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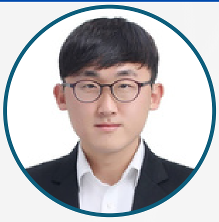

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Fabrication of anisotropic skeletal muscle using in situ magnetic fields supplemented bioprinting process

Abstract: Skeletal muscle consists of uniaxially aligned myofibers, which can provide unparalleled functionalities, such as mechanical support and contractility. In cases of a critical injured tissues which are irreversible, implantation of an artificial bioconstructs that mimicks the native specified architecture have shown promising results. Previously, various strategies including cell electrospinning, in situ E-field stimulation, and 4D fabrication techniques have been utilized to obtain alignment of cells and provide appropriate topographical cues. Here, we have formulated a novel bioink consisting of GelMA, C2C12 myoblast, and magnetic particles (Fe2O3) to induce alignment of the magnetic particles and provide a topographical cue. To induce the alignment of magnetic particles, an in situ magnetic field parallel to the nozzle was provided. Additionally, UV light was irradiated directed onto the glass nozzle simultaneously during extrusion in order to crosslink the GelMA component. As a result, cellular alignment using DAPI/Phalloidin images indicated a significant alignment of cells that were exposed to in situ M-field compared to conventional group. Similarly, the myogenic activities of the cells evaluated using DAPI/myosin heavy chain (MHC) immunofluorescent staining and RT-PCR indicate that that in situ M-field have significantly upregulated the myogenic activities. To further elucidate the in vitro findings, the bioconstructs were implanted into a volumetric muscle loss (VML) defect in mice. The results indicated that muscle regeneration and functional recovery in mice that received the bioconstruct obtained using in situ M-field were significantly higher than in those that received the control bioconstruct. Based on these promising results, we cautiously estimate that the situ M-field assisted bioprinting system can be applied in the fabrication of therapeutics for VML defects.

Keywords: Tissue engineering, stimulus-assisted bioprinting, Magnetic field, Skeletal muscle regeneration

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