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.

Kayla Harpold (she/her/hers) is a third year medical student who is currently undecided, but loved doing research in dermatology, and is keeping her options open.

What is your most important takeaway from your research experience?

"Even though COVID messed up the original plans, because it was online, I learned a new skill (bioinformatics in R software) I wouldn't have had it been in person. Also, Dr. Turner was wonderful to work with and really took the time to guide me during IMPRS and further my understanding both in his research and also in the field of dermatology as a whole. Science doesn't solve anything without quality people behind it."