3/2019
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ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Food for thought ...
Kathrin Herrmann et al.
Beyond the 3Rs: Expanding the use of human-relevant replacement methods in biomedical research

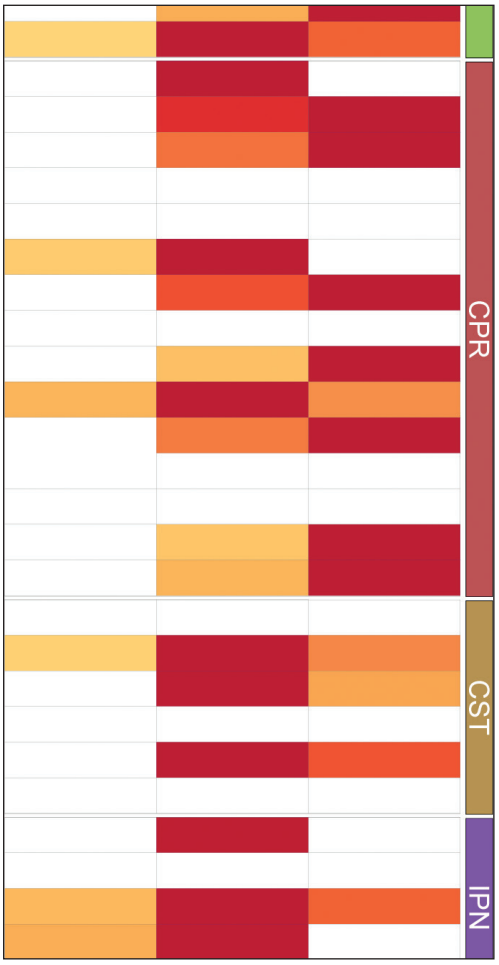
Research Article
Christy M. Foran et al.
A modular approach for assembly of quantitative adverse outcome pathways

Research Article
Haojian Li et al.
Improved defined approaches for predicting skin sensitization hazard and potency in humans

Research Article
Nitin H. Patel et al.
Comparison of *in chemico* skin sensitization methods and development of *in chemico* skin photosensitization assays

Research Article
Diego Marescotti et al.
How complex should an *in vitro* model be? Evaluation of a complex 3D alveolar model with transcriptomic data and computational biological network models

Research Article
Outi Huttala et al.
Presence of vasculature results in faster insulin response in adipocytes in novel *in vitro* vascularized adipose tissue model



Research Article
Aline Chary et al.
An *in vitro* coculture system for the detection of sensitization following aerosol exposure

Research Article
Maria Leontaridou et al.
The impact of precision uncertainty on predictive accuracy metrics of non-animal testing methods

Research Article
Susana Proença et al.
Insights into *in vitro* biokinetics using virtual cell based assay simulations

BenchMarks
Stevie van der Mierden et al.
Software tools for literature screening in systematic reviews in biomedical research

BenchMarks
Christiaan Karreman et al.
SUIKER: Quantification of antigens in cell organelles, neurites and cellular sub-structures by imaging

Short Communication
Letters
Meeting reports
Corners

Springer Spektrum

Dear readers,

we are very pleased to announce the winner of the ALTEX Prize 2019: Fabian Grimm, formerly of the Texas A&M University, now at ExxonMobil Biomedical Sciences, Inc. will be awarded the prize for the best manuscript published in ALTEX during 2018 at the social event of the EUSAAT Congress this October. Congratulations!

We are thrilled that the impact factor of ALTEX has increased further to 6.183. A warm thank you to all scientists who entrust the journal with their manuscripts, to the reviewers who invest their time to appraise the manuscripts and share their critical thoughts and questions with the authors, and to our staff, who shape and polish the texts and figures into articles. It is encouraging to witness the increasing recognition of work on alternatives to animal experiments by the scientific community.

2019 marks the 60th anniversary of the 3Rs, first proposed in the *Principles of Humane Experimental Technique*. This is an excellent time to take a look at how far the field has come and to think about what could be done to more effectively protect animals given the new tools and models that are now becoming available. Kathrin Herrmann, Francesca Pistollato, and our North American editor Marty Stephens provide Food for Thought … on a strategy to step into the next decade.

An adverse outcome pathway (AOP) describes the chain of events leading from an initial trigger to a health issue. Christy Foran and colleagues present a way to model how much deflection of one element will set off the subsequent element of the chain in order to build a quantitative AOP that can predict the relative level of an adverse effect different substances will have on a system.

Haojian Li et al. alert us to the issue that prediction models are often based on data from relatively few substances of which usually more are positive than negative. Using the large Cosmetics Europe database, they have compared data-rebalancing ensemble learning models to improve the predictivity of defined approaches for skin sensitization assessment.

Some skin sensitizers only become active allergens upon exposure to light. Nitin Patel and colleagues demonstrate that modifications of *in chemico* skin sensitization assays that include UV irradiation identify known photosensitizers based on their ability to bind model peptides representing the haptenization process in the skin.

Two manuscripts present work on different versions of the same multi-cell type 3D alveolar model. Diego Marescotti et al. show the contributions of each of four cell types to the functionality of the model using biological network models. They compare the transcriptional profile of their model to that of other *in vitro* airway models and human lung tissue and show that complex model systems built from multiple cell types in a more physiological state closely approach the profile of normal human lung tissue. Aline Chary et al. develop a modification of the model involving also dendritic-like cells to discriminate between respiratory sensitizers and irritants. They describe differences in cytokine release and surface marker expression that allow identification of low and high molecular weight respiratory sensitizers.

