of accommodating various classes of antibiotics and did not result in cytotoxicity in mammalian fibroblasts or adipose stem cells

Conclusions: An antibiotic-loaded collagen-rich hydrogel is capable of controlled antibiotic release without local cell death. A human-derived hydrogel possessing essential proteins for wound repair that is capable of eluting therapeutic levels of antibiotic is an exciting prospect in the field of chronic wound healing.

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Nerve Growth Factor Derives From Pericytes And Smooth Muscle Cells After Extremity Trauma

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Purpose: Neurotrophic factors like nerve growth factor (NGF) have been described in the literature as a crucial regulator in developmental biology and inflammation of musculoskeletal tissues. While extremity trauma has been shown to elicit re-engagement of developmental programs like NGF upregulation and invasion of new sensory nerve endings in a mature organism, the source of NGF has remained largely unknown. In a validated extremity trauma mouse model, we have previously demonstrated a significant attenuation of injury site re-innervation by sensory fibers following inhibiting of afferent neural signaling and NGF binding of its receptor TrkA. Given this significant impact of NGF on sensory reinnervation of injured soft tissues and downstream bone formation, we examined the source of NGF after extremity trauma using single cell transcriptomic and reporter proteomic technologies.

Methods: A 30% dorsal burn and Achilles transection was performed. The tendon site tissues were harvested from baseline (t0) and day 3, 7, and 21 (n=3-4/group) after induction. Samples were prepared for library generation on a 10x Genomics Chromium Controller, sequenced on a Illumina HiSeq 4000, and analyzed with Cell Ranger Software for pre-processing and alignment to the mm10 genome. Downstream analyses including unsupervised clustering and canonical correlation analyses were performed with Seurat. Immunofluorescent (IF) labeling of cellular markers including αSMA was performed using NGF-eGFP reporter mice at baseline, and at 1,3 and 9 weeks after injury (n=2-3/group).

Results: To localize cell specific *Ngf* expression from injured soft tissue, 9 cell clusters were defined across all timepoints: mesodermal (*Prrx1*) populations including *Acta2*$^{+}$ pericyte/vascular smooth muscle (SMC) and *Pdgfra*$^{+}$ mesenchymal cells, two *Pecam1*$^{+}$ endothelium, and four inflammatory cell populations (mixed, B cell, T cell, and neutrophil). *Ngf* was found uniquely enriched in the pericyte/SMC cluster in a composite view. These pericytes/SMCs were found in increasing number and *Ngf* expression across timepoints, peaking at day 21. To further characterize this joint cluster (1273 cells), the pericyte/SMC cluster was isolated and blindly re-clustered to produce new sub-clusters, distinguishing *Pdgfrb* (platelet derived growth factor receptor beta)^{high} *Prrx1*^{high} *Abcc9*$^{+}$ pericytes from *Acta2*^{high} *Pln*$^{+}$ *Myh11*^{high} SMCs; an uncharacterized cluster with 24 cells was discarded from analysis. Of these two sub-clusters, vascular SMCs demonstrated the highest *Ngf* expression at baseline (mean normalized *Ngf* expression of 0.52 [in 41% of cells] vs 0.28 [in 23% of cells]. IF of NGF-eGFP reporter mice show robust NGF co-localization with αSMA^{+} SMCs.

Conclusions: This is the first work characterizing the pericyte and vascular SMC as a major contributor to NGF signaling at an extremity injury site. The fine resolution defining the cellular source of NGF provides insight into potential mechanisms correlating nascent nerve and vascular growth given the intersection of these pathways at the level of pericytes and myofibroblastic SMCs that will inform future candidate therapeutics to improve extremity trauma healing and re-innervation.