





P. Artursson has made a significant career in the research of pharmacy, especially in drug absorption, disposition and delivery. He has made globally pioneer research contribution in development of *in vitro* models for the prediction of drug absorption through small intestine. Current research interests are directed towards predictive pharmacokinetics (ADMET) and biopharmaceutics in drug discovery and development. In particular, the

P. Artursson is listed as one of the world 100 most cited scientists in Pharmacology and Toxicology since 2004 (ISI). He has published about 150 original articles, 18 review articles and 18 book chapters.

Professor Erik Walum  
Vice-president of the  
Björn Ekwall Memorial Foundation  
[walum@glucoxbiotech.com](mailto:walum@glucoxbiotech.com)  
[www.bemf.eu](http://www.bemf.eu)

[illegible]

## Felix Wankel Animal Welfare Award

Marcel Leist, co-director of CAAT-Europe at the University of Konstanz, has been awarded the Felix Wankel Animal Welfare Award for his work on in vitro test systems in the area of reproductive toxicology. The work used differentiating stem cells to model human nervous system development and disturbances. He shares this prestigious award with Stephan Reichl, who was recognized for his work on human cornea models. The Felix-Wankel research prize is



the session with a presentation on the use of the social amoeba *Dictyostelium* as a new model for early identification of emetic liability of drugs.

The final session of the meeting focussed on epigenetics in toxicology and linked IVTS 2012 with the Industrial Genotoxicity Group (IGG) of the UK Environmental Mutagenesis Society (UKEMS). Lorraine Young (University of Nottingham) gave us a fantastic introduction to epigenetics and how understanding epigenetic modifications during embryonic development may provide insights into our understanding of functional relevance. Nessa Carey (Pfizer) followed with some interesting human-relevant examples of where epigenetics may be involved such as foetal alcohol syndrome and development of anticancer drugs which target the epigenome of cancer cells. She also highlighted how such drugs are used and the importance of intergenerational transmission of epigenetic changes.



Stephanie Ravenscroft receiving her award from Pratibha Mistry (IVTS Chair, I) and Karl Herbert

Early career scientists at the meeting were eligible for either their poster or oral presentation to be included in the meeting competition. The IVTS 2012 winner was, Stephanie Ravenscroft (University of Liverpool), for her poster "The role of endothelial cells in drug-induced cardiotoxicity". Stephanie was awarded a £200 prize, free Society membership for a year and will be invited to present her work at the IVTS 2013 meeting.

**International Conference of Alternatives to Animal Experimentation**  
26-27 January, Almada, Portugal

As the first event of this kind to be held in Portugal, the conference specifically aimed at promoting the debate and sharing of information regarding the 3R's policies on animal use and highlighting the replacement of animal models for suitable and ethical alternatives, such as *in vitro* and *in silico* models, as well as alternative experimental designs.

The event was organized by the Portuguese Society for Humane Education (SPeDH) and co-sponsored by the Almada City Council, the European Partnership for Alternative Approaches to Animal Testing (EPAA), Hotel Melia Capuchos, Fundação Luso-Americana para o Desenvolvimento (FLAD), Liga Portuguesa para os Direitos do Animal (LPDA) and Mercado do Site.

The conference had approximately 100 participants coming from universities, animal facilities, research laboratories, regulatory agencies, cosmetic industry, animal welfare NGO's as well as general public willing to learn more on this subject.

The vast majority of Portuguese students and researchers attending the congress were positively impressed by the alternatives presented at the conference and became interested on the subject. The general public gained valuable tools to be more participative as decision makers and people from different backgrounds and different perspectives on the animal experimentation issue gained more knowledge and respect towards each other, allowing for constructive dialogues. All Portuguese participants agreed that Portugal needs to have more investment in the field of Alternatives to Animal Experimentation and after this conference this is one step closer to happening.

