

ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Food for thought ...

Thomas Hartung

**Rebooting the generally
recognized as safe (GRAS)
approach for food additive
safety in the US**

Research Article

Jorid B. Sørli, Yishi Huang,
Emilie Da Silva et al.

**Prediction of acute
inhalation toxicity using
in vitro lung
surfactant inhibition**

Research Article

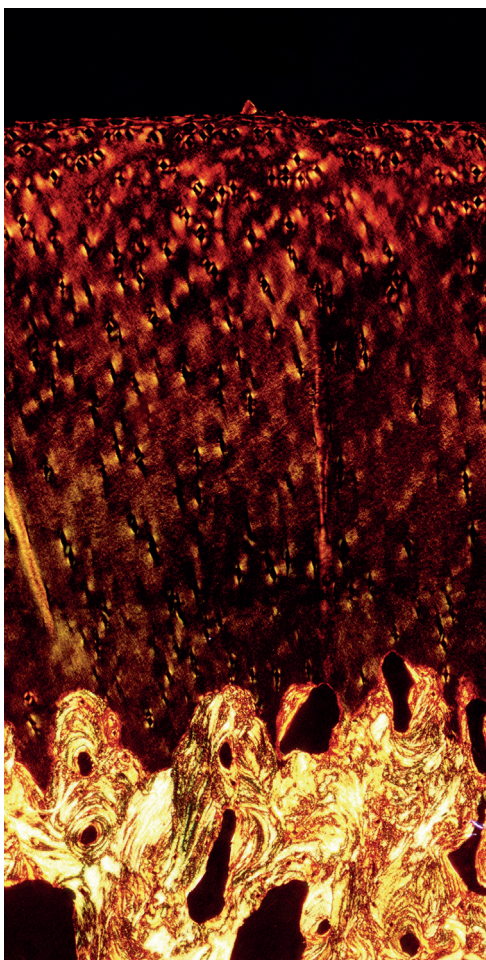
Julita Stadnicka-Michalak,
Melanie Knöbel, Anže Županič
and Kristin Schirmer

**A validated algorithm
for selecting non-toxic
chemical concentrations**

Research Article

Weihsueh A. Chiu, Kathryn Z.
Guyton, Matthew T. Martin et al.

**Use of high-throughput
in vitro toxicity screening
data in cancer hazard
evaluations by IARC
Monograph Working
Groups**



Research Article

Vivian H. M. Mouser,
Noël M. M. Dautzenberg,
Riccardo Levato et al.

***Ex vivo* model unravelling
cell distribution
effect in hydrogels
for cartilage repair**

Review Article

Carola R. Daniel,
Raphael Labens, David Argyle
and Theresia F. Licka

**Extracorporeal perfusion
of isolated organs
of large animals – Bridging
the gap between *in vitro*
and *in vivo* studies**

Consensus Report

Jan van der Valk, Karen Bieback,
Christiane Buta et al.

**Fetal bovine serum (FBS):
Past – present – future**

Meeting reports

Comment

Corners

**Dear readers,**

2018 has already brought some changes to ALTEX. I am very pleased that Martin L. Stephens, Senior Research Associate at CAAT, has agreed to take over the post of North American Editor of ALTEX from Joanne Zurlo, who retired at the end of 2017. Thank you, Joanne, for your support of ALTEX over the past five years!

Our new website at www.altex.org is online! Its new manuscript and issue management system allows authors to follow the progress of their manuscripts throughout the review and production process and the website offers an updated selection of functions for readers. The production of the journal remains in the hands of the dedicated ALTEX team, who will also still be in personal contact with authors and reviewers to ensure that their manuscripts are prepared with care to the high standard you are accustomed to. The printed issues of ALTEX now no longer contain the News or Calendar of Events – instead these are updated on the website continuously.

We are all personally concerned with the safety of our food. In the United States, substances may be added to processed foods if they are “generally recognized as safe” (GRAS). However, this does not mean that reliable safety data is available for all such GRAS substances. The FDA and the US Grocery Manufacturer Association are under pressure to update the system. Thomas Hartung’s Food for Thought ... explains their ongoing efforts and highlights how new approaches, especially replacement and refinement methods, can be included in the safety assessment process, an opportunity to harness modern, validated methodology and reduce or replace animal tests at the same time.

