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*“Bone repair in response to mast cell immunotherapy”*

Osteoimmunology is a rapidly developing interdisciplinary research field, which studies the molecular interplay between the immune system and the skeletal system. The highly ordered sequence of events in bone repair is heavily dependent on very specific interactions between cells of the skeletal, vascular and immune systems. While bone regeneration and repair is successful in the majority of patients, the success rate drops significantly in patients with underlying chronic disorders such as osteoporosis, diabetes or infection. Over 100,000 fractures develop a non-union each year in North-America. Non-unions of fractures represent an enormous burden of illness to patients and an escalating economic challenge to the healthcare system. Adjunct therapies currently used to promote healing in patients at risk of non-union include bone grafts and recombinant growth factors, which can cause significant morbidity in themselves, are used in over 1.5 million cases in North America yearly. Immunotherapy may prove to be a safer and more cost-effective alternative to promote bone repair. Mast cells, which carry many of the factors released during the inflammatory phase of bone healing, are present at all stages of the repair process. They migrate to the injury site in response to allergens or during the early inflammatory phase of bone repair and soft tissue repair. Taken together with their capacity to respond to specific stimuli, this identifies mast cells as potential immunotherapeutic targets for assisted bone repair. In recent work, we demonstrated impaired bone healing and the development of fibrous non-unions in mast cell deficient mice (Behrends et al., 2014) as well as in mice exposed to acute systemic inflammation (Behrends et al., 2017). The bone healing in mast cell deficient mice was significantly disorganized (Ramirez Garcia Luna et al. 2017), with mice exhibiting non-unions in association with impaired neovascularization. The goal of this proof-of-concept study is to determine if adoptive transfer of mast cells will restore normal bone repair in mast cell deficient mice. The proposed research is built on the global hypothesis that mast cells play a pivotal role in bone repair by coordinating the recruitment and/or activity of vascular, skeletal and immune cells in the bone healing micro-environment.