

ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Food for thought ...

Federica Madia et al.

Making better use of toxicity studies for human health by extrapolating across endpoints

Research Article

Marilena P. Etna et al.

Optimization of the monocyte activation test for evaluating pyrogenicity of tick-borne encephalitis virus vaccine

Research Article

Jon P. Joelsson et al.

Azithromycin has lung barrier protective effects in a cell model mimicking ventilator-induced lung injury

Research Article

Moritz Pfeiffenberger et al.

The *in vitro* human fracture hematoma model – a tool for preclinical drug testing

t⁴ Workshop Report

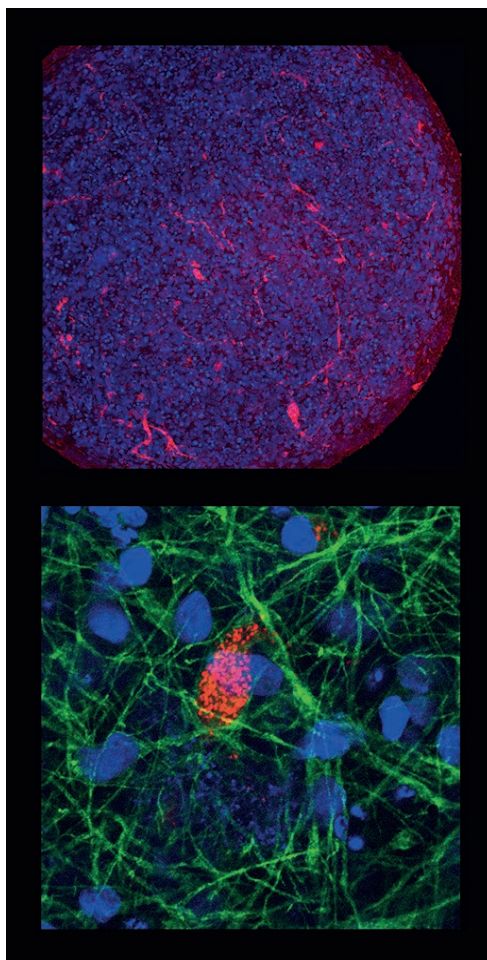
Costanza Rovida et al.

Internationalization of read-across as a validated new approach method (NAM) for regulatory toxicology

Consensus Report

Ans Punt et al.

New approach methodologies (NAMs) for human-relevant biokinetics predictions: Meeting the paradigm shift in toxicology towards an animal-free chemical risk assessment



Research Article

Zunwei Chen et al.

Rapid hazard characterization of environmental chemicals using a compendium of human cell lines from different organs

Research Article

Britta Wareing et al.

The kinetic direct peptide reactivity assay (kDPRA): Intra- and inter-laboratory reproducibility in a seven-laboratory ring trial

Research Article

Andreas Natsch et al.

Predictivity of the kinetic direct peptide reactivity assay (kDPRA) for sensitizer potency assessment and GHS subclassification

Short Communication

C. Korin Bullen et al.

Infectability of human BrainSphere neurons suggests neurotropism of SARS-CoV-2

BenchMarks

Jaffar Kisitu et al.

Chemical concentrations in cell culture compartments (C5) – free concentrations

Letter

Meeting Reports

Corners





Dear readers,

This last issue for 2020 completes my first decade as editor of ALTEX, and I would like to express my heartfelt gratitude to my colleagues, who have all been on the team from the start, for their unfailing enthusiasm and dedication, which made this such a fulfilling and successful time.

Starting off the issue, Federica Madia and colleagues provide Food for thought ... by introducing different approaches aiming to use existing data to predict the results of other regulatory endpoints that would otherwise require animal testing. Their aim is to reduce redundancy and promote and expand the use of non-animal methods for regulatory purposes.

The t⁴ Workshop Report by Costanza Rovida and co-authors lays out the main issues that need to be addressed for the read-across approach for toxicity assessment to gain better regulatory acceptance worldwide and explains how new approach methodologies can contribute. Biokinetics, which is one of these main issues, is dealt with in more detail in a Consensus Report by Ans Punt and co-authors. Biokinetics can inform on relevant chemical concentrations and metabolites that need to be considered in *in vitro* tests. The article discusses how this bottleneck can be unblocked by harnessing new technologies but also by forming an OECD expert group on biokinetics to steer the process.

