

# The Mechanism of Action by Which p38 Alpha/Beta Regulate DUX4 Gene Expression

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Facioscapulohumeral Muscular Dystrophy is one of the most common muscular dystrophies within the United States. However, very little research has been conducted in comparison to other dystrophies. Facioscapulohumeral Muscular Dystrophy is a disorder characterized by muscle weakness that starts in the face, shoulders, and upper arms and eventually spreads to the rest of the skeletal muscles. This is a direct result of the misexpression of the DUX4 gene which produces a toxic protein that causes muscle cell death. The purpose of this study was to link either p38 alpha or beta to the inhibition of RNA induced transcriptional silencing (RITS) in order to further my understanding of each isoforms role in FSHD pathology. Comparison of p38 alpha knockout cells and p38 beta knockout cells to a control cell line showed that when Protein X is knocked down in cells with and cells without p38 beta there is no significant difference in Dux4 target mRNA levels which correlates p38 beta with the inhibition of RITS. Statistical analysis showed that the data collected was extremely significant which supports the hypothesis that p38 beta interferes with the endogenous silencing mechanism RITS and that p38 alpha works independently of the inhibition of the RITS pathway to promote DUX4 transcription. This research provides a better understanding of the p38 pathway which enables scientists to more effectively develop a therapy for Facioscapulohumeral Muscular Dystrophy.