

The European Society of Toxicology In Vitro

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July 2014

Editorial

Dear ESTIV members.

Here is the latest edition of the ESTIV newsletter. It was great to meet most of you in Egmond aan Zee, at the ESTIV Congress 2014. In the Newsletter you will find an update on what has happened in the world of *in vitro* toxicology, the developments that took place in the last six months and what we look forward to in the future. In this regard, I would also like to express my gratitude to CELLTOX, our affiliated Society, and its activity.

Congratulations to Tuula Heinonen, the recipient of the 2014 Björn Ekwall Memorial Award. Prizes awarded to Young Scientists during ESTIV 2014 are also reported here. demonstrating the involvement and the of the "new generation" researchers in vitro toxicology. Information on the fourth annual developmental toxicity (DNT) alternative Conference and a brief fascinating description of the connection between Alzheimer's disease, research and toxicology complete this newsletter. Information on upcoming courses, debates, meetings and workshops are included in the Newsletter as well.

I hope you find this Newsletter informative, useful and enjoyable at the same time.

Best wishes, Francesca Caloni

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Message from the President

Dear members,

I am pleased to introduce our summer Newsletter which addresses amongst other our ESTIV 2014 Congress. The Congress marked the 20th Anniversary of ESTIV, officially established in 1994 in Paris, France. Inspired by new scientific advances and technologies, a special acknowledgement to the organizers who offered us not only a warm welcome in The Netherlands but also a scientifically and socially stimulating program. During the four days we have witnessed the advances made in a variety of areas to meet toxicological, pharmacological and regulatory merging scientific needs related to in vitro toxicology. In particular the animated debate session illustrated how the replacement of animal testing represents a true scientific and societal need, and that predictive value (in vivo and in vitro), quality and human relevance are important issues to be considered to prompt advances implementing in vitro toxicology methods and in replacing animal testing.

During the congress we had our General Assembly in which a new ESTIV Executive Board has been nominated due to the end of term of a number of our board members. In particular, a warm acknowledgement to all members that leave behind a remarkable contribution to our society: Dr. Greet Schoeters (past president), Dr. Alison Gray (Secretary), Dr. Maria Laura Scarino (Elservier's contact), Erwin Roggen (organizer ESTIV 2012) and Asa Fex Svenningsen (students representative). Also

a friendly welcome to the new board members motivated to support ESTIV's current and future activities: Dr. João Barroso (sponsors). Dr. Helena Kandárová (communication) and Prof. Paul Jennings (affiliations and EC grants). We also welcome our two new financial auditors Dr. Sieng Horsbasch and Dr. Paul Daly, and greatly acknowledge the dedicated work of the financial auditors. Prof. Blaauboer and Prof. Horst Spielmann. ESTIV will continue to promote in vitro toxicology in the upcoming years and for this purpose it has invested and will continue to invest in organizing practical and/or applied training courses. Furthermore it will continue to strengthen collaboration with similar scientific associations and strategic stakeholders such as ECHA and ECVAM.

In the Newsletter you will also find reports on the latest scientific events and an agenda with the upcoming meetings, workshops and congresses. In particular, the new nominee for the Bjorn Ekwall Memorial Award has been announced - congratulations to Dr. Tuula Heinonen! Besides her professional accomplishments, Tuula is chairman of the Scandinavian Society for Cell Toxicology, an affiliated society of ESTIV. Finally, I raise your attention to the publication of the ECHA report on the use of alternatives to animal testing.

Wishing you an enjoyable reading!

With best regards,

Chantra Eskes ESTIV President

ESTIV 2014

ESTIV2014, the 18th International Congress on *in vitro* Toxicology took place in Egmond aan Zee, The Netherlands, June 10-13, 2014.



In total 277 people were present in Egmond aan Zee, coming from 33 countries from all over the world.



In addition to the scientific sessions, two new events were introduced: a career session for young scientists and a debate with the topic "Can we get rid of animal experimentation in toxicology within 5 years?".



The social events included a congress diner and after party, a visit to Alkmaar with scooters ('step' in Dutch) and boat trip, and a party on the beach. The weather was excellent for these events.



The local organisation looks back to a successful meeting with excellent speakers, good discussions with the participants and interesting exhibitors (17).