The monocyte activation test was developed to replace pyrogenicity testing in rabbits for parenteral products. Marilena Etna et al. have successfully optimized the test for batch release of tick-borne encephalitis virus vaccines. The assay is shown to be highly sensitive also for this product but requires an adaptation of the validity criteria.

Patients on ventilators are at risk of developing ventilator-induced lung injury (VILI) owing to mechanical stress. Harnessing their human cell model of VILI to investigate the protective effects of azithromycin, which are unrelated to its antibacterial activity, Jon Joelsson and colleagues show that the cell model can be used to elucidate the mechanistic basis of such anti-inflammatory and barrier-protective effects, supporting its relevance as a non-animal model of VILI.

When a bone is fractured, blood cells from ruptured vessels and bone marrow cells together form a fracture hematoma, within which bone healing starts. Moritz Pfeiffenberger et al. present a novel model of the human fracture hematoma, based on primary human cells cultured under hypoxic conditions, with which either drug-induced inhibition of fracture healing or the rescue of delayed fracture healing can be modeled. Thus, this human-relevant method lends itself to the replacement of animal experiments in early preclinical studies of fracture healing.

Back to back papers by Britta Wareing et al. and Andreas Natsch et al. report on the kinetic direct peptide reactivity assay (kDPRA), a modification of an OECD test guideline test,

which differentiates between strong and weak skin sensitizers. The predictivity of the kDPRA is comprehensively proven based on 180 chemicals in the first paper, and its inter- and intra-laboratory reliability is successfully demonstrated in the second paper. Based on the recommendations of the independent peer review, it is expected that the kDPRA soon will be included in the OECD TG 442C so that it can replace animal tests currently performed for subclassification of skin sensitizers.

Zunwei Chen and colleagues present a high-throughput *in vitro* screening model to assess the toxicity of environmental chemicals based on a panel of five cell types representing liver, nervous system, heart and endothelium, and a matrix of different endpoints. They find that this model is a conservative and fast alternative to *in vivo* tests that can deliver essential risk information for decision-making, e.g., in response to chemical spills.

Reports of neurological symptoms in COVID-19 patients raised the question whether the virus can infect the brain. Korin Bullen and team set out to answer this question in the human induced pluripotent stem cell-derived *in vitro* Brain-Sphere model, in which they found that the ACE2 receptor is expressed. They show evidence of a productive infection with SARS-CoV-2 in a small population of neural cells, indicating that infection of the brain could endanger vulnerable patient populations.

The BenchMarks article by Jaffar Kisitu explores the difference between nominal and free concentrations of chemicals, what factors affect the free concentration, and how it can be estimated. These considerations are essential for comparison of effective concentrations in different *in vitro* assays or their extrapolation to other models or applications.

A letter by Katharina Hohlbaum et al. reports on a survey on the views of animal facility and scientific staff on non-aversive mouse handling after a lecture and discussion on the subject. Meeting Reports on ways to increase the availability of human tissue for research purposes, *in vitro* strategies for food and environmental safety, and COVID-19-related research projects as well as the Corners provide insight into recent 3R-related activities. Please note that current news and upcoming events, including many insightful webinars, are published on our website.

Finally, we wish to thank you, our authors, reviewers, subscribers, readers, members and sponsors, for your continued support of ALTEX in 2020 and hope you and your families stay safe and healthy.

Sonja von Aulock and the ALTEX Edition Editorial Office with Franz P. Gruber and the Board of ALTEX Edition



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Cover Picture

BrainSpheres infected with SARS-CoV-2 analyzed at 72 hpi for viral M protein (red) in relation to neuronal marker MAP2 (green) and nuclei (blue) by immunofluorescence. Excerpt of Fig. 2 from Bullen et al., 665-671.

Aims and Scope

The journal ALTEX – Alternatives to Animal Experimentation publishes open access academic articles on the development and implementation of alternatives to the use of animals for scientific purposes and informs on international developments in this field.

ALTEX publishes research articles, concept articles, opinion articles, reviews, consensus reports, short communications, letters, comments, corners and meeting reports. Current news and events are posted online.

Manuscripts submitted to ALTEX are evaluated by two expert reviewers. The evaluation takes into account the scientific merit of a manuscript and its contribution to animal welfare and the 3R principle.

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