Calcitriol, the active form of vitamin D3, significantly inhibits apoptosis through reduction of oxidative stress and is a potential key stimulator of triglyceride accumulation. This study investigates the novel use of calcitriol for improving adipose tissue survival by reducing inflammation and phagocytic tissue clearance.

**METHODS:** In vitro, adipose tissue from 3 human donors was cultured for 48 hours in 1% oxygen and 0, 15.6, 62.5, and 250 nM calcitriol. Tissue viability was assessed, and quantitative reverse transcriptase polymerase chain reaction was performed to measure genes related to hypoxia or inflammation. In vivo, an immunocompromised mouse model was used to evaluate the impact of calcitriol on fat graft outcomes. Lipoaspirate tissue (0.3 ml) from 3 human donors was implanted bilaterally on the mouse dorsum and assessed at multiple time points out to 12 weeks. Study groups included lipoaspirate incubated with calcitriol for 60 minutes before injection or thrice weekly intraperitoneal calcitriol injections. Study outcomes included residual graft volume (%) and graft injury as observed through histology.

**RESULTS:** Under hypoxic culture conditions, calcitriol did not significantly impact adipocyte viability in vitro but did decrease expression of inflammatory cytokines including SOD1, IFNγ, and interleukin-6. In vivo, lipoaspirate submersion before grafting increased graft retention at 1 week ($P = 0.081$, not statistically significant) and 4 weeks ($P < 0.05$), whereas intraperitoneal calcitriol injections significantly increased fat graft volume retention at both 1 and 4 weeks ($P < 0.01$). Results from 12-week data are pending.

**CONCLUSION:** Calcitriol, an Food and Drug Administration–approved drug with known immunomodulatory properties, seems to be a promising drug for improving long-term fat grafting outcomes. In vitro, calcitriol exhibited anti-inflammatory properties and hypoxic tissue had decreased expression of inflammatory cytokines SOD1, IFNγ, and interleukin-6. In vivo, calcitriol submersion and intraperitoneal injection both significantly increased fat graft volume retention by 4 weeks. Used in tumescent fluid, calcitriol has potential as a simple, economical means of increasing fat graft retention.

**Quality- and Quantity-cultured Peripheral Blood Mononuclear Cell Improve the Fat Graft Vascularization and Survival**

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**INTRODUCTION:** Fat grafting is a valuable technique in soft-tissue reconstruction. However, ischemia of the grafted tissue with subsequent necrosis and tissue loss impede us from having satisfying long-term results. Recently, the quality and quantity (QQ) culture has been established to increase the vasculogenic potential of endothelial progenitor cells in peripheral blood-derived mononuclear cells (MNCs). Our experiment was designed to test whether QQ-cultured MNC (MNC-QQ) can contribute to vasculogenesis in the human fat graft and decrease the tissue loss.

**METHODS:** Adipose tissue and peripheral blood were harvested from healthy subjects. Fat grafts were created with peripheral blood-derived MNC (N = 16), MNC-QQ (N = 16), and stromal vascular fraction (N = 16) before grafting in BALB/c nude mice, and compared to nonenriched control fat grafts (N = 16). Grafts were explanted after 1 and 7 weeks and analyzed by weight persistence, immuno-histochemistry, and quantitative polymerase chain reaction.

**RESULTS:** Weight persistence after 7 weeks was significantly higher in the MNC-QQ group (89.8% ± 3.5%) and SVF group (90.1 ± 4.2) compared to control (70.4% ± 6.3%). With 96.6 ± 6.5 vessels/mm², grafts in the MNC-QQ group had the most dense vessel network and scored significantly better than control (70.4 ± 5.6 vessels/mm²). MNC-QQ exerted a direct effect on vasculogenesis by integrating in vessels, and a paracrine VEGF-mediated effect. Tissue consisting of fibrosis and perilipin-positive adipocytes was unchanged among all groups.

**CONCLUSIONS:** QQ-cultured MNC containing endothelial progenitor cell stimulates the formation of a blood vessel network in the fat graft and enhances the graft survival, indicating its potential for clinical fat grafting.

