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Induced pluripotent stem cells for modeling neuromuscular disorders: development of disease-specific assays, live cells functional testing and drug design

Mégane Delourme, Camille Laberthonnière, Stefano Testa, Leslie Caron, **Frédérique Magdinier**.

Marseille Medical Genetics, INSERM-Aix Marseille Université, La Timone School of Medicine. Marseille. France

Frederique.magdinier@univ-amu.fr

Induced pluripotent stem cells (iPSC) represent an innovative, easily obtained and renewable stem cell source. This somatic cell-derived model that can be derived without considerable ethical issues has generated significant enthusiasm for its potential application in basic and translational research or development of new therapeutics.

In particular, patient-specific iPS-derived tissues and latterly, organoids offer attractive platform to model a wide range of diseases but also personalized or regenerative medicine.

Compared to other tissues, only a limited number of large-scale protocols describe the production of mature skeletal muscle fibers from human iPSCs (hiPSCs). We developed a procedure for simultaneous differentiation of hiPSC into muscle cells and motor neurons, that generates innervated and contractile multinucleated skeletal muscle fibers with sarcomeric organization and formation of neuromuscular junction. Our protocol permits the production of expandable skeletal muscle progenitor cells and mature skeletal muscle fibers that can be maintained and regenerates on the long-term.

These *in vitro* muscle constructs can be used for the exploration of skeletal muscle differentiation for basic research, disease modeling and drug discovery. Our “muscle in a dish” model has been used to successfully model a number of neuromuscular disorders. By combining transcriptomics with artificial intelligence, we were able to design specific pipelines for a comprehensive understanding of the molecular, cell biological and functional properties of hiPSC-derived muscle tissue in diseases.

Overall, this strategy opens a wide range of opportunities for disease modeling, personalized medicine for patients in diagnosis deadlocks, drug design or tissue bioengineering and bioprinting.