ES and IPS cells as a model for Facioscapulohumeral muscular dystrophy

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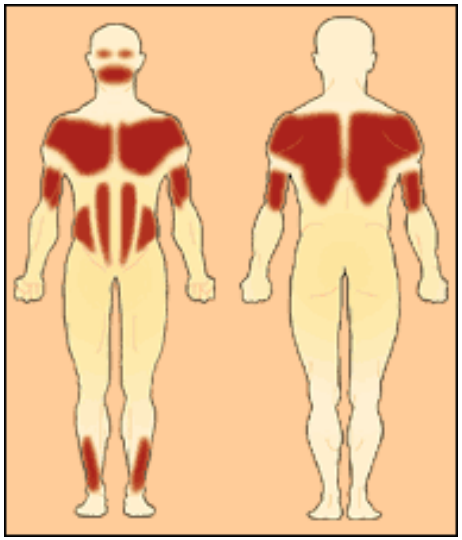
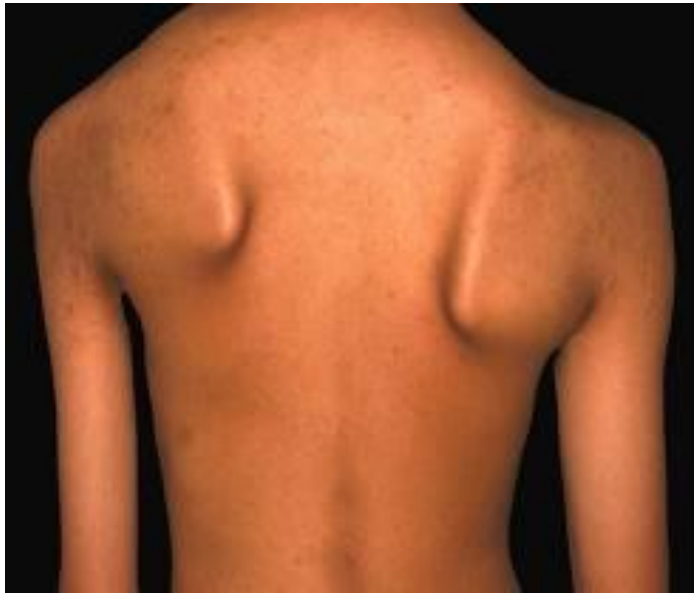
Suitable diseases model

- **Study the mechanism of the diseases;**
- **Search for specific therapy.**

Facioscapulohumeral Muscular Dystrophy (FSHD)

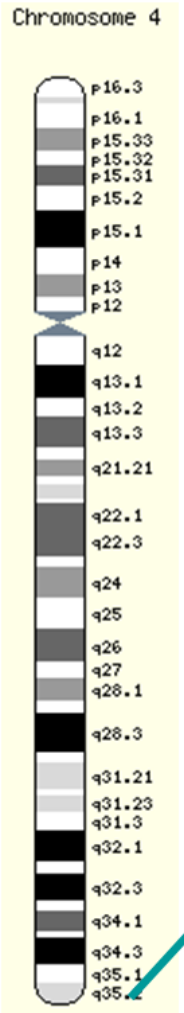
- FSHD is an autosomal dominant inherited disorder
- Third most common inherited neuromuscular condition (1:8000)
- Disease onset is unusual before the age of 10
- Muscles on the face are first affected, then the symptoms are progressive
- **There is no specific treatment**.

