Dear readers,

the 12th World Congress on Alternatives and Animal Use in the Life Sciences in August finally brought the community together again to exchange, connect, and reenergize our work towards our common goal of replacing, reducing, and refining animal experiments and improving the health and safety of humans, animals, and the environment. We can already look forward to WC13 in Rio de Janeiro, Brazil in 2025!

In this last issue of *ALTEX* for 2023, Thomas Hartung considers how artificial intelligence techniques such as machine learning and deep learning can benefit toxicology. The article gives an overview of the upcoming technologies and argues that thoughtful design and responsible development and application of these tools can drive evidence-based toxicology forward.

In the third part of a series of papers on the analysis of skin sensitization data, Andreas Natsch uses a new expanded database with a larger set of chemical potency values to retrain regression models and compare these. He concludes that the human DSA04 dataset is too small and biased to be used as a key dataset for potency prediction, and that the predictivity of the *in vitro* models is similar to that of the LLNA-based models.

Gwen van de Wall and colleagues assess how well results from animal experiments have translated to human clinical trials. In their scoping review they find no evidence of different translational success rates among pharmacology, neuroscience, and cancer research; however, in a different study approach, they find different rates of success for clinical trials among different medical research fields. Further analysis may lead to the identification of factors that determine translational success or failure.

While methods to predict peak plasma concentrations of drugs without the use of animals have been developed, this has not yet been translated to food-related compounds. Takashi Kitaguchi and colleagues find that a combination of *in silico* methods and *in vitro* data from small intestinal epithelial cells (hiPSC-SIEC) predicts peak plasma concentrations of 20 food-related compounds within a factor of 10 of reported values.

The new approach methodologies developed for skin sensitization testing include different test methods assessing the binding of a chemical with skin proteins, i.e., the molecular initiating event in the adverse outcome pathway. Nathalie Alépée et al. compare these methodologies, share an extensive database, and show that all methods have problems predicting poorly water-soluble chemicals and that the DPRA and ADRA produce very similar results. They also discuss the use of new categorization thresholds for specific applications.

Hagen Eike Keßel and colleagues delve into the intricacies of statistics, demonstrating the impact that analysis variants have on the results of benchmark concentration determinations, their confidence intervals, and the final hazard classification. They use case studies on a large existing dataset produced by a developmental neurotoxicity *in vitro* battery; however, the insights also can be translated to other datasets.

Christian Rodriguez Perez et al. explore how Swiss animal protection legislation deviates from Russell and Burch's original definition of the 3Rs. They identify one risky departure and discuss how this could be mitigated, and how Swiss law could be applied more effectively.

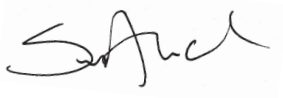
The microphysiological system constructed by Katrina Wisdom and colleagues follows how T cells migrate through 3D endothelium and a stromal barrier to lung tumor cells. This model could help to develop more effective methods to promote T cell infiltration of lung tumors and improve patient response to immunotherapy. Experiments using chemoattractants and inhibitors of translocation effectively characterize the system.

Catharine Krebs et al. investigate the concept of animal methods bias, in which animal data is requested to validate studies produced using non-animal methods during the publication process where they may not be necessary. Their initial survey supports that scientists do sometimes carry out animal experiments solely in anticipation of reviewer requests, are asked to add animal data to studies in some cases, and that they sometimes do not find these requests justified. This survey is complemented by a report on a workshop held on further developing this topic.

In their BenchMarks contribution, Anna-Katharina Holzer et al. discuss the concept of acceptance criteria in relation to new approach methodologies. They explain why such criteria need to be set explicitly to determine the validity of each test run, and they introduce the different types of acceptance criteria.

Meeting Reports, Corners, and a Book Review round off the issue. Note that the ALTEX website hosts a calendar of events such as conferences and webinars and keeps you up to date with developments in the field via announcements.

With best wishes,



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