Dirk Petersohn, J Clinic Toxicol, 2018, Volume 8
DOI: 10.4172/2161-0495-C1-027

The Phenion® full-thickness skin model: A versatile tool for efficacy and toxicological testing of dermally applied compounds

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Skin is the site of first contact for many chemicals like topically applied dermo-pharmaceuticals, cosmetics or intra-cutaneous injections used in e.g. aesthetic medicine. Traditional two-dimensional monolayer cultures of skin cells are limited in modelling those exposure scenarios. In contrast, Phenion® Full Thickness skin models mimic native human skin in its histological architecture and in a wide spectrum of physiological and biochemical properties. Primary human keratinocytes form a fully differentiated epidermis. It is connected through basement membrane proteins with the underlying dermis which comprises a unique and stable collagen meshwork populated with fibroblasts of the same donor. These conditions boost the de novo synthesis of extracellular matrix proteins like elastin and collagens. Its biological equivalence with human skin makes the tissue model perfectly suited for efficacy testing of substances, e.g. for the intra-cutaneous injection of new hyaluronic acid formulations which are intended to activate gene and protein expression of extracellular matrix molecules. Additionally, toxicological assessments can reliably be performed, as exemplified hereafter for genotoxicity studies. Primary human skin cells in the Phenion® FT skin model keep their normal cell cycle control and DNA-repair competence while additionally exhibiting the xenobiotic metabolism of skin. Beside others, these features make the skin model an ideal tool to be combined with an established toxicological read-out parameter to develop the 3D Skin Comet assay. Recently, the first phase of an ongoing validation exercise has been finalized showing an excellent predictivity in the five participating, international laboratories. Meanwhile, the 3D Skin Comet assay has successfully been used to support the toxicological safety assessment of three cosmetic ingredients. The complete validation data set is expected to build the basis for a broader regulatory acceptance for product risk assessments where the dermal route of exposure is most relevant.

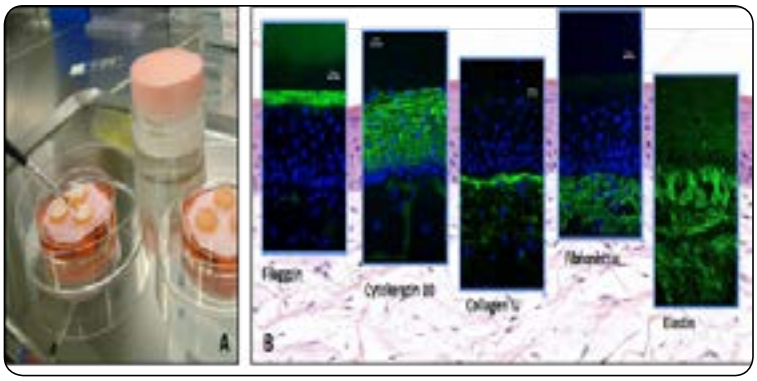

Figure 1: Phenion® Full Thickness skin model mirrors native human skin. (A) Skin models during substance application. (B) Cross section of a paraffin- embedded skin model (background), overlaid with immunofluorescence pictures of the tissue. Blue- DAPI, green- proteins as indicated labeled with FITC-linked antibodies.

Recent Publications

1. Ackermann K et al. (2010) The Phenion full-thickness skin model for percutaneous absorption testing. Skin Pharmacol. Physiol. 23(2):105-112.
2. Jäckh C et al. (2011) Characterization of enzyme activities of Cytochrome P450 enzymes, flavin-dependent monooxygenases, N-acetyltransferases and UDP-glucuronyltransferases in human reconstructed epidermis and full-thickness skin models. Toxicol In Vitro. 25(6):1209-1214.
3. Meloni M, Farina A and de Servi B (2010) Molecular modifications of dermal and epidermal biomarkers following UVA exposures on reconstructed full-thickness human skin. Photochem. Photobiol. Sci. 9(4):439-447.

4. Mewes K R et al. (2007) Elastin expression in a newly developed full-thickness skin equivalent. Skin Pharmacol. Physiol. 20(2):85-95.
5. Reisinger K et al. (2018) Validation of the 3D Skin Comet assay using full thickness skin models: transferability and reproducibility. Mutat Res. 827:27-41.

Biography

Dirk Petersohn studied biology and conducted his PhD studies at the University of Cologne, Germany on the topic of tissue specific gene regulation in the human nervous system. After his Postdoc studies on wound healing mechanisms in the team of Professor Doctor Thomas Krieg, he joined Henkel AG & Co KGaA in 1998. Since than he held various positions in research and development and is currently the Director of Henkel's Department of Biological and Clinical Research. Additionally, he Vice-Chairs at Cosmetics Europe's Steering Scientific committee and Chairs the Task Force Skin Tolerance that is developing approaches to assess skin sensitization of chemicals without the use of animals.

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