Linz 06: Interesse an Alternativmethoden ungebrochen

Universität Linz, 2.6.-4.6.2006

Am diesjährigen Linzer Kongress wurde erstmals auf die Tagungssprache englisch gesetzt – und dies mit Erfolg. Der Kreis der Teilnehmenden konnte stark erweitert werden. Aus 25 europäischen Ländern sowie Australien, USA, Kanada und Sri Lanka reisten Interessierte an, um sich im Bereich der Alternativmethoden auf den neusten Stand zu bringen. Die Bedeutung des Kongresses wurde in diesem Jahr noch dadurch unterstrichen, dass er als offizielle Veranstaltung im Rahmen der österreichischen EU-Präsidentschaft stattfand, und dass ECVAM, eine Teilorganisation der EU-Kommission, die für die Validierung von Alternativen zu Tierversuchen zuständig ist, als Mitorganisatorin auftrat.

Die Zusammensetzung der Tagungsteilnehmer war wieder charakteristisch für die ausgewogene Meinungsvielfalt, die seit Jahren an den Linzer Veranstaltungen bestimmend ist: Etwa 34% der Teilnehmerinnen und Teilnehmer kamen von Universitäten, 27% aus der Industrie, 23% von mit Tierversuchen und Zulassungsverfahren befassten Behörden, 16% von Tierschutzorganisationen. Alle vier Säulen, die überall in Europa die nationalen Plattformen für Alternativmethoden tragen, waren also gut vertreten.

Auch in diesem Jahr lag einer der Schwerpunkte auf der Chemikalien- und Kosmetik Politik. Zudem wurden Themen wie die akute und chronische Toxizität, die „Gute Zellkultur Praxis" sowie ethische und rechtliche Aspekte intensiv diskutiert. Die Ökotoxikologie war diesmal mit nur zwei Beiträgen allerdings im Vergleich zu früheren Jahren sehr schwach besetzt. Bleibt zu hoffen, dass dieses Thema 2007 wieder eine zentralere Rolle einnehmen wird.

Am Gesellschaftsabend des Kongresses wurden verschiedene Preise vergeben:

Der mit 25.000 CHF dotierte Preis der Doerenkamp-Zbinden Stiftung wurde vom Präsidenten der Stiftung, Franz P. Gruber, an **David Dewhurst** (Universität Edinburgh) übergeben. Dewhurst erhielt den Preis für seine hervorragenden Leistungen bei der Entwicklung und Evaluierung tierversuchsfreier Unterrichtsmethoden, vor allem in der Pharmakologie. Der *ALTEX*-Preis 2006 wurde (leider in Abwesenheit) der Erstautorin **Marion Krug** vom Paul-Ehrlich-Institut in Langen für ihren Artikel „Serologische Testmethoden als Ersatz für Infektionsversuche an Ferkeln zur Wirksamkeitsprüfung von E. coli-Muttertierimpfstoffen" (*ALTEX 22, 2005*, 111-116) verliehen. Der vom FFVFF Zürich gespendete Preis ist mit CHF 2.000 dotiert und beinhaltet die Einladung zum Linzer Kongress sowie eine dreijährige Mitgliedschaft bei MEGAT. Die Posterpreise, die mit je € 220,- plus einem Jahresabonnement von *ALTEX* dotiert sind, wurden an **Markus Binder et al.** "*A metabolic activation system for the embryonic stem cell test*", **Andrew Knight et al.** "*Animal carcinogenicity studies: Implications for the REACH System*" und **Johanna Schanz** „Vaskularisiertes Lebertestsystem als Alternative zu Tierversuchen" vergeben.

Im Anschluss an die Preisverleihungen stellte sich der neu im Amt befindliche Professor für „*In vitro* Methoden zum Tierversuchsersatz" an der Universität Konstanz vor. **Marcel Leist**, dessen Lehrstuhl für 10 Jahre mit jährlich 300.000 € von der Zürcher Doerenkamp-Zbinden Stiftung finanziert wird, schilderte kurz seine wissenschaftliche Laufbahn und bat die anwesenden Kongressteilnehmer um Kooperation.

Auch in diesem Jahr werden ausgewählte Beiträge des Kongresses in *ALTEX* publiziert und den Tagungsteilnehmern zur Verfügung gestellt. Möglich gemacht wird dies durch ein Sponsoring der Stiftung FFVFF (Fonds für versuchstierfreie Forschung). Trotz Weltkongress haben sich die Organisatoren entschieden, auch 2007 einen Linzer Kongress abzuhalten. Er findet vom 28. bis 30. September 2007 wiederum an der Johannes Kepler Universität Linz statt.

