

# Skin bioengineering: from laboratory to clinic to industry

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The field of wound healing, whether for wounds with loss of substance, chronic ulcers or extensive burns, is of great economic, clinical and social importance. Our laboratory has long been interested in the search for new treatments for these ailments, based on skin Tissue Engineering techniques. A crucial aspect in this type of technique is the choice of the appropriate materials and methods to generate the scaffold that, containing the cells, provides mechanical consistency, three-dimensional shape and adequate signaling to the modelled tissue. Although there are many possibilities (natural, artificial and mixed polymers), and our laboratory has tested several of them, due to the biological properties of fibrin and its involvement in healing, we have obtained the best results with fibrin-based hydrogels, obtained mainly by polymerizing the fibrinogen present in human blood plasma or of commercial origin.

With these scaffolds, and using cells obtained from small biopsies, we have developed and patented 'basic' 3D equivalents of human skin, containing a lower dermal compartment and an upper compartment consisting of a well-differentiated epidermis. Although initially designed for the treatment of extensive burns, they were eventually used in different types of acute, chronic or surgical wounds, as well as in the production of 'humanised mice' for research uses.

Moreover, these skin equivalents proved to be an excellent platform from which, with appropriate optimizations, to develop new applications such as obtaining human skin by 3D bioprinting or developing mini 'organs on chips' (OoCs), which are useful in the necessary analysis of the efficacy and/or toxicity of new drugs, cosmetics and chemicals for human use. An additional advantage of OoCs is that they can be equipped with sensors that allow real-time measurement of the production of physicochemical and biochemical markers of interest in the modelled tissue or process.

Looking ahead, we are pursuing developments in several directions, such as: 1) Increasing the performance of skin equivalents by introducing materials that improve the properties of the scaffold or the equivalent (e.g., graphene). 2) Applying these developments to the modelling of tumour or inflammatory skin diseases of high prevalence and clinical importance (e.g. psoriasis). 3) Developing 3D cultures and OoCs containing other components present in the skin (e.g. immune or sensory) to achieve more 'mature' skins. 4) Equip OoCs with sensor and actuator systems to make them more effective and useful.