Funded PhD Project: Myoepithelial and immune cell dynamics in the mammary terminal duct lobular unit during postnatal development

Supervisor: Dr Kate Hughes, Department of Veterinary Medicine, University of Cambridge
Co-Supervisor: Prof Clare Bryant, Department of Veterinary Medicine, University of Cambridge

Within the bilayered structure of the mammary gland, myoepithelial cells form the basal epithelial layer, express alpha-smooth muscle actin, and have contractile properties necessary for milk expulsion. Myoepithelial cells are recognised to be of significance in the progression of both mammary neoplasms and mastitis. However, in spite of their critical role in milk expulsion, and the importance of myoepithelial cells in mammary pathological processes, very little is known about the contribution of this cellular compartment to the postnatal cycle of mammary development and remodelling associated with puberty, pregnancy, lactation, and post-lactational regression. This project will elucidate the role and cellular interactions of myoepithelial cells in the mammary microenvironment in health. By defining the periods during which myoepithelial cells are dividing, the relationship of myoepithelial cells with immune cells, and the impact of hormones and growth factors on myoepithelial cell behaviour, the project will provide a deeper understanding of the role of the mammary basal epithelial compartment. This data will facilitate future identification of functions and interactions of myoepithelial cells that can be used in translational medicine to develop novel therapeutic strategies for mastitis and mammary neoplasia. This research will also seek to define the mammary microenvironment in non-traditional model species that are promising alternative models to rodents. Whilst rodents provide highly tractable model systems, the mouse mammary gland is fundamentally different from the human breast. This project will exploit the similarities between the mammary gland of non-traditional model species and the human breast to delineate the replication patterns, cellular interactions, and role of myoepithelial cells in these species.

The student will receive bespoke scientific training in:
1. Imaging: The student will gain rigorous training in imaging techniques applicable to a range of biological problems, including dual colour immunohistochemistry and immunofluorescence in 2D tissue sections, CUBIC tissue clearing, and deep 3D imaging. The student will be trained in appropriate selection of antibodies (including corroborative western blotting) and identification of relevant control tissues. The student will be fully trained in image acquisition using light and confocal microscopy.
2. Image interpretation: The supervisor is a veterinary pathologist who will provide detailed training in histology and image interpretation including use of scanned slides and software including Fiji and Imaris. Collaborator Prof Paul Rees will provide expertise in automated image analysis.
3. Tissue culture/organoid culture: The student will be fully trained in general tissue culture and in vitro techniques and particularly those techniques relevant to organoid culture such as enzymatic dissociation of tissues, maintenance of organoids in matrigel, and organoid harvest.
4. Mammary gland biology: The supervisor is a mammary gland biologist with experience of mammary gland biology and pathology across a range of species. The student will be exposed to mammary tissues from non-traditional model species and will learn about the differences, advantages, and limitations of these species compared to mice. The student will collect mammary tissues from a range of species and in doing so will learn the principles of anatomical dissection and tissue handling as well as appropriate tissue preservation.
5. Immunology: Co-supervisor Prof Clare Bryant will provide expertise and specialist training in immunology, particularly relevant to the interactions between myoepithelial cells and macrophages and T-lymphocytes.
6. Scientific writing and presentation including scientific communication to non-specialist audiences.
8. Statistics
9. There will be opportunities for the student to participate in teaching and demonstrating

Funding: Fees (at UK rate) and a stipend of £15,285 per annum for three years will be provided by the Anatomical Society.

How to apply: Contact the Supervisor to discuss before submitting an application via the Applicant Portal by: 15th January 2021. Applicants will be invited to attend an interview in the week beginning 25th January 2021.
More info on application process here: http://www.vet.cam.ac.uk/grad/Prospectivestudents/apply.