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Muscle atrophy in vitro: a lesson from cisplatin

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Adult skeletal muscle cells are multinucleated syncytia with a peculiar cytoskeletal apparatus, relatively resistant to apoptosis but susceptible to atrophy when catabolic inputs exceed. Among molecular mechanisms involved in muscle atrophy induced in vitro by cisplatin (CisPt), a widely used chemotherapic drug, dysfunctional autophagy emerged as an important contributing factor. Macroautophagy is a physiological process, necessary in skeletal muscles to clear abnormal proteins and organelles, mainly mitochondria, and to maintain an efficient mass (Sandri, 2011). Here we sought to morphologically characterize macroautophagy in vitro in C2C12 myotubes, at 5 days of differentiation, exposed to CisPt from 4h up to 24h, and its dependence on tubulin cytoskeleton. Furthermore we tested taurine, a 2-aminoethanesulfonic acid, previously beneficial in CisPt exposed renal cells (Rovetta et al., 2012). Confocal, transmission and scanning electron microscopy were adopted to solve these points. Main findings were that 10-50 microM CisPt stimulated macroautophagy very early in myotubes but it persisted even at 24h, when autophagolysosomes increased and LC3-positive puncta accumulated beneath sarcolemma. At this time, nucleolar segregation, mitochondria damage, disaligned myotubes and sarcolemma blebbings were observed. Taurine plus 50 microM CisPt reduced autophagolysosomes density, ameliorated mitochondria and rescued atrophy. We suggest that taurine, by modulating proper autophagy, might be considered a reliable strategy to control muscle wasting.

References

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Key words
Atrophy, C2C12, Cisplatin, Transmission electron microscopy, Scanning electron microscopy.