

Dermal Equivalents produced with an innovative elasto-mimetic hydrogel

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Type of contribution desired: ORAL POSTER

Candidating to best presentation award for PhD students/young scientists*

Keywords : hydrogel, Synthetic elastin protein, DGL, dermal equivalent

ABSTRACT

The dermis is the layer of the skin that provides flexibility and strength to the skin. It is principally composed of fibroblasts, responsible of the production and regulation of the extracellular matrix (ECM). While collagen is widely used as scaffolds for dermal equivalents, it has weak mechanical properties, batch-to-batch variability and risk of pathogen transfer. Interestingly, as well as collagen, the dermal matrix comprises a high amount of elastin, which provide its elasticity. Therefore, we hypothesized that a hydrogel integrating a synthetic elastin protein (SEP) with similar physicochemical properties as tropoelastin would be beneficial to recapitulate a dermal equivalent.

A hydrogel composed of poly-lysine dendigrfts (DGL) and PEG encompassing the SEP was developed and evaluated as a support for the formation of an efficient dermal equivalent. To allow cell colonization in 3D, hydrogels were made porous by particulate/leaching technique. We demonstrated that hydrogel's mechanical properties can be modified by changing the ratio of DGL/PEG components, allowing to obtain a porous hydrogel with a complex modulus (15.2±2 and 17.1±2.7 KPa with SEP) close to the values reported for skin [1]. Human fibroblasts could homogeneously colonize the porous matrix after 21 days of cell culture and synthesize their own ECM. Interestingly, unlike collagen gels, no contraction was observed. Cell density in the hydrogels was increased when the SEP was incorporated, and cells were able to infiltrate deeper and synthesize collagen I further in the hydrogel (Figure 1). No significant effect was observed in the production of proMMP2 or active MMP2 between both conditions by zymography (after 8 and 20 days). To understand the effect of the SEP on the hydrogel formulations, fibroblasts were seeded on the surface of dense hydrogels (2D). We observed an increased in migration due to the presence of the SEP, by following fibroblasts on a 16hrs Time-lapse. Similarly, SEP had an effect in spreading and proliferation, as was indicated by an increase of ki67 positive cells in 2D studies. To conclude, this porous hydrogel containing an SEP allows to efficiently produce a dermis equivalent without retraction. Ongoing experiments involve further characterization of the ECM quality and eventually produce a full skin equivalent.

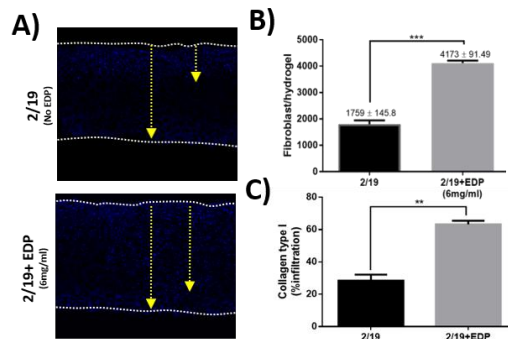


Figure 1 A) Cellular infiltration (in blue cell nucleus) B) Cell density from image analysis C) Presence of collagen type I after 21 days cell culture

ABSTRACT SUBMISSION

To be submitted **before Feb. 22nd**, 2019 online at <https://biomatsante.sciencesconf.org>

Biomat – Materials for Health Congress – June 3-7 2019 – La Grande Motte, France
