

Vascular Link with FSHD

Background: Facioscapulohumeral muscular dystrophy (FSHD) is caused by deletions within a tandem array of D4Z4 repeats on chromosome 4q35. In addition to muscle degeneration, most patients with FSHD develop abnormalities of the retinal vasculature. Previous work has suggested that muscle degeneration in FSHD results from increased expression of genes proximal to the deletion, including *FRG1*.

Objectives: To reexamine this mechanism and identify pathways that are abnormally regulated early in the disease process.

Methods: We prospectively studied gene expression in skeletal muscle in patients with FSHD (n = 19) vs healthy individuals (n = 30) and patients with myotonic dystrophy type 1 (n = 12). We used oligonucleotide microarrays for global analysis of gene expression and reverse transcriptase-PCR (RT-PCR) to assess expression or alternative splicing for particular genes.

Results: Expression of *FRG1* was not increased in patients with FSHD, either by microarray analysis or quantitative RT-PCR. Among genes on 4q35, only *LRP2BP* showed upregulation that was specific to FSHD. However, neither *LRP2BP* nor *FRG1* showed imbalance of allelic expression by RT-PCR. After filtering out genes that showed similar dysregulation in other forms of muscular dystrophy, only 44 genes were specifically upregulated early in FSHD. Among these, 34 genes were characterized or partially characterized, of which 11 (32%) had a role in vascular smooth muscle or endothelial cells.

Conclusion: Expression of genes on chromosome 4q35 was normally regulated in the early stages of facioscapulohumeral muscular dystrophy. Our results support a possible link between muscular dystrophy and retinal vasculopathy in facioscapulohumeral muscular dystrophy.
