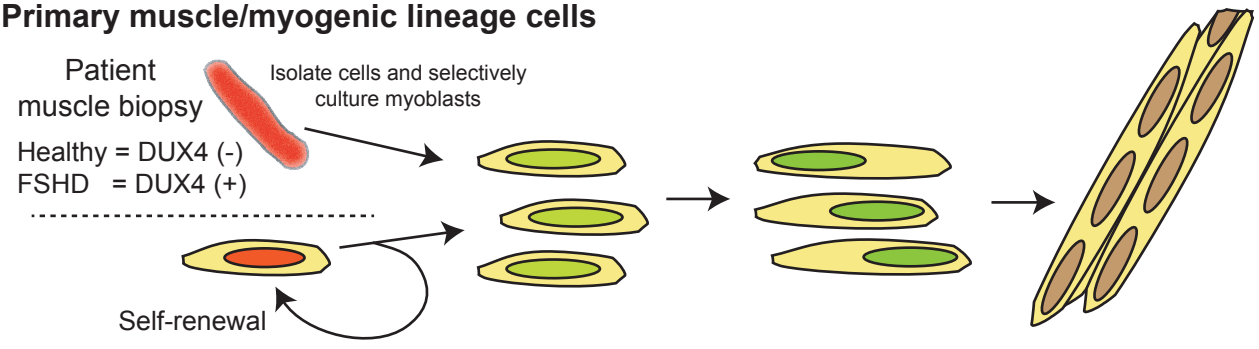
Human FSHD cellular models

Ultimately, FSHD is uniquely human and, whenever possible, maintaining the human context is the best system.

Human cellular systems include muscle biopsy, muscle biopsy-derived muscle cells, immortalized myoblasts, fibroblasts, lymphoblastoid cells, and induced pluripotent stem cells (iPSCs).

Uses: gene expression studies, biomarker discovery, drug screening, testing therapeutic approaches. Need cells from FSHD and healthy controls. Ideally isogenic cells or from first-degree relatives.

Primary muscle/myogenic lineage cells



Immortalized myoblasts

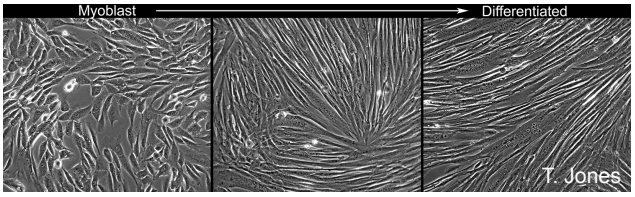
Myoblasts

\+ Telomerase (*hTERT* - prevents telomere loss)
\+ CDK4 (maintains myogenic lineage)

Establishment of clonal myogenic cell lines from severely affected dystrophic muscles - CDK4 maintains the myogenic population

Guido Stadler[1], Jennifer CJ Chen[2], Kathryn Wagner[3], Jerome D Robin[1], Jerry W Shay[1], Charles P Emerson Jr Jr[2], Woodring E Wright[1*]

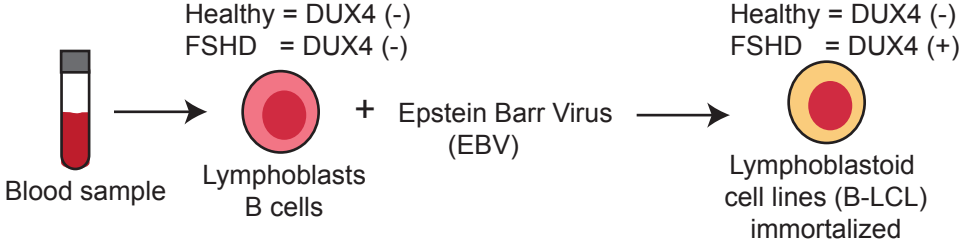
Skeletal Muscle (2011) 1:12



Lymphoblastoid cells

Benefits:
Can express DUX4
Immortal

Limitations:
Not myogenic



Large family cohorts of lymphoblastoid cells provide a new cellular model for investigating facioscapulohumeral muscular dystrophy

Takako I. Jones [a,1], Charis L. Himeda [a,1], Daniel P. Perez [b,*], Peter L. Jones [a,1,**]

[a] *The Department of Cell and Developmental Biology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655, USA*
[b] *FSH Society, 450 Bedford Street, Lexington, MA 02420, USA*

Neuromuscular Disorders (2017) 27:221-238.