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Nachzutragen sind noch folgende Beiträge, die aus Zeit- und Platzgründen im Verzeichnis der Linzer Abstracts in *ALTEX 2/06* fehlten.

Poster

Standardisation of an *in vitro* method to quantify angiogenesis

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The process of angiogenesis includes sprouting of new vessels from pre-existing ones, their remodelling and regression. Angiogenesis plays a key role in many pathological processes particularly growth and metastasis of tumours. Both, the stimulation of angiogenesis to generate new vessels in ischemia and the inhibition of angiogenesis, so called anti-angiogenesis, to arrest growth and metastasis of tumours, are promising therapeutic concepts. Studies on angiogenesis, which are done particularly in animal models, are a pre-requisite for the determination of the angiogenic or angiostatic effect of substances. We have established a method for quantitation of angiogenesis *in vitro* based on microvascular endothelial cells isolated from the ovary of slaughtered cattle (Bahramsoltani and Plendl, *ALTEX* 2005). In opposite to *in vivo* systems this method includes the staging of angiogenesis in strictly defined steps and thus allows quantitation of all phases of angiogenesis up to the development of capillary-like structures. Validation of the method in our laboratory showed that routine and reproducible accomplishment should be possible for different investigators with a maintainable effort of time and costs. The aim of our current efforts is to develop a standardised method independent from the cells. For this reason we cultivate different endothelial cell lines (human myocardium and dermis) and investigate whether the steps of the angiogenic cascade *in vitro* found for the bovine can be assigned to these cultures. This standardisation which is a pre-requisite for the use of the method in different laboratories would allow to replace a number of preclinical *in vivo* tests in angiogenesis research.

Poster

Computed tomography as a non-destructive method for reduction of animal use

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Up to now the use of microcomputed tomography, also known as µCT, has been successfully used in different branches of science for study of opaque objects. In biology the technology is well adapted to the study of bones and soft tissues of animals. In the meantime the CT technology has experienced a lot of refinements, which give more additional information on the analysed subjects. The greatest advantage is the chance of *in vivo* screening due to higher scan speed and lower radiation dose to the laboratory animals. This has established a basis for long-term studies which meets the necessity of lowering the quantity of tested animals. LaTheta, the laboratory µCT scanner, has been developed to combine these advantages and has been optimised for *in vivo* body composition analysis of small laboratory animals. LaTheta enables easy longitudinal monitoring of the internal organs and the measuring of bones as well as adipose tissues due to its low radiation dose (two range 2 to 8 mSv) and advanced evaluation software. High resolution pictures with high contrast make the analysis a lot easier. Up to date in search for time saving and non-destructive methods for *in vivo* analysing of small animals a µCT provides a lot of advantages to biomedical research. Among accurate outcomes and better statistical evidence the ability to perform *in vivo* analysis results directly in reduction of animal use.

Lecture

Funding Alternatives Research in the European Union, 2007-2013

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In the current Research Framework Programme, the European Union has invested more than 90 MIO € to develop robust, effective, non-animal testing methods that withstand the requirements of international validation.

Funding has come mostly from the priorities Life sciences, genomics and biotechnology for health; Policy support and Sustainable development, global change and ecosystems (http://www.cordis.lu/fp6/lifescihealth.htm; http://cordis.europa.eu/fp6/support.htm; http://cordis.europa.eu/sustdev/environment/).

Topics covered by Integrated projects (IP) (usually large projects funded around 9 MIO € for maximum 5 years) and Specific Targeted Research projects (STREP) (smaller research projects funded around 2.5 MIO € for maximum 3 years) include high throughput techniques with genomic approaches to genotoxicity and carcinogenicity, the development of specific cell (this includes research on human embryonic stem cells) and organ toxicity assays and the application of *in vitro* cell and sensor technologies to replace *in vivo* animal studies. Intelligent testing strategies, kinetic studies applied to product screening and to the development of pharmaceutically-relevant lead compounds are also considered.

A range of networks, fora and workshops are funded through Specific Support Actions (SSA) [support measure (workshops, conferences, study, etc.)] , aimed at paving the way for new activities and informing/involving representatives of stakeholder groups, raising awareness on the use of alternative methods in New Member States and Candidate Countries, promote new biosensor-based technologies for the Three Rs, and analyse the mechanisms of nuclear hormone receptors to bridge the gaps between *in vitro* and *in silico*.

