The reconstituted human epidermis, RHE: A suitable model to evaluate the effects of environmental pollutants on skin homeostasis

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The skin, the largest body organ, referring to its surface and weight, is chronically exposed to environmental stress factors, such as ultraviolet (UV) and ozone (O₃), or to pollutants of anthropic origin, such as cigarettes smoke or diesel/gasoline fuel exhaust. The skin provides the first barrier against the outdoor stressors, it is mainly composed of two main compartments, the epidermis, the outermost layer and the dermis, rich of fibroblasts, nerves and vessels.

The epidermis

The ability of the skin to work as an effective barrier, depends also on the characteristics of the epidermis. This protective envelope comprises the stratum corneum (corneocytes), a physical barrier against both penetrations of dangerous substances and excessive trans-epidermal water, electrolyte and protein loss; more deeply, a corneocytes-bound intercellular hydrophobic matrix, forms a chemical barrier against the entry of environmental contaminants, including ambient particulate matters or pathogens. Finally, the deepest layer of the epidermis, is constituted by humoral and cellular components of the adaptive immune system that represent an immunological barrier [1].

Skin exposure to environmental pollutants

It is well known that exposure to pollutants affects the skin barrier functions and that chronic exposure of the cutaneous tissue to stressors such as UV light, ozone and particulates matter induces oxidative stress, inflammation, and can result in cutaneous premature aging. Concerning ozone, it has been demonstrated that stratum corneum, as the outer skin barrier, is the main target of oxidative damage [2,3] which leads to the generation of a cascade of bioactive molecule able to react with lipids, proteins and even DNA.

In this scenario, the development of formulations for a selective mode of protection from different pollutants, is extensively being explored.

Nowadays, the use of excised skin is still considered greatest approach for the developing of novel skin therapeutics. However, both the logistic limitations of an “ex vivo” study with human epidermis explants and the differences between human and animal skin, limits the use of animal models.

In this context, even if keratinocytes cell cultures have been extensively studied with the aim to understand the usages of pollution-protective substance and although some promising result as have been achieved, often it is difficult to extrapolate the data to real life due to the model limitations. Therefore, all these issues have driven the search for novel realistic three-dimensional skin models.

The reconstituted human epidermis, RHE, skin model

RHE is a tissue model composed of human epidermal keratinocytes that develop a fully-differentiated epidermal tissue, containing all...
viable (stratum basale, stratum spinosum, and stratum granulosum) and nonviable (stratum corneum) cell layers, after air-liquid interface cultivation on polycarbonate membranes: in about two weeks a fully differentiated cultured epidermis is reconstituted.

RHE reliably resemble in vivo structures, both morphologically and biochemically; they are metabolically and mitotically active, have a lipid profile very similar to human epidermis, and express normal epidermal differentiation markers such as keratin 1/10, profilaggrin, and involucrin. They are all grown in serum-free media system and are highly reproducible lot to lot.

The first in vitro Skin model goes back to the early 1980s [4] and over time several other academic laboratories have reported successful reconstruction of epidermis using similar techniques. These epidermal reconstruction models are suitable for basic research interest aimed at obtaining a better overall understanding of skin physiology. Over the years RHE are used in a broad range of applications including disease modeling after pollutants skin exposure. In addition, they are very useful to understand the protective effect of specific formulation since it is possible to apply to the RHE the final product.

In contrast, 2D keratinocytes model, grown in liquid culture conditions limits the used to compounds water soluble unless solvent such as ethanol are added to help study. Finally, 2D models do not show the expression of these differentiation markers, indicating a non-differentiated profile [5].

**Conclusion**

The important functions of skin make it a principal organ for body health and physiology. Accordingly, pharmacological and biomedical research necessitates appropriate test systems for finding novel drugs and treatments to protect the skin from pollutants insult. The constant advance in the field of in vitro skin models provide improved efforts, which more closely represent in vivo conditions. In particular, the RHE, is finely tuned for improving the knowledge of skin ageing and of physiological and biochemical pathways involved in its barrier role.

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**References**


