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# YY1 and MyoD are transcriptional activator and inhibitor, respectively, of the *DUX4* gene that causes facioscapulohumeral muscular dystrophy (FSHD).

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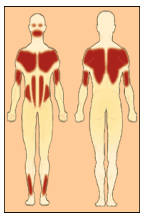
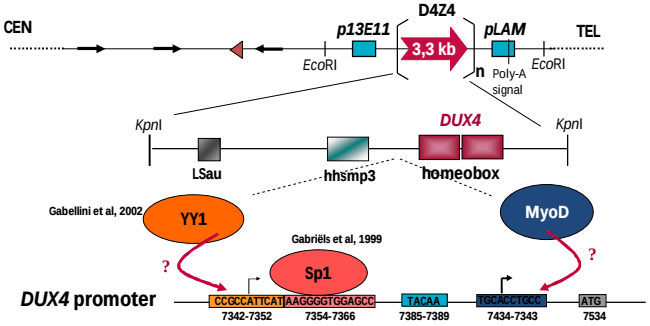
## FSHD



Facioscapulohumeral muscular dystrophy is a dominant hereditary disease with a prevalence of 1/17,000.
It is characterized by weakness and atrophy of the muscles progressing from the face to the lower limbs

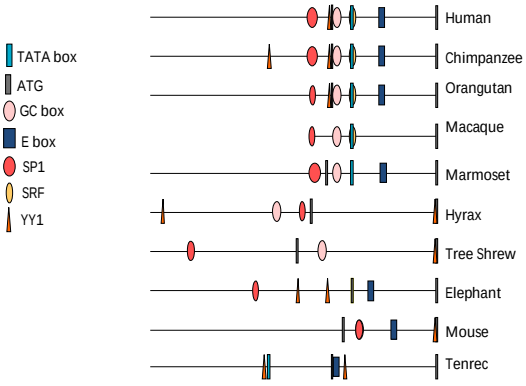
## The *DUX4* gene

The *DUX4* gene is expressed at the mRNA and protein levels in FSHD myoblasts and muscle biopsies but not in controls.




The *DUX4* promoter is more active in muscle cells compared to other cell types. An inhibitory complex containing YY1 was described in non muscle cells and shown to bind to a *cis*-element in the *DUX4* promoter that covers a DUX4 transcription start site. In addition, an E box (MyoD binding site) maps 3' of the TACAA box and covers the second transcription initiation site that is more often used in myoblasts.

The *DUX4* promoter has been well conserved in mammalian evolution.




In conclusion, we propose that *DUX4* expression can occur in FSHD myotubes because YY1 and MyoD are degraded at this differentiation stage.

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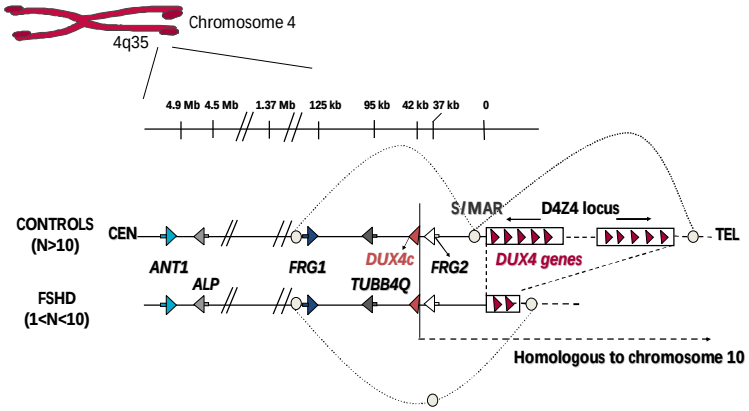
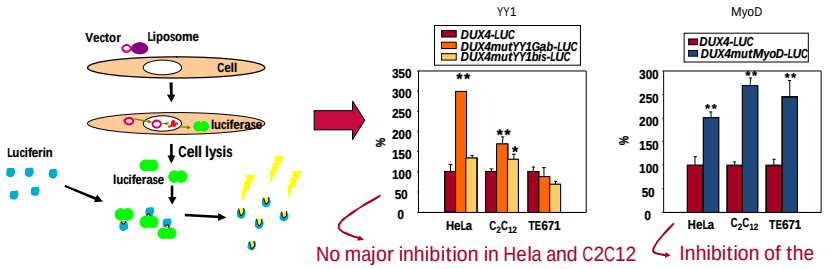
## The FSHD locus in *4q35*




In non-affected individuals, the locus comprises 11-100 tandem copies of a 3.3-kb element named D4Z4 that contains the DUX4 gene. The FSHD deletions reduce the D4Z4 copy numbers to 1- 10 and activate genes in the vicinity by chromatin loop alterations.

## Transient expression of *DUX4* promoter fused to the *LUC* reporter

Lipofection of muscle or non-muscle cells and luciferase assay: test of mutated cis-elements

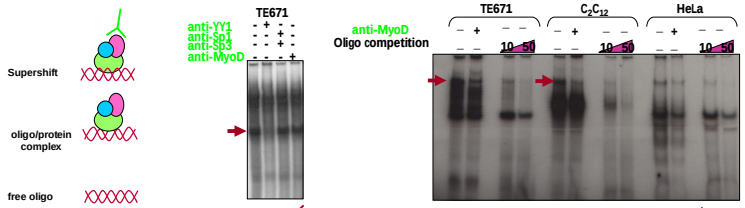



No major inhibition in Hela and C2C12 cells. Weak activation in TE671 cells.

Inhibition of the promoter activity

## Binding of YY1 and MyoD on their *cis*-element

Electrophoretic Mobility Shift Assay (EMSA)




YY1 and MyoD bind to their *cis*-element

Chromatin Immuno-Precipitation (ChIP)