Specifics about the meeting, abstracts, program and sponsor and exhibitor information can be found on the website (www.estiv2014.org) and the meetings app: http://m.twoppy.com/estiv2014/

Jan van der Valk

ESTIV Young Scientist Awards

ESTIV, in collaboration with Elsevier, Celltox, Invitrom and ESACT provided awards at the 2014 ESTIV Congress in order to motivate the participation of students and young scientists at ESTIV Congresses. The high quality of students and young scientist presentations has made it difficult to choose.

The Elsevier-ESTIV Award for Best Oral Presentation was granted to Marije Strikwold from the Wageningen University, The Netherlands for her presentation on the "Assessment of potential embryotoxicity a series of p-substituted phenols by an integrated QSAR-in vitro-PBK approach" The award includes a one year subscription to "Toxicology in Vitro" and 500 Euros.

The Elsevier-ESTIV Award for Best Poster Presentation was granted to Stefania Vernazza from the Università degli studi di Genova, Italy for her poster entitled "Development of in vitro testing strategies for toxicity evaluation of mixtures derived from discarded laboratory animals". The award includes a one year subscription to "Toxicology in Vitro" and 500 Euros.

The European Society on Animal Cell Technology (ESACT) Award was granted to Maaria Ginai from the Loughborough University, United Kingdom for her poster entitled "Assessment of drug transport in human renal proximal tubule cells towards development of a bioartificial kidney to model drug interactions". The award consists of a travel and invitation to participate to the ESACT 2015 meeting taking place in Barcelona, Spain.

ESTIV bursaries: a total of five bursaries of 500 Euro for PhD-students and young scientists were provided to S. Alghamdi (UK), T. Baccarin (Spain), M. Ezechias (CZ), S. Mohammadi (Turkey) and E. Zorzan (Italy).

INVITROM bursaries: two bursaries of 500 Euro for PhD-students members of INVITROM presenting their research work at the ESTIV2014 congress were provided to K. Buyl (Belgium) and A. Domínguez (Spain).

CellTox bursaries: two bursaries of 1000 Euro for young Italian scientists CellTox members presenting their research work at the ESTIV2014 congress was provided to S. Giusti (Italy) and S. Vernazza (Italy)-.

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Nomination Dr. Tuula Heinonen as the recipient of the Björn Ekwall Memorial Award 2014

At its Annual Board Meeting January 16, 2014, Stockholm, Björn Ekwall Memorial Foundation (BEMF) nominated Dr. Tuula Heinonen from Finland as the recipient of the Björn Ekwall Memorial Award 2014.



Dr. Tuula Heinonen

Dr. Tuula Heinonen (Ph.D., Adjunct Professor, Director of FICAM) from the School of Medicine, University of Tampere, Tampere, Finland has been nominated for the Björn Ekwall Memorial Award in recognition of her achievements in promotion and implementation of alternative methods by developing human cell based tissue/organ models, as well as by establishing the Finnish Centre for Alternative Methods (FICAM).

Dr. Heinonen defended her PhD thesis in 1982 in the field of toxicology, University of Turku; in 1984 she became adjunct professor in toxicology at the University of Turku and in 1993 adjunct professor in biochemistry at the University of Helsinki. Dr. Heinonen has worked as scientist at the Institute of Occupational Health (1979-83) and as toxicologist and in leading research positions in pharmaceutical industry (1983-2007). The special areas of Dr. Heinonen are toxicological risk evaluation and regulatory toxicology. She has worked at School of Medicine, University of Tampere from 2007 on first at Cell Research Centre, and after the establishment of FICAM in 2008 as director of it. Dr. Heinonen and her group develop human cell based tissue models for biomedical research and toxicology. The focus of Dr. Heinonen is on the development and validation of better methods for the prediction of human effects by using human cell based tissue models and tests instead of animal experiments. The first validated model developed by Dr Heinonen's group is angiogenesis model applicable for both biomedical and toxicological purposes.

Dr. Heinonen has developed FICAM to a high-level research laboratory with an official GLP-status and ability to function in method validations coordinated by EURL-ECVAM (European Union Reference Laboratory for Alternatives to Animal Testing). The staff of FICAM (about 20) consists of professors, senior scientists, doctoral students and technicians. In addition to research Dr. Heinonen will educate scientists organising high level courses on alternative methods in FICAM and by giving lectures also in other universities in Finland.

Dr. Heinonen is member of several international and national expert groups and the Finnish representative in the PARERE (Preliminary Assessment of Regulatory Relevance) network in EU. She has been the President of the Finnish Society of Toxicology (FST) 1998-2000. In 2010 she became the President of the Scandinavian Society for Cell Toxicology (SSCT). She is Vice President of European Consensus Platform Alternatives (ECOPA), President of the Finnish Consensus Platform for Alternatives (FINCOPA). and European Registered Toxicologist (ERT).

