Muscle regeneration can be irreversibly impaired by traumatic injuries, despite the high regenerative capacity of skeletal muscle. The objective of this study is to modulate and enhance the regenerative process via myogenic growth factors and in conjunction with rehabilitative exercise for the treatment of volumetric muscle loss.

To enhance the regenerative potential of injured skeletal muscle, insulin growth factor-like-1 (IGF-1)-laden nano-patterned anisotropic scaffolds were fabricated by an extrusion process, followed by overnight incubation with IGF-1. Individual scaffolds released a cumulative total of 1250 ng ± 150 ng of IGF-1 in vitro over the course of 21 days. When implanted into a murine injury model by ablation of the tibialis anterior muscle, the growth factor laden scaffolds in conjunction with voluntary caged wheel exercise could significantly improve the density of isolectin+/CD31+ perfused microvessels by greater than 3-fold in comparison to treatment of constructs without IGF-1. Enhanced myogenesis was also observed in the muscle treated with the IGF-1 laden scaffolds combined with exercise compared to the same IGF-1 laden scaffolds transplanted into mice that did not receive exercise. Furthermore, the abundance of neuromuscular junctions was greater when treated with IGF-1 laden scaffolds in conjunction with exercise, in comparison to the same treatment without exercise.

These findings demonstrate that voluntary exercise improved the regenerative effect of growth factor-laden scaffolds by augmenting vascular regeneration and myogenesis, and has important translational implications in the therapeutic design of off-the-shelf therapeutics for the treatment of traumatic muscle injury.