

# ALTEX

## ALTERNATIVES TO ANIMAL EXPERIMENTATION

### Food for thought ...

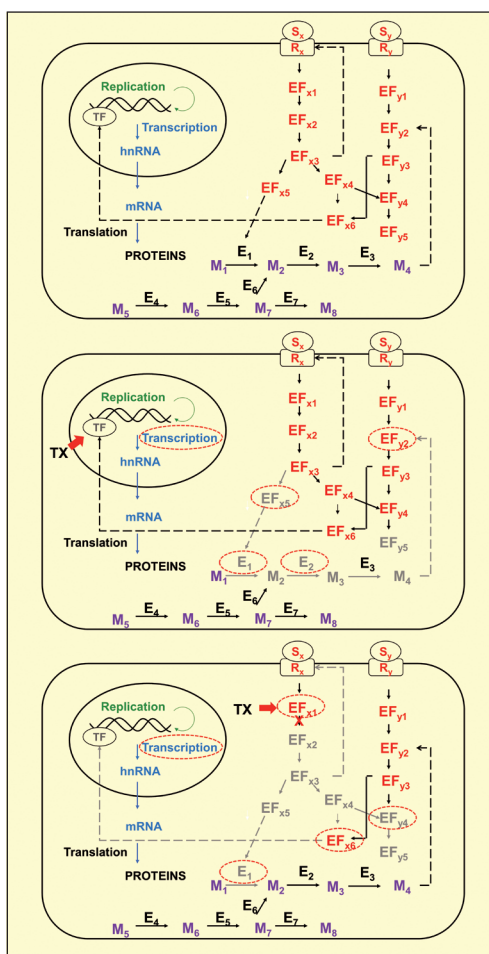
Gian Paolo Rossini and  
Thomas Hartung:

### Towards tailored assays for cell-based approaches to toxicity testing

Marcel Leist, Brett A. Lidbury,  
Chihai Yang, Patrick J.  
Hayden, Jens M. Kelm,  
Stephanie Ringeissen, Ann  
Detroyer, Jean R. Meunier,  
James F. Rathman, George R.  
Jackson, Jr., Gina Stolper,  
and Nina Hasiwa:

### Novel technologies and an overall strategy to allow hazard assessment and risk prediction of chemicals, cosmetics, and drugs with animal-free methods

Leonarda J. van den Broek,  
Frank B. Niessen, Rik J.  
Scheper, and Susan Gibbs:  
**Development, validation,  
and testing of a human  
tissue engineered  
hypertrophic scar model**



Ronald Sroka, Kathrin Weick,  
Stefanie Steckmaier, Bernd  
Steckmaier, Radka Blagova, Ina  
Sroka, Mojtaba Sadeghi-  
Azandaryani, Johann Maierl,  
and Claus-Georg Schmedt:

### The ox-foot-model for investigating endoluminal thermal treatment modalities of varicosis vein diseases

### t4 workshop report:

Bas J. Blaauboer, Kim  
Boekelheide, Harvey J. Clewell,  
Mardas Daneshian, Milou M. L.  
Dingemans, Alan M. Goldberg,  
Marjoke Heneweer, Joanna  
Jaworska, Nynke I. Kramer,  
Marcel Leist, Hasso Seibert,  
Emanuela Testai, Rob J.  
Vandebriel, James D. Yager,  
and Joanne Zurlo:

### The use of biomarkers of toxicity for integrating in vitro hazard estimates into risk assessment for humans

Letter  
Erratum  
Conference reports  
Workshop reports  
Calendar of events  
Corners  
News



**Dear readers,**

This last issue of ALTEX for 2012 strikes a good balance between primary research establishing novel alternative methods to animal experiments and the presentation of strategies aiming to harness the power of available *in vitro* alternative methods to improve hazard assessment and risk prediction of chemicals, drugs, biocides, or cosmetics.

Van den Broek and colleagues present a model of hypertrophic scars, i.e., scars that are raised, itchy, and painful. The model is based on reconstructed epidermis on a dermal matrix with adipose derived mesenchymal cells and represents hypertrophic scar formation both microscopically and biochemically. Drugs currently used to treat scars improved a selection of parameters, and a potential new drug improved a different set of parameters, suggesting a combination treatment strategy might be most effective. This model promises an improvement of the understanding and the treatment of hypertrophic scars. Sroka et al. report on progress made with the ox-foot-model, which uses ox feet taken from animals slaughtered for food production at an abattoir to optimize surgical procedures to destruct veins by applying energy to the inside of the vein by laser light. Insights gained from the ox feet have been used to design trials for the treatment of varicose veins using these innovative procedures. The manuscript provides a detailed illustrated description of the preparation procedure which has also been found of use for training purposes. And in their letter Cánovas and Bird propose the use of converted human AB serum as a replacement for fetal bovine serum in cancer and primary endothelial cell line culture.

An animal-free strategy for hazard assessment and risk prediction of chemicals by combining novel technologies into an iterative process is put forward by Leist et al., and the various steps are illustrated by examples from the authors' areas of research. This approach aims to incorporate data from methods that have not yet been formally validated into the overall assessment process. Rossini and Hartung provide Food for thought ... on how cells probably have only a limited number of pathways whose disturbance by toxins will lead to problems manifesting in toxicity. If key points of these pathways can be defined, fairly simple cell-based tests that indicate triggering of these key points can be used to identify unknown toxins. This strategy is complemented by a  $t^4$  workshop report by Blaauboer et al. defining how such key points, called "biomarkers of toxicity," may be defined, what criteria they must ful-

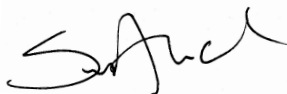
fill, and how their triggering can be extrapolated quantitatively and regarding kinetic information to *in vivo* toxicity prediction to contribute to the overall risk assessment.