Dr. Heinonen is Associate Editor of "Frontiers in Toxicology" (from 2010 on), Guest Editor of Toxicology *in Vitro* Special Issue 2013, and reviewer in several toxicological journals. Her list of publications includes thirty articles in peer reviewed scientific Journals, and dozens of pharmaceutical study reports.

The BEM award is handed out to Dr. Tuula Heinonen in the 9th World Congress on Alternatives and Animal Use in the Life Sciences 24-28.08.2014 in Prague where she will give also the BEM-lecture.

Hanna Tähti, FICAM

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CAAT Hosts the 4th International Conference on Alternatives for Developmental Neurotoxicity (DNT) Testing

CAAT hosted the fourth annual developmental toxicity (DNT) alternatives conference on May 12-14th in Philadelphia. Pennsylvania. With expert speakers from the U.S. and Europe, the seventy participants including research scientists, regulators, industry representatives, academics, and paediatricians — came together to discuss the development of new, alternative methods neurotoxicity testing of chemicals, including in vitro human cells, computer models and non-mammalian (zebrafish and C. elegans).

CAAT Director Thomas Hartung spoke of the critical need for this research. "Developmental neurotoxicity cannot be effectively studied with rats. If we want to understand the causes neurodevelopmental disorders, we need a new, 21st century toxicology — a toxicology based upon studying human cells at the molecular level. DNT4 brought together the best minds from around the world to help us better understand whether and how chemicals affect vulnerable, growing nervous systems — so we can better protect public health and address the rise in developmental disorders."

The conference was sponsored by CAAT, the Alternatives Research & Development Foundation (ARDF), Boehringer Ingelheim, CropLife, the Doerenkamp-Zbinden Foundation, the Environmental Protection Agency, the Human Toxicology Project Consortium, The Humane Society of the United States, the Society of Toxicology, and the European Commission.

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CELLTOX Workshop on Alternative methods: Present and Future.



The Italian Association for *in Vitro* Toxicology (CELLTOX, www.celltox.it) organized the workshop on "Alternative methods: Present and Future". The workshop objectives 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 was hosted by Chiara Motta who invited Celltox to the historical Biology Department of the University of Naples Federico II and was supported by the University of Milano Bicocca (UniMIB, Italy), Department of Earth and Environmental Sciences. More than 50 participants attended the workshop, coming mainly from Academia (teachers, researchers PhD fellows and students).

Experts from both the legislative and the regulatory areas, from the basic to the innovative applied biological and toxicological research provided their expertise and transferred their knowledge. Chiara Motta from the University of Naples was the chair who stimulated, most of all the students, to get involved into the use of alternative methods and the application of the 3Rs, and to consider them as the possibility for a future job. The topics were divided into the following lectures:

- "History of the 3Rs and of Alternative Methods" Chiara Urani, University of Milan Bicocca
- "Alternative Methods: National and European Regulatory Context" – Isabella De Angelis, Istituto Superiore di Sanità
- "Validation of Alternative Methods to animal experiments" Federica Madia, EURL ECVAM Joint Research Centre
- "Alternative Methods: how they are used by the Pharmaceutical Industry" – Lucia Golzio Consultant Altran

"Alternative Methods: 3D models and new technologies" – Giovanna Mazzoleni, University of Brescia

All lectures were very intense, attended with great interest by the participants, and followed by pleasant and fruitful discussions. We realized the big need for having workshops aimed at the scientific divulgation of the 3Rs culture. Certain that the "seed" of the 3Rs culture has been planted into new fields, we are going to work into this direction, implementing stronger connections between researches and developing more and more reliable alternative methods.

What can health research learn from toxicology?

Research into Alzheimer's disease has made slow progress and there is still no disease-modifying therapy. A new paper (Langley GR, 2014) suggests that research would benefit from a paradigm change resembling the current transition in toxicology.

There have been many late-stage clinical trial failures of compounds tested for Alzheimer's disease in transgenic mice, the dominant models. With the inevitable limitations of species and strain variations, the quest to improve animal studies seems outdated when advanced techniques could be applied to human-relevant models.

