

ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Food for thought ...

Roberta S. Santos et al.

**Sex and media:
Considerations
for cell culture studies**

Research Article

Fabian A. Grimm et al.

**A human population-based
organotypic *in vitro* model
for cardiotoxicity screening**

Review Article

Lindsey K. Borton and

Kelly P. Coleman

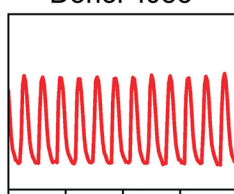
**Material-mediated pyrogens
in medical devices:
Applicability of the *in vitro*
monocyte activation test**

Research Article

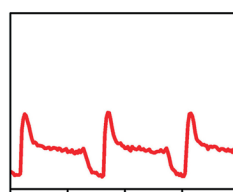
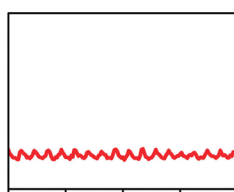
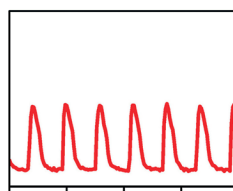
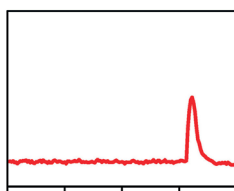
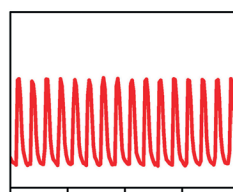
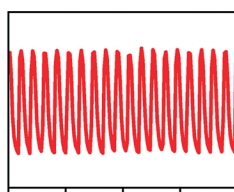
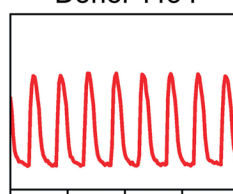
Ann-Cathrin Volz et al.

**Completely defined
co-culture of adipogenic
differentiated ASCs and
microvascular
endothelial cells**

Donor 1083



Donor 1434



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Research Article

Alexander Edwards et al.

**Adaptation of the
human Cell Line Activation
Test (h-CLAT) to
animal-product-free
conditions**

Research Article

Aldo Dekker et al.

**Replacement of
foot-and-mouth disease
virus cattle tongue
titration by *in vitro*
titration**

Research Article

Rita Palmeira-de-Oliveira et al.

**Testing vaginal irritation
with the Hen's Egg
Test-Chorioallantoic
Membrane Assay**

Research Article

Brian D. Chapron et al.

**Reevaluating the role
of megalin in renal
vitamin D homeostasis using
a human cell-derived
microphysiological system**

Letters

Meeting Report

Corners





Dear readers,

ALTEX Edition is very pleased to welcome its new members R2N and Cruelty Free International, who joined during this year, as well as EUSAAT, who will join in 2019. We are grateful to all our members and sponsors for their continuing support, which enables us to keep the article processing costs (APCs) at a reasonable level, to waive the APCs for authors whose institutions have no means to cover them, and to continue to produce a printed version of ALTEX in addition to the open access version. To find out about the benefits we offer our members, please visit [doi:10.14573/altex.aed](https://doi.org/10.14573/altex.aed) or see the membership application form on page 527.

A special thank you goes to the reviewers of the manuscripts published in ALTEX during this year. The time you take to thoughtfully review your colleagues' papers and prepare constructive suggestions is highly appreciated by the authors and by ALTEX.

This issue of ALTEX is an excellent example of the multitude of different, overlapping aspects covered in the field of new approach methods. Are the cells we work with in culture male, female, or something in between, and does their sex affect how they respond to challenges? And how do common endocrine-active components of cell culture media influence these reactions? Roberta Santos and colleagues provide Food for Thought ... on these questions that many have never thought to ask.

Whereas most scientific approaches are reductionist, trying to draw general conclusions for the human population from experiments in single cell lines or inbred mouse strains, Fabian A. Grimm et al. consider how differences between human individuals can be assessed experimentally and factored into a model to better predict potential toxic effects of test substances on the heart of the many different individuals in the human population.

Two contributions assess the use of established new approach methods for novel applications. *In vitro* pyrogen tests were developed more than twenty years ago with the main aim of ensuring that batches of injectable medication are not contaminated with fever-provoking substances. Lindsey K. Borton and Kelly P. Coleman now review the evidence that such tests also can be used to ensure that medical devices will not induce fever reactions, either by releasing pyrogenic substances themselves or via surface contaminations collected during production. Similarly, Palmeira-de-Oliveira et al. show that the Hen's Egg Test-Chorioallantoic Membrane Assay (HET-CAM), which was originally developed for eye irritation testing more than thirty years ago, can also be used to predict irritation to the vaginal epithelia by products intended for this specific use.

In vitro cell culture still widely relies on the use of fetal bovine/calf serum (FBS/FCS). Both the papers by Alexander Edwards and colleagues as well as Ann-Cathrin Volz and colleagues focus on replacing this undefined component in their assays. In the first case this is done for an OECD Test Guideline assay for skin sensitization, demonstrating that the test fulfills its purpose equally well in the ab-

sence of animal-product derived components. In the second case, the target is a basic research model of vascularized fatty tissue and the aim is to improve the robustness and reproducibility of the assay by using more defined components. Here, finding the right balance of components led to a gain of functionality with the endothelial cells organizing themselves into capillary-like structures.

The efficacy of vaccines against foot-and-mouth disease in cattle is tested in challenge experiments where immunized animals are exposed to the virus. Dekker et al. have compiled data from titrations of challenge strains done on cattle tongues over thirty years and compared these with data from *in vitro* titrations with the same samples. They conclude that the *in vitro* titrations are more robust and are suited to replace the *in vivo* approach.

And finally, Chapron et al. show using human kidney cells in a microphysiological system that the role of megalin in vitamin D homeostasis is different in humans than in rats, challenging a hypothesis on the pathophysiology of chronic kidney disease that was formulated on the basis of rodent models. This contribution is an example of how new approach methods are finding their use in basic research and can be used to argue against confirming *in vitro* results obtained using human models with animal experiments.

Reports on the difficulty to reproduce findings reported in scientific papers, termed the "reproducibility crisis", have initiated the proposal to attribute statistical significance to results only when the p value is lower than 0.005 instead of 0.05. In their letter, Konradin Metze and colleagues point out how this change would drastically increase the use of animals and offer alternative suggestions. In his letter, Tilo Weber exposes the worrying development that the stringent ethical evaluation of animal experiments, which should be detailed in each application and be included in the non-technical summary published online, is being reduced to empty phrases or general references to websites of associations that promote animal experiments.

CAAT, Cruelty Free International, and EU-ToxRisk bring you up to date on their recent activities; please visit www.altex.org for an overview of other current developments and conference dates.

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