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Morpho-functional approaches to highlight skeletal muscle response to cell death inducers

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Cell death has been long described, with continuously growing interest, in a variety of tissues and models. Its presence in muscle disorders stimulated us to study it in striated muscle tissue, in particular, in " in vitro" differentiated myotubes. Apoptosis is a regulated mechanism of cell death which occurs in the absence of plasmalemma disruption, but with cell and organellar component swelling. It plays a crucial role in skeletal muscle pathology, in denervation and disuse [1]. Recently, "autophagy", an intriguing phenomenon characterized by progressive deletion of cell components, could have a role in skeletal muscle death progression, also acting as a survival mechanism. Here, in vitro C2C12 skeletal muscle cells were exposed to etoposide, H_2O_2 or staurosporine and cell response has been investigated by means of morpho-functional approaches. Myotubes appeared more resistant than myoblasts to apoptotic induction. In particular, etoposide- or H_2O_2-treated myoblasts showed characteristic apoptotic features, visualized also in etoposide-treated myotubes characterized by a diffuse DNA cleavage presence. After H_2O_2 exposure, necrotic cells could be observed and myotubes exposed to staurosporine, evidenced late apoptotic features and secondary necrosis. The coexistence of normal and apoptotic nuclei within the same fiber has been demonstrated, in particular in the case of etoposide and staurosporine treatments. The deletion of a single nucleus can occur without the death of the entire myotube, evidencing that a multinucleated cell dies 'more slowly'. After the majority of stimuli, autophagic vacuoles could be diffusely revealed in myotube cytoplasm. They could preserve muscle cell integrity counteracting chemical treatments, or could activate death pathways. It is the case of etoposide drug, which induced skeletal muscle apoptosis in the presence of an autophagic flux impairment. These findings reveal that apoptosis, necrosis and autophagy coexist in muscle biology and, ultrastructural analyses appear a useful approach for highlighting and describing these processes.

References

[1] Salucci et al. (2013) The peculiar apoptotic behavior of skeletal muscle cells. Histol Histopathol 28: 1073-87.

Keywords

Myotubes, chemical triggers, apoptosis, autophagy