Human FSHD cellular models

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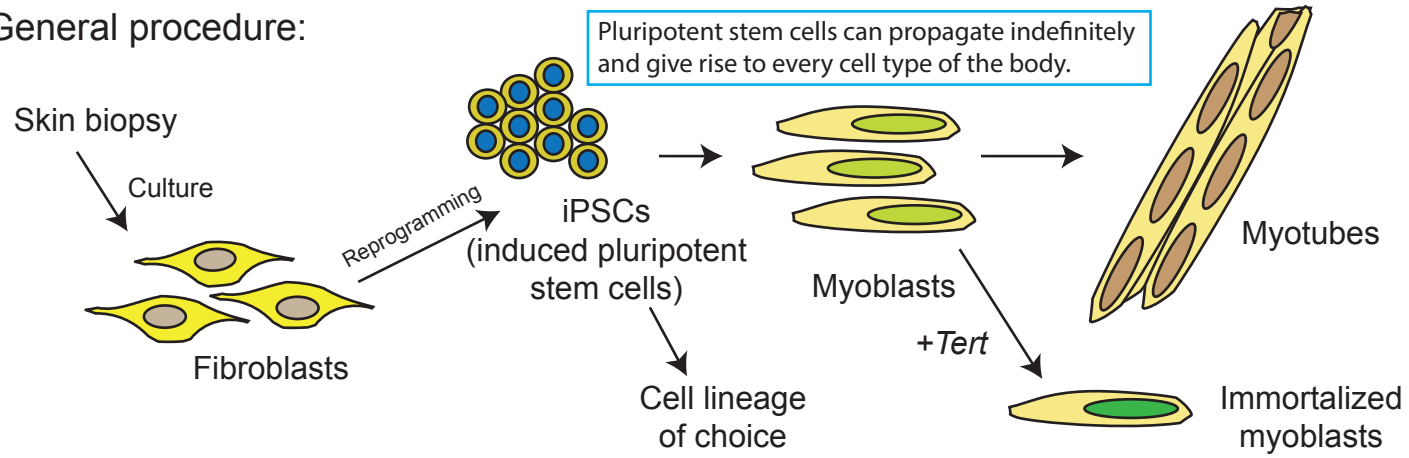
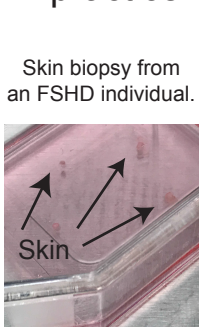
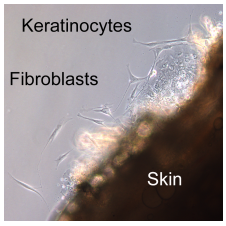
Generating patient-derived myogenic cells from fibroblasts (skin biopsy).

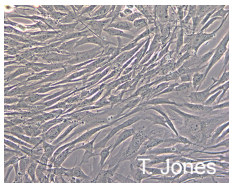
General procedure:



In practice:



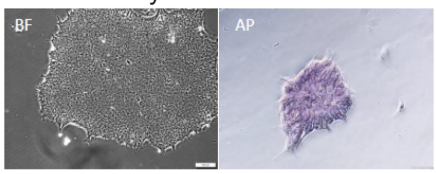


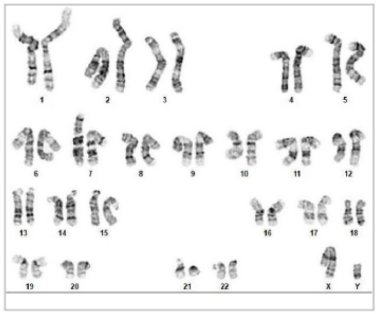


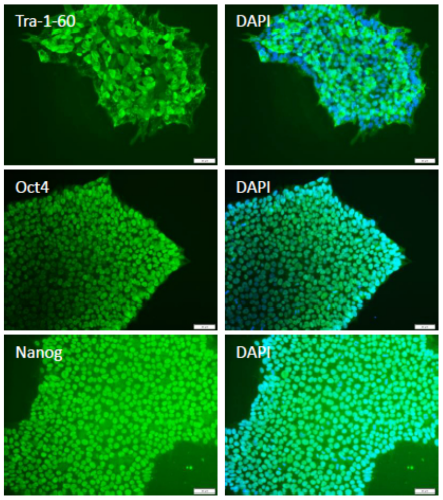
Fibroblasts growing out from skin biopsy in culture.

Reprogramming

iPSC colony: successful creation of stem cells from an individual's skin.







The iPSCs have a normal # of chromosomes and express all the markers of stem cell pluripotency.

Key resources: Isogenic (same patient) iPSC lines; thus, the only genetic difference between the healthy and FSHD1 cells is the FSHD1 D4Z4 deletion.

Lab Resource: Multiple Cell Lines

Stem Cell Research 40 (2019) 101560.

Generation of genetically matched hiPSC lines from two mosaic facioscapulohumeral dystrophy type 1 patients

Erik van der Wal[a], Bianca den Hamer[a], Patrick J. van der Vliet[a], Merve Tok[b], Tom Brands[c], Bert Eussen[c], Richard J.L.F. Lemmers[a], Christian Freund[d], Annelies de Klein[c], Ronald A.M. Buijsen[a], Willeke M.C. van Roon-Mom[a], Rabi Tawil[e], Silvère M. van der Maarel[a], Jessica C. de Greef[a,*]

Roughly 4% of spontaneous FSHD1 patients are mosaic (the deletion happens after fertilization) and therefore their bodies are a mixture of healthy and FSHD1 cells.

For an excellent review: Xia *et al*., "Human iPSC models to study orphan diseases: Muscular Dystrophies" (2018) *Current Stem Cell Reports* 4(4):299-309.