**CELLTOX Course – March to June 2013:**  
"Alternative methods – replacement"





The Italian Association for in Vitro Toxicology (Celltox, [www.celltox.it](http://www.celltox.it)) organized the first training course on "Alternative methods – replacement". The objectives of this course were within the aims of the Association: *"...to promote the use of in vitro systems in pharmacological and toxicological research...and to organize courses to train young researchers..."*.

The event, for its high scientific and innovative content and also for being organized without external sponsoring, was accredited as ECM (Education Continuous in Medicine) at the Italian Ministry of Health by assigning 5 credits per module.



CELLTOX Board members (from left to right): L. Golzio (Secretary), M. Meloni (President), G. Mazzoleni, C. Urani (Treasurer)

The event was supported by the University of Milano Bicocca (UniMIB, Italy) and by the Ethic Committee of the same University, and hosted by the Department of Earth and Environmental Sciences of UniMIB.

More than 40 participants attended, coming from Academia (teachers, researchers, PhD students), Hospitals, Private and Public Research Institutes and Laboratories, and Industry, with many heterogeneous backgrounds (e.g., Biological and Environmental Sciences, Biotechnology, Pharmacy, Veterinary Medicine, Medicine).

The lessons were divided into 4 modules of one day each from March to June.

Experts both from the legislative and regulatory areas, and from the basic to very innovative applied biological and toxicological research provided their expertise and exchanged their knowledge.

The topics addressed were divided into:

- Module I: "Actuality on Alternative Methods"
- Module II: "Regulatory and applicative aspects"
- Module III: "The models for the alternative methods - 1"
- Module IV: "The models for the alternative methods - 2"

All modules were very intense and followed with great interest by the participants at the end of the lectures. Pleasant and fruitful discussions continued during lunch time and at the end of the day. All the participants briefly presented their fields of activity. Interestingly, for many of them it was the first introduction to alternatives and this experience represented a basis to start introducing alternative methods in their respective research programs.

The event produced a "think tank" committed to disseminate the principles of the 3Rs and to give new ideas and stimuli to the Association.

The organizers acknowledge all the speakers for their willingness and enthusiasm in presenting their areas of expertise, and their ability to stimulate the interest and active discussions from participants.



Participants to CELLTOX Course 2013

We, as organizers, aimed at responding the big need for courses on the scientific divulgation of the 3Rs culture. Certain that the "seed" of the 3Rs culture has been planted



The NOTOX film is available on the project website: <http://www.notox-sb.eu/film>

The two test guidelines had originally been adopted in 2009 for the identification of serious eye damage/eye irritation of chemicals further to retrospective validation by the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) in collaboration with EURL ECVAM and the Japanese Center for the Validation of Alternative Methods (JaCVAM). Additional validation of the two tests showed their usefulness also for the identification of chemicals not requiring classification for serious eye damage/eye irritation (i.e. non-irritant chemicals), thus leading to the revision of the test guidelines under the co-lead of EURL ECVAM and the Netherlands.





[illegible]

As part of our ongoing support to early career scientists, 2013 saw the launch of the IVTS mini-fellowship scheme. The scheme has been set up to aid research training opportunities for scientists in techniques which are not available at their home institution. The fellowships are designed to allow early career scientists to set up collaborations with established scientists, learn new techniques useful for their own research, and to promote further career development particularly in the field of *in vitro* toxicology research. The scheme is open to IVTS members that are either students currently enrolled on a PhD Programme or Post-doctoral Scientists within 10 years of obtaining their PhD. More details about this new scheme can be found on our website: <http://www.ivts.org.uk/site/early-career-support/>. Although the closing date for this year's submission has passed, we intend to make this an annual scheme.

[illegible]

Attention veterinarians, lab technicians, animal technicians, and all who work with laboratory animals: The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) now is accepting proposals for the 2014 Science-based Refinement Awards (formerly the Animal Welfare Enhancement Awards).

