

# ALTEX

## ALTERNATIVES TO ANIMAL EXPERIMENTATION

### Food for thought ...

Lena Smirnova, Nicole Kleinstreuer, Raffaella Corvi et al.

**3S – Systematic, systemic, and systems biology and toxicology**

### Food for thought ...

Russell S. Thomas, Richard S. Paules, Anton Simeonov et al.

**The US Federal Tox21 Program: A strategic and operational plan for continued leadership**

### Research Article

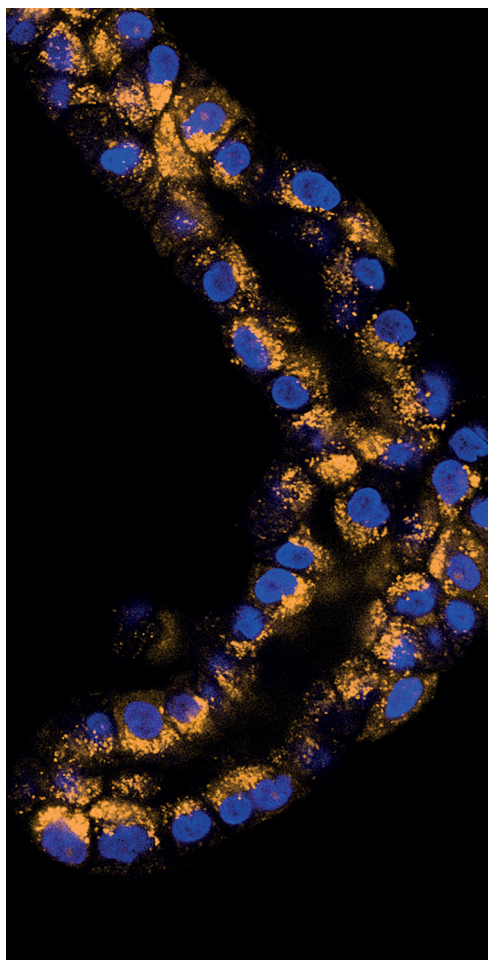
Serena Manganelli, Benoît Schilter, Emilio Benfenati et al.

**Integrated strategy for mutagenicity prediction applied to food contact chemicals**

### Consensus Report

Erwin van Vliet, Jochen Kühnl, Carsten Goebel et al.

**State-of-the-art and new options to assess T cell activation by skin sensitizers: Cosmetics Europe workshop**



### Review Article

Katy Taylor, Laura Rego and Tilo Weber

**Recommendations to improve the EU non-technical summaries of animal experiments**

### Research Article

Philipp F. Secker, Lisanne Luks, Nadja Schlichenmaier and Daniel R. Dietrich

**RPTEC/TERT1 cells form highly differentiated tubules when cultured in a 3D matrix**

### Research Article

Johannes Delp, Simon Gutbier, Stefanie Klima et al.

**A high-throughput approach to identify specific neurotoxicants / developmental toxicants in human neuronal cell function assays**

### BenchMarks

**Normalization of data for viability and relative cell function curves**

Meeting reports  
Corners



**Dear readers,**

We are pleased to hear that the Swiss Competence Center 3RCC is up and running under the direction of Chantra Eskes. The 3RCC will take over the support of research and educational activities in Switzerland from Stiftung Forschung 3R. First insights into the center will be given by Dr Eskes at the Swiss Animal Protection STS conference in Olten this May, which you will find advertised on our website and in this issue. In Italy, the Centro 3R, a collaboration between the universities of Pisa and Genoa to promote the 3Rs in research and education was inaugurated as described in the meeting report written by its director Arti Ahluwalia and collaborators. We wish both centers a smooth start and the best of success in their endeavors.

This issue of ALTEX starts off with two Food for Thought ... contributions. Lena Smirnova and colleagues discuss the challenges facing the replacement of systemic animal tests, i.e., reproductive and developmental toxicity, carcinogenicity and chronic toxicity tests. The authors argue that a combination of systematic reviews and other evidence-based approaches with systems biology and toxicology will be needed to achieve the highly complex goal of predicting effects that develop over long time spans or affect fertility or the offspring. Rusty Thomas and collaborators from EPA, NTP, NCATS, and FDA introduce the new strategic and operational plan of the Tox21 program. Tox21 has generated an enormous amount of data on thousands of chemicals using *in vitro* assays. Future goals are to develop or improve assays to close data gaps, integrate existing data from *in vivo* assays and develop performance standards to achieve regulatory acceptance of this nonanimal data.

Concerns have been growing about untested chemicals leaching from packaging materials into food. Serena Manganelli and colleagues harness different computer algorithms developed on the basis of *in vitro* data to develop a strategy that identifies potentially mutagenic chemicals with high accuracy among a wide range of structures. The strategy, which will be made available as a free software application, may also be applicable to predict the mutagenicity potential of chemicals used for other applications.

T cell activation is the only key event in the skin sensitization adverse outcome pathway for which no mature *in vitro* method is currently available. Erwin van Vliet and co-authors report on the status quo and the consensus reached at a Cosmetics Europe Workshop on how to improve and evaluate respective methods that are under development and how they may be integrated into testing strategies to best predict skin sensitization potential.

