Alternative methods and *in vitro* skin 3D tissue models: What's new for toxicity testing and cosmetic?

Edith Flaire[1,2], Rachida Nachat-Kappes[3], Camille Laporte[6], Marie-Françoise Harmand[1], Marina Simon[1], Christian Poinsot[1]

[1]Groupe ICARE. Biopôle. Rue Emile Duclaux 63360 Saint Beauzire
[2]UMR 1019 INRAE-University Clermont-Auvergne, UNH (Human Nutrition Unity), ECREIN Team, 63000 Clermont-Ferrand, France
[3]InnovSkin, 63140 Chatel-Guyon, France
[4]Institut Universitaire de Technologie, Université Clermont Auvergne, UMR INSERM-UCA, U1240, France
[5]Univ. Grenoble Alpes, CEA-Leti: division for Biology. 38000 Grenoble. France

Presenting author edith.filaire@groupeicare.com

INTRODUCTION

Evaluation of absorption through the skin barrier and the irritation potential of drugs, pesticides and more generally chemicals can be carried out using *in vitro*, *ex vivo* and *in vivo* models, skin toxicology testing in the cosmetics and pharmaceutical industries being used to identify whether new compounds are toxic to human skin. For many years, toxicological studies have been performed on animals. However, the use of animals has long been a matter of controversy. Indeed, concerns have raised about animals' sentience, and whether the justification for harms is acceptable[1]. In consequence, there is a strong need for more representative human models, which are reproducible, easy to use and cost-effective. Guidelines of standardized and codified methods for the testing and assessment of chemicals have been produced by the Organization for Economic Cooperation and Development (OECD). In July 2021, several new non-animal-based OECD Test Guidelines were also published, without including the three-dimensional (3D) cell culture approach. Use of this last approach can provide potential solutions with more complex organotypic models. This approach has already been used in cosmetics industry following a complete banning cosmetic developed through animal testing in the European Union since 2013 (EU Regulation no. 1223/2009). Other developments of human-based three-dimensional *in vitro* testing models such as the 3D bioprinting technology enable the simultaneous deposition of multiple types of human skin cells, and the generation of *in vitro* 3D vascularized skin models with dynamic perfusion and microfluidic devices known as skin-on-a-chip, which are good candidates for tissue modeling. They enable a more physiological transport of nutrients and permit a high-throughput and less expensive evaluation of drug candidates in terms of toxicity, efficacy, and delivery[2]. Next-generation organoids including not only skin components (keratinocytes, fibroblasts, and dermal collagen) but also immune cells to study the role of innate and adaptive immunity are also investigated[3]. This conference presents the different 3D skin models available, highlighting the advantages and disadvantages of the existing models and focuses on recent innovative 3D cell culture with their future applications.

CONCLUSION

The development of Organ-on-a-chip (OCC) technology is promising for generating engineered models for drug testing. However, most OOC models are based on a single type or tissue. The next step is to generate multi-OOC platforms that emulate entire biological processes[4]. Besides the challenges, the technology needs to be validated and accepted by the regulatory bodies as an efficient method for testing newly developed drugs. Collaboration between researchers, regulatory bodies and the industry would be necessary to obtain this validation.

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