Nature Reviews Endocrinology **11**, 65 (2015); published online 2 December 2014; doi:10.1038/nrendo.2014.211

THYROID FUNCTION

Inactivation of T_3 in muscle stem cells

New research reveals that type 3 deiodinase is upregulated in muscle stem cells in response to acute skeletal muscle injury, which reduces intracellular T_3 signalling.

Domenico Salvatore and colleagues developed a *dio3*-floxed mouse model to selectively ablate type 3 deiodinase in the muscle stem cell compartment. Skeletal muscle regeneration was found to be severely impaired in these mice. Salvatore and co-workers determined that this impairment was due to apoptosis of muscle stem cells as a result of high intracellular levels of T_3.

The lack of type 3 deiodinase meant that the cells could not process excess levels of T_3, leading to promotion of the apoptotic pathway. Thus, "type 3 deiodinase-mediated thyroid-hormone inactivation is a survival factor for muscle stem cells and this mechanism is exploited *in vivo* during muscle regeneration and normal muscle homeostasis," explains Salvatore.

Which environmental and cellular signals coordinate this process is currently unknown, but the researchers are hoping to shed light on this problem. "Our next aim will be to characterize the molecular determinants through which intracellular T_3 affects the balance between proliferation and differentiation in muscle cells and profoundly affects their behaviours," says Salvatore.

Salvatore also notes that improved understanding of the action of T_3 in muscle stem cells could have therapeutic implications. For example, drugs could be developed that modify deiodinase activity and so improve regeneration, which could be used to treat muscle atrophy in elderly people.

Claire Greenhill

Original article Dentice, M. *et al*. Intracellular inactivation of thyroid hormone is a survival mechanism for muscle stem cell proliferation and lineage progression. *Cell Metab*. doi:10.1016/j.cmet.2014.10.009