MyoD helps stem cells proliferate in response to muscle injury

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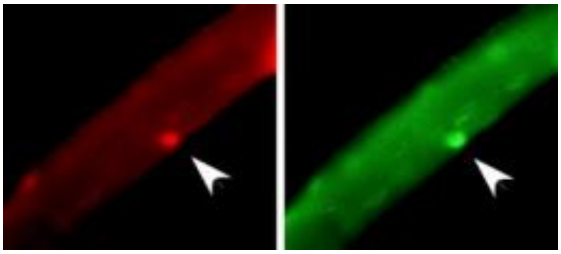

Activated muscle stem cells express MyoD (red) and Cdc6 (green) as they begin to proliferate. Credit: Zhang, K., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200904144.

The master regulator of muscle differentiation, MyoD, functions early in myogenesis to help stem cells proliferate in response to muscle injury, according to researchers at Case Western Reserve University. The study appears online Jan. 4 in the *Journal of Cell Biology*.

MyoD is a transcription factor that activates muscle-specific genes as myoblast precursors differentiate and fuse to form mature muscle fibers. But MyoD is also expressed at an earlier stage of myogenesis when quiescent stem cells rapidly expand in number to generate the myoblasts needed to repair tissue damage. The transcription factor's function in this proliferative phase is unknown.

The team found that MyoD bound to the promoter of CDC6, a gene that

initiates DNA replication, suggesting that MyoD might activate Cdc6 expression in muscle stem cells to promote their reentry into the cell cycle and rapid proliferation. Indeed, Cdc6 was expressed shortly after MyoD in stimulated muscle progenitors, and knocking down MyoD reduced Cdc6 production and slowed cells' entry into S phase. MyoD works in conjunction with transcription factors from the E2F family. E2F3a activated the CDC6 promoter with MyoD, but was replaced by the repressive family member E2F4 as myoblasts began to differentiate.

Senior author Nikki Harter now wants to investigate how the transcription factors cooperate to control Cdc6 expres-sion—initial results suggest that MyoD recruits E2F3a to the promoter region. The researchers also propose that a related protein, Myf5, might control Cdc6 transcription in MyoD's absence, acting as a backup mechanism to ensure that muscle stem cells expand to repair tissue damage.

More information: Zhang, K., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200904144

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