Improving reconstructed skin models by mechanical stimulation in organ-on-chip devices

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Physiological tissues are exposed to different mechanical stimuli in the human body. Mimicking these constraints in microsystems contributes to the establishment of more complex and functional organs-on-chip. Regarding the skin, the current *in vitro* models fail to reproduce the permeability characteristics of a native skin. According to previous study, the integration of a cyclic stretching function in a conventional protocol of reconstructed skin improved the maturity of the *in vitro* model. Here, we have developed a novel microfluidic system that integrates a reconstructed skin under dynamic perfusion and mechanical stimulation. The device combines the integration of hyper-elastic and porous materials made of polyethylene foam, reproducing the air-liquid interface under mechanical stimulation. The hyper-elastic membrane deforms under the effect of a pressure generated by the actuation liquid. During its deformation, the hyper-elastic membrane comes into contact with and deforms the foam located above it without any leakages or alteration of the foam.

We showed thanks to an indirect cytotoxic assay that this non-conventional foam material is suitable for tridimensional cell culture. We have demonstrated that the resulting reconstituted skin was well structured by a dermis populated by homogeneously distributed fibroblasts and a correctly stratified and differentiated epidermis. Moreover, we have observed a good expression of filaggrin (biomarker of terminal differentiation) by keratinocytes in the superficial layer.

This well controlled stretching system could be a promising device for mechanical stimulation of a skin model and could potentially be used for other biological models.

This work opens new perspectives for the design of new organoids on chip with integrated mechanical actuation.

Congrès. Berlin. MPS / Eurooc 2023