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

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INTRODUCTION

The deregulated molecular network causing FSHD skeletal muscle dysfunction is still a major research topic. Recent meta-analyses (Banerji et al, 2015), highlighted the HIF1-α axis as critically disturbed in FSHD muscles. HIF1-α is a master regulator of oxygen homeostasis and its sustained stabilization in skeletal muscle might affect muscle mass through metabolic disturbances or an increased sensitivity to oxidative stress.

AIM

Our goal is to investigate potential relationships between DUX4 and HIF1-α and its contribution to muscle dysfunction in FSHD.

EFFECT OF HIF1α ACTIVATION IN HUMAN MYOBLASTS IN PROLIFERATION, DIFFERENTIATION AND FUSION

Hypoxic conditions increase HIF1-α protein level with a concomitant increase in proliferation rate

Hypoxia induces early myogenic differentiation but reduces myoblast differentiation into multinucleated myotubes

EFFECT OF DUX4 ACTIVATION ON HIF1α IN DUX4-INDUCIBLE HUMAN MYOBLASTS

Proliferation

4 Days of Differentiation

DUX4 inhibits HIF1-α nuclear protein level in proliferating myoblasts

52% of HIF1-α positive nuclei were DUX4 positive

CONCLUSION

FSHD is linked to a greater sensitivity of muscle cells to oxidative stress. Using transcriptomic studies, we have found that HIF1-α signalling is deregulated in FSHD. Expression of DUX4 in human myoblasts associates with HIF1-α signalling, and we are investigating this association with the DUX4-induced phenotype.

Acknowledgements: Thuy Hang NGUYEN holds a fellowship from FRIA (F.R.S.-N.R.S.)
Funding: F.N.R.S Belgium, Amis FSH

Medical Research Council

AMIS FSH