

### **3D bioprinted infected skin model as a platform for drug and therapies screening**

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Skin is the largest human organ and it is the barrier between the human body and external environment. Skin-on-a-chip models are for sure fundamental for in vitro drug testing and they are replacing conventional 2D cell culture and animal models. Bacteria-induced infections is one of the major clinical challenges for effective skin repair and regeneration after an injury or in some pathological conditions.

Methacrylated gelatin (GelMA) was synthesized and dissolved in culture medium, adding photo-initiator. Human fibroblasts were then encapsulated in GelMA and 3D printed. Immediately after printing the architectures were photopolymerized and human keratinocytes were seed on top of them. Air Liquid Interface culture started and new medium was supplied and refreshed every two days. The models were analysed after 14 and 31 days. After 31 days the models were wounded and infected with both gram positive (*S. Aureus*) and gram negative (*E. Coli*) bacteria. The infection lasts 24h. At this point, the infected models were treated with penicillin-streptomycin.

After 31 days the skin was improved than after 14 days: the epidermis was thicker with good cytokeratin, filaggrin and CD29 expression, fibroblast began to produce collagen type I and  $\alpha$ -sma, marker of the skin fibroblasts becoming able to participate in wound healing process. After 31 days it was also observed elongation of fibroblasts into the matrix and change in shape of epidermis, that became more compact.

Observing the behaviour of bacteria on the wounded model after the penicillin-streptomycin treatment it was possible to notice that the wound allows the bacteria to grow more but it also permits the antibiotic to better operate, obtaining an enhanced anti-bacterial effect.

For these reasons, the 3D bioprinted infected skin model could be used in the future as a realistic platform for drugs and therapies screening to have predicting results and to avoid the use of animals in clinical trials.