Subtitled "Building the European research area of knowledge for growth", the Seventh Framework Programme, FP7, will cover the period 2007-2013 and is designed to respond to the competitiveness and employment needs of the EU. FP7 will continue to support research on the Three Rs, through similar instruments as now (IP, STREP and SSA) under the themes devoted to Health, Food, Agriculture and Biotechnology, as well as Environment and Nanosciences and under the Joint Technology Initiatives.

This presentation will provide a review of FP6 contracts in the field of the Three Rs and an introduction to FP7, focussing on the relevant scientific areas and funding tools (the first call is expected to be published in 2007).

Lecture

Virus and prion contaminations in animal cell culture

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Virus and prion contaminations in animal cell culture Otto-Wilhelm Merten, Généthon, Evry, France Abstract: In contrast to microbial and mycoplasmal contaminations, which can be relatively easily detected, viral contaminations present a serious threat because of the difficulty in detecting some viruses and the lack of effective methods of treating infected cell cultures. While some viruses are capable of causing morphological changes to infected cells (e.g. cytopathic effect) which are detectable by microscopy some viral contaminations result in the integration of the viral genome as provirus (this causes no visual evidence) by means of modification of the cellular morphology. Virus production from such cell lines, are potentially dangerous for other cell cultures (in research labs) by cross contaminations, or for operators and patients (in the case of the production of injectable biologicals) because of potential infection. The only way to keep cell cultures for research, development, and the biotech industry virus-free is the prevention from contaminations. Cell cultures can become contaminated by the following means: firstly, they may already be contaminated as primary cultures (because the source of the cells was already infected), secondly, they were contaminated due to the use of contaminated raw materials, thirdly, they were contaminated via an animal passage, or finally via handling errors of the operator. A further threat for cell culture and the use of biologicals produced with cell culture is the contamination by the misfolded prion protein (PrPSc). As for viral contamination, its presence cannot be easily detected, there is no treatment, and cells can be contaminated via contaminated primary cultures or contaminated raw materials. This overview presents the main causes of virus and prion protein (PrPSc) contaminations animal cell culture, methods for prevention and some of the most important detection methods.

Lecture

EACHing out for animals

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REACH, the EU Chemicals Policy (Registration, Evaluation and Authorisation of Chemicals) objectives were to improve the protection of human health and the environment through the better and earlier identification of the properties of chemical substances. However, the original Commission paper on REACH would have resulted in the use of millions of animals in testing. To decrease the number of animals tested, a number of objectives must be considered during the development of the legislation: data-sharing, early pre-registration, the exemption of cosmetic ingredients and importantly the development, validation and acceptance of non-animal test methods. The European Parliament adopted a large number of amendments during the first-reading phase of the legislation, which would significantly reduce the number of animals used. The Council's Common Position did not consider many of these amendments, however, the text is an improvement on the original text. It is important during second-reading that further changes are made to ensure there is a further decrease in the number of animals required to be tested under REACH.

Lecture

The COLIPA strategy for the development of *in vitro* alternatives

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The cosmetics industry regards consumer safety as its top priority and its commitment to phase out animal tests is long standing: Since 1992, SCAAT has coordinated activities towards development of non animal alternative methods, contributing to their validation. *In vitro* tests are needed to identify relevant aspects of the complex interactions of a chemical with human skin, eye and other target tissues.

The Colipa/SCAAT research programme on alternative methods/strategies to animal testing focuses on the main areas of need and expertise within the cosmetics industry: skin and eye irritation, skin allergy and genotoxicity. This research comprises the understanding of biological mechanisms, method/strategies development, method optimisation, as well as prevalidation and validation in collaboration with the European Centre for the Validation of Alternative Methods (ECVAM). The Task Force (TF) Skin Tolerance currently runs projects to develop *in vitro* test systems to identify potential allergens and irritants. The TF Eye Irritation is focussed on the underlying physiological mechanisms of eye irritation and recovery to identify *in vitro* endpoints more predictive of the *in vivo* human response to chemicals and is working in close collaboration with ECVAM. TF Genotoxicity plans to support research projects in order to improve the predictive capacity of the current *in vitro* battery. For all TFs a major challenge is to develop an appreciation of how to use their data output for risk assessment in addition to hazard identification. Risk assessment for chemicals used as ingredients also covers systemic exposure. The acceptance of a method to assess percutaneous absorption *in vitro* (OECD 428) was a major success for our TF.

In cooperation with academia, industry, scientists and regulators, our strategy tries to combine the best scientific approaches resulting in alternative methods for the most appropriate safety assessment of cosmetics, taking into account the 2009 and 2013 deadlines.