

## **The pathogenesis of inflammation in knee osteoarthritis and its effect on muscle function**

C. van der Poel,<sup>1</sup> P. Levinger,<sup>2</sup> I. Levinger<sup>2</sup> and N.C. Walsh,<sup>3</sup> <sup>1</sup>Department of Human Biosciences, La Trobe University, VIC 3086, Australia, <sup>2</sup>Institute of Sport, Exercise & Active Living, Victoria University, Melbourne, VIC 8001, Australia and <sup>3</sup>Bone, Joint, Cancer Unit, St Vincent's Institute, Melbourne, VIC 3065, Australia.

Osteoarthritis (OA), is a painful degenerative joint disorder affecting 1.62 million Australians. OA is characterized by progressive loss of articular cartilage and aberrant bone formation. In knee OA, loss of quadriceps muscle mass, strength and function in the affected legs is also a common feature which contributes to impaired quality of life through deterioration of functional abilities. It is not known if loss of muscle mass and strength in knee OA occurs as an indirect result of reduced limb use, or if muscle itself is a direct target of the degenerative processes active in OA. Since impaired muscular function is a major determinant of daily function and disability, understanding the underlying mechanisms of the loss of muscle mass and function in patients with OA is essential.

To induce OA in mice, the medial menisco-tibial ligament was transected (DMM surgery) resulting in joint instability and a level of OA at 4 weeks equivalent to that observed in the human OA condition. 12-week old male C57Bl/6 mice underwent either DMM or sham surgery in the right knee. *Tibialis anterior* (TA) muscle function was assessed *in situ* at 1, 4, and 8 weeks post-surgery (n = 10 all groups).

At 1 week post surgery, there was no significant difference in any tetanic or twitch force characteristics assessed. At 4 and 8 weeks post surgery there was a significant decrease in both the absolute (Po) and specific (sPo) force of tetanic TA contractions of the DMM mice compared to sham ( $P < 0.05$ ). At 4 and 8 weeks post DMM surgery there was no significant change in twitch force production (Pt) or time to peak tension (TPT). However, in the 4 and 8 week post DMM surgery groups, there was a significant increase in the twitch force relaxation rates (1/2 RT) compared to the sham controls ( $P < 0.001$ ).

It has been traditionally thought that the loss of muscle strength in patients with OA is associated with the onset of joint pain and the accompanying changes in gait and muscle use. However, this study demonstrates that changes in muscle function can be observed within skeletal muscle before any overt changes in gait are visible. Understanding the mechanisms of muscle loss in OA may lead to improved rehabilitation for patient's pre-and post-knee replacement surgery.