Some impregnation products, used for example to waterproof shoes or flooring, have been reported to cause toxicity to humans upon inhalation. Sørli et al. introduce a nonanimal method to test inhalation toxicity using synthetic surfactant, which mimics the surface tension-reducing properties of surfactant in the human lung. Comparison of the results with animal tests, which the group has refined to require fewer animals and cause less suffering by introducing a humane endpoint, showed good correlation of the results, picking out all products that had been associated with human intoxication cases and all that caused toxic effects in mice. The method may also be suitable for other chemicals that need to be tested for their inhalation toxicity.

Identifying the highest concentration of a chemical that can be used before it has toxic effects and causes cells to die allows us to characterize the substance’s effects and the cellular mechanisms it sets in action. The approach developed by Stadnicka et al. to calculate this non-toxic concentration (NtC) considers both measured and modelled data and was tested successfully in two model systems. It can be applied both to choose suitable substance concentrations for a variety of *in vitro* systems and to refine animal experiments.

The ToxCast™ program is an ongoing effort to screen thousands of chemicals in hundreds of assays to assess their potential risk. These data are collated with other data on the chemicals by the Tox21 collaboration. Chiu et al. describe three case studies on chemicals in which they investigate whether and how ToxCast/Tox21 data can contribute information about how these chemicals cause cancer. Such information can contribute to the risk evaluation of these chemicals in their respective International Agency for Research on Cancer (IARC) Monographs. The group finds that the ToxCast/Tox21 data can fill some information gaps but calls for further high throughput screening methods to address other hallmarks of cancer causing agents not yet covered by the tests.

Filling up cartilage defects with chondrocytes arranged in a suitable three-dimensional matrix is a promising approach to improving cartilage repair. Mouser and colleagues study what concentration of chondrocytes is best and how they should be distributed throughout a hydrogel used to plug defects made in sections of cartilage from equine joints obtained from the slaughterhouse. Samples were cultured over two months. Such *ex vivo* studies can help to reduce the number of animal experiments performed to optimize the methodology.

Experiments on organs obtained from the slaughterhouse under conditions that sustain their function do not provide results at the same speed as *in vitro* experiments; however, they can be the key to obtaining biological information that depends on the different cell types of the organ being in their natural 3-dimensional arrangement and able to communicate with each other without performing experiments on live animals. This field of research has directly benefited transplantation surgery by determining how best to conserve the function of organs outside of the body. Daniel and colleagues review the development of the *ex vivo* organ perfusion methodology, the status of the field and opportunities for the future.

Fetal bovine serum (FBS) or fetal calf serum (FCS) is still an almost universal supplement used in large amounts in cell culture. However, it is associated with a variety of scientific, ethical, safety and supply problems. Jan van der Valk and colleagues explain the history and problems of FBS use and argue for the replacement of FBS with more ethical and, where possible, chemically-defined substitutes based on the successes of these approaches in the field.

Looking forward with you to what further developments 2018 has in store for the 3Rs,

Sonja von Aulock
Editor in chief, ALTEX

ALTEX

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Address

Society ALTEX Edition, Weinmannngasse 86
8700 Kuesnacht ZH, Switzerland
Phone: +41 44 380 0830, Fax: +41 44 380 0832
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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Cover Picture

Picrosirius red staining of cartilage and bone of osteochondral plugs in culture. Excerpt of Fig. 2 from Mouser et al., 65-76.

Aims and Scope

ALTEX is devoted to the open access publication of scholarly articles on alternatives to the use of animals for scientific purposes according to the 3R concept of Russell and Burch: Replace, Reduce and Refine. Articles describing experiments involving the use of animals for scientific purposes must attest that experiments were performed according to the ethical standards set in the instructions to authors and must be described in detail in accordance with the ARRIVE or GSPC guidelines.

ALTEX publishes research articles, short communications, reviews, as well as comments, corners, news and meeting reports.

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.

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