Modernising the paradigm for Alzheimer's disease research and drug discovery, in parallel with toxicology, would involve a shift of focus and resources towards human species-specific *in vitro*, *in vivo* and *in silico* models, probed with 21st-century tools. For example, neurons with the classic cellular hallmarks of Alzheimer's disease have now been produced from patient-derived induced pluripotent stem cells.

Systems biology enables the discovery of human disease pathways and networks at multiple scales, providing novel drug targets. Adding human exposomic and epigenomic data could allow the elucidation of complete pathways of disease, from exposure to outcomes – similar to the adverse outcomes pathway concept in toxicology.

A discussion is needed on how best to incorporate 21st-century advances into a strategic new framework for Alzheimer's disease research, based primarily on human – not animal – disease pathways. Humane Society International is also working to extend the paradigm change to health research and drug discovery across the board: the benefits could be life-saving.

Gill Langley, Humane Society International glangley@hsi.org

CELLTOX participates to the PhD Program in Translational Medicine



The PhD Program in Translational and Molecular Medicine (DIMET) interdisciplinary and inter-departmental project of the University of Milano-Bicocca, aimed to accelerate the translation of discoveries into a mode of delivery that will benefit human health. The translational research program will train, at the European level, novel hybrid researchers that will be able to rapidly translate scientific advances to the patient's advantage. Building such international translational highways requires innovative educational models and career paths, with the aim of providing crossdisciplinary training for PhDs and MDs with potential bench-to-bedside round trips.

In frame of the DIMET educational activities, Dr. Giovannoni Roberto (UNIMIB), Dr. Tiranti Valeria (IRCCS Foundation Neurological Institute "C.Besta") and Dr. Torsello Antonio (UNIMIB) organized a three-days course on "Experimental models in translational medicine: how to produce and how to use them" in Milan open to Ph.D. students and

researchers. The course was aimed to provide students and researchers the information about production and possible application of *in vivo* and *in vitro* models in biomedical applications. Dr. Meloni, president of CellTox Association, contributed to this event with a comprehensive presentation on how the *in vitro* models could expand the potentiality of toxicology and pharmacology studies, both in terms of necessary reduction of animal use in the experiments and in terms of efficacy of several *in vitro* assays.

Participants of the event appreciated the integrated *in vitro/in vivo* approach that expands the scientific benefits for researchers applying these different techniques for several scopes.

ECHA publishes the report on alternatives to animal testing

On 2 June, ECHA published the second report on the use of alternative to testing on animals for the REACH regulation. A total of 38'000 dossiers have been analyzed from the ECHA registration database. The report shows that registrants make use of alternative testing methods and strategies.

Building categories and predicting substance properties by read-across is the most widely used method. Combining information together from different sources (weight-of-evidence) is the second most common method, followed by computer modelling ((Q)SAR).

In vitro methods have been used to provide information on skin and eye irritation, and skin corrosion. Since 2011, the number of such tests has grown from 442 to 1'410, representing a 3.2 fold increase. In addition, almost 20% of the analysed dossiers contained in vitro studies, either alone or combined with other information.

http://echa.europa.eu/web/guest/about-us/the-way-we-work/plans-and-reports

Courses calendar



25-29 January 2015

ESTIV and APTox organize a training course **Applied** *in vitro* **Toxicology Course** Lisbon, Portugal

http://estivtraining.webs.com/

Meetings calendar



24-28 August 2014

9th World Congress on Alternatives and Animal Use in Life Sciences: "Humane Science in the 21st Century"

Prague, Czech Republic www.wc9prague.org

28-29 August 2014

WC9 Practical Training Course on Alternative Methods: Skin and Eye *In Vitro* Toxicity

as a satellite meeting to the 9th World Congress on Alternatives to Animal Experiments (WC9) in Prague, Czech Republic.

http://www.wc9prague.org/satellitemeetings/course-on-alternative-methods/

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7-10 September 2014

EUROTOX - 50th Congress of the European Societies of Toxicology

Edinburgh, United Kingdom http://www.eurotox2014.com/

16-17 October 2014

Annual meeting of the French Society of Toxicology: Alertes et Risques Toxicologiques en 2104: Evaluation et Perception
Annecy, France
http://www.sftox.com/

23-24 October 2014

3rd Symposium on **Fish and Amphibian Embryos as Alternative Models in Teratology and Toxicology**

Aulnay-sous-Bois, Paris, France https://www.ufz.de/fish-frog-embryo/

10-11 November 2014

Annual meeting of the UK *In Vitro* Toxicology Society

Astra Zeneca's Alderley Park, Macclesfield, Cheshire, UK

http://www.ivts.org.uk/site/ivts2014/

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12 November 2014

Third Annual Meeting of the American Society for Cellular and Computational Toxicology will feature a plenary lecture by Robert Kavlock, Deputy Assistant Administrator for Science, Office of Research and Development, US EPA, and be focused around the topic of AOPs and their use as a framework to develop new tools for chemical assessment. The meeting will be held on the NIH campus in Bethesda, Md and will feature oral and poster presentations, a panel discussion, and a reception.

www.ascctox.org.

