



## Meeting report

# Futuristic Approach to Alternatives

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A one day seminar, “Futuristic Approach to Alternatives,” sponsored by the Indo-French Centre for the Promotion of Advanced Research (IFCPAR/CEFIPRA) and co-sponsored by L’Oréal India, was organized at the Indian Institute of Technology Bombay (IITB), Mumbai, India, on November 17, 2015. Dr Abhijit Majumder, Department of Chemical Engineering, IITB, and Dr Jose Cotovio, L’Oréal Research & Innovation, Aulnay, France, were the Indian and French coordinators, respectively. This was the first national event on alternative methods hosted by an IIT, a group of autonomous Indian institutes with the President of the country as the *ex officio* visitor and with their council directly under the President of India. This highlights the importance the concept of alternatives has gained in India in recent times. India’s recent ban of testing of cosmetics and cosmetics ingredients in animals and of import of cosmetics tested on animals has created an urgent need for development of alternative approaches for animal testing and their validation to meet the regulatory guidelines. Sixteen institutes of high academic repute, 15 industry (beauty & hygiene, pharmaceuticals and chemistry), international experts, regulatory community, NGOs, scientists and students attended the seminar.

Dr **Yogendra Kumar Gupta**, All India Institute of Medical Sciences (AIIMS), New Delhi, delivered the keynote address and said “man and animals are an evolving relationship”, and “equal partners on planet earth” and “animals do not consent to be subjected to experiments, so the responsibility and accountability are in the hands of the scientists and regulators.” He underlined the need to adopt or develop and validate multiple tools and organ-on-chip models in series to evaluate systemic effects of new molecules. Dr **Christian Pellevoisin** (EPISKIN Academy, France) and Dr **Namita Misra** (L’Oréal Research and Innovation, Bangalore, India) spoke about alternative toxicological methods for hazard evaluation and risk assessment that can replace animal use while ensuring human safety when formally validated. Current validated tests address topical and acute toxicities. Integrated approaches to testing and assessment (IATA) hold the promise to support risk assessments that cannot be made on the basis of single *in vitro* / *in silico* test methods.

Dr **Mahendra Sonawane**, Tata Institute of Fundamental Research (TIFR), Mumbai, elaborated upon the embryological and genetic advantages of zebrafish, especially the mutant forms of disease models, for small molecule screening and drug discovery and highlighted their use for assessing the

mechanisms involved in the maintenance of epidermal integrity. Dr **Prabha Nair**, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, emphasized how artificial tissues/organs can be used for toxicity testing. She said that 3D open porous scaffold structures would enhance their mechanistic properties as well as degradability and discussed how 3D scaffolds developed for tissue engineering in regenerative medicine can be adopted for 3D *in vitro* test models. Dr **Gilles Marcou**, University of Strasbourg, France, focused on drug-induced hepatotoxicity / drug-induced liver injury (DILI). He introduced the HepG2, Hepa-RG and KaLy *in vitro* models and went on to explain how his team came up with a validated DILI prediction as a combination of theoretically calculated parameters and measured *in vitro* biological data. Dr **Kareenhalli V. Venkatesh**, Chemical Engineering Department, IITB, spoke on systems engineering perspectives of human metabolism. Elaborating upon systems analysis and quantitative approaches, he introduced the concept of “interactomics”. His research group has developed a cell-to-human framework comprising five modules, i.e., data mining, networking, modeling, experiment and validation, to address human physiology and diseases. Dr **Dhananjaya Dendukari**, Achira Labs, Bangalore, presented a cost-effective approach of designing and producing microfluidic device in which silk yarn coated with different reagents is woven into a patch of fabric which can be used to perform simple capillary flow based tests.

