Biochip reduces the cost of manufacturing in vitro skin

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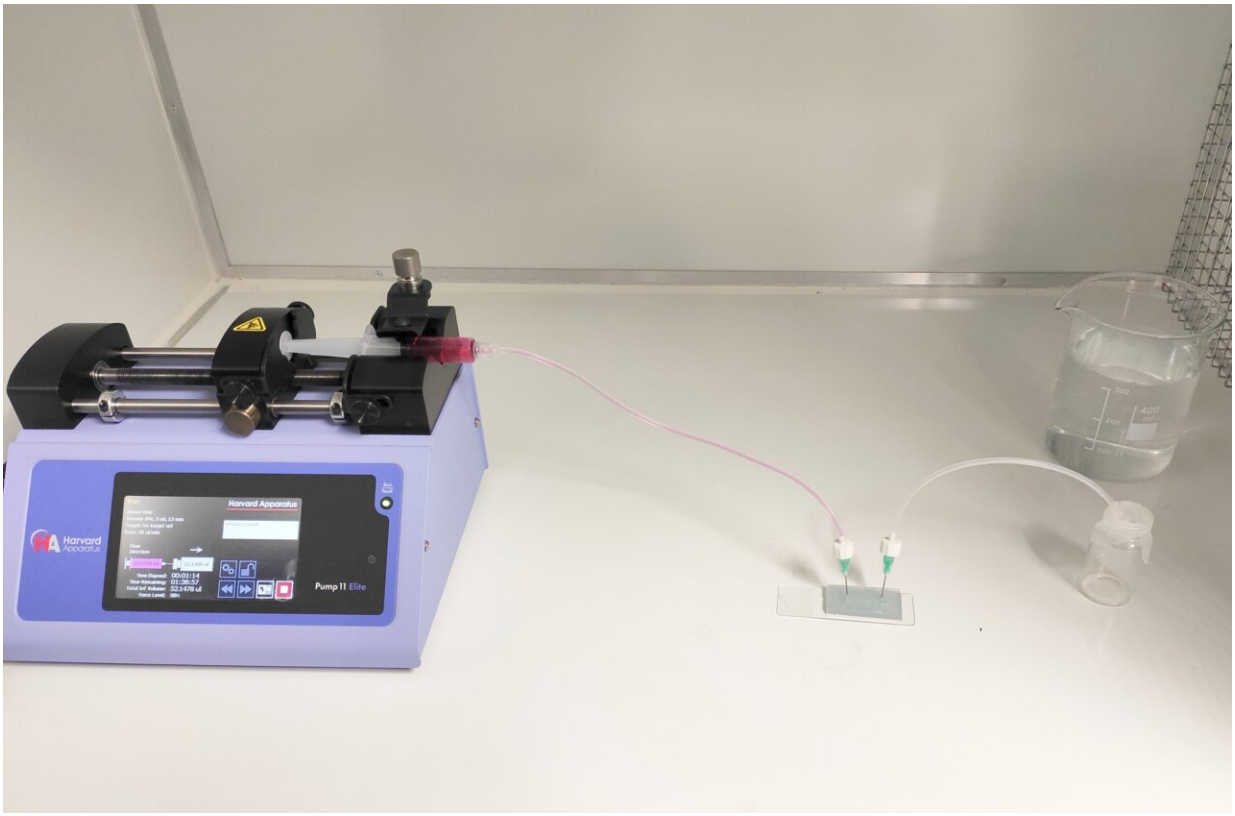

The biochip enables in vitro skin culture to be grown inside the biochip. The flows are controlled by highly accurate syringe pumps. Credit: UC3M

Researchers from the Universidad Carlos III de Madrid (UC3M), the Universidad Politécnica de Madrid (UPM) and other entities have designed a new biochip, a device that simplifies the process of

manufacturing in vitro skin in the laboratory and other complex multi-layer tissues. Human skin modeled using this device could be used in medicine and cosmetic testing, which would reduce the cost of these preclinical trials.

This biochip is made of biocompatible and micromachined adhesive vinyl sheets. "Most microfluidic devices are developed using ultraviolet lithography, a very expensive and complex technique that requires highly specialized instruments and highly qualified staff. In contrast, our technology is very cheap, accessible for any laboratory, and versatile, as its design can be modified virtually for free," explains one of the researchers, Leticia Valencia, from the Tissue Engineering and Regenerative Medicine-Integrative Biomedicine (TERMeG-INTEGRA) research group at the UC3M's Department of Bioengineering and Aerospace Engineering.

The biochip enables in vitro skin culture to be grown inside the biochip. It is divided into two overlapping channels, separated by a porous membrane: blood flow is simulated in the lower channel; skin is generated in the upper channel, which is nourished by the culture medium that flows through the lower channel via the membrane. "All flows are controlled by highly accurate syringe pumps and the procedure is performed in a cell culture room and a sterile environment. The biochips are incubated in a humidity-controlled atmosphere with 5 percent CO_2 and a temperature of 37°C," explains another of the scientists involved in this line of research, Ignacio Risueño, from the UC3M's Department of Bioengineering and Aerospace Engineering.

This platform and the techniques developed have been tested in a proof of concept that consisted of the generation of a three-dimensional skin with its two main layers. The dermis was modeled using a fibrin hydrogel, while the epidermis was created using a keratinocytes monolayer that is seeded onto the fibrin gel. In addition, the researchers

developed a new method for controlling the height of the dermis based on parallel flow, a technique that allows an in-situ deposition process of the dermal and epidermal compartments.

This research work does not have a clinical objective but rather is aimed at replacing animal models in medicine and cosmetic testing, as these tests could be carried out on this microfluidic platform directly. In fact, EU directives forbid the manufacture of cosmetic products that have been tested on animals and encourages the application of the 3Rs (Replacement, Reduction and Refinement) in animal research.

"Although it cannot be directly applied to a patient in a clinical setting, it would allow studies on personalized skin models to be carried out. This would consist of taking cells via a biopsy of a patient and creating the skin model in the microfluidic device using their skin cells. This could be used as a patient-specific check to look at a particular patient's response to a treatment or medication," say the researchers.

Both the biochip and protocols developed could be extrapolated to any other complex tissue that has the same structure as skin. In addition, it could be used to model tissues consisting of a single monolayer of cells more easily, as in most "organs on a chip." This cell culture system simulates the main functional aspects of living organs but on a microscopic scale, which can be used to develop new drugs and a lower-cost alternative to testing on animals in toxicology studies and clinical trials.

Future challenges lie in securing a mature skin, in other words, a skin with a completely differentiated epidermis, with all of its layers. In addition, integrating biosensors that enable the condition of the skin to be monitored in real time could be studied, as well as trialing this model as a testing method.

More information: L. Valencia et al, A new microfluidic method enabling the generation of multi-layered tissues-on-chips using skin cells as a proof of concept, *Scientific Reports* (2021). DOI: 10.1038/s41598-021-91875-z

Ignacio Risueño et al, Generation of a Simplified Three-Dimensional Skin-on-a-chip Model in a Micromachined Microfluidic Platform, *Journal of Visualized Experiments* (2021). DOI: 10.3791/62353

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