with corneal neurotization (30.1 % ± 12.7 vs. 0.0 % ± 0.0, p < 0.001). All rats without corneal neurotization treatment developed progressive corneal epithelial breakdown, while only one rat with corneal neurotization developed a corneal ulceration that healed within one week (p = 0.047). Eighty percent of rats without corneal neurotization developed a corneal perforation after tarsorrhaphy removal, in comparison to no rats with corneal neurotization (p = 0.008). Corneal neurotization treatment also significantly decreased corneal scarring. Contains representative images demonstrating significant corneal scarring, perforation (A) and ulceration (B) in a rat without corneal neurotization seven days after tarsorrhaphy removal and improved ocular surface health in a rat treated with corneal neurotization (C/D).

CONCLUSION: Corneal neurotization decreases breakdown of the corneal epithelium in rats with NK and prevents perforation and scarring. This data demonstrates that axons reinnervating the cornea improve corneal epithelial maintenance and repair, although further research using this model is required to investigate the underlying mechanism. These findings support clinical studies showing that corneal neurotization improves ocular surface health and preserves vision in patients with NK.

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23

FK506 Binding Protein Expression Within the Injured Peripheral Nerve

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PURPOSE: The mechanism of action of FK506 on peripheral nerve is still unknown despite the growing interest in local FK506 delivery for enhancing axon regeneration. In this study, we analyzed the expression of FK506-binding proteins (FKBPs), a family of immunophilins that act as receptors for FK506, within the injured peripheral nerve and following local FK506 administration. We investigated the expression of FKBP-12 and FKBP-52 which have been shown to mediate immunosuppressive and neurotrophic properties of FK506 within the central nervous system, respectively.

METHODS: Using transgenic Thy1-GFP+ rats expressing green fluorescent protein (GFP) to visualize peripheral axons, the sciatic nerve was transected and repaired either with or without local FK506 delivery using a particulated FK506 delivery system. In a sham group, the sciatic nerve was not injured. Seven days post repair, immunostaining for FKBP-12 and FKBP-52 proteins, Schwann cells (S100), and macrophages (ED-1) was performed to determine the localization and/or co-expression of the proteins within the longitudinal sections of injured and intact sciatic nerve.

RESULTS: With and without FK506 local delivery, FKBP-52 was specifically expressed in Schwann cells in both the proximal and distal stumps adjacent to the site of sciatic nerve injury, 7 days post-repair, as seen in longitudinal nerve sections. FK506 delivery promoted an obvious elevation of Schwann cell proliferation in the distal nerve stump as compared to the nerves without FK506 delivery. FKBP-52 expression was minimal in the regions of the proximal and distal nerve stumps not adjacent to the injury. FKBP-12 was mainly expressed in the vacuoles of the degenerated nerve fibers in the distal nerve stump, with minimal expression in the proximal nerve and at the site of nerve injury. Both FKBP-12 and FKBP52 expression were not detectable within the intact nerves.

CONCLUSION: The mechanism of action of FK506 on nerve regeneration has not been completely characterized. Our findings suggest that FK506 acts on the Schwann cells at the site of injury, accounting, at least in part, for the profound enhancement of nerve regeneration when applied locally. FKBP-52 expression within the injured peripheral nerve. FKBP-12 expression within the injured peripheral nerve.

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24

Successful Control of Virtual and Robotic Hands using Neuroprosthetic Signals from Regenerative Peripheral Nerve Interfaces in a Human Subject

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PURPOSE: Regenerative Peripheral Nerve Interfaces (RPNIs) show promise in controlling neuroprosthetic devices. We have implanted and recorded from RPNIs in 3 human subjects. Here, we present the results from our longest implanted subject with a distal transradial amputation.

METHODS: An RPNI consists of a muscle graft that is neurotized by the distal end of a transected peripheral nerve. Once revasularized and reinnervated, the RPNI muscle graft serves as a stable bioelectric amplifier for efferent nerve action potentials and produces recordable electromyography (EMG) signals. The subject was implanted with RPNIs on the residual median, ulnar, and dorsal radial nerves. Using ultrasound, RPNIs were located, and percutaneous fine-wire bipolar electrodes were inserted for acute EMG recordings. Temporal features of the EMG waveforms (100-500Hz) were used for decoding algorithms.

RESULTS: Eight months post-surgery, we recorded 300–400µV EMG signals from the median RPNI with signal-to-noise ratio (SNR) of 24.2 and 100–120µV EMG signal from the ulnar RPNI with SNR of 5.84. Additionally, EMG from residual muscles was obtained including the flexor digitorum superficialis with 100–120µV signals, SNR of 6.30, and flexor pollicis longus with ~1mV signals, SNR of 47.8. With these signals, the subject controlled a virtual robotic hand in real time with 96% accuracy, choosing 1 of 4 movements within 212 trials. Importantly, the subject controlled a physical Touch Bionics iLimb neuroprosthetic hand with 100% accuracy, choosing 1 of 3 movements within 100 trials.

CONCLUSION: RPNIs harness neural signals from transected peripheral nerves with sufficient amplitude and fidelity to control an advanced neuroprosthetic limb.

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Discovery Of Unique Immune Cell Subsets During The Development Of Capsular Fibrosis

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PURPOSE: Capsular fibrosis is the most common long-term complication after breast implant-based augmentation. The cellular alterations that underlie capsular fibrosis are still barely understood. The identification of cell types in the implant area can provide clues in determining the pathophysiology of the fibrotic changes to find a medical cure. Here, using an in vivo mouse model with silicone implants we analyze the cell types present in the capsule over time. Next, we use single cell analysis to characterize these cells to determine their involvement in fibrotic capsule development.

METHODS: Capsular fibrosis was induced by inserting a customized silicone implant (same shape and filling as a human silicone breast implant) in C57/B6 mice. A paravertebral incision was performed on the dorsum of the mice and the implant was placed in a subcutaneous pocket. Explantation was done on day 15, day 30 and day 90 by resecting the implant with the surrounding capsule en-block for SEM and TEM. The capsule itself was digested and cells were immunostained with CD45, EpCam, CD31, CD11b, F4/80 and Col I. Cells were subjected to further analysis by fluorescence-activated cell scanning (FACS). Single cells were sorted and subjected to single cell transcriptional analysis. H&E, Trichrome and Picosirius Red as well as immuno-staining were performed on the capsules.

RESULTS: FACS analysis revealed that the major cell types in the fibrotic capsule across all time-points were immune cells, not fibroblasts or endothelial cells. The immune cells could be classified as: (i)CD45+/CD11b+/F4/80+ (macrophages), (ii)CD45+/CD11b+/F480- (myeloid cells, including dendritic cells) and (iii)CD45+/CD11b-/F4/80- cells. On day 15, the maximum number of cells was CD45+/CD11b+/F4/80+ (mean:76.61%, SEM:5.13%) and there were no cells that were CD45+/CD11b-/F4/80-. On day 30 the CD45+/CD11b+/F4/80+ cells were reduced and the CD45+/CD11b-/F4/80- cells were statistically significant population (mean:57.35%, SEM:8.78%). The most interesting finding was that CD45+/CD11b-/F4/80- cells that were not found at earlier time-points were seen on day 90 (mean: 27.2%, SEM:3.67%) and there was a further reduction in the macrophage population. The macrophages were found to deposit Coll both by FACS and immunostaining of sections. Scanning electron microscopy and Transition electron microscopy were used to confirm the presence of these immune cells and collagen deposition. We are currently using single cell analysis to understand the