

## Effects of Tempol and Tiron on tetanic force in skeletal muscle preparations from rat and mouse incubated at 37°C and 38°C

*J.N. Edwards, C. Van Der Poel, G.D. Stephenson, Zoology, La Trobe University, Bundoora, Vic, Australia*

It has been suggested that the drop in muscle performance at elevated physiological temperatures is due to increased production of superoxide ( $O_2^{\bullet}$ ), which decreases the capacity of the contractile apparatus to produce force [1]. In this study, we investigated whether the deterioration in tetanic force production at physiological temperatures (37-38°C) in rat and mouse skeletal muscle is due to increased production of  $O_2^{\bullet}$ . For this, we measured tetanic force production in rat EDL bundles and whole EDL muscles of mice at 37-38°C, in the absence and presence of Tiron, a commonly used, membrane permeable  $O_2^{\bullet}$  scavenger, and Tempol, a nitroxide  $O_2^{\bullet}$  dismutase mimic.

Male Long Evans rats, and both male and female mice (C57BL/10) were killed by Fluothane overdose. Fibre bundles from rat EDL muscle, and intact EDL muscles of mice were dissected and then attached to a force transducer, whilst bathed in a Krebs-Ringer bicarbonate buffer solution, 'bubbled' with carbanox and tetanically stimulated. Extracellular  $O_2^{\bullet}$  was measured using the cytochrome C assay 1.

Results show that after 30min at 37-38°C,  $O_2^{\bullet}$  production in resting muscle was greater in both rat EDL bundles and intact mouse EDL muscles by at least one order of magnitude, compared with muscle preparations maintained at room temperature (22°C). Tetanic force decreased markedly after the unstimulated rat and mouse muscle preparations were exposed to 37-38°C respectively and recovered only little after 90min at 22°C.

The addition of 20mM Tiron or 1mM Tempol in the Krebs-Ringer solution caused greater recovery in tetanic force in both muscle preparations. These data indicates that: 1) the increased production of  $O_2^{\bullet}$  in the resting muscle at physiological temperatures contributes to the decreased ability of the mammalian muscle to produce force, and 2) 20mM Tiron and 1mM Tempol partially protect intact skeletal muscle from oxidative stress caused by  $O_2^{\bullet}$ .

(1) van der Poel, C. & Stephenson, D.G. 2002. *Journal of Physiology*, 544, 765-776.