**Exploring the Relationship Between DUX4 and Hypoxia-Inducible Factor (HIF1α)**

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**Background:** Examining FSHD skeletal muscle molecular networks reveals pathways involved in hypoxic response and oxidative stress to be critically disturbed, with HIF1α being of particular interest (Banerji et al., 2015, 10.1098/rsif.2014.0797).

**Objectives:** Our goal is to investigate potential relationships between DUX4 and HIF1α and its contribution to muscle dysfunction.

**Results:** Human DUX4 inducible myoblasts were cultured under normoxia or hypoxia. Immunofluorescence studies showed that hypoxia increases HIF1α protein levels, with a concomitant increase in proliferation rate. Hypoxia however, reduced myogenic differentiation into multinucleated myotubes. DUX4 induction reduces differentiation, and preliminary data indicates that HIF1α levels are altered upon DUX4 expression, depending on the differentiation state. 52% of induced myoblast nuclei with DUX4 also contained HIF1α protein. In vivo studies are ongoing, and include a murine model based on an intramuscular injection of a DUX4 expression vector followed by electroporation.

**Conclusion:** FSHD is linked to a greater sensitivity of muscle cells to oxidative stress. Using transcriptomic studies, we have found that HIF1α signalling is deregulated in FSHD. Expression of DUX4 in human myoblasts associates with HIF1α signalling, and we are investigating this association with the DUX4-induced phenotype.