Store-operated Ca^{2+} entry in intact skeletal muscle fibres from healthy and dystrophic mice

T.R. Cully,[1] J.N. Edwards,[1] D.G. Stephenson,[2] O. Friedrich[1] and B.S. Launikonis,[1] [1]School of Biomedical Sciences, The University of Queensland, St. Lucia, QLD 4072, Australia and [2]Department of Zoology, La Trobe University, Melbourne, VIC 3086, Australia.

Store-operated Ca^{2+} entry (SOCE) is a mechanism that involves an influx of extracellular Ca^{2+} in response to store-depletion during work in skeletal muscle. It has been suggested that SOCE may be deregulated in dystrophic skeletal muscle activating proteolytic enzymes and triggering necrosis. To test this we stained the cytoplasm of wild-type (wt) and mdx fibres with fluo-4AM to image Ca^{2+}. By adding Ca^{2+} to the external solution of the Ca^{2+}-depleted fibres, we observed a low amplitude fluorescence transient in wt fibres (n= 5). In contrast, mdx showed no such transient (n=8) under the same conditions. Upon the application of caffeine, the sarcoplasmic reticulum (SR) of both wt and mdx released SR Ca^{2+} as indicated by an increase in fluorescence showing that the SR has refilled with Ca^{2+}. The results also show that SOCE must deactivate when the SR is refilled with Ca^{2+} in both wt and mdx fibres and that mdx fibres must have a more efficient SR terminal cisternae for sequestering Ca^{2+} from the junctional space as it enters through the transverse tubules during SOCE, preventing Ca^{2+} from escaping to the bulk cytoplasm. SOCE influx was also found to be increased three times in mdx (n=3) compared to wt fibres. This finding is consistent with previous work that found SOCE proteins Stim 1 and Orai 1 to be increased three-fold in mdx fibres (Friedrich *et al.*, 2008). We conclude that while SOCE is upregulated in mdx muscle, it is not functionally compromised, consistent with SOCE playing a compensatory role in mdx mouse muscle.

Friedrich O, Edwards JN, Murphy RM, Launikonis, BS. (2008) Proceedings of the Australian Physiological Society **39**: 19P.