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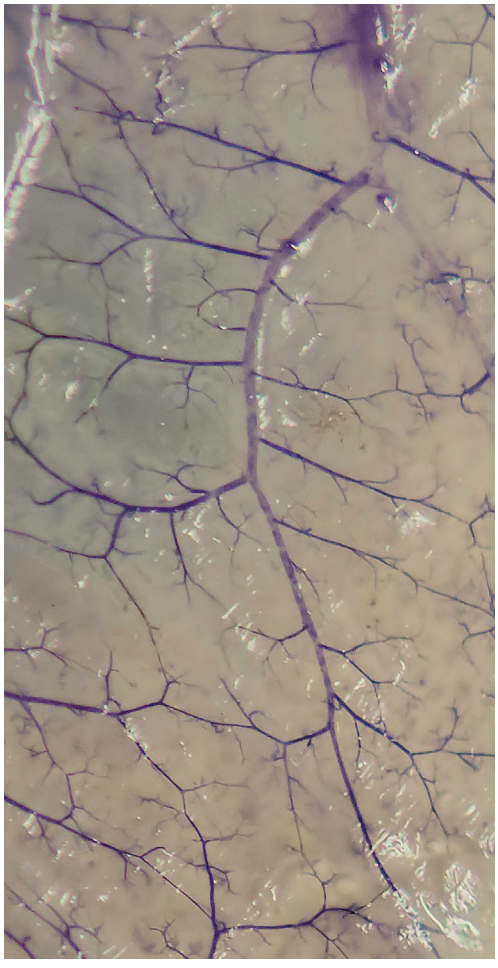
ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION



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Dear readers,

Many *in vitro* experiments involve exposing cells to a fixed amount of a substance and measuring an outcome of interest after a chosen time. Pharmacology teaches us that to characterize a drug we need to know not only how it works but also how much of the applied dose reaches the blood stream, how it is distributed to the various organs, how it is processed in the liver and how and over what time it is excreted. These parameters are also relevant for *in vitro* experiments and for translating information from *in vitro* tests to *in vivo* predictions for toxicological safety assessments. If a would-be toxin is not absorbed into the organism, it cannot have harmful effects. But if a seemingly harmless substance is metabolized in the liver to a toxin, it is a liability. The importance of ADME for alternative methods in toxicology is this issue's Food for Thought … by Katya Tsaioun and colleagues.

Nongenotoxic carcinogens are cancer causing agents that do not directly interact with DNA but cause or promote cancer by other mechanisms. Currently there is no defined strategy to identify such substances. Miriam Jacobs et al. propose such a strategy that can provide the necessary information for regulators to make well-founded decisions. Designing the strategy has identified what kinds of tests reflecting mechanisms of cancer initiation or propagation still need to be developed to fill out the strategy at its different decision levels.

Pesticide residues in food have been linked to a decrease in human fertility. Cédric Pisani and colleagues investigated the possible mechanisms of action of two pesticides using the seminiferous tubules of pubescent rats grown in culture over three weeks. These were assessed for changes in mRNA and protein expression at different time points when exposed to either or both pesticides. The results show what effects the pesticides have on the cells, point towards useful biomarkers by which to test for these effects in a more efficient manner, and demonstrate that mixtures of pesticides, as they are often used in agriculture, can lead to stronger or different effects than either substance alone. This is a first step towards addressing the challenge of assessing the toxicological risk posed by mixtures of substances.

Artificial skin tissue can be grown using the relevant cell types, however it cannot be connected to and fed via the blood system as natural tissue would be because it lacks vasculature. Florian Groeber et al. overcame this drawback by clearing a piece of pig intestine of cells and reseeding it with endothelial cells via the blood vessels and with skin cells via the surface. This model can add a further dimension to *in vitro* skin testing and research as well as open new possibilities for grafting of wounds.

Ilona Kosten and collaborators present a new *in vitro* model of the inner surface of the human mouth and compare its response to allergens to that of a model of skin epithelium. The antigens activated the immune cells in both models but via different mechanisms and they also caused differential changes in surface markers. This is in line with observations that different tissues react differently to allergens and indicates that a single tissue will not suffice for the purpose of sensitization testing.

In a short communication, Amy Clippinger and colleagues investigate why to date only few antimicrobial cleaning products have been tested for their eye irritation potential using an *in vitro* and *ex vivo* EPA-endorsed approach instead of the *in vivo* test and suggest measures to promote the use of the alternative approach in the future. And in a second short communication, Joaquín Valdés et al. describe cultures of rat retinae that respond to sugar changes in the medium that emulate diabetes with cell death of retinal neurons as well as photoreceptors, especially cone receptors. The model may provide insight into the mechanisms of diabetic retinopathy without using live animals.

EU Directive 2010/63 calls for more detailed reporting of animal use for scientific purposes by member states, especially including the number of genetically modified animals bred but not used in experiments and the severity of animal experiments. Katy Taylor and Laura Rego have compiled this data for the year 2014 and uncover numerous shortcomings to report the required information by the member states.

As always, current news, corners and the calendar of events inform you of relevant developments in the 3Rs field.

We thank you for your continued support of and interest in ALTEX in 2016 and look forward to the innovations and breakthroughs that await us in 2017.

Sonja von Aulock
and the ALTEX Editorial Team: Franz P. Gruber, Thomas Hartung, Hans Peter Hoesli, Michael M. Hughes, Goran Krummenacher, Petra Mayr, Carolin Rauter and Joanne Zurlo with Mardas Daneshian and the Board of ALTEX Edition

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