

# ALTEX

## ALTERNATIVES TO ANIMAL EXPERIMENTATION

### Food for thought ...

Thomas Steger-Hartmann et al.

**Introducing the concept of virtual control groups into preclinical toxicology animal testing**

### Research Article

Liana Kramer et al.

**Modeling chemotherapy-induced peripheral neuropathy using a nerve-on-a-chip microphysiological system**

### †4 Workshop Report

Uwe Marx et al.

**Biology-inspired microphysiological systems to advance patient benefit and animal welfare in drug development**

### Opinion Article

Peter M. J. Bos et al.

**Towards an animal-free human health assessment: Starting from the current regulatory needs**

### Research Article

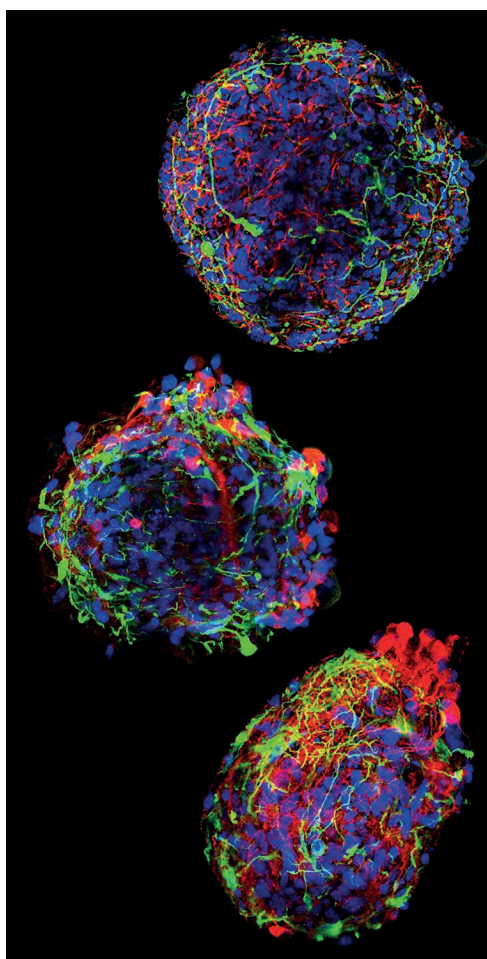
Markus Brüll et al.

**Incorporation of stem cell-derived astrocytes into neuronal organoids to allow neuro-glial interactions in toxicological studies**

### Research Article

Julia Wallstabe et al.

**Inflammation-induced tissue damage mimicking GvHD in human skin models as test platform for immunotherapeutics**



### Research Article

Alžbeta Lišková et al.

**Evaluation of phototoxic and cytotoxic potential of TiO<sub>2</sub> nanosheets in a 3D reconstructed human skin model**

### Research Article

Fenxia Hou et al.

**Performance of a novel *in vitro* assay for skin sensitization based on activation of T lymphocytes**

### Research Article

Domenico Gadaleta et al.

**Automated integration of structural, biological and metabolic similarities to improve read-across**

### Research Article

Yevheniia Nesterenko et al.

**Strategy to replace animal-derived ECM by a modular and highly defined matrix**

Letter

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Corners





## Dear readers,

We are pleased to announce that Dr Pilar Prieto of the EU Commission Joint Research Centre (JRC), Ispra, Italy is the winner of the ALTEX Prize 2020 as first author of the article “Investigating cell type specific mechanisms contributing to acute oral toxicity”. The article was selected by the ALTEX Editorial Board, the Board of ALTEX Edition and the ALTEX editorial office as the best article published in ALTEX during 2019. The award will be presented at the 11<sup>th</sup> World Congress on Alternatives and Animal Use in the Life Sciences in Maastricht in 2021. The annual ALTEX Prize is kindly sponsored by the Doerenkamp-Zbinden Foundation.

In this year’s Journal Citation Report, ALTEX achieved an Impact Factor of 5.787 – it’s second highest to date. The five-year IF now stands at 5.329. We are thrilled that the field of alternatives to animal experiments is consistently gaining attention in the scientific arena thanks to the excellent contributions from our authors and the valuable work of our reviewers.

This issue’s Food for Thought ... contribution introduces the concept of using virtual control groups in preclinical animal experiments as is already implemented in clinical trials. Thomas Steger-Hartmann presents the project initiated by an alliance of pharmaceutical companies to build a database from legacy data and test the concept, which potentially could reduce respective animal use by 25%.

