Creatine preserves the myogenic capacity of oxidant-stressed C2C12 myoblasts through mitochondrially-targeted mechanisms.

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Creatine (Cr) is a nutritional supplement promoting a number of health benefits, whose use is spreading in the prevention of muscle aging and treatment of neuromuscular maladies (Wallimann, 2007). Indeed Cr has been shown to be beneficial in disease-induced muscle atrophy, improve rehabilitation and afford mild antioxidant activity (Tarnopolsky, 2011). The beneficial effects of its supplementation are likely to derive from pleiotropic interactions. In accord with this notion, we previously demonstrated that multiple, pleiotropic effects account for the capacity of Cr to prevent the differentiation arrest caused by oxidative stress in C2C12 myoblasts, namely: increased expression of muscle regulatory factors mRNA, antioxidant activity, amelioration of energy status and preservation of mitochondrial damage (Sestili, 2015).

Given the importance of mitochondria in supporting the myogenic process, here we further explored morphologically, cytofluorimetrically and biochemically the protective effects of Cr on the structure, function and networking of these organelles in C2C12 cells differentiating under oxidative stressing conditions (acute exposure to 0.3 mM H_2O_2); the effects on the energy sensor AMPK, on PGC-1α, which is involved in mitochondrial biogenesis and its downstream effector Tfam were also investigated.

Our results indicate that damage to mitochondria are crucial in the differentation imbalance caused by oxidative stress and that the Cr-prevention of these injuries is invariably associated with the recovery of the normal myogenic capacity. We also found that Cr- activates AMPK and induces an up-regulation of PGC-1α expression, two events which are likely to contribute to the protection of mitochondrial quality and function.

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