The contractile properties of slow and fast skeletal muscle from protease activated receptor-2 null mice

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Protease activated receptor-2 (PAR-2) is a member of a family of G-protein coupled receptors that are activated by proteolytic cleavage. PAR-2 activation results in the initiation of multiple intracellular signalling cascades that regulate a number of cellular processes, including the response to injury and cell survival (Ossovskaya and Bunnett, 2004). As PAR-2 is highly expressed in developing myoblasts in culture, and is reported to influence muscle proliferation and differentiation (Chinni *et al.*, 2000; Jenkins *et al*., 2000), PAR-2 has been proposed to play a role in skeletal muscle development and regeneration. However, the effects of PAR-2 on adult skeletal muscle function and contractile phenotype are unknown. The aim of this study was to compare the contractile properties of slow and fast skeletal muscle from PAR-2 null and control, wild-type mice.

Experiments were performed on 17-18 week old female PAR-2 null (n = 6) and wild-type littermate control mice (PAR-2 Wt, n = 6). Mice were anaesthetised (sodium pentobarbitone, 40 mg/kg, i.p) and the *soleus* (mainly composed of slow-twitch fibres) and *extensor digitorum longus* (EDL, mainly composed of fast-twitch fibres) muscles were surgically removed and attached to a force transducer system. Muscles were maintained in mammalian Krebs Ringer solution (pH 7.3) bubbled with Carbogen (5% CO_2 in O_2) at 25°C. Twitch force characteristics, the force-frequency relationship, maximum specific force and rate of fatigue and post-fatigue recovery were compared in *soleus* and EDL muscles from PAR-2 null and PAR-2 Wt mice. All values are expressed as means ± SEM.

The absence of PAR-2 in EDL muscles resulted in a 44% reduction in the time to fatigue compared to Wt controls (time taken to reach ~20% of pre-fatigue force; null: 475.0 ± 63.18 s; Wt: 269.0 ± 37.02 s, $P < 0.05$). However, the twitch time to peak, maximum rate of force development and half relaxation times, were not significantly different in the EDL muscles of PAR-2 null and Wt control, as were the force-frequency relationship, maximum specific force output and post-fatigue recovery rate. No significant differences in the contractile properties of *soleus* muscles were found between the PAR-2 null and Wt mice.

These findings indicate that the absence of PAR-2 receptors significantly alters the contractile function of fast-twitch skeletal muscle. The marked increase in fatigue resistance, in the absence of changes in contractile and relaxation times in the PAR-2 null EDL muscles, suggests that the absence of PAR-2 receptors may alter fatigue resistance through alteration of cellular metabolic components rather than a fibre type transition.

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Jenkins AL, Chinni C, De Niese MR, Blackhart B & Mackie EJ. (2000) *Developmental Dynamics* **218**, 465-71.

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