Congress reports on Animal Law and Ethics and Linz 2012 as well as workshop reports on practical aspects in the application of new legislation and on improvements for 3Rs in daily practice as well as Corners and News keep you up to date with recent prizes and open calls as well as other developments in this dynamic area.

Looking forward to 2013, the most decisive political development for the field of alternatives to animal experiments promises to be the implementation of the final ban on animal testing for cosmetic ingredients, which is due to come into force on March 11. It is clear that there are currently no validated full replacements to the repeated dose toxicity, reproductive toxicity, and toxicokinetic assays which are to be banned, and the legislation allows postponement of the ban under these conditions. Therefore, it is encouraging to read in the response by the government of Sweden on a stakeholder questionnaire regarding this ban and its possible postponement: "The ban on cosmetic testing and marketing of products containing animal-testing ingredients is based on an ethical choice against testing for cosmetic purposes. The view of the Swedish government is that the ban should be enforced as planned...the 2013 ban should remain as an incentive to develop alternative methods" (<http://bit.ly/TNwRSO>). The European Commission is expected to put forward a legislative proposal later this year, either to maintain or delay the 2013 ban. The European Parliament and Council will then debate and vote on the proposal. We will keep you posted on this issue.

ALTEX is pleased to announce that Joanne Zurlo, Center for Alternatives to Animal Testing (CAAT) and Johns Hopkins Bloomberg School of Public Health, Baltimore, has joined our US editorial office as North American Editor. Joanne will introduce herself in the next issue. After the second issue on the topic of compassion, our German-language journal TIERethik, which explores the human-animal relationship, has published a third issue focusing on animal experiments. We would also like to call your attention to the upcoming issue of ALTEX Proceedings on the alternatives session at the last Indian Science Conference, which will be published online early 2013.

Thank you for your interest in and loyalty to ALTEX. Season's greetings and best wishes for a Happy New Year,



Sonja von Aulock

and the ALTEX team: Franz P. Gruber, Thomas Hartung, Hans Peter Hoesli, Carol Howard, Michael M. Hughes, Goran Krummenacher, Petra Mayr, Carolin Rauter, and Joanne Zurlo

## International Symposium on

# Alternative *in vitro* methods to characterize the role of Endocrine Active Substances (EASs) in hormone-targeted tissues

December 17<sup>th</sup> 2012

Aula Pocchiari

Istituto Superiore di Sanità, ROME, Italy



|      |                                     |  |
|------|-------------------------------------|--|
| 8.00 | <b>Registration of participants</b> |  |
| 8.30 | <b>Welcome address</b>              | <b>Umberto Agrimi</b> , Head of Food Safety and Veterinary Public Health Department<br><b>Loredana Musmeci</b> , Head of Environment and Primary Prevention Department |
| 8.40 | <b>Symposium opening</b>            | <b>Isabella De Angelis</b> and <b>Stefano Lorenzetti</b>   |

### INTRODUCTIVE SESSION

8.50 **Thomas Hartung**

*Endocrine disruption as the pilot of mapping the human toxome*

9.10 **Costanza Rovida**

*Implementation of regulatory issues*

9.30 **Alberto Mantovani**

*Endocrine Active Substances / EASs: understanding modes of action for risk assessment*

9.50 **Johann Steinkellner**

*Exploration of alternative methods for toxicity assessment of pesticide metabolites*

10.10 **Serena Cinelli**

*Improving test methods in the spirit of the 3Rs; the point of view of a contract research organization*

10.30 **Coffee break**

### SESSION 1: EASs in reproductive-targeted tissues

11.00 **Stefano Lorenzetti**

*A prostate perspective on male fertility and EASs: from toxicogenomics to phenotypic anchoring*

11.20 **Marcello Spanò**

*Human sperm (epi)genetic biomarkers to assess the impact of EASs on male reproductive function*

11.40 **Luana Paulesu**

*In vitro effects of EASs in human placenta*

### SESSION 2: EASs in different hormone-targeted tissues

12.00 **Igor Bendik-Falconnier**

*Endocrine active nutrients explored in human bone cell cultures*

12.20 **Robert A Smith**

*The use of cell models in determining neuronal responses to EASs*

12.40 **Arti Ahluwalia**

*Dynamic in-vitro organ models of metabolism*

13.00 **General discussion**

13.30 **Lunch**

### SESSION 3: EASs and kinetics

14.30 **Emanuela Testai**

*The role of biokinetics in in vitro tests and in the interpretation of results*

14.50 **Frédéric Yves Bois**

*Physiologically-based modeling of ovarian steroid hormones synthesis for EASs' health risk assessment*

15.10 **Daniel R. Dietrich**

*EASs contra human & environmental health: relevant or playground for merchants of doom?*

15.30 **General discussion**

16.00 **Concluding remarks**

### Scientific Secretariat

Dr. LAURA NARCISO, Department of Food Safety and Veterinary Public Health, Istituto Superiore di Sanità, Rome (I)  
Phone +39.(0)64990-2512 - Fax +39.(0)64990-3014 - e-mail: [laura.narciso@iss.it](mailto:laura.narciso@iss.it).

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## USA

Subscription service USA:

Center for Alternatives to Animal Testing (CAAT),

615 N. Wolfe St. W7032, Baltimore, MD, 21205, USA.

Phone: 410-614-4990, Fax: 410-614-2871,

e-mail: caat@jhsph.edu

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