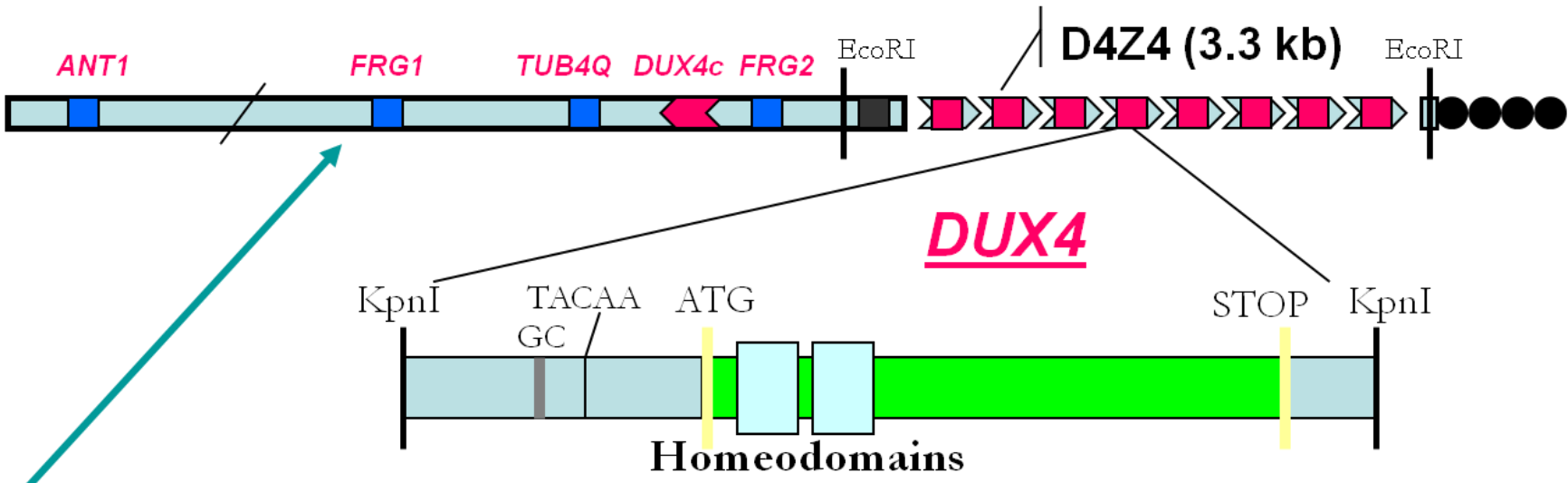




Deletion on chromosome 4 is a reason for FSHD

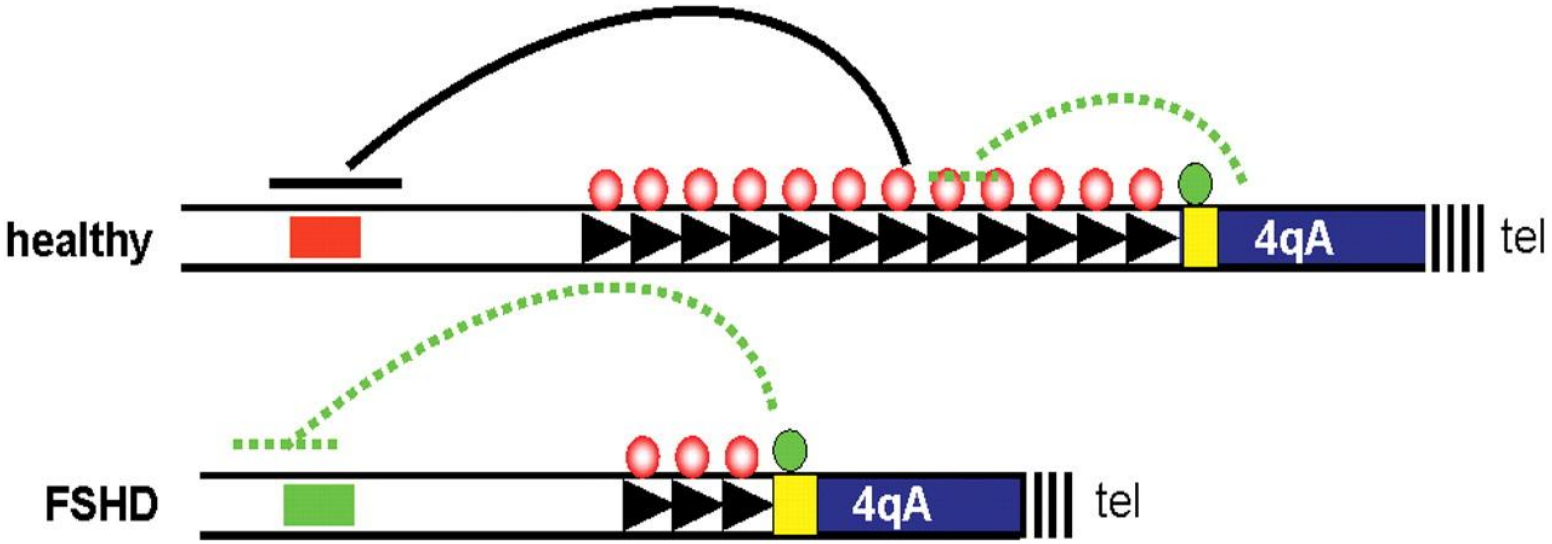
Is DUX4 a key player in the molecular mechanism?





