



Workshop report

First Training on Alternatives to Animal Experimentation in Tunisia

Sarrah M'Barek¹, Christian Pellevoisin², Christophe Chesné³, Francois Busquet⁴ and Ouajdi Souilem⁵

¹Unit of Functional Proteomics and Organic Food Preservation, High Institute of Applied Biological Sciences of Tunis (ISSBAT), University of Tunis El Manar, Tunisia; ²Episkin Academy, Lyon, France; ³Biopredic International, Saint-Gregoire, France; ⁴CAAT-Europe, University of Konstanz, Konstanz, Germany; ⁵Laboratory of physiology and pharmacology, National School of Veterinary Medicine, University of Manouba, Sidi Thabet, Tunisia

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1 Introduction

The training course entitled “From *in vivo* models to cell models” took place at the National School of Veterinary Medicine (ENMV) of Sidi Thabet (University of Manouba) on February 23-26, 2015. It was organised by ICLAS (International Council for Laboratory Animal Science), ATSAL (Tunisian Association for Laboratory and Animal Science) and ENMV (National School of Veterinary Medicine of Tunisia) and was the outcome of an international collaboration with CAAT-Europe, Episkin Academy and Biopredic International. Thirty-four participants with different educational backgrounds, i.e., researchers, teacher-researchers, veterinarians, pharmacists, biologists and doctors, PhD or master degree students and from different regions of Tunisia, i.e., Tunis Capital, Greater Tunis, Bizerte, Kef (North), Monastir, Sousse (Central South), attended the training. There were Tunisian and three international speakers. The language used in the talks, debate and workshops was French.

Prof. Souilem, Tunisian National ICLAS Representative, introduced the training. He surveyed the animal ethical bases and the evolution of man's perception of animals through the ages and according to civilizations and countries. He asked that “Every scientist should take in consideration the respect of animal and its intrinsic value before the application of 3Rs.”

Dr M'Barek gave an overview of different alternative methods and their status of validation. She introduced different international organisations for the validation of alternative methods, in particular EURL ECVAM (European Union Reference Laboratory for Alternatives to Animal Testing). She also distributed a questionnaire aimed to assess the Tunisian scientists' awareness and knowledge of alternative methods. As there is neither existing data on the topic nor statistics of animal testing or alternative methods in Tunisia, analysis of this data will help development of alternative methods and

prioritize installation of validated alternative tests in the country. The first analysis of the questionnaires indicates that, as in Europe, laboratory animal species mostly used for scientific purposes are rodents, especially mice and rats. However, local species, in particular dromedary (*Camelus dromedarius*) or desertic rodents (*Meriones* and *Psammomys*), are also used.

Dr Masmoudi from Tunis El Manar University showed how cell culture minimized the number of animals needed to perform an experiment. She presented a new cell culture platform dedicated to teaching which is supported by the World Bank and started in 2012. She reported on the enthusiasm among the majority of her students on using alternatives in practical work instead of sacrificing animals. This talk launched a long, constructive debate because many teachers present at the meeting were very interested in Dr Masmoudi's new teaching approach. They asked about all the experimental conditions and details of this new experience with the prospect of transferring this technology to their universities.

Three workshops consisted of practical works and were respectively organized by ATSAL/Pasteur Institute of Tunis, Biopredic International and Episkin Academy. The informal form of the handling session is a good opportunity for discussions with participants, which can build networks between scientists from public institutions and private companies to prepare and support the regulatory evolutions in Tunisia. A further workshop, organized by CAAT-Europe, was an open discussion which offered the opportunity to discuss collaborative projects (medium and long term) with the scientific and medical community as well the industry represented by the Tunisian Chemistry Technical Center. The subject was the setting up of a test platform in Tunisia to fulfil the implementation of the REACH (Registration Evaluation, Authorisation and Restriction of Chemicals) regulation. The representatives of the above mentioned international organisations actively participated in the workshops.



Group photo of participants with instructors

2 Contributions

2.1 Contribution from ICLAS (International Council for Laboratory Animal Science)

ICLAS is an international umbrella organization, the aim of which is to advance human and animal health by promoting the ethical care and use of animals in research worldwide. Tunisia has integrated ICLAS since 1998 and ICLAS considers the National School of Veterinary Medicine of Sidi Thabet as a platform to diffuse laboratory animal sciences in French-speaking Africa. Prof. J. R. Maisin (past ICLAS President) made a great effort to drive ICLAS activities in the region since 1997 in coordination with the Tunisian National ICLAS Representative, Prof. O. Souilem. 3Rs principles and the international guiding principles for biomedical research involving animals (ICLAS/CIOMS) and OIE recommendations on laboratory animal welfare was provided to all participants and discussed in this training.

