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DISSERTATION TITLE: *The role of myogenin and HIF-1α in the plasticity of adult skeletal muscle*

Adult skeletal muscles are able to adapt in response to various factors such as exercise and disease. These changes occur in fully-formed muscle fibres, and do not require cell death or regeneration. How exactly these changes occur is not yet fully understood. In this thesis, we present two factors, myogenin and HIF-1α, which are able to induce significant changes in adult muscle, and therefore may play a key role in this adaptation.

Myogenin is a factor that is primarily found in slow muscles, which have a rich blood supply and are fatigue-resistant; as opposed to paler fast muscles which tire quickly. We show that by reducing myogenin in the living adult slow muscle, the muscle fibres become faster. By this we mean that we see changes in the type of fibres found, the size and a metabolic marker. When we analysed fast and slow muscles, we noted that although myogenin is found in both types, we mostly see a modified, or inactive, form in fast muscle. When we overexpressed a form of myogenin that cannot be inactivated, we saw that the fast muscles became notably slower.

Lack of oxygen, or hypoxia, can induce changes in adult muscle, and often occurs during training. HIF-1α is a factor that is activated in response to low levels of oxygen. We report that more HIF-1α is found in fast muscles than slow, and that overexpressing this factor makes muscles faster. We see also that stimulating slow muscle with a fast nerve pattern results in higher levels of HIF-1α.

Based on these results, we suggest that myogenin is an important factor in the regulation of slow muscle, and that HIF-1α is key to fast muscle signalling pathways. By finding out what factors are responsible for changes in skeletal muscle, we are more able to both understand muscle adaptation, and to be able to treat changes related to disease.