The focus of these awards is to elicit scientific evidence to support the enhancement of the

PDF Poster Available for download and distribution at: [http://altweb.jhsph.edu/news/2012/sci\\_based\\_refinement\\_awards%202014.pdf](http://altweb.jhsph.edu/news/2012/sci_based_refinement_awards%202014.pdf)

More information can be found at:  
<http://caat.jhsph.edu/programs/awards/AWE/2014/index.html>.

[illegible]

In 2013, the EPAA will grant a €3000 prize to a laboratory technician involved in implementing and raising awareness of Replacement, Reduction and Refinement of animal testing.

While most of the current Three Rs prizes and awards target scientists, much of the processes using animals for safety science are actually performed by laboratory technicians and animal care takers. The purpose of this prize is to target those actually implementing alternative approaches to animal testing and raise awareness of their role for the day to day implementation of Three Rs principles and, in particular, for seizing opportunities for further Refinement. Animal technicians mainly contribute to one main 'R' – Refinement and this is what the prize should focus on. Most animal technicians are not working on replacement or reduction. In addition there are few prizes for the neglected R of refinement. It is the hardest R to provide sound scientific evidence on. Therefore, this prize is an opportunity to first, recognise animal technicians as opposed to scientists and second, promote refinement – the R that has the benefit for the animals that still need to be used in experiments. Refinement refers to improvements to scientific procedures and husbandry which minimise actual or potential pain, suffering, distress or lasting harm and/or improve animal welfare in situations where the use of animals is unavoidable.