Every country in the European Union is obliged to inform the public on what animal experiments are being performed there in the form of non-technical summaries (NTS). Katy Taylor and colleagues investigate where countries are posting NTS online and in what form. Based on their analysis of the content of NTS published by two countries over one year each, they make constructive recommendations on how NTS can be improved to provide information on all relevant aspects to interested parties.

They call for institutions responsible for gathering and publishing NTS to control that the information content fulfils the requirements of Directive 2010/63/EU and to provide NTS within a reasonable timeframe.

Alveolar type I cells form the lung's alveoli where gaseous exchange takes place. They are in close contact with macrophages, which protect them from damage by organic or inorganic particles in the air. Stefanie Kletting et al. have developed a model that combines two cell lines that emulate the respective primary cells' properties at the interface between liquid and air. They find that the model closely reflects the functionality of the lung's air-liquid interface and will be useful to study the uptake and safety of inhaled substances *in vitro*.

A second, highly physiological *in vitro* model, here of the nephron's proximal tubule in which reabsorption and secretion take place, is presented by Philipp Secker and colleagues. This is achieved by culturing a renal proximal tubule epithelial cell line in a three-dimensional matrix. This issue's cover picture impressively shows how the cells arrange themselves into a tubular structure. They express transporter proteins at the appropriate surfaces and the model responds to cisplatin in a manner that more closely models the human toxic response than can be achieved in two-dimensional culture.

Toxicity to the central or peripheral nervous system is a hazard for which most substances have never been tested. Johannes Delp et al. report the results of running the high-throughput *in vitro* NeuroTox and PeriTox tests on a library of 75 compounds. The two-step testing strategies confirm hits and differentiate specific neurotoxicity from general cytotoxicity. Both tests each picked up unique substances known to affect only the central or peripheral nervous system, respectively, and also jointly confirmed the neurotoxic potential of substances that had already tested positive in a previous neurotoxicity test. These tests will allow the screening of large numbers of chemicals without using animals.

Meeting reports and corners bring you up to date on developments in the 3Rs field. More international news can be found on <https://www.altex.org>.

Finally, we are pleased to introduce BenchMarks, a new series in ALTEX dealing with technical issues such as data generation, analysis, presentation, and interpretation coordinated by Marcel Leist. The series aims to call attention to common mistakes in *in vitro* research and to refresh and add to our knowledge of best practice using relevant examples. The first BenchMarks contribution by Alice Krebs et al. deals with normalization of data to 100%.

Hoping you enjoy this exciting new issue of ALTEX,

Sonja von Aulock  
Editor in chief, ALTEX

# LINZ 2018

21st European Congress on Alternatives to Animal Testing

# EUSAAT 2018

18th Annual Congress of EUSAAT

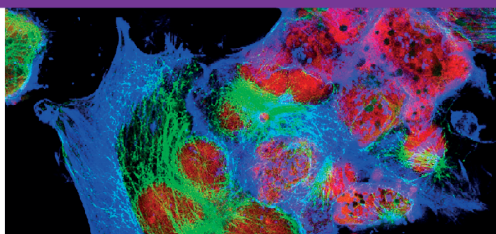
# EUSAAT

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Alternatives to Animal Testing

The European 3Rs Society

[www.eusaat-congress.eu](http://www.eusaat-congress.eu)

**23 – 26 September 2018 – University of Linz, Austria**



## Call for abstracts

### Topics/tentative sessions

- International progress in 3Rs research: New funding initiatives & global cooperation
- Refinement & Reduction: welfare, culture of care, best practice approaches, avoidance of severe suffering
- Replacement – advanced molecular technologies for implementation of 3Rs: bio-printing, -omics technologies, systems biology approaches
- 3D Models & multi-organ-chips (MOC), human-organ-chips (HOC)
- Stem cell models and technology (hiPS, ES, mES, miPS)
- In Silico Models: toxicology & efficacy of drugs, chemicals & cosmetics
- Disease Models using HUMAN cells, tissues and organs
- Implementing EU Dir 63/2010 - update on legal and ethical issues
- 3Rs in education and academia
- REACH I – the most frequently used alternatives: „Read Across, WoE (Weight of Evidence) & QSAR“
- REACH II – meeting the 2018 deadline!
- Advanced safety testing of cosmetics and consumer products
- Alternatives to animal testing in food safety, nutrition and efficacy
- Specific Endpoints of Toxicity: repeated-dose toxicity, inhalation, sensitization, reproductive & developmental toxicity (mEST & hEST), carcinogenesis, nanotoxicology
- Neurotoxicology & Developmental Neurotoxicology (DNT)
- Ecotoxicology
- Efficacy and safety testing of drugs, medical devices & biopharmaceuticals (incl. vaccines, blood components, allergens, somatic cells, gene therapies, tissues, recombinant therapeutic protein and living cells used in cell therapy)
- Intra- and interspecies differences – translational aspects
- Advanced GMO models – CRISPR/Cas in vivo & in vitro
- Biological barriers: lung, gut, kidney & skin, blood-brain & blood-saliva barriers
- Initiative for Implementing Serum Free Culture Media
- „Young Scientists“ session
- Free communications

### Deadlines for the submission of abstracts:

for oral presentations: **31 May 2018**

for posters: **31 May 2018**

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