3D skeletal muscle model

Created on: 04-12-2020 - Last modified on: 08-12-2020

Contact person

Lieven Thorrez

Organisation

Name of the organisation Katholieke Universiteit Leuven (KUL)

Department Development and Regeneration

Specific Research Group or Service Research group muscles and movement

Country Belgium

Geographical Area Flemish Region

SCOPE OF THE METHOD

The Method relates to	Animal health, Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	myoblasts, fibroblasts, endothelial cells derived from human muscle tissue

DESCRIPTION

Method keywords

Coculture

Myoblasts

endothelial cells

Bio-artificial muscle

Intramuscular injection

Compound testing

Scientific area keywords

tissue engineering

Muscle model

Skeletal muscle

Atrophy

Sarcopenia

Cachexia

Hypertrophy

Tissue development

mechanobiology

Method description

We tissue-engineer *in vitro*, skeletal muscle consisting of aligned myofibers. To create the so-called bio-artificial muscle (BAM), human muscle progenitor cells are expanded, and a 3D construct is created by mixing the cells with a hydrogel. The cell-gel mix is cast into custom-made silicone molds with end attachment sites and then differentiated for 1 week. The passive forces generated in the contracted hydrogel align the myogenic cells parallel to the long axis of the contracted gel such that they fuse into aligned multinucleated myofibers. This results in the formation of a 2 cm long and ~1.5 mm tick human BAM construct with endothelial networks. In addition, by co-culture with endothelial cells, interspersed endothelial networks can be created.

Lab equipment

- Incubator,
- Biology safety cabinet,
- Custom molds,
- Fluorescence microscope.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

The model system allows for extensive biochemical, physical, cellular and electrical characterization of the effect of adding compounds, different extracellular matrix components or different cell types to investigate the effects on muscle development, morphology and function. It thus bridges the gap between 2D culture systems and *in vivo* experiments related to muscle tissue.

Challenges

- Limited size of the constructs imposed by the limit of passive diffusion of nutrients and gases.
- Developmental stage of the muscle is comparable to foetal tissue, but can be stimulated to induce maturation (involves longer culture time).

Modifications

- Integration with flow system, stimulation methods are under development.
- Cells derived from mouse, pig, rabbit, and cow muscles can also be used.

Future & Other applications

Besides further development toward regenerative medicine, such a muscle model can also be used to study mechanisms underlying myogenesis, vasculogenesis, and drug effects, administered either to the medium surrounding the muscle either by injection in the muscle.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Gholobova D., Decroix L., Van Mulyder V., Desender L., Gerard M., Carpentier G., Vandenburgh H. and Thorrez L. (2015) Endothelial network formation within human tissue-engineered skeletal muscle Tissue Eng. Part A 21 2548–58. doi.org/10.1089/ten.tea.2015.0093

Gholobova D., Gerard M., Terrie L., Desender L., Shansky J., Vandenburgh H., Thorrez L. Coculture Method to Obtain Endothelial Networks Within Human Tissue-

Engineered Skeletal Muscle. Methods Mol Biol. 2019; 1889:169-183. doi: 10.1007/978-1-4939-8897-6_10
Gholobova, D. et al. Human tissue-engineered skeletal muscle: a novel 3D in vitro model for drug disposition and toxicity after intramuscular injection. Sci. Rep. 8, 12206 (2018)
Thorrez, L., DiSano, K., Shansky, J. & Vandenburgh, H. Engineering of Human Skeletal Muscle With an Autologous Deposited Extracellular Matrix. Front. Physiol. 9, 1–11 (2018)
Gholobova D., Terrie L., Mackova K., Desender L., Carpentier G., Gerard M., Hympanova L., Deprest J. and Thorrez L. Functional evaluation of prevascularization in one-stage versus two-stage tissue engineering approach of human bio-artificial muscle. Biofabrication 12 (2020) 035021. doi.org/10.1088/1758-5090/ab8f36

Links

Research group muscles and movement

Coordinated by

Financed by