Bioengineered constructs combined with exercise enhance stem cell-mediated treatment of volumetric muscle loss.

Journal: Nat Commun

Publication Year: 2017

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PubMed link: 28631758

Funding Grants: Molecular regulation of stem cell potency

Public Summary:
Major trauma often results in volumetric muscle loss which is associated with partial or complete loss of skeletal muscle strength and function. Current treatments of this condition show limited efficacy. In this study, we generated biological scaffolds in which we embedded muscle stem cells and other supporting cell types. We then transplanted these scaffolds into the injured muscles of mouse models of both acute and chronic volumetric muscle loss. Our subsequent analysis revealed that this treatment resulted in improvement of structural regeneration of the injured muscles. In addition, force restoration and nerve growth were readily detectable in recipients of this transplantation approach. These data suggest that stem cell-based therapies aimed to engineer tissue in vivo may be effective to treat volumetric muscle loss.

Scientific Abstract:
Volumetric muscle loss (VML) is associated with loss of skeletal muscle function, and current treatments show limited efficacy. Here we show that bioconstructs suffused with genetically-labelled muscle stem cells (MuSCs) and other muscle resident cells (MRCs) are effective to treat VML injuries in mice. Imaging of bioconstructs implanted in damaged muscles indicates MuSCs survival and growth, and ex vivo analyses show force restoration of treated muscles. Histological analysis highlights myofibre formation, neovascularisation, but insufficient innervation. Both innervation and in vivo force production are enhanced when implantation of bioconstructs is followed by an exercise regimen. Significant improvements are also observed when bioconstructs are used to treat chronic VML injury models. Finally, we demonstrate that bioconstructs made with human MuSCs and MRCs can generate functional muscle tissue in our VML model. These data suggest that stem cell-based therapies aimed to engineer tissue in vivo may be effective to treat acute and chronic VML.