Department of Veterinary Medicine

Available PhD Project:

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Project Title: The role of wnt signalling in equine stress fractures

Description: Long bone fractures in horses have significant welfare and economic implications to the horseracing industry, in addition to the damage to the image of the sport, particularly when they occur to high profile animals or during high profile events. At the current time, strategies to reduce the effects of long bone fractures consist of prevention and early recognition of fractures and improving treatment. Key to the prevention of fractures is a clear understanding of their aetiopathogenesis. Long bone fractures occur either due to a one off overload incident or due to repetitive microdamage and subsequent weakening, such as associated with high intensity exercise. These latter fractures are commonly termed 'stress fractures (SF)' and can present either as overt failure of the bone or as a cause of leg pain and lameness.

Whilst it is known that high intensity exercise causes stress fracture, the exact mechanism linking exercise and catastrophic bone failure remains poorly understood, making targeted prevention difficult. In a recent previous study we have demonstrated that a signalling protein, sclerostin, made by load sensing cells residing in bone ('osteocytes'), is up-regulated next to fracture lines in damaged front leg metacarpal bones (one of the commonest sites of fracture). The aim of this PhD is to expand this observation and to investigate, more fully, the role of wnt signalling in equine stress fracture. In this PhD studentship we aim to determine the following: 1) the skeleton-wide importance of this observation; 2) the role of related signalling proteins that are known, in other species and under other conditions, to be sensitive to load; 3) the intrinsic differences in responses between osteocytes isolated from normal and damaged bones to known factors and load.

The specific aims of this project are:

1. Validate the observation that sclerostin increases at sites of clinical SF in the racing TB.
2. To define which other wnt signaling pathway components are involved in SF.
3. To determine which other mechanically sensitive osteocytic proteins involved in bone cell homeostasis or mineralization are involved in SF.
4. To determine whether there is evidence for hypoxia at the site of SF.
5. Generate equine osteocytes and characterize responses to hypoxia and mechanical load.

The successful candidate will become part of Dr Henson's research group which is embedded within the Division of Trauma and Orthopaedic Surgery, Addenbrooke's Hospital under the overall leadership of Professor Andrew McCaskie. This produces an environment where basic and clinical scientists interact with a 'One Health' agenda. Within the Division of Trauma and Orthopaedic Surgery there are comprehensive laboratory facilities with all the specialist equipment that is required for completion of this project. For example, tissue culture facilities, a molecular biology laboratory and a histology suite that includes a cryostat with bone cutting knife. The student will learn specific laboratory skills and more general transferable skills. Laboratory skills that will be learnt include tissue culture, PCR, immunohistochemistry, mechanical loading and tissue processing. General transferable skills will include data collection, accurate record keeping, data analysis, academic writing and presentation skills.

Funding:
This project is not funded. Prospective students would be expected to apply for funding opportunities either through the University (http://www.vet.cam.ac.uk/grad/Prospectivestudents/funding) or other sources.

How to apply:
Contact the Supervisor to discuss before submitting an application.
More details on how to apply here: http://www.vet.cam.ac.uk/grad/Prospectivestudents/apply