Predictions !!!

4q35A locus is open and transcriptionally active in FSHD

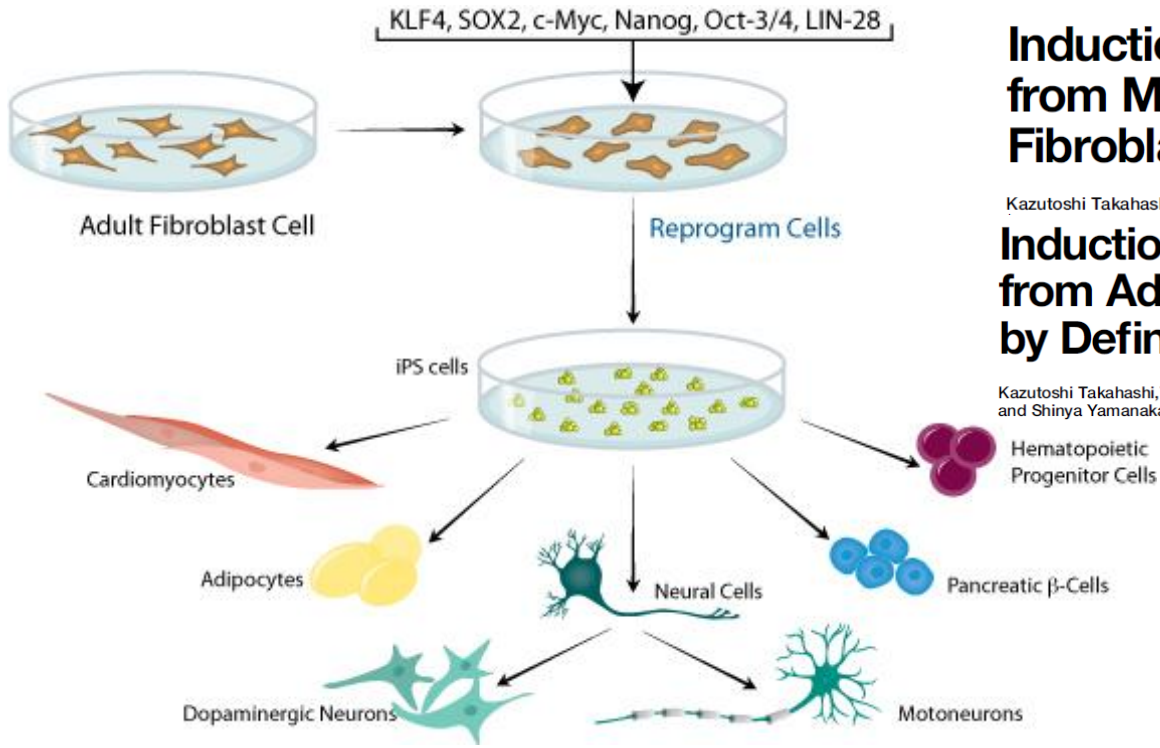


Bickmore and van de Maarel; 1993

How to overcome the limitations of MSC, tissue specific stem cells or embryonic stem cells?

- Limited potential for cell proliferation and differentiation
- Formation of tumors
- Donor specific
- Ethical issues

Induced pluripotent stem cells (IPS cells)



Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors

Kazutoshi Takahashi[1] and Shinya Yamanaka[1,2,*]

