

## Role of mechanosensitive channels in skeletal muscle damage and muscular dystrophy

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Muscles which are stretched during contraction are liable to a mild form of muscle damage including immediate weakness and delayed stiffness, soreness and swelling. In muscular dystrophy, which is characterized by profound muscle degeneration, stretch-induced damage is more severe and recovery incomplete. We have studied the mechanisms involved by measuring ionic changes in single fibres following a short series of stretched contractions. Intracellular sodium shows a slow increase after stretched contractions, not seen after isometric contractions, which can be prevented by either  $Gd^{3+}$  or streptomycin (Yeung *et al.*, 2003). Both  $Gd^{3+}$  and streptomycin block a class of mechanosensitive channels (MSCs), permeable to both  $Na^+$  and  $K^+$ , present in mammalian muscle fibres (Franco-Obregon & Lansman, 2002). In *mdx* mice, which lack dystrophin, muscles showed an increased resting  $[Na^+]_i$  and a greater increase in  $[Na^+]_i$  following stretched contractions which was also blocked by the above agents. We have previously shown that stretched contraction increase resting  $[Ca^{2+}]_i$  but reduced tetanic  $[Ca^{2+}]_i$  (Balnave & Allen, 1995). Recently we found that  $Gd^{3+}$ , streptomycin or a potent blocker of MSCs, GsMTx4, could prevent the rise in resting  $[Ca^{2+}]_i$  and simultaneously increased the tetanic  $[Ca^{2+}]_i$  from the reduced level observed after stretched contractions. In both wild-type and *mdx* muscles the reduced force following stretched contractions was partly reversed by MSC blockers, presumably as a consequence of the increased tetanic  $[Ca^{2+}]_i$  noted above.

These data suggest that MSCs are present in both wild-type and *mdx* muscle and are persistently opened by stretched contractions. The subsequent entry of  $Na^+$  and  $Ca^{2+}$  may have roles in the reduced force and perhaps other aspects of muscle damage.

- (1) Balnave CD & Allen DG (1995). Intracellular calcium and force in single mouse muscle fibres following repeated contractions with stretch. *J Physiol* 488, 25-36.
- (2) Franco-Obregon A & Lansman JB (2002). Changes in mechanosensitive channel activity following mechanical stimulation in skeletal muscle myotubes from the *mdx* mouse. *J Physiol* 539, 391-407.
- (3) Yeung EW, Head SI & Allen DG (2003). Gadolinium reduces short-term stretch-induced muscle damage in isolated *mdx* mouse muscle fibres. *J Physiol* 552, 449-458.