## Recent Publications of ESTIV members

- Clotworthy M, Archibald K (2013) Advances in the development and use of human tissue-based techniques for drug toxicity testing. *Expert Opin Drug Metab Toxicol*. May 20. [Epub ahead of print]
- Coecke S, Pelkonen O, Batista Leite S, Bernauer U, Bessems J, Bois F, Gundert-Remy U, Loizou G, Testai E, Zaldívar JM (2013) Toxicokinetics as a key to the integrated toxicity risk assessment based primarily on non-animal approaches. *Toxicol In Vitro* 27, 1570-1577.
- Devreese M, Pasmans F, De Backer P, Croubels S (2013) An in vitro model using the IPEC-J2 cell line for efficacy and drug interaction testing of mycotoxin detoxifying agents. *Toxicology in Vitro* 27, 157-163
- Fahy GM, Guan N, de Graaf IAM, Tan Y, Griffin L, and Groothuis GMM. (2013) Cryopreservation of precision-cut tissue slices. *Xenobiotica* 43(1), 113-132
- Groothuis GMM and de Graaf IAM (2013) Precision-cut intestinal slices as in vitro tool for studies on drug metabolism. *Curr Drug Metab* 14(1), 112-119
- Guan N, Blomsma SA, Fahy GM, Groothuis GMM and de Graaf IAM (2013) Analysis of gene expression changes to elucidate the mechanism of chilling injury in precision-cut liver slices. *Toxicol in Vitro* 27(2), 890-899
- Gunness P, Mueller D, Shevchenko V, Heinzle E, Ingelman-Sundberg M and Noor F (2013) 3D organotypic cultures of human HepaRG cells: a tool for in vitro toxicity studies. *Toxicol Sci* 133 (1), 67-78
- Hadi M, Westra IM, Starokozhko V, Dragovic S, Merema MT and Groothuis GMM. (2013) Human precision-cut liver slices as an ex vivo model to study idiosyncratic drug-induced liver injury. *Chem Res Toxicol*. 26(5), 710-720
- Hadi M, Dragovic S, van Swelm R, Herpers B, van de Water B, Russel FGM, Commandeur JNM and Groothuis GMM. (2013) AMAP, the alleged non-toxic isomer of acetaminophen, is toxic in rat and human liver. *Arch Toxicol* 87(1), 155-165
- Hamers T, Legler J, Blaha L, Hylland K, Marigomez I, Schipper CA, Segner H, Vethaak AD, Witters H, de Zwart D and Leonards PE (2013) Expert opinion on toxicity profiling--report from a NORMAN expert group meeting. *Integr Environ Assess Manag* 9(2), 185-191
- Hoelting L, Scheinhardt B, Bondarenko O, Schildknecht S, Kapitza M, Tanavde V, Tan B, Lee QY, Mecking S, Leist M, Kadereit S (2013) A 3-dimensional human embryonic stem cell (hESC)-derived model to detect developmental neurotoxicity of nanoparticles. *Arch Toxicol* 87(4), 721-733
- Jennings P (2013) Stress response pathways, toxicity pathways and adverse outcome pathways. *Archives of toxicology* 87(1):13-4 doi:10.1007/s00204-012-0974-4
- Juan-Garcia A, Manyes L, Ruiz MJ, Font G (2013) Applications of flow cytometry to toxicological mycotoxin effects in cultured mammalian cells: A review. *Food Chem Toxicol* 56, 40-59.
- Juan-Garcia A, Manyes L, Ruiz MJ, Font G (2013) Involvement of enniatins-induced cytotoxicity in human HepG2 cells. *Toxicol Lett* 218, 166-173
- Krug AK, Kolde R, Gaspar JA, Rempel E, Balmer NV, Meganathan K, Vojnits K, Baquie M, Waldmann T, Ensenat-Waser R, Jagtap S, Evans RM, Julien S, Peterson H, Zagoura D, Kadereit S, Gerhard D, Sotiriadou I, Heke M, Natarajan K, Henry M, Winkler J, Marchan R, Stoppini L, Bosgra S, Westerhout J, Verwei M, Vilo J, Kortenkamp A, Hescheler J, Hothorn L, Bremer S, van Thriel C, Krause KH, Hengstler JG, Rahnenführer J, Leist M, Sachinidis A (2013) Human embryonic stem cell-derived test systems for developmental neurotoxicity: a transcriptomics approach. *Arch Toxicol* 87(1), 123-14
- Leist M, Hartung T. Inflammatory findings on species extrapolations: humans are definitely no 70-kg mice. *Arch Toxicol* 87(4), 563-567
- Leite, SB, Wilk-Zasadna I, Zaldivar JM, Airola E, Reis-Fernandes MA, Mennecozzi M, Guguen-Guillouzo C, Chesne C, Guillou C, Alves PM, Coecke S (2012) Three-Dimensional HepaRG Model As An Attractive Tool for Toxicity Testing. *Toxicol Sci*. 130(1):106-16
- Lu H, Fernandez-Franzon M, Font G, Ruiz MJ (2013) Toxicity evaluation of individual and mixed enniatins using an in vitro method with CHO-K1 cells. *Toxicol in Vitro* 27, 672 – 680
- Lundberg K, Albrekt AS, Nelissen I, Santegoets S, de Gruij TD, Gibbs S and Lindstedt M (2013) Transcriptional profiling of human dendritic cell populations and models – unique profiles of in vitro dendritic cells and implications on functionality and applicability. *PLoS One* 8(1), e52875
- Murk, AJ, Rijntjes, E, Blaauboer, BJ, Clewell, R, Crofton, KM, Dingemans, MML, Furlow, JD, Kavlock, R, Köhler, J, Opitz, R, Traas, T, Visser TJ, Xia, M and Gutleb, AC (2013) Mechanism-based testing strategy using in vitro approaches for identification of thyroid hormone disrupting chemicals. *Toxicol in Vitro* 27(4), 1320-1346
- Niu X, de Graaf IAM and Groothuis GMM. (2013) Evaluation of the intestinal toxicity and transport of xenobiotics utilizing precision-cut slices. *Xenobiotica* 43(1), 73-83
- Nogueira DR, Morán MC, Mitjans M, Martínez V, Pérez L, Vinardell MP (2013) New cationic nanovesicular systems containing lysine-based surfactants for topical administration: Toxicity assessment using representative skin cell lines. *Eur J Pharm Biopharm* 83(1), 33-43