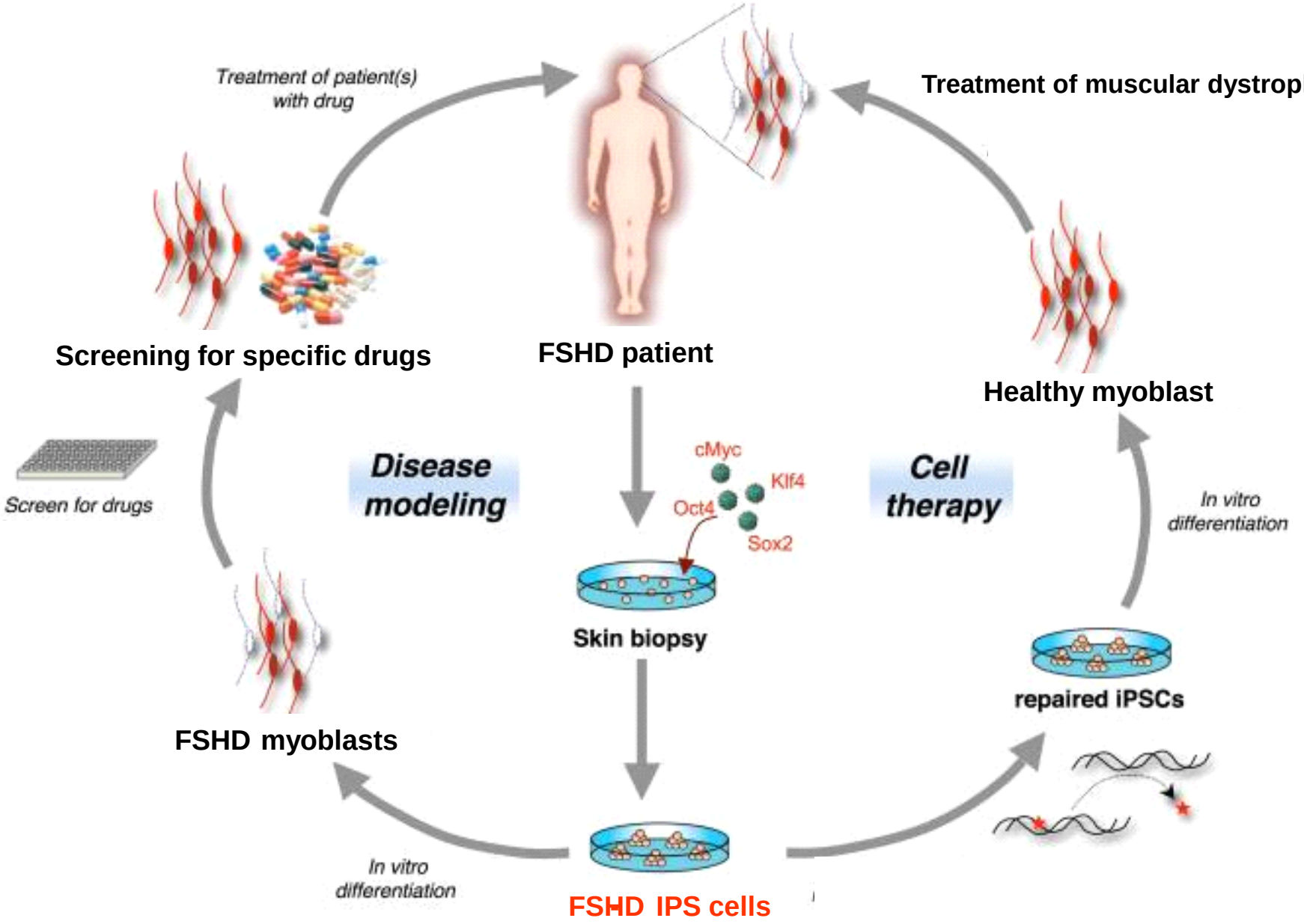
Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,[1] Koji Tanabe,[1] Mari Ohnuki,[1] Megumi Narita,[1,2] Tomoko Ichisaka,[1,2] Kiichiro Tomoda,[3] and Shinya Yamanaka[1,2,3,4,*]

Parkinson's Disease Patient-Derived Induced Pluripotent Stem Cells Free of Viral Reprogramming Factors

Frank Soldner,[1,4] Dirk Hockemeyer,[1,4] Caroline Beard,[1] Qing Gao,[1] George W. Bell,[1] Elizabeth G. Cook,[1] Gunnar Hargus,[2] Alexandra Blak,[2] Oliver Cooper,[2] Maisam Mitalipova,[1] Ole Isacson,[2] and Rudolf Jaenisch[1,2,*]

Why IP Stem cells?



Conclusions

- **DUX4 as initial trigger of the molecular mechanism of FSHD**
- **Control and specific induction of DUX4 in cells- *in vitro* model for FSHD**
- **iDUX4-animal model for FSHD**
- **FSHD-IPS cells- *in vitro* model for FSHD**
- **Prove of principle for cell therapy with gene corrected IPS cells**

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