



BSMB Satellite Symposium Report –Wednesday 8th September

Tendon Biology and Pathology - written by Stephanie G Dakin

The second Tendon Satellite Symposium organised by Graham Riley was held at the Thomas Paine Study Centre, University of East Anglia, Norwich on Wednesday 8th September 2010. The meeting began focusing on growth and development of tendon, with an enlightening lecture from **Ronen Schweitzer** (Portland, Oregon) describing the 'Genetic analysis reveals the modular nature of limb tendon differentiation and matrix assembly' in the mouse. Normal limb development is dependent on co-ordinated differentiation and patterning in musculoskeletal disease. Ronen emphasised the importance of Scleraxis and TGF β as key factors in the induction and maintenance of the developing tendon. His elegant studies and superb images illustrated the different stages of development of the mouse limb bud, showing the onset of tenocyte proliferation is different in the mouse autopod and zeugopod. Tendon development is dependent on the presence of cartilage in the autopod, in contrast muscle is crucial for normal zeugopod development, emphasising the mutual interdependence between muscle and tendon in the developing mouse embryo.

Mohammed Hajhosseini (Norwich) reported the importance of FGFs in tendon development, suggesting that the putative roles of FGF10 are to induce the formation of tendon in a paracrine fashion in the mouse autopod and the formation of a specific subset of limb tendons from a migratory cell population in the zeugopod. This exciting research in the embryo provides a solid foundation for further investigation of the role for FGFs in adult tissues.

The second session focused on the mechanobiology of tendon and its adaptation to mechanical load. **Mads Konsgaard** (Copenhagen) gave a comprehensive overview of the literature on human tendon adaptation, integrating some of the latest findings from his own laboratory. These included some elegant studies using in vivo microdialysis in human subjects that have shown Collagen I synthesis peaks 24 hours after exercise, and is still elevated at 72 hours. These findings have important implications for determining appropriate training intervals, potentially helping to reduce the incidence of tendon injury. Inactivity has rapid detrimental effects upon tendon as the mechanical properties of tendon dramatically diminish in comparison to other tissues. Findings correlating the mechanobiology of tendon with ageing seem to be diverging in the human field and further investigation is necessary to explore this relationship.

Eleanor Jones (Norwich) presented 'Strain regulation of metalloproteinases in human tenocytes'. The findings from her in vitro experimental work thus far have shown that cell to cell contact is crucial for mediating mechanotransduction and mechanical strain regulates protease and matrix genes at the mRNA level. Specifically MMP2, MMP3 and MMP13 gene expression were reduced after mechanically straining tenocytes after 48 hours, in contrast ADAM12, Collagen I and

elastin increased. Eleanor concluded that TGF β activation is also an important factor involved in regulation of strain in human tenocytes in vitro.

After the lunch break, the third session commenced with talks centred on the molecular pathophysiology of tendinopathy. **Chavaunne Thorpe** (London) presented the findings from her work focussing on tendinopathy in the equine athlete. She hypothesised that matrix turnover would differ in functionally distinct tendons (the Common Digital Extensor vs. the Superficial Digital Flexor tendon). The results of her study showed collagen turnover was more rapid in extensor tendons and that the equine SDFT is more prone to matrix modifications and accumulation of damaged collagen which may be important predisposing factors to injury.

Raewyn Poulson (Oxford) later discussed oxidative stress and the role of forkheads in human rotator cuff tendon degeneration. The findings from her study suggested oxidative stress was important factor in the development of this injury and transcription factors FOXO1 & 3 may afford protection against some effects of oxidative stress albeit at the cost of reduced cell proliferation.

The final session entitled 'Latest developments in the treatment of tendinopathy' included talks from both medical and veterinary perspectives emphasising the importance of information exchange across species to improve our management strategies for injury. **Nicola Maffulli** (London) gave an energetic account of current therapeutic practices in the human field. Nicola emphasised the importance of standardising the terminology (to define treatment!), then progressed to discuss the altered metabolism of injured tendon, with a greater propensity to form scar tissue and the enigma behind mechanisms of pain in the injured Achilles tendon. Multiple therapeutic regimes currently exist for the management of this condition although randomised controlled studies are currently lacking. Nonetheless, Nicola reported an excellent outcome in 25/48 patients with chronic Achilles tendinopathy that underwent surgical longitudinal tenotomies.

Roger Smith (The Royal Veterinary College) concluded the meeting discussing the role of cell therapy in the treatment of equine tendinopathy. Superficial digital flexor tendon (SDFT) injury is a substantial cause of wastage in the racing industry with reported prevalence of 43% in racing equine athletes with re-injury occurring in 56% horses (Dyson 2004), not surprising as this tendon is subjected to 1 tonne at peak loading concentrated over a region with a cross sectional area of 1cm²! Core lesions tend to develop in the injured equine tendon providing a suitable receptacle for cell based therapies. An in vivo experimental study was conducted in 10 horses, hypothesising implantation of autologous bone marrow derived mesenchymal progenitor cells into tendons with naturally occurring SDFT injury would synthesise a matrix more representative of tendon, thus reducing fibrosis and resulting in a better functional outcome than saline controls. The results of this in vivo study (5 BMMSC treated and 5 control horses) showed that after a controlled exercise programme for 6 months, after euthanasia and tissue harvest stem cell treated tendons showed improved histological organisation of tendon architecture, better crimp pattern and reduced cellularity and lower GAG content. Hence initial findings suggest stem cell treated tendons are functionally, morphologically and compositionally more like normal tendon in comparison to saline controls. Moreover, data from over 100 horses treated clinically thus far suggests that re-injury rate is reduced from 56 to 26% in stem cell treated horses in comparison to those managed conservatively. It is hoped that the findings from these studies may facilitate the translation of this therapy into the human arena.

We are all very grateful for the immense hard work from Graham Riley and his team at UEA for organising this fantastic and hugely informative tendon symposium and look forward to the next one in the near future.