3D Cell Printed Muscle Tissue for Functional Muscle Recovery

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Introduction

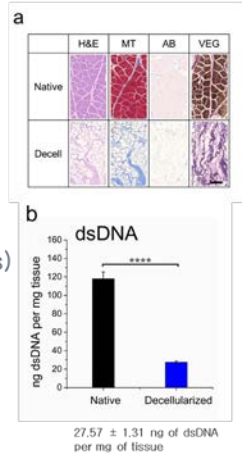
Volumetric muscle loss (VML) is an irrecoverable injury generally more than 20% muscle loss. The decellularized extracellular matrix (dECM) approach has been extensively investigated. In this study, we developed pre-vascularized muscle tissue constructs for VML treatment using muscle dECM (mdECM) bioink through 3D cell printing. The regenerative capability of muscle tissue constructs was evaluated through implantation in a rat model of the VML defect.

Materials and Methods

Human muscle cells and human umbilical vein endothelial cells (HUVECs) were encapsulated in mdECM and vascular-derived dECM (vdECM) bioink. Pre-vascularized skeletal muscle constructs were fabricated in the gelatin granule reservoir. To create the models of VML injuries, 10-week-old Sprague Dawley rats were anesthetized, and 40% of the tibialis anterior muscle was removed from each rat. The 3D cell printed muscle constructs were implanted and sutured at both ends. Masson's Trichrome staining, immunofluorescence staining, and functional assessment were conducted at four weeks post-impanation.

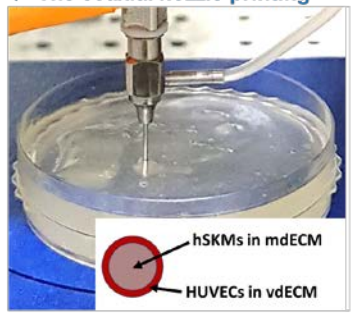
dECM bioink & cell preparation

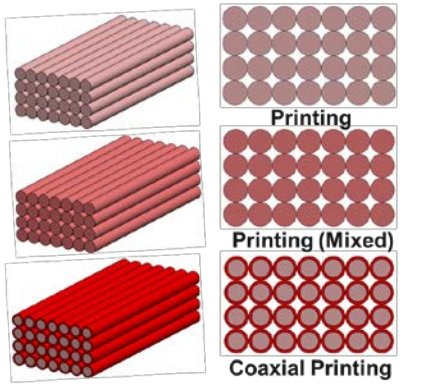
- Skeletal muscle dECM (mdECM)
  - porcine tibialis anterior (TA) muscle
- Vascular dECM (vdECM)
  - porcine descending aortas
- Human skeletal muscle cells (hSKMs)
- Human umbilical vein endothelial cells (HUVECs)



Fabrication of vascularized muscle construct

◆ The coaxial nozzle printing





Endothelial cells Myoblasts

- **Vascularized skeletal muscle construct**
  - Two types of cells and bioinks were considered for fabrication of vascularized muscle.
  - Coaxial nozzle printing was applied.

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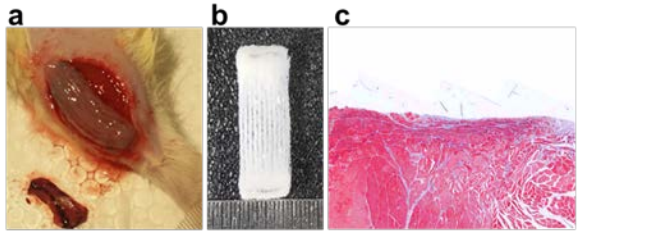
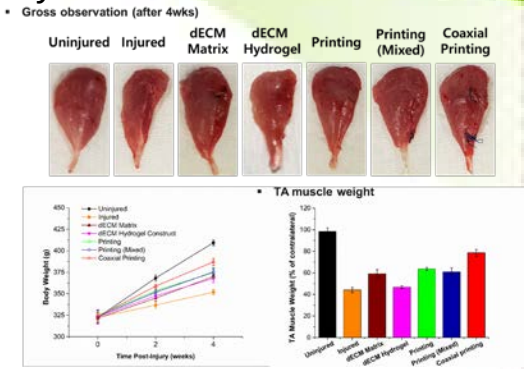
Results

In vitro assessments showed that the pre-vascularized muscle tissue construct that was formed by a coaxial nozzle (coaxial group) exhibited enhanced contractile force and myotube and endothelial network formation. In vivo results revealed that the muscles treated with the coaxial group greatly improved de novo muscle fiber regeneration, vascularization, and innervation. Most importantly, the pre-vascularized muscle tissue construct achieved 85% functional recovery in VML injuries.



A 3D cell printed skeletal muscle construct and treatment of a VML injury. (a) A 3D cell printed skeletal muscle construct implanted in a VML injury model. (b) A 3D cell printed skeletal muscle construct. (c) A coaxial group implanted muscle stained with Masson's Trichrome at four weeks post-implantation.



Conclusion

In this study, we developed a pre-vascularized muscle construct using 3D cell printing and a coaxial nozzle. We expect that these results will provide a blueprint for the future development of engineered human-scaled muscle tissues for VML injury treatment.