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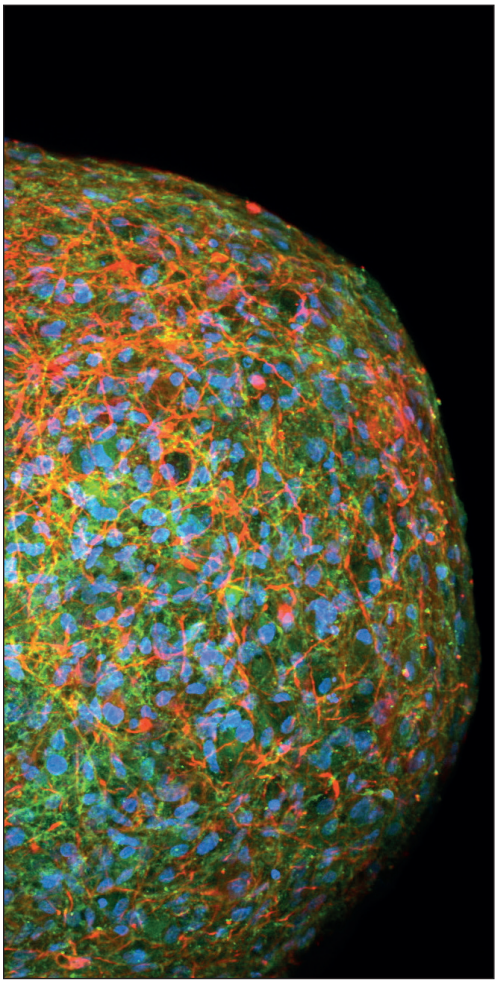
ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION



Springer Spektrum

Dear readers,

We are excited to announce that ALTEX has started a collaboration with the OECD in the review of adverse outcome pathways submitted to the AOP-Wiki and will publish manuscripts generated within this process as AOP Reports. An AOP Report provides an overview of an AOP description, which conforms with OECD GD 344 and has been entered into the AOP-Wiki (https://aopwiki.org/), and describes its 3R relevance and potential application. We are looking forward to the first submissions.

The participants of the EUSAAT 2022 Congress in September clearly enjoyed this in-person meeting and welcomed the networking opportunities that virtual meetings cannot fully replicate. The ESTIV Congress in Barcelona on November 21-25 is an opportunity to continue and expand the discussions started in Linz and learn more about what is hot in *in vitro* toxicology.

This issue starts with a Food for thought … contribution that I wrote with colleagues from CAAT. It calls on scientists in the field of alternatives to animal experimentation to engage more with the public and with policymakers to explain why human biology-based methodologies are necessary and should be supported. Audience-specific communication and preparation of evidence-based messages can help to improve the effectiveness of such outreach activities.

In their study, Qin Wang and colleagues employ a 3D neural spheroid model to detect potential neurotoxicity of drug candidates. They first challenge their model with a large set of pharmaceuticals for which clinical and preclinical data is available to determine cut-offs for their seven endpoints and optimize the accuracy of their approach. They report that the resulting *in vitro* test system has a higher specificity and sensitivity than the animal safety studies and conclude that it is suitable to identify compounds that may be neurotoxic during early drug discovery.

3D spheroids are also the model of choice of Ji-Eun Seo et al., who optimize spheroids generated from the liver cell line HepaRG for genotoxicity testing in the CometChip assay. They test the model with direct-acting and indirect-acting genotoxicants/carcinogens, and with compounds that have shown contradictory results *in vitro* versus in animal experiments. They find that the 3D spheroids have a higher sensitivity than 2D *in vitro* cultures of the same cell line to detect genotoxicants/carcinogens and are more comparable with primary human hepatocytes.

To be able to replace the use of dogs as experimental animals, we need to understand for what purposes they are used. Sherry Ward and Pamela Osenkowski categorize the uses of dogs for biomedical research in the US noted in recent grants and publications and identify the most common uses. They note that basic information typically reported for experimental animals and required by the ARRIVE guidelines on reporting of *in vivo* experiments is sometimes missing or incomplete in publications.

Pharmaceutical products intended for parenteral use must be free from pyrogenic (fever-inducing) contamination. The study presented by Ruth Daniels and colleagues describes the first product-specific GMP validation of the *in vitro* monocyte activation test for testing of three therapeutic monoclonal antibodies. The data for one of the antibodies has contributed to a successful product license application to the EMA.

A set of two articles by Andreas Natsch and Frank Gerberick explores the possible variations and applications of the OECD's defined approaches on skin sensitization. In the first paper, the results achieved with different combinations of two or all three guideline assays are compared using a comprehensive database of *in vitro* and *in vivo* results. The authors find that the predicted points of departure (PoD) are very robust and the misprediction factor is low in most cases. In the second paper, the authors compare different testing sequences to determine how they can be planned most efficiently to generate a PoD in parallel to hazard identification and GHS subclassification.

The article by Patrick Farrell and colleagues and the t^4 Workshop Report by Daniel Krewski et al. complete the *Special Issue* Development of an Evidence-Based Risk Assessment Framework (doi:10.14573/altex.22S2). Farrell et al. describe how health risks of deficiency and excess, for example of nutrients, can be assessed by using categorical regression. They envisage that this method will allow the use of diverse data sets, including data obtained using new approach methodologies, for risk assessment. The Workshop Report describes how the framework was developed and pieces together the outcomes of the associated workshop to present a preliminary evidence-based risk assessment framework.

Animalfree approaches in Parkinson's Disease research are discussed in a second t^4 Workshop Report by Manuela Cassotta et al. Further meeting reports describe a workshop on the replacement of fetal bovine serum in cell culture and the Third Virtual Summer School. The Corners bring you up to date with the latest international developments.

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