Low dose formoterol administration improves limb muscle function in dystrophic *mdx* mice

L.J. Harcourt[1], J.G. Ryall[1], D.R. Plant[1], M.N. Sillence[2], G.S. Lynch[1], [1]Physiology, University of Melbourne, Melbourne, Australia, [2]Agriculture, Charles Sturt University, Wagga Wagga, NSW, Australia

Formoterol is a long-acting β_2-adrenoceptor agonist (β_2-agonist) that causes muscle hypertrophy in rats at lower doses than other β_2-agonists,[1] and therefore may have therapeutic potential for pathologies where muscle wasting is indicated, including muscular dystrophy. We tested the hypothesis that low dose formoterol administration would ameliorate the dystrophic pathology in skeletal muscles of the *mdx* dystrophic mouse, a widely used animal model of Duchenne muscular dystrophy. Ten week old *mdx* and wild type C57BL/10 ScSn mice were administered formoterol (25 Î¼g/kg/day, *i.p.*) or saline vehicle for 4 weeks. This dose was chosen because we have determined previously that it is sufficient to cause skeletal muscle hypertrophy in rats[1]. At the conclusion of treatment, mice were anaesthetised and isometric contractile properties of isolated EDL (fast-twitch) and soleus (predominantly slow-twitch) muscles and diaphragm muscle strips were determined *in vitro* using well described methods.[2] Absolute force producing capacity was greater in EDL and soleus muscles of formoterol treated wild type and *mdx* mice, functional improvements that correlated with greater muscle masses and median fibre sizes in treated mice. In diaphragm muscles from formoterol treated mice, median fibre size was 18.1% and 25.4% greater than in untreated mice but these morphological changes did not affect functional properties. Our findings indicate that formoterol administration improves the force producing capacity of fast- and slow-twitch dystrophic muscles by increasing median fibre size. Similar increases in the size of fibres in the *mdx* diaphragm highlight formoterol's therapeutic potential but further investigation is warranted.

Supported by the Muscular Dystrophy Association (USA).

(1) Ryall JG, Plant DR, Lynch GS. FASEB Journal. 2004; 18 Suppl: A747.
(2) Gregorevic P, Plant DR, Leeding KS, Bach LA, Lynch GS. American Journal of Pathology. 2002; 161:2263-2272.