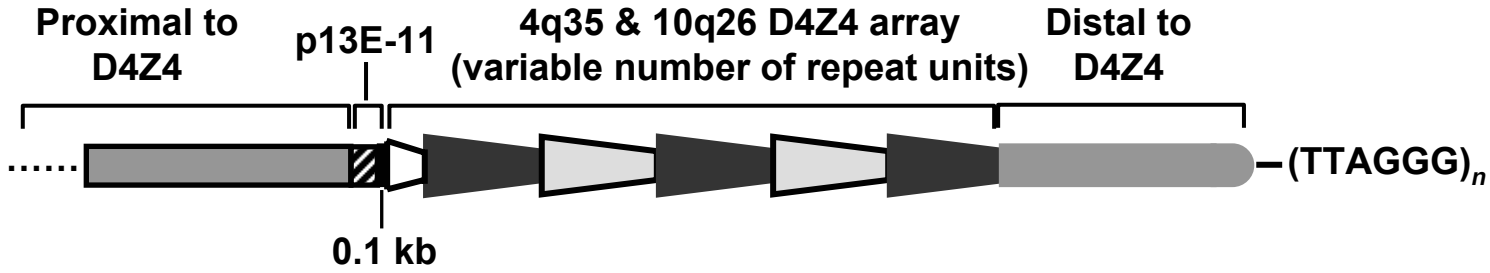
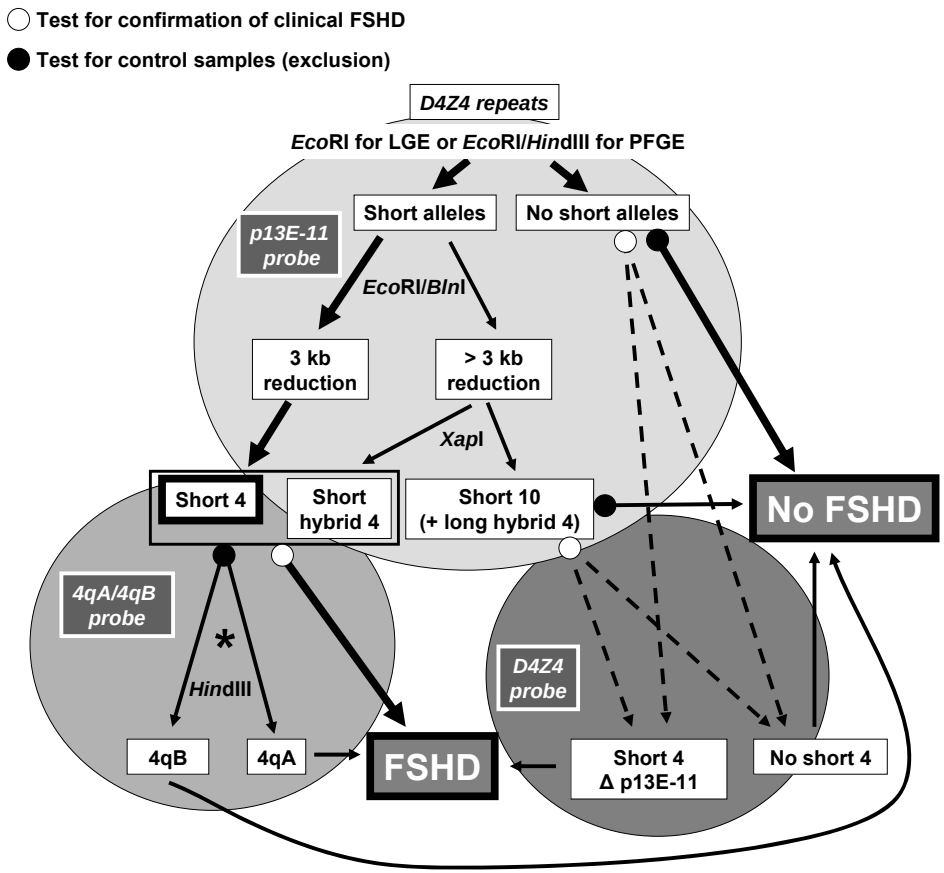
Map of the FSHD-linked D4Z4 repeat array and proximal regions: Essentially the same structures are seen at 4q35 and 10q26



FSHD, facioscapulohumeral muscular dystrophy, is an autosomal dominant disease affecting about 20,000 people in the US. It is diagnosed by detecting characteristic muscular symptoms, but most especially by pulsed-field gel electrophoresis to detect a short D4Z4 array on one chromosome 4. Cartoon (not to scale) showing the size-polymorphic D4Z4 array and p13E-11, a marker sequence. Patients with <11 D4Z4 repeat units at 4q35 (short array) almost always have the disease and those The sequence between the D4Z4 array and the telomeric hexamer repeats is about 15-25 kb and is polymorphic (4qA vs. 4qB). All reported D4Z4 patients with short 4q35 D4Z4 arrays (~95% of all FSHD patients) have the 4qA distal sequence. However, this polymorphism almost always need not be considered during molecular diagnosis because with a few exceptions, individuals with a short D4Z4 array all have the 4qA distal allelic region. Black or gray trapezoids, essentially identical, tandem 3.3-kb *Kpn*I fragment D4Z4 repeat units. White trapezoid, the 0.9- kb region from the start of the array to the first *Kpn*I site in D4Z4. (unpublished figure)

FSHD molecular diagnosis flowchart



Flowchart for the molecular diagnosis of FSHD for confirmation (clinical FSHD) as well as exclusion (clinically no FSHD) purposes. Recommended enzyme digestions and hybridization with three sets of hybridization probes (three shaded circles), starting with the p13E-11 probe, are shown for molecular diagnosis of FSHD. The chromosomal location (4 or 10) of the D4Z4 array is indicated and whether the size of the array is within the range for FSHD linkage (short). Most frequent outcomes for either PFGE or LGE analysis for FSHD are shown with thick arrows. The dotted arrows indicate recommended rehybridization for confirmation of FSHD with the 1-kb D4Z4 probe for all LGE tests and for PFGE tests that reveal less than four long arrays. However, for all PFGE assays, it is preferable to include rehybridization with the D4Z4 probe to detect infrequent complications, such as array distributions that might hide an FSHD-associated deletion encompassing p13E-11. From: Ehrlich, M., Jackson, K., Tsumagari, K., Camano, P. and Lemmers, R.J.F.L. (2007) Improved hybridization analysis of D4Z4 repeat arrays linked to FSHD. *Chromosoma* 116, 107-116.