2.2 Contribution from CAAT-Europe

The European Union (EU) is spearheading worldwide efforts when it comes to the use of laboratory animals for scientific purposes. In the context of the EU internal market, one of the competences of the European Commission is to negotiate bilateral agreements on behalf of the EU member states with other countries. These discussions are currently taking place between EU and other non-EU countries such as Tunisia or USA within its TTIP (Transatlantic Trade for Investment Partnership). EU laws (e.g., Directive 2010/63/EU, REACH, ban on animal testing for cosmetics, etc.) are also becoming a part of the “package” that non-EU countries need to negotiate/implement to sell their products on the EU market, which represents half a billion of consumers. As a direct consequence, the use of alternatives to animal testing becomes also a clear need for these countries. Having this in mind, CAAT-Europe has decided to increase the dissemination of 3R’s state-of-the-art beyond EU borders. The

economical and political context gives an added opportunity to discuss the topic next to the ethical and scientific aspects. CAAT-Europe’s involvement in Tunisia was to advocate alternatives to animal testing and to provide the necessary support, know-how and network to add to existing and local expertise and bridge those with training activities on 3R’s. **Dr Busquet** aimed to create momentum and present new models (e.g., *in silico*, *in vitro* and organs-on-a-chip), current state-of-the-art in the EU, the paradigm shift in toxicology (e.g., adverse outcome pathways) as well as to introduce the zebrafish embryo toxicity test as a low-cost but valuable model for academic research purposes.

2.3 Contribution from Episkin Academy

Episkin SA, a subsidiary of L’Oréal, is a pioneer in supplying *in vitro* human reconstructed epidermis (RHE) and epithelial tissue models (corneal, gingival, vaginal...) worldwide. The workshop in Tunisia was the opportunity to access to a large number of scientists coming from different areas, i.e., basic and applied science as well as public laboratories. In the first part of the workshop “3D models: Reconstructed Human Epidermis and Skin,” Dr Pellevoisin gave an overview of the regulatory context, the concept of alternative methods and how to validate them. The second part illustrated the industrial applications of tissue engineering to assess safety and efficiency of chemicals, cosmetics, drugs or medical devices. During the handling session, all participants learnt how to assess the irritancy potential of 2 products in a real situation with living tissues. This 4 hour session was based on the OECD TG 439 for *in vitro* skin irritation of chemicals, a regulatory method using reconstructed human epidermis (RHE), which is robust, widely used, easy to handle and easy to implement.

2.4 Contribution from Biopredic International

Biopredic International aimed to show veterinary students, doctors and scientists how human hepatic HepaRG cell cul-



ture, a new *in vitro* tool promoted by Biopredic, was developed over the last 5 years. The cells became a popular model for cytochrome P450 (CYP) induction studies (to study drug-drug interactions, a regulatory requirement) and were included recently in an OECD draft test guideline after being validated in a multicenter laboratory study coordinated by EURL EC-VAM. The established CYP induction application of the cells, together with new applications related to predicting cholestatic side effects, and the more industrial/biotechnological aspects around the scale up of the production of the cells were covered. **Dr Chesné** gave the perspective of a small biotechnology company dealing with the aspects of patenting, production and application of an *in vitro* system.

3 Conclusion

The first training on alternative methods was successful and received a very positive feedback amongst the participants. With such scientific events on 3Rs in Tunisia we hope on the one hand to initiate within the participants an innovative way

of thinking about care and use of laboratory animals and a changing attitude towards animal testing as well as to develop an interest and spread education about animal welfare and alternatives in all the Tunisian scientific community. On the other hand, in a close future, we hope to offer the possibility to all participants and maybe the whole Tunisian scientific community to use some of the validated alternative methods that will be established in Tunisia or to give them all the information available and educational support to set up a validated alternative method by themselves.

Correspondence to

Sarra M'Barek
High Institute of the Applied Biological Sciences
of Tunis (ISSBAT)
University of Tunis El Manar
Tunisia
Phone: +216 71 573 721
e-mail: mbareksarra@gmail.com

Workshop report

No alternatives? Animal experimentation and the future of research

Mardas Daneshian

Center for Alternatives to Animal Testing – Europe, University of Konstanz, Germany

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Owing to the rapid scientific developments the scientific landscape around alternatives to animals in research and testing has received noticeably increased attention from the manifold stakeholders interested in human-relevant methodologies and humane approaches in recent years. Now, the new interest of politics in the field of alternatives also endorses its societal and economic significance. In many countries, e.g. UK, USA, China and Brazil, annual allocations of governmental funds for research on non-animal approaches have been substantially increased, and now also in Germany the interest of politics in this field has awakened.

On October 2, 2015 the Green Party (*Bündnis90/Die Grünen*), which received 8.4% of the vote in the last par-

liamentary elections in Germany, invited experts to discuss the possibilities, hurdles and possible measures to facilitate competitive research in the field of alternatives. Under the headline “No alternatives? Animal experimentation and the future of research” a technical discussion was moderated by Nicole Maisch, spokesperson for animal welfare policy, and Kai Gehring, spokesperson for research policy of the Green parliamentary group at the parliamentary building Paul-Löbe-Haus in Berlin.

Participants of this panel discussion, held in front of 80 politicians and stakeholders, were Prof. Ellen Fritsche, Leibniz Institute of Environmental Medicine and Head of CERST, Dr. Reyk Horland, Head of Business Development at TissUse