Dear readers,

The inaugural Microphysiological Systems World Summit will take place in New Orleans, Louisiana from May 30 to June 3, 2022. Building on the two virtual pre-conferences in 2021, the organizers have put together an exciting scientific program and aim to establish an international MPS society. This hybrid event can be attended in person or remotely. Keep a lookout for the Abstract Book, which will be published in *ALTEX Proceedings* ahead of the conference.

Staying on the subject, with this issue we introduce the first contributions to a *Special Issue* on Microphysiological Systems in Drug Development and Safety Testing, which is being compiled by the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) Microphysiological Systems (MPS) Affiliate. All content of the *Special Issue* can be viewed at doi:10.14573/altex.22S1.

Terry Van Vleet introduces the background and aims of the *Special Issue* in an editorial. In a review article, Diane Ramsden and colleagues explore the potential role MPS can play in the discovery and development of oligonucleotide therapeutics (ONTs), which are novel medicines that target gene expression. They argue that because ONTs are often species-specific, human cell-based MPS may be better suited for characterizing their pharmacology, ADME, and toxicity than animal models. Szczepan Baran et al. report on a workshop of the IQ MPS Affiliate with the Food and Drug Administration (FDA) on how complex *in vitro* models, including MPS, are already being used by pharmaceutical companies and within the FDA, and on how the technology can be evaluated and qualified for different contexts of use.

In this issue's Food for Thought … contribution, Sebastian Hoffmann et al. offer their insight on how evidence-based methodology can help to assess and potentially reduce uncertainties in the health risk assessment of exposure to chemicals.

Given the myriad potential variations of engineered nanomaterials (ENMs), testing their safety in animals is not feasible. High-throughput new approach methodologies (NAMs) may be more suited and informative. To identify opportunities for the use of NAMs in ENM testing, Elijah Petersen et al. compile information on the types of ENMs that are of interest to the different relevant US federal agencies and on the guidance for ENM testing that is already in place.

Knowing that valproic acid and some of its analogues cause fatty degeneration of the rodent liver, Nanette Vrijenhoek and colleagues compare how the expression pattern of a panel of 3000 relevant genes in human hepatocytes changes when challenged with 18 analogues of valproic acid. The authors integrate this biological information into a read-across strategy to improve the prediction of the safety profile of the analogues and underpin it with a mechanistic explanation for the differences in activity among the analogues.

Ans Punt et al. investigate how different ways of characterizing 44 chemicals as input for a computer model of human physiology-based kinetics affect its prediction of the maximum concentration a chemical would reach in serum (C_{max}). By comparing the models' outputs to legacy data on these chemicals from animal experiments, the authors identify the best methods of characterizing the chemicals to gain results that approach the *in vivo* results.

Much of the research in the 3Rs field focuses on developing and applying models representing humans. Charlotte Deschamps and colleagues turn our attention to *in vitro* models of the digestive tract of dogs. Such models that include the different gut compartments and gut microbiota have potential uses in research on dog food and veterinary drug development.

Seeing that the numbers of fish embryos or larvae used for proteomics studies to date range over three orders of magnitude, Laura Langan and Bryan Brooks investigate the minimal number of fish embryos and larvae needed per sample for reliable and sensitive proteomics studies to inform environmental chemical safety assessments.

A letter by Miriam Jacobs et al. calls attention to the potential uses of concentration-response data in the development of new *in vitro* test guidelines and requests test developers to provide such quantitative data in their submissions to regulatory bodies. Laure-Alix Clerbaux and colleagues report on the 3rd CIAO AOP Design Workshop while Shihori Tanabe et al. report on the first two Mystery of Reactive Oxygen Species Conferences.

The Corners include a special tribute to Horst Spielmann on the occasion of his 80th birthday. Congratulations!

Last but not least, a BenchMarks contribution by Giorgia Pallocca and colleagues kicks off a new mini-series considering the complexities of the question "Are animals useful as a model?" This first part of the series lays out the many facets of the question and focusses on the aspect of robustness, also termed reliability or reproducibility.

Hoping you enjoy this issue of ALTEX,

Sonja von Aulock
Editor-in-chief