## The role of reactive oxygen species on stretch-induced muscle damage in dystrophic mice

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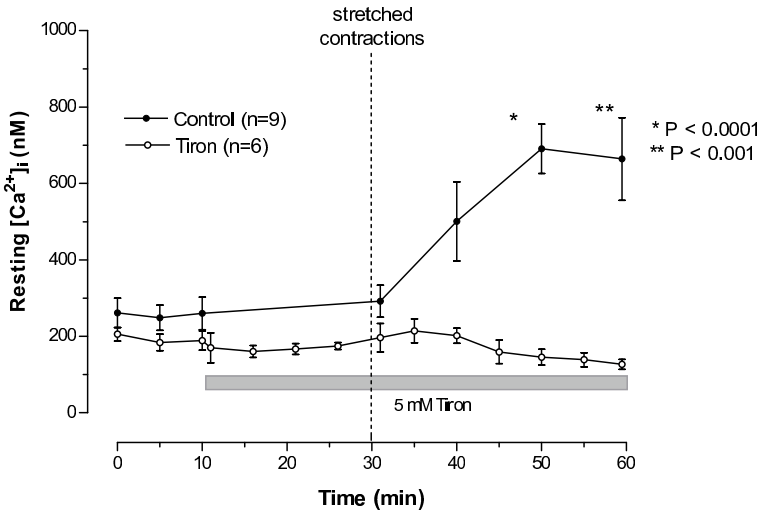
Recently we showed that *mdx* (animal model of Duchenne muscular dystrophy) muscle fibres are more susceptible to stretch-induced muscle damage and there is an associated rise in resting $[Ca^{2+}]_i$ (Yeung *et al*., 2005). We propose that elevated $[Ca^{2+}]_i$ causes reactive oxygen species (ROS) production, leading to muscle damage. Thus treatment with ROS scavenger may exert a protective effect against stretch-induced muscle damage. To test this hypothesis, single fibres isolated from the flexor digitorum brevis of the *mdx* mice were subjected to 10 stretched contractions (eccentric contractions), stretched by 30 % of optimal length ($L_o$) during each tetanus. Measurements of intracellular calcium with fluo-4 were obtained using confocal microscopy. Calibration of fluo-4 intensities were performed using the procedure described by Kao *et al*. (1989).

The resting $[Ca^{2+}]_i$ in the *mdx* fibres was 227 ± 44 nM (n = 5), significantly higher than that in the wild-type fibres (100 ± 6 nM, n=3, P < 0.05). Under control conditions in the *mdx* muscle, $[Ca^{2+}]_i$ increased slowly following stretched contractions to 690 ± 64 nM (n= 9) after 20 min. The ROS scavenger 4,5-dihydroxy-1,3-benzenedisulfonic acid (Tiron, 5 mM) was applied during and for 30 min following the stretched contractions in 6 *mdx* fibres. Not only did Tiron prevent the rise in $[Ca^{2+}]_i$ (145 ± 21 nM, P<0.0001) at 20 min, it also improved the force following stretched contractions from 35 ± 4% to 59 ± 7 % (P<0.05).

These results indicate that production of ROS play a role in stretch-induced muscle damage in *mdx* fibres and, further, suggest that ROS may have a role in the activation of stretch-activated channels which produce the $Ca^{2+}$ entry.




Kao, J.P., Harootunian, A.T. & Tsien, R.Y. (1989) *Journal of Biological Chemistry*, **264**, 8179-84.

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