MRI-UQ Winter Research Project Description

Project title:	**Determine whether osteoporosis dysregulates osteomac and/or inflammatory macrophage number and phenotype in bone marrow and osteal tissues**
Project duration:	Please outline the length of the project. *10 weeks*
Description:	Resident tissue macrophages are present within virtually all tissues throughout life contributing to tissue homeostasis, tissue specific physiology, damage suppression and innate immune surveillance. Our group identified the resident macrophages within bone lining tissues (osteal macrophages or osteomacs) and have demonstrated their role in maintaining bone homeostasis. Osteomacs regulate the maintenance and bone forming activity of osteoblasts and can also influence the bone resorbing actions of osteoclasts. Therefore osteomac detection and subsequent response to elevated systemic inflammation represents a potential cellular mechanism mediating systemic inflammation-driven imbalances in bone turnover. We have recently demonstrated that deletion a single cell surface molecule gene that has resident macrophage-restricted expression resulted in a 50% reduction in resident macrophage frequency in bone and bone marrow. It also resulted in a significant reduction in bone volume. Therefore osteomac number and function may be a key cellular mechanism controlling bone health. To extend on these observation we will examine bone and bone marrow residence macrophage number and phenotype in two different mouse strains that sit on either end of the spectrum with respect to peak bone density: C57Bl/6 and C3HeJ. We will also compare bone and bone marrow residence macrophage number and phenotype between male and female mice at different ages. Bone is a sex-dependent organ with males reaching a higher peak bone density than females and the females having greater risk of osteoporosis in later life. This is mimicked in C57Bl/6 mice with rapid and profound bone loss initiating approximately 10 weeks of age in female but not male mice. Macrophage populations will be assessed by multiplexed flow cytometry analysis of bone marrow and bone preparations to quantify number and characterize the phenotype of resident macrophages between strains and across an aging time course. Antibody panels will include markers of macrophage activation status. Hind limbs will be processed for *in situ* analysis using immunohistochemistry to specifically assess whether the physical distribution of osteomacs and their interactions with other bone effector cell populations vary between stains or during aging.

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Expected outcomes and deliverables:	Osteoporosis costs the Australian healthcare system between $2.75 and 7.5 billion/year. This burden will continue to intensify due to population ageing and growing prevalence of comorbidities that increase fracture risk and poor fracture healing outcomes. Better understanding of key driver of achieving and maintaining peak bone mass is needed to develop more effective methods of detecting this 'silent' disease before significant bone loss has occurred, leading to a fragility fracture. This project represents a first step in identifying whether altered macrophage biology plays a direct role in dysregulated bone turnover leading to osteoporosis.
Suitable for:	Interested students need to be diligent, meticulous, inquisitive and self-motivated. Flexibility in working hours will be required. Knowledge of immunology and flow cytometry theory and/or hands on experience, are highly desirable. Project will be based at the Translational Research Institute in Woolloongabba.
Primary Supervisor:	Associate Professor Allison Pettit
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