Four years after their first t<sup>4</sup> workshop report on microphysiological systems (MPS), Uwe Marx and colleagues take a look at how far this field has progressed, showcasing progress on a technical and organizational level and proposing a roadmap to efficiently progress MPS to their full potential. The main challenges they identify for developers are achieving a closed vascular system and procuring consistent good-quality cells of all relevant types. Misaligned expectations of the different stakeholder groups are often stumbling blocks that must be overcome by constructive, open communication. In line, the opinion article by Peter Bos and colleagues gives insight into the perspective of regulators, who need specific data to perform risk assessments within their legal framework. They call for intensive, open collaboration of scientists with regulators at early stages of test development to ensure that new tests are tailored to provide information that regulators can use. While keeping the overall goal of a paradigm shift towards non-animal risk assessment in mind, we should appreciate that each new test contributes towards achieving this overall mind-shift.

The closer we are edging towards modeling human physiology *in vitro*, the more we are learning about the contributions of different cell types, their architecture and their environment. Markus Brüll and colleagues report on adaptations made to an *in vitro* model for neurotoxicity testing that make the model more versatile and adaptable to different research questions, including speeding up organoid production, studying neurites separately from soma, and including astrocytes and microglia. With regard to cell environment, Yevheniia Nesterenko et al. present a strategy to replace the use of animal-derived fibronectin as an extracellular matrix coating with a recombinant human self-assembling protein poly-

mer modified with a fibronectin domain. They demonstrate the material’s equivalence in the migration inhibition of neural crest cells assay and are willing to share it with others who wish to test it. In order to predict whether new chemotherapeutics will cause damage to peripheral nerves, Liana Kramer et al. have developed a rat nerve-on-a-chip model that indicates whether compounds cause changes in nerve conduction velocity, nerve tissue fine structure and/or toxicity in order to replace respective animal experiments.

Next to nerves, skin is a major topic in this issue. Cellular therapies, like organ transplants, carry the risk of eliciting graft versus host disease (GvHD). Julia Wallstabe et al. have designed a non-animal model of this form of undesired immunity by adding lymphocytes or the signaling molecules they release upon activation to human skin models. As the ensuing tissue damage can be controlled with immunosuppressants, the model may be used to predict GvHD or to test new therapeutic approaches in a human-relevant setting. Alžbeta Líšková et al. employ reconstructed human skin to assess whether titanium dioxide nanoparticles, which are widely used in sunscreen or cosmetics, are cytotoxic or phototoxic in comparison to reference substances. While demonstrating that the nanoparticles are inert when tested in a relevant model, they confirm the suitability of the assay for photo-irritation assessment of topically applied substances. Fenxia Hou and colleagues now have built an *in vitro* assay for skin sensitization hazard based on the activation of T cells, i.e., the fourth key event in the adverse outcome pathway, and investigated how it can add to the tests for the other key events in the identification of skin sensitizers.

Read-across looks at the known activity of similar compounds to predict the activity of untested compounds. Traditionally, this similarity is assessed only on a structural basis. Domenico Gadaleta et al. present an automated procedure to identify chemical analogues for read-across based on structural, biological and metabolic similarity and test its accuracy on two databases of liver toxins.

If you are experienced with cell culture work, please consider joining the GCCP 2.0 scientific advisory committee as requested in the Letter by David Pamies et al.

Owing to the coronavirus pandemic, many conferences, webinars and other educational activities on the 3Rs have moved online. For example, WC11 will be hosting two webinars on the 3Rs in COVID-19 research in August. Please keep checking our Events page to benefit from these opportunities to stay up-to-date about alternatives to animal experiments. Recent meetings and other 3R activities are summarized in the Meeting Reports and the Corners.

Hoping you stay healthy and productive despite the current circumstances,

Sonja von Aulock



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Follow instructions for authors posted on the ALTEX website.

### Cover Picture

Neuro-glial interaction upon long-term culture and plating of mixed organoids. Confocal optical sections of co-culture organoids with 20% Astro. KN in the organoids. Organoids were fixed and immunostained after 1, 3 or 4 weeks in culture. Excerpt of Fig. 5 from Brüll et al., 409-428.

### 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.

ALTEX Proceedings publishes Abstract Books and Proceedings of scientific conferences. TIERethik is a German-language journal devoted to the bioethics of the relationship between animals and humans.

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