**Nanofiber System for Sustained Release of Insulin-like Growth Factor 1 Nanoparticles to Nerve and Muscle**

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INTRODUCTION: Despite extensive research efforts, no therapeutic agents are currently clinically indicated for the treatment of peripheral nerve injuries. Insulin-like growth factor 1 (IGF-1) is an ideal therapeutic candidate because it can accelerate axonal regeneration and also minimize the deleterious effects of prolonged denervation on muscle and Schwann cells. However, given its short half-life, a practical delivery system is needed to stabilize the protein and provide sustained release to target tissues. Using a novel encapsulation method, we demonstrated sustained release of bioactive IGF-1 from nanoparticles, in vitro, and improved nerve regeneration and functional recovery, in vivo. An optimized carrier system to maintain the nanoparticles at target tissue sites for the duration of drug release and avoid frequent redosing is now needed. We, therefore, developed a biocompatible nanofiber hydrogel composite that could be loaded with IGF-1 nanoparticles; fine-tuned its drug release kinetics in vitro and in vivo; and applied it in a chronic denervation median nerve model to assess its impact on functional recovery.

METHODS: An injectable nanofiber-hydrogel composite system (made of PCL nanofibers covalently bonded to hyaluronic acid) was developed by electrospinning. Its 3-dimensional structure was formulated to mimic that of fat extracellular matrix. The release kinetics of this delivery system were then optimized in vitro and in vivo (using ELISA and immunofluorescent staining) to achieve controlled release of IGF-1 at therapeutic levels (≈10 times EC50) for a prolonged period. Finally, using a chronic median nerve denervation model, we tested the effects of this modality on axonal regeneration, Schwann cell senescence, muscle atrophy, and muscle force.

RESULTS: The level of synthetic mimicry between our drug-delivery system and extracellular matrix fat was noted to confer high levels of biocompatibility as evidenced by a minimal inflammatory response 25 days postinjection. The release kinetics of IGF-1 from the nanofiber system were then optimized in vitro and in vivo (using ELISA and immunofluorescent staining) to achieve controlled release of IGF-1 at therapeutic levels (≈10 times EC50) for a prolonged period. Finally, using a chronic median nerve denervation model, we tested the effects of this modality on axonal regeneration, Schwann cell senescence, muscle atrophy, and muscle force.

CONCLUSION: We introduce a novel drug delivery system in which IGF-1 nanoparticles are combined with a nanofiber hydrogel carrier to provide sustained local concentrations of bioactive IGF-1 within target nerve and muscle. This therapeutic approach has the potential to improve functional outcomes via enhanced axonal regeneration and maintenance of denervated muscle and Schwann cells. IGF-1 and the polymer components of the engineered delivery system are currently used in Food and Drug Administration-approved formulations and devices, which will facilitate clearance of regulatory hurdles.

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Self-propagating Autologous Skin Substrate for the Treatment of Cutaneous Defects: Clinical Series of the Utilization of a Novel Therapy for In Vivo Full-thickness Skin Regeneration

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INTRODUCTION: The rate of incidence of full-thickness chronic and acute dermal wounds is increasing and becoming a significant burden on healthcare systems. Large and complex wounds, which are unable to heal on their own, or reconstruction patient management strategies that have failed to fully close wounds are frequently treated by skin grafting, a procedure that is over 2-millennia old and is still being used as a conventional treatment option. Split-thickness skin grafts (STSGs) have not demonstrated neogeneration of dermal appendages (hair follicles, sweat and sebaceous glands, etc) or full-thickness skin replacement and consequently are prone to contraction, fibrosis, infection, and morbidity. Skin grafting requires surgeons and an operating room, which inherently produces a barrier to patients and the wound care community, including nonsurgical clinicians and midlevel providers. Here we investigate outcomes from a multi-institutional case series of early clinical use of a novel autologous homologous skin construct (AHSC) for complex wounds. A retrospective cohort study at 9 institutions between December 1, 2017, and July 23, 2018, of 15 patients (age range, 7–72 years) with wounds which