

## **The role of $\beta_2$ -adrenoceptors in skeletal muscle regeneration after myotoxic injury**

F. Beitzel<sup>1</sup>, M.N. Sillence<sup>2</sup>, G.S. Lynch<sup>1</sup>, <sup>1</sup>Physiology, University of Melbourne, Melbourne, Australia, <sup>2</sup>Agriculture, Charles Sturt University, Wagga Wagga, NSW, Australia

$\beta_2$ -adrenergic stimulation of skeletal muscle can promote hypertrophy and influence muscle fibre phenotype.<sup>1</sup> Increased muscle force producing capacity after chronic  $\beta_2$ -adrenoceptor agonist administration has indicated potential for promoting muscle repair after injury.<sup>2</sup> There is a marked increase in  $\beta_2$ -adrenoceptor density in regenerating muscles, suggesting a physiological role for  $\beta_2$ -adrenoceptor-mediated mechanisms in muscle regeneration.<sup>2</sup> The aim of this study was to examine the  $\beta_2$ -adrenoceptor population during muscle regeneration and test the hypothesis that  $\beta_2$ -adrenergic signalling affects regeneration of fast- and slow-twitch muscles after myotoxic injury. Male rats (275-300g) were anaesthetised with ketamine-xylazine, and the extensor digitorum longus (EDL) and soleus muscles of the right hindlimb were surgically exposed and injected with a maximal volume of bupivacaine hydrochloride, to cause complete destruction of all muscle fibres. The EDL and soleus muscles of the contralateral hindlimb served as uninjured controls. Rats received either fenoterol (1.4 mg/kg/day, *i.p.*) or an equivalent volume of saline for 2, 5 or 7 days post-injury. After treatment, rats were anaesthetised and EDL and soleus muscles excised for analysis. Radioligand binding assays identified a ~2-fold increase in  $\beta_2$ -adrenoceptor density in EDL muscles at all time points after injury. In soleus muscles,  $\beta_2$ -adrenoceptor density was reduced to 53% of control values at 2 days post-injury, but returned to control levels by 5 and 7 days post-injury. Fenoterol treatment resulted in marked downregulation of  $\beta_2$ -adrenoceptors in both regenerating EDL and soleus muscles by 5 days post-injury. These findings indicate that  $\beta_2$ -adrenoceptors present during muscle repair are functional and may play an important role in influencing the phenotype of regenerating fast-and slow-twitch muscles.

*Supported by the Muscular Dystrophy Association ( USA ).*

- (1) Ryall J, Gregorevic P, Plant DR, Sillence MN and Lynch GS. American Journal of Physiology. 2002; 283:R1386-R1394.
- (2) Beitzel F, Gregorevic P, Ryall JG, Plant DR, Sillence MN and Lynch GS. Journal of Applied Physiology. 2004; 96:1385-1392.