Fatty tissue is more than an energy store. Outi Huttala and colleagues show that allowing vascularization of adipose tissue by culturing adipocytes together with human umbilical cord vein endothelial cells allows it to respond faster to insulin and modulates its response to other angiogenic or adipogenic chemicals in comparison to the same model in the absence of vasculature. This well characterized, complex *in vitro* model provides the basis to study the functionality of human adipose tissue without the use of animals.

In developing a test for a biological activity, one naturally aims to find a readout and define a cut-off that clearly discriminates between positive and negative substances. However, the reality is that some substances are falsely identified as positive or negative, respectively. Using data from skin sensitization testing, Maria Leontaridou and colleagues show that evaluation of a test's predictivity is more informative and allows a better comparison with other tests if it includes a description of the variability and the upper and lower limits.

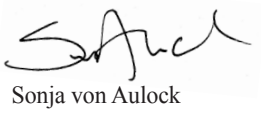
Challenging cells with a chemical seems like one of the simpler parts of a test until you start to ask how much of the chemical you add actually reaches the cells and how this is influenced by the composition of the medium, the incubation vessel, and the chemical's own properties. Susana Proença et al. model the biokinetics of substances in *in vitro* tests to determine the concentrations that are available to the cells under different conditions to allow comparison of results from different tests.

A short communication by George Helman and colleagues introduces a read-across workflow on the EPA CompTox Chemicals Dashboard, and the two letters share experience of the "Valley of Death" between developing and actually implementing an alternative method and ask how often applications for animal experiments are actually rejected in Germany.

The BenchMarks series continues with two contributions: Stevie van der Mierden and colleagues explore literature screening tools for systematic reviews and Christian Karreman et al. introduce an image analysis application they have developed to quantify colocalized fluorescence signals of overlapping cells.

Four Meeting Reports and six Corners bring you up to date on recent and upcoming activities in the 3Rs field; you can find news and a calendar of upcoming events at https://www.altex.org.

Enjoy this issue of ALTEX and see you in Linz in October.



Sonja von Aulock
Editor in chief, ALTEX

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Address
ALTEX Edition
Romanshornerstr. 90
8280 Kreuzlingen, Switzerland
e-mail: editor@altex.org

ALTEX Edition Editorial Office USA
Martin L. Stephens (North American Editor)
Thomas Hartung
Michael M. Hughes

Address
Johns Hopkins University Baltimore
615 N Wolfe Street
W7032 Baltimore, MD 21020, USA
Phone: +1 443 287 2515, Fax: +1 410 614 2871
e-mail: msteph14@jhu.edu

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Submissions
Follow instructions for authors posted on the ALTEX website.

Cover Picture
Biological network analysis of the effects of he addition of immune cells to a complex 3D alveolar model. Excerpt of Fig. 7 from Marescotti et al., 388-402.

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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LINZ 2019

22nd European Congress on Alternatives to Animal Testing

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19th Annual Congress of EUSAAT

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The European 3Rs Society

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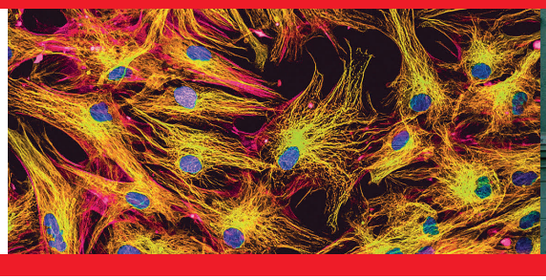
NEW DATE!

10 – 13 October 2019 – University of Linz, Austria



Call for abstracts

Topics/tentative sessions

- Refinement: best practice approaches, animal welfare, avoidance of severe suffering, culture of care
- Reduction: transparency, reproducibility and translational aspects (species differences)
- Replacement: advanced technologies for implementing the 3Rs
- 3Rs in education and academia
- 3R Centers in Europe & international
- International progress in 3Rs research
- 3D Models & multi-organ-chips (MOC), human-organ-chips (HOC)
- Biological barriers
- In Silico Models: toxicology & efficacy of drugs, chemicals & cosmetics, new approaches for biomedical research
- Disease models using HUMAN cells, tissues and organs
- Efficacy and safety testing of drugs, medical devices & biopharmaceutics
- REACH
- Advanced safety testing of cosmetics and consumer products
- Alternatives to animal testing in food safety, nutrition and efficacy
- Specific Endpoints of Toxicity
- Neurotoxicology & Developmental Neurotoxicology (DNT)
- Ecotoxicology
- Stem cell models and technology
- Implementing EU Dir 63/2010
- Ethical & legal issues
- Advanced GMO models – CRISPR/Cas in vivo & in vitro
- Initiative for implementing Serum Free Culture Media
- Publication policies with regard to animal experiments and the 3Rs principles
- An integrated interdisciplinary approach to animal-free nanomaterial and chemical safety assessment: Results of the in3 project
- Vaccines & the 3Rs
- „Young Scientists" session
- Free communications

Deadlines for the submission of abstracts:

for oral presentations: 14 June 2019
for posters: 14 June 2019

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Congress office and further information

appl communications & consulting e. U. | Helmut Appl
A-4225 Luftenberg/Donau | Laimbauerweg 15 | mob/fax: +43 676 410 47 12 | mail: congress2019@eusaat-congress.eu

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