



QUANTIFICATION OF CELL STREAMS IN EPIDERMAL WOUND HEALING USING A 3D IN VITRO CULTURE MODEL OF HUMAN SKIN AND WHOLE-SLIDE IMAGING

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Skin homeostasis and re-epithelialization are dynamic, self-organizing processes, in which a stream of keratinocytes originating from proliferating cells in the basal layer of the epithelium and is heading towards its surface. Under wound healing these cell streams are substantially altered in their direction and extent to achieve fast re-epithelialization of the skin. Local cellular decisions thereby coordinate migration, proliferation and differentiation in space and time.

We used 3D organotypic in vitro cultures of human skin (EFT-400, MatTek) to develop an experimental wound healing model allowing the quantitative analysis of re-epithelialization under a time series of 10 days. We performed spatially structured histological sectioning of the paraffin embedded wound model, specific immunohistochemical staining and subsequent microscopic whole-slide imaging of the sections. Computational image analysis of the tissue sections allowed the quantification of the spatial-temporal process of tissue re-epithelialization during wound healing on a single-cell level. At first the velocity of the extending epidermal tongue was quantified. Subsequently, a first quantitative description of re-epithelialization comprising proliferative index, differentiation behavior, and cell migration was obtained.

For the first time our approach combined spatial reorganization of 3D in vitro skin cultures with whole slide imaging for obtaining comprehensive quantitative view on wound healing. Our results serve as a first step towards a multi-scale model that can be used to explore pathologies or potential therapies in epidermal wound healing.

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