaneya Chimalakonda[2]

[1](Senior Principal Investigator - Pharmaceutical Candidate Optimization)
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[2](Director, Clinical Pharmacology and Pharmacometrics, Biostats, CP&P – BMS, LVL, NJ)

2. Lean liver volume as a potential scaler for in vitro-in vivo extrapolation of drug clearance in obesity. Jaydeep Sinha[1,*], Stephen B Duffull[1], Bruce Green[2] and Hesham S Al-Sallami[1]

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3. Biodistribution, Pharmacokinetics and Metabolism of siRNA based therapeutics: Vikrant Gohil[1] and Kusum Gupta[2]

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4. Advancement of in silico and in vitro techniques in ADMET profiling of drug discovery

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Schedule:

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Revision Due: February 28, 2020

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Final manuscripts due: March 20, 2020

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