

**Dear readers,**

Starting off into 2019, a good New Year's resolution for scientists in our field could be to take a step back and invest some time into looking at how we design, analyze, and report our experiments and to question whether we are up to date with the most recent guidelines that have been developed to aid us to make the most of our work and ensure that others can reproduce and build on the results. To start you off in this direction, Thomas Hartung and colleagues give an overview of activities and guidelines to improve reporting standards and introduce a CAAT-led initiative focused on such standards specifically for *in vitro* studies in this issue's Food for thought ... As a practical start, Jaffar Kisitu et al. discuss concepts and problems around the use of concentrations, doses, their units, and how they are displayed in BenchMarks.

Related issues are discussed in two papers on the zebrafish embryotoxicity test. When a new method is established and multiple laboratories start to use it, inconsistent results between laboratories may be the result of variations made to adapt or improve the protocol. Jon Hamm et al. interviewed different laboratories performing the zebrafish embryotoxicity assay, which is an alternative to the acute fish toxicity test, to identify and differentiate between variations that are likely to have limited *versus* major influence on the results. This information will lead to guidance that can improve the consistency of results between laboratories. In line with this, Anita Birke and Stefan Scholz have retested six narcotic compounds, reported to be incorrectly classified in the zebrafish embryotoxicity assay. When tested in accordance with the OECD TG 236, which requires the measurement of actual exposure concentrations, the substances were classified correctly.

In another research article that uses vertebrate embryos before the last third of gestation (when pain reception becomes possible), Eva Petrovova and colleagues report on the use of the chorioallantoic membrane of the chick and quail embryo to follow the growth of the avian blood vessels into a bioengineered scaffold developed to repair bone defects. A scaffold that is amenable to vascularization allows a better supply of nutrients to bone cell precursors and will thus likely better support bone regeneration.

The synovial membrane lines the capsule of joints and shows pathological changes both in rheumatoid as well as osteoarthritis. Mathijs Broeren et al. have developed and characterized a 3-dimensional *in vitro* model of this membrane containing fibroblast-like and macrophage-like cells, which can be nudged towards either disease state by exposure to TNF $\alpha$  or TGF $\beta$ , i.e., cytokines that are linked to the respective diseases. This human cell-based model may be used to test drugs designed to treat or modulate either disease.

Predicting systemic toxicity of a chemical by non-animal methods is highly challenging because so many different organ systems throughout the body can be affected. Pilar Prieto et al. have compiled the toxicity mechanisms of 114 chemicals for which both *in vivo* and *in vitro* toxicity data are available. This information can form the basis for the development of adverse outcome pathways

and integrated approaches to testing and assessment. But can an adverse outcome pathway, i.e., the chain of events leading from chemical exposure to an adverse health event, be used to predict chemical hazard not only qualitatively but quantitatively? Edward Perkins and colleagues have developed three successful approaches to test this using *in vitro* data and discuss how they can be used in a regulatory context for decision making.

Bacterial sepsis is a highly lethal disease. Many drug candidates that were promising in mouse and rat models failed in humans. Wen Chung et al. have developed a model in which pig spleens from the abattoir are perfused with pig blood to study the invasion and colonization of the organ by bacteria. They can monitor how pneumococci added to the blood are collected by the spleen and grow into clusters after phagocytosis by resident macrophages. Owing to both the architecture of the spleen and the immune system of pigs and humans being more similar, the information gained from the pig organs may translate better to the human patient than data from rodent studies.

Anesthesia and pain management are key elements of the treatment of patients undergoing surgery. But what role does this play when experimental animals are subjected to surgery? Kathrin Herrmann and Paul Flecknell evaluated over 500 German animal research proposals submitted during one year to determine how pain is assessed and managed in mice and rats before, during, and after surgery, and whether adequate anesthesia is regularly provided.

When Allergan announced in 2011 that they had developed an approved cell-based assay to test batches of botulinum toxin that could replace almost all such testing on animals, it was thought that other companies would soon follow suit and numbers of animals used for this purpose would drop dramatically. Katy Taylor et al. find that this is still not the case. They trace the developments in this field and discuss them from the perspective of an animal protection organization.

China's strategy and challenges around adopting alternative methods for cosmetics testing is explained in a letter by Fei-ya Luo and colleagues, and meeting reports and corners provide a synopsis of recent activities. Please consult our website for current news from the field of alternative methods and to plan your participation in 3Rs related events in 2019.

Wishing you continued success in your scientific endeavors.

Sonja von Aulock  
Editor in chief, ALTEX