Profiling the impact of CSF1-c treatment on osteomacs and osteoclasts

Research Project Overview

Project title:	**Profiling the impact of CSF1-Fc treatment on osteomacs and osteoclasts**
Project duration:	4 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 imbalances in bone turnover. The proliferation, differentiation, and survival of both resident tissue macrophages (such as osteomacs) and osteoclasts depends upon macrophage colony stimulating factor (CSF-1). Treatment with CSF-1 during the early anabolic phase of fracture healing enhances soft callus formation in mice. However, the short in vivo half-life of CSF-1 makes it cost-prohibitive as a therapeutic agent. CSF1-Fc has similar biological activity to CSF-1 with a significantly extended circulating half-life. We have preliminary data suggesting that CSF1-Fc is effective at promoting fracture healing, demonstrated by increased strength of the healing fracture site at 4 weeks post-injury. In this project we are seeking to understand the impacts of a range of CSF1-Fc treatment regimens (intensive: 4 x daily injections; sustained: 4wks of bi-weekly injections or 4wks of weekly injections) on bone homeostasis. Hind limbs will be processed for *in situ* analysis using

	immunohistochemistry and histological stains to specifically assess changes in osteomacs and osteoclasts under the different treatment regimens. This will inform whether treatment regimens suitable for promoting fracture healing have impacts on skeletal homeostasis.
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. Currently there are no broadly applicable pharmaceutical therapies for enhanced healing of fragility fractures. This project represents a key step in determining whether a novel therapeutic agent may be suitable for this purpose.
Suitable for:	Interested students need to be diligent, meticulous, inquisitive and self-motivated. Flexibility in working hours will be required. Knowledge of immunology and immuno-staining theory and/or hands on experience, are desirable. Project will be based at the Translational Research Institute in Woolloongabba.
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