27 November 2014

Animal Replacement Science 2014: Improving relevance to human disease -

challenges, innovations and applications-Charles Darwin House, London

www.animalreplacementscience.com

Workshops calendar

3-5 September 2014

Adverse Outcome Pathways: From Research to Regulation — Workshop exploring how regulatory, industrial, and NGO stakeholders can work together to advance research activities on various adverse outcome pathways to regulatory use efficiently and effectively. Sponsored by the Program Interagency National Toxicology Center for the Evaluation of Alternative Toxicological Methods (NICEATM), Physicians Committee for Responsible Medicine (PCRM), The European Union Reference Laboratory for Alternatives Testing (EURL ECVAM). and Animal endorsed by the Society of Toxicology. Will be held at the NIH Natcher Conference Center in Bethesda, Md, Sept. 3-5, 2014. The workshop will features scientific talks, case studies, breakout group discussions, and a hands-on demonstration of the OECD AOP-Knowledge Base tool set. More information and registration can be found on the web site: http://ntp.niehs.nih.gov/go/41374.

Recent Publications of ESTIV members

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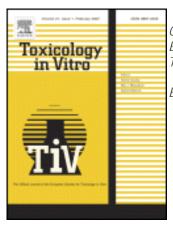
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Toxicology in vitro



Official Journal of the European Society of Toxicology in vitro

Editors: Daniel Acosta.

ESTIV Corporate member



W e Innovate Healthcare

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology. inflammation, metabolism and CNS. Roche is also the world leader in in vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. In the pharmaceutical research field, Roche is committed to support in vitro approaches to assess efficacy and toxicity of compounds, as a sign of its strong commitment with the 3R-principle.

http://www.roche.com



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https://www.vito.be/EN/HomepageAdmin/Ho me/home/Pages/Homepage.aspx

ESTIV Affiliated Societies

Associazione Italiana Tossicologia In vitro - CellTox

Dutch-Belgium Society for *In vitro* Methods–INVITROM

UK In vitro Toxicology Society - IVTS

Scandinavian Society for Cell Toxicology – SCCT

ESTIV membership fee

Membership fee

The membership for an individual member for 2014 is € 30.00. If you are also a member of one of the affiliated societies (CellTOX, SSCT, INVITROM, IVTS), the membership amount to € 18.00.

Method of Payment

Bank Transfer

RABOBANK, IBAN #: NL20 RABO 0101 4857 51

BIC: RABONI 2U

Attention of: ESTIV

Polderkade 1, NL-5345 RR Oss, The Netherlands Due to the high costs of applying for and cashing EuroCheques, please do not use this means of payment.

It is also possible to pay the membership fees by our convenient and secure online credit card payment services (PayPal), To use these services, please visit the ESTIV website at:

http://www.estiv.org/member.html

Laura Suter-Dick

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ESTIV e-mail list

ESTIV has an e-mail list, which has the potential to be a very valuable resource. There are many types of questions that you could pose to the list, whether you are a junior or a senior scientist. To send a message to all ESTIV members on the list (presently more than 200 colleagues), simply address your estiv@freelists.org

This is a "closed" list, which means the "list-owner" (Elsa Casimiro) is able to select who is allowed to join. Only ESTIV members will receive the message. However, please note that this list should not be used to send confidential messages or attachments as these are uploaded to the 'freelists' archive that can be accessed by the general public. If you have never received a message from the ESTIV list, it is because you have not informed us of your e-mail address. Please correct this by sending a message to me at secretariat@estiv.org and your name will be added.

Elsa Casimiro

"ESTIV also owns a group on LinkedIn, to communicate and to allow ESTIV members to update each other on career moves, etc. The group is only open to ESTIV members. Search for the group "ESTIV" and register".

ESTIV Executive Board Members

EXECUTIVE BOARD	POSITION	E-Mail
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