scRNA-Seq Identifies IL-1 Responsive Cell Subsets in the Skin Injury-induced Inflammatory Response

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Inflammation is an integral aspect of skin wound healing; however, the mechanisms that regulate inflammatory cascades in this context are not well defined. To better understand how skin inflammation impacts wound healing, we developed an *ex vivo* skin culture system to model key aspects of the inflammatory phase of wound healing. In this model, a defined set of proinflammatory cytokines and chemokines, mirroring those produced in wounds *in vivo*, are produced when mouse or human skin biopsies are cultured *ex vivo*. We refer to this pattern of cytokine and chemokine induction as the skin injury-induced inflammatory response. Previous studies in our laboratory demonstrated this response is initiated by the cytokine, interleukin 1 alpha (IL-1α). To understand the cellular sources and targets of IL-1α during the skin injury-induced inflammatory response, skin biopsies from mouse tail skin were cultured *ex vivo* for 8 hours followed by processing for single cell RNA sequencing (scRNAseq). Using bioinformatic software, R, and the package, Seurat, analysis of scRNAseq data from this experiment identified 22 distinct cell population clusters. While no populations exhibited significant expression of *Il1a* transcripts, multiple cell populations expressed *Il1r1* transcripts, which encodes the ligand-specific subunit of the IL-1 receptor. Notably, fibroblast, endothelial cell and stromal cell clusters were characterized by expression of *Il1r1* and the skin injury-induced inflammatory response transcripts *Il6, Cxcl1* and/or *Csf3*. Furthermore, Reactome Pathway Analysis suggested the Il-1 signaling axis was activated in these cell populations. This information provides a basis for future studies to understand how IL-1 signaling in fibroblasts, endothelial cells and stromal cells impacts wound healing *in vivo*, which could in turn lead to novel therapeutic approaches to clinically relevant outcomes.