Dr **Anne Gourmelon** made a presentation on OECD (Organisation for Economic Co-operation & Development) guidelines. The OECD plays a pivotal role in the harmonization of test methods for pre-clinical chemical safety testing, and in the promotion of alternative methods that follow the principles of the 3Rs (replacement, reduction, refinement of animal testing). India is an adherent to the Mutual Acceptance of Data system at OECD and will in future be a heavy user of the advanced test methods; it is therefore essential to maintain good communication and strengthen collaboration between stakeholders across countries. Dr **Nilesh Joshi**, Blue Turtle Biotechnologies, USA, presented the perspectives of a start-up biotechnology company and emphasized the need for low-cost alternative testing systems. Dr **Aditya B. Pant**, CSIR-Indian Institute of Toxicology Research, Lucknow, India, spoke about the present situation of alternatives in India. He opined that the use of animals is inevitable in research and higher studies and called for country-specific standard operat-



ing procedures for the use of animals for experimental and educational purposes.

The participants were assigned to five discussion sessions on cellular and lower animal models, *in silico* and systems biology, future technologies, challenges and expectations of industry, and regulation and implementation.

The outcomes were presented in a common session. This was followed by a panel discussion on “Animal Studies in India: Challenges and the road ahead”.

Proposals were made to form a consortium for alternatives research in India to support networking of the stake-holders, to organize this meeting annually, and to approach the

government to open a center of excellence for alternatives research.

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## Meeting report

# New Alternative Models for In Vitro Toxicology

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On June 21, 2016, a meeting was held on “New alternative models for *in vitro* toxicology studies,” chaired by Prof. Giovanna Mazzoleni and Prof. Francesca Caloni and organized by CELLTOX, the Italian Association of *in vitro* Toxicology, in partnership with MISTRAL (Integrated Models for Prevention and Protection in Environmental and Occupational Health) Research Center, University of Brescia, Italy. The meeting was hosted by the Faculty of Medicine and Surgery, University of Brescia. The aim of the meeting was to present new *in vitro* methodologies and their applications in different areas, from veterinary toxicology to neurotoxicology.

Prof. **Francesca Caloni** (DIMEVET, University of Milan), president of CELLTOX, presented a lecture entitled “Predictive models in veterinary toxicology: *in vitro* epithelial barrier.” The main concept was the use of *in vitro* 3D epithelial barrier models as predictive tools for toxicological adverse effects of xenobiotics and their bioavailability in animals and humans. In the area of veterinary toxicology it is critical to emphasize the importance of species-specific predictive tools, like the porcine small intestinal epithelial cell line, JPEG-2 (Zagabresky, 2013), the bovine mammary epithelial cells, BME-UV (Al-Bataineh, 2012) and the 3D dog skin equivalent model air-liquid interface (Serra, 2007) to evaluate the absorption, bioavailability, metabolism, and toxicity of natural or synthetic xenobiotics, alone or in mixtures. Moreover, a species-specific bovine primary granulosa cell model was

introduced as a predictive tool for endocrine disruptor effects (EATS mechanisms) (Petro, 2012).

Dr **Susanna Alloisio** (ETT, Genoa) presented a sensitive *in vitro* tool useful to detect and evaluate neurotoxicity not only of pure chemicals, such as pesticides or drugs, but also of mixtures of not completely known composition, such as environmental biotoxins and herbal oils. The approach evaluates the spontaneous electrical activity developed by primary neuronal networks derived both from embryonic or neonatal mouse cortex grown on microelectrode array (MEA) chips. The major advantages of this *in vitro* cell-based model are the ability to reproduce to a great extent the functional activity of CNS *in vitro* and the ability of MEAs to automatically record neuronal activity over several days or weeks. Several cultures can be monitored in parallel and followed for days or weeks. The sensitivity, versatility and high throughput make the MEA-based assay useful for the screening of chemicals and mixtures. Furthermore, a specific multiparametric analysis is performed in order to evaluate more accurately the effects of chemicals on neuronal functional activity and their neurotoxic potential (Alloisio, 2015, 2016).

Dr **Marisa Meloni** (Vitroscreen, Milan) presented the topic “Adipocytes: scaffold free microtissues for preclinical and toxicology applications.” Her group developed human-adipocyte spheroids. These 3D adipose microtissues