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PURPOSE: Meaningful recovery of motor function following peripheral nerve injury requires timely reinnervation of muscle before atrophy occurs. In contrast, sensory recovery is thought to be less time-sensitive because sensory receptors are relatively spared from atrophy. Conventional wisdom holds that meaningful sensory recovery can be achieved regardless of the duration of delay. However, this thinking has been challenged by recent insights from animal research demonstrating that Schwann cells within the distal stump lacking axonal interaction senesce and lose their capacity to support axonal regeneration. The clinical implications of these experimental findings remain unclear. In this study, we systematically examined the literature for cases of secondary nerve repair to determine the relative impact of delay on sensory vs. motor recovery.

METHODS: We reviewed all articles describing outcomes following repair of median, ulnar, and radial nerves from 1970–2018. We performed a meta-analysis of patient outcomes to determine the differential effect of delay on motor and sensory recovery. We fit a linear mixed effects model with change in BMRC recovery score as the outcome. We included duration of delay, motor vs. sensory classification, interaction between outcome and delay, and pre-operative functional score as fixed effects. We included a random subject effect to account for multiple observations on the same subject. We then performed backwards step-wise regression utilizing additional covariates (type of nerve, location of injury, type of nerve, an interaction between delay and motor vs. sensory, and an interaction between type of nerve and motor vs. sensory as significant predictors of recovery (p<0.05). The effect of delay on recovery remained significantly different for motor vs. sensory groups after adjustment (p<0.01). Moreover, our model allowed us to predict recovery based on type of nerve, injury location, and delay.

RESULTS: Out of 1621 screened articles, 21 articles with a total of 448 patients met inclusion criteria. After adjusting for preoperative score, we found that the negative effects of delay are more than twice as large for motor recovery than sensory recovery (p<0.01). Backwards step-wise regression yielded a final model that included pre-operative score, motor vs. sensory classification, delay, location of injury, type of nerve, an interaction between delay and motor vs. sensory, and an interaction between type of nerve and motor vs. sensory as significant predictors of recovery (p<0.05). The effect of delay on recovery remained significantly different for motor vs. sensory groups after adjustment (p<0.01). Moreover, our model allowed us to predict recovery based on type of nerve, injury location, and delay.

CONCLUSION: This study demonstrates that delayed nerve repair has a greater deleterious effect on motor than sensory functional recovery. This finding supports the hypothesis that chronic denervation of the distal regenerative pathway has a modest effect on motor and sensory recovery in comparison to the more pronounced effects of muscle atrophy on motor recovery. Importantly, this study provides the first model that can predict motor and sensory recovery following nerve repair based on the duration of delay.

QS20

HIF-1\textalpha Deletion Modulates the Ratio of Treg/Th17 cells in CD4 T Cells and Improves Vascularized Composite Allotransplantation Survival under Costimulatory Blockade

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PURPOSE: Hypoxia-inducible factor (HIF-1α) regulates the balance between effector T cells (Teff) and regulatory T cells (Tregs) by enhancing Th17 development (helper T cell subtype) and attenuating Tregs development via degradation of FoxP3, whose expression defines Tregs. The balance between Tregs and Th17 cells impacts allograft survival. This study investigates the consequence of HIF-1α deficiency on T cell differentiation and vascularized composite allograft (VCA) survival using knockout mice.

METHODS: To assess the effect of HIF-1α deficiency upon T cell subtypes differentiation, naïve CD4+ T cells derived from wild type (WT) and HIF-1α deficient (HIF-1αfl/flCD4CreC57BL/6) mice were incubated in 2 types helper T cell subtypes (Th1 and Th17) and Tregs-skewing conditions. Degrees of IFN-γ, IL-17A and FoxP3 expressions were then quantified. Mixed lymphocyte reaction (MLR) was then used to assess effect of HIF-1α deficiency on CD4+ T cell proliferation. To evaluate effect on VCA survival, 13 WT and 15 HIF-1αfl/flCD4CreC57BL/6 mice received osteomyocutaneous allografts from Balb/c mice. Immunosuppressive regimen consisted only of co-stimulatory blockade (1 mg anti-CD154 at POD 0, 0.5 mg CTLA4Ig at POD 2). Allograft survival, ratios of Tregs/Teff subpopulations in the periphery and within the allograft were assessed.

RESULTS: Unlike from WT mice, the naïve CD4+ T cells from HIF-1αfl/flCD4CreC57BL/6 mice not expressed IFN-γ and IL-17A after incubated in Th1 and Th17-skewing conditions. However, those cells still expressed FoxP3 in Tregs-skewing conditions although the degree of expression was lower than WT mice (p<0.01). HIF-1α deficient CD4+ T cells did not result in T cells proliferation during MLR analysis. In the transplanted mice, a higher ratio of Tregs/Th1 cells and Tregs/Th17 cells in the periphery was observed in tolerant animals and lower ratio of both in graft rejecting animals (p<0.05). With co-stimulatory blockade, improved allograft median survival time (MST) occurred with HIF-1αfl/flCD4Cre-mice compared to WT mice (MST = 100 vs 36.5 days, p<0.01). Infusion/adoptive transfer of 5x10⁶ Th17 cells at POD 0 in HIF-1αfl/flCD4Cre-recipients disrupted allograft survival (MST = 60 days).

CONCLUSION: HIF-1α deficiency affects the differentiation of naïve CD4+ T cells, ratio of Tregs/Teff, and improves allograft survival in the setting of co-stimulatory blockade. Targeting potential mechanisms involved in CD4+ T cell differentiation, such as HIF-1α, may be a viable treatment approach in improving allograft tolerance.

QS21

Leadership In Plastic Surgery

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PURPOSE: The pathway to leadership in plastic surgery remains uncertain, but it is thought that exceptional training represents a key to success. Studies have shown that 39% of academic plastic surgeons have been trained by the same 10 programs in the US (Gast, Kuzon, Adelman, & Waljee, 2014), which demonstrates that institutional training is integral to establishing a career in academic plastic surgery. However, the impact of training on the development of leadership skills remains unclear. The present study aims to determine the relationship between training and leadership within the field of plastic surgery.

METHODS: First, a cross-sectional study was conducted in June 2018 to examine the demographics and training background of plastic surgery faculty currently holding leadership positions within academic programs accredited by the Accreditation Council for Graduate Medical Education. The data was gathered from institutional websites. Second, a retrospective review was conducted in July 2018 to examine the demographics and training background of the current and past presidents of leading plastic surgery societies (American Association of Plastic Surgeons, American Society of Plastic Surgeons, Plastic Surgery Foundation, and Plastic Surgery Research Council). The data was gathered from society websites and other electronic media. Frequencies were calculated to determine the number of leaders who trained at each institution during either their plastic surgery residency or fellowships.

RESULTS: Among the 287 institutional leaders (112 chairs or chiefs, 109 residency directors, and 66 fellowship directors) 90 training programs were identified that contributed to their training. However, the top ten training programs