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"Discovering Which Macrophage Subtypes Are Involved in Regeneration"

Mice and humans both share the ability to regenerate digit tips. Following amputation of the distal third of a digit tip, the bone, tissue, skin, nerves, and nail entirely regrow. In contrast, amputation proximal to this point results in permanent tissue loss and scar formation. With this model, we have a way to compare a regenerating injury and a non-regenerating injury to find pathways that control regeneration.

After injury, macrophages populate the damaged tissue. This influx of macrophages leads to inflammation, histolysis, re-epithelialization, revascularization, and cell-proliferation within the digit tip. The exact role a macrophage plays after injury depends on its subtype (i.e. pro-inflammatory versus anti-inflammatory, pro-angiogenic, pro-fibrotic, etc.). While we have previously shown that macrophages in general are necessary for this regeneration, it is unknown which subtypes of macrophages are specifically responsible.

In order to discover which macrophage subtypes are responsible for regeneration, we analyze data taken from single cell RNAseq studies in the digit tip. In these studies, samples were taken from the digit tips of mice at 10 and 14 days after amputation in the regenerating and non-regenerating injury. We upload the single cell data into R Code, and analyze the data using Seurat, a package of R Code that specializes in single-cell genomics. Using this, we group the macrophages within each sample into clusters and plot these clusters on a UMAP. Once plotted, we analyze the UMAPs and label each cluster with its respective subtype. Then, we can cross-reference between the UMAPs to discover which macrophage subtypes are more present in regenerating samples than non-regenerating samples.

If macrophages are responsible for driving regeneration over scar-formation, we expect to find populations of macrophages that are unique to the regenerating digit compared to the non-regenerating digit amputation. Knowing which macrophage subtypes are present in the regenerating digit will help us identify which ells to target for future therapies.