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Oxidative stress-induced S100B accumulation in myoblasts converts myoblasts into brown preadipocytes via an NF-κB/YY1/MIR-133 axis and NF-κB/YY1/BMP7 axis

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Muscles of sarcopenic people show hypotrophic myofibers and infiltration with adipose and, at later stages, fibrotic tissue. The origin of infiltrating adipocytes resides in fibro-adipogenic precursors, nonmyogenic mesenchymal progenitor cells, and satellite cells, the adult stem cells of skeletal muscles. Myoblasts and brown adipocytes share a common Myf5+ progenitor cell, and cell fate decision depends on levels of BMP7, a TGF-β family member; high BMP7 levels cause Myf5+ progenitor cells to differentiate in brown adipocytes. When expressed at relatively high levels as observed in myoblasts from sarcopenic humans, intracellular S100B, a Ca2+-binding protein of the EF-hand type (1), exerts anti-myogenic effects that are reversed by S100B knockdown (2,3). We show that ROS-activated NF-κB induces accumulation of S100B that causes myoblasts to convert into brown preadipocytes via 1) an NF-κB/YY1 axis that negatively regulates the promyogenic and anti-brown adipogenic miR-133 with consequent accumulation of the pro-brown adipogenic transcription factor, PRDM16, and 2) an NF-κB/YY1/BMP7 axis with resultant BMP7 autocrine activity. Also, culturing L6C8 (S100b-overexpressing) myoblasts (2) in adipocyte differentiation medium causes NF-κB-dependent upregulation of S100B expression, which precedes and is required for lipid droplet formation. Lastly, S100B knockdown in myoblast-derived brown adipocytes reconvert them into fusion competent myoblasts. Thus, S100B is a major molecular determinant of cell fate decision of proliferating myoblasts; while modulating myoblast differentiation (2,3), at high levels S100B promotes myoblast-brown adipocyte transition, which might have pathophysiological implications in sarcopenia.

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References

[1] Donato et al. Functions of S100 proteins. Curr Mol Med 13, 24-57.
[2] Tubaro et al. (2010) S100B protein in myoblasts modulates myogenic differentiation via NF-κB-dependent inhibition of MyoD expression. J Cell Physiol 223, 270-282. doi: 10.1002/jcp.22035.
[3] Beccafico et al. (2011) Human muscle satellite cells show age-related differential expression of S100B protein and RAGE. Age 33, 523-541, DOI: 10.1007/s11357-010-9197-x.

Keywords

Myoblast; brown adipocyte; chronic oxidative conditions; S100B; sarcopenia.