Localization of IL-1α Responsive Dermal Populations in an Ex Vivo Human Model of Wound Healing

Andrej Sikoski[1], Krish Jayapranu, Hong-Ming Zhou[2], Yunglong Liu[4,5,6,7], Xiaoling Xuei[5], Hongyu Gao[5], & Matthew J. Turner[2,3,8]

Indiana University School of Medicine[1]; Departments of Dermatology[2] ; Microbiology & Immunology[3] ;; Center for Computation Biology and Bioinformatics[4] ; Medical & Molecular Genetics[5]; Biostatistics[6]; Informatics and Computing[7]; Richard L. Roudebush VA Medical Center[8]

While playing a critical role in skin wound healing, the inflammatory phase of this process is poorly understood. To gain a better understanding of the inflammatory phase of wound healing, we developed an ex vivo skin culture model of skin injury-induced inflammation. Previous work in our laboratory showed ex vivo culture of human skin induces an interleukin 1 alpha (IL-1α)-dependent response characterized by increased transcript and protein levels for the inflammatory cytokines/chemokines, IL-6, CXCL1, and CSF3. However, the cellular sources of these factors in ex vivo cultured human skin have not been determined. Prior work with ex vivo cultured mouse skin and single cell RNA sequencing suggested fibroblasts and endothelial cells were potential cellular sources for these inflammatory mediators. The current studies used spatial transcriptomics analysis of ex vivo cultured human skin to localize the IL-1α target cell populations/skin tissue regions that produce IL-6, CXCL1 and CSF3. The Visium Gene Expression Solution platform (10x Genomics Inc.) was used to generate spatial transcriptomics data from skin specimens preserved immediately after biopsy or after skin culture for 24 hours. Loupe Browser version 5.1.0 (10x Genomics Inc) was used for data analysis to identify and characterize cell populations/regions expressing *IL6*, *CXCL1*, and *CSF3* and associated differentially expressed genes (including cell type-specific transcripts). Notably, these IL-1α-induced transcripts were localized to the parent dermis region cluster. Analysis of subclusters in the dermal region showed differential expression of these inflammatory transcripts in regions enriched with either or both fibroblast and endothelial cell specific-type markers. Potential novel markers of this inflammatory response, like *SOD2,* were identified and warrant future investigation. Subsequent studies in identifying the targets of IL-1α in skin inflammation is called for, as they may lead to better understanding of this processes in wound healing and better clinical outcomes.