HDAC4 is necessary for satellite cell differentiation and muscle regeneration.

Nicoletta Marroncelli[a], Chiara Noviello[a], Silvia Consalvi[b], Valentina Saccone[b], Pier Lorenzo Puri[b], Eric N. Olson[c], Sergio Adamo[a] and Viviana Moresi[a].

[a] *Dept. of Anat., Histol., Forens. & Orthop. Sciences, Sapienza University of Rome, Italy*

[b] *Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Fondazione Santa Lucia, 00143 Rome, Italy*

[c] *Dept. of Molecular Biology, University of Texas Southwestern Medical Center, Dallas, TX, USA*

In response to injury, skeletal muscle exhibits high capacity to regenerate and epigenetics controls multiple steps of this process (Giordani et al., 2013). It has been demonstrated *in vitro* that completion of muscle differentiation requires shuttling of histone deacetylase 4 (HDAC4), a member of class IIa HDACs, from the nucleus to the cytoplasm and consequent activation of MEF2-dependent differentiation genes (McKinsey et al., 2000). *In vivo*, HDAC4 expression is up-regulated in skeletal muscle upon injury, suggesting a role for this protein in muscle regeneration. With the aim to elucidate the role of HDAC4 in skeletal muscle regeneration, we generate mice lacking HDAC4 in the satellite cells ($HDAC4^{fl/fl}$;$Pax7^{CE}$ Cre). Lack of HDAC4 inhibits satellite cell differentiation. Despite having similar amount of sorted cells, HDAC4 KO satellite cells proliferate less and have less pax7 than controls. Importantly, muscle regeneration in vivo is impaired in $HDAC4^{fl/fl}$;$Pax7^{CE}$ Cre mice. These results are confirmed by molecular analyses of the expression of myogenic markers. All together, these data delineate the importance of HDAC4 in muscle regeneration and suggest a protective role in response to muscle damage.

References

(1) Giordani L, Puri PL. Epigenetic control of skeletal muscle regeneration: Integrating genetic determinants and environmental changes. FEBS J. 2013 Sep;280(17):4014-25.

(2) McKinsey TA, Zhang CL, Lu J, Olson EN. Signal-dependent nuclear export of a histone deacetylase regulates muscle differentiation. Nature. 2000 Nov 2;408(6808):106-11.

Keywords

Histone acetylation, chromatin remodeling, transcriptional regulation of gene expression, satellite cell commitment, muscle repair.