IJAE
Vol. 121, n. 1 (Supplement): 162, 2016
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

S100B protein regulates myoblast and macrophage functions in skeletal muscle regeneration

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Regeneration of acutely injured skeletal muscles relies on a tightly controlled chain of cellular and molecular events, but a complete picture of factors concurring to the regeneration process is still missing. Extracellular S100B protein inhibits myoblast differentiation and stimulates myoblast proliferation by activating its canonical receptor, RAGE (receptor for advanced glycation endproducts), or bFGF/FGFR1 depending on myoblast density (1-4). S100B is released by damaged muscle tissue early after injury in advance of bFGF release, with declining release thereafter (4). We show that S100B is required for correct timing of skeletal muscle regeneration after acute injury. S100B expands the myoblast population, attracts macrophages to damage sites, promotes macrophage polarization into M2 (pro-regenerative) phenotype and reduces fibroblast proliferation. Also, S100B is transiently induced in and released by infiltrating macrophages under the action of proinflammatory and antiinflammatory cytokines, and effects of macrophage-derived S100B sum up with those of myofiber-released S100B. S100B's effects are mediated by RAGE during the first 3 days after injury, however during the myoblast proliferation phase/macrophage M2 phase (i.e. at days 4-6 post-injury) S100B also activates bFGF-FGFR1 to stimulate myoblast proliferation and macrophage M1/M2 transition. Thus, S100B is a major molecular determinant of timed muscle regeneration after acute injury by virtue of its regulatory effects on myoblasts and macrophages.

This work was supported by grants from MIUR PRIN-2010R8JK2X_004, AFM-Téléthon 16260 and Fondazione CRP 2012.0241.021.

References

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Keywords
Muscle regeneration; S100B; RAGE; bFGF/FGFR1; myoblasts; macrophages.