Three-Step Method For Universal Enrichment, Expansion, And Maturation Of Skeletal Muscle Cells Derived From Human Pluripotent Stem Cells

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OTHER INFORMATION

KEYWORDS

Enrichment, expansion, maturation, skeletal muscle cells, SMC, human pluripotent stem cells, hPSC, muscle progenitor cells, myogenesis, method, RNA sequencing, NGFR, ERBB3, PAX7+ human fetal SCs, human induced pluripotent stem cells, hiPSCs, neuromuscular

CATEGORIZED AS

- **Medical**
  - Disease: Metabolic/Endocrinology
  - Disease: Musculoskeletal Disorders
  - Other
  - Research Tools
  - Screening
  - Stem Cell
  - Therapeutics
- **Research Tools**
  - Cell Lines

RELATED CASES

2017-217-0

SUMMARY

UCLA researchers have developed a novel method for enriching, expanding, and maturing populations of skeletal muscle progenitor cells (SMPCs) from human pluripotent stem cells (hPSCs).

BACKGROUND

Skeletal muscle is one of the only organ systems endowed with an endogenous stem cell, the satellite cell (SC). However, the events controlling the timing and specification of SCs and early progenitors during human myogenesis have remained poorly defined. There is a need for a method to identify these early developmental cells prior to generating equivalent SMPCs from hPSCs with robust *in vitro* myogenic ability and *in vivo* engraftment potential.

INNOVATION

- Method for universal enrichment, expansion, and maturation of skeletal muscle cells derived from human pluripotent stem cells
- RNA sequencing to perform the first-ever myogenic profile of different stages of human fetal and hPSC derived muscle
- Identified that NGFR and ERBB3 are expressed by PAX7+ human fetal SCs

APPLICATIONS

- Generating skeletal muscle from hPSCs using an integrated three-step enrichment, expansion, and maturation procedure
- Directed differentiation protocol to improve myogenic activity *in vitro* and *in vivo*
- Regenerative
- Approaches for Duchenne's muscular dystrophy
- Applicable to multiple protocols and disease lines (e.g. human neuromuscular diseases, muscular dystrophy, metabolic and mitochondrial disease)

ADVANTAGES

This method enables:

- Development of human neuromuscular diseases, muscular dystrophy, metabolic and mitochondrial disease-based models that require functional myofibers
- Improved understanding of human muscle development, maturation, and aging
- The ability to generate adult-like skeletal muscle and/or skeletal muscle progenitor cells or satellite cells for autologous transplantation therapies
- A delivery system (the corrected skeletal muscle stem cells) for delivery of gene edited cells (i.e. CRISPR/Cas9 corrected muscle stem cells)
- Myofiber derived niche *in situ* to support and/or target PAX7+ cells *ex vivo*
- The ability to develop co-culture and 3-dimensional models with functional human skeletal muscle to study disease and basic biology
- Inhibition of TGF improves hPSC muscle maturation in the following ways: (i) Improved myogenic fusion *in vitro* and *in vivo;* (ii) Activation of adult myosin isoforms; (iii) Organized sarcomeres as measured by electron microscopy; (iv) Increased expression of transcription factors that regulate skeletal muscle maturation
- Significant engraftment *in vivo* with potential for systemic delivery of stem cells to muscles

STATE OF DEVELOPMENT

The method has been successfully demonstrated.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20210139854	05/13/2021	2017-217
Belgium	Published Application	2018/128779	07/12/2018	2017-217
Switzerland	Published Application	2018/128779	07/12/2018	2017-217
Germany	Published Application	2018/128779	07/12/2018	2017-217
European Patent Office	Published Application	2018/128779	07/12/2018	2017-217
France	Published Application	2018/128779	07/12/2018	2017-217
United Kingdom	Published Application	2018/128779	07/12/2018	2017-217
Ireland	Published Application	2018/128779	07/12/2018	2017-217

Netherlands (Holland)	Published Application	2018/128779	07/12/2018	2017-217	

RELATED MATERIALS

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- M.R. Hicks, A.D. Pyle, The Path from Pluripotency to Skeletal Muscle: Developmental Myogenesis Guides the Way, Cell Stem Cell, 2015.

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Small Molecule Generation of Multinucleated and Striated Myofibers from Human Pluripotent Stem Cells Equivalent to Adult Skeletal Muscle

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