Poster Title: Novel Role of Megakaryocytes in the Skeletal Response to Mechanical Loading

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Abstract:
Megakaryocytes (MKs) are the largest and rarest of the cell types in bone marrow. MKs not only play a vital role in thrombopoiesis but are also known to regulate bone mass. Indeed, MKs stimulate osteoblast proliferation and bone formation through a direct cell-to-cell interaction. Bone mass is regulated by mechanical stimulation, primarily through the mechanical sensing osteocytes. Interestingly, MKs are also known to be responsive to mechanical stimulation. Therefore, we hypothesized that bone formation induced by mechanical loading could be attributed, in part, to MK-mediated stimulation of bone formation. To accomplish this, we selectively ablated MKs (~50% reduction) in some mice using diphtheria toxin (DT). The right tibia of mice underwent mechanical loading 5 days/week for 2 weeks. Upon completion of the study, platelets and MKs were measured, and both loaded and non-loaded tibia were analyzed for bone-related parameters via microCT and histomorphometric assessments. Results indicated successful >50% reduction in MKs and platelets. Male and female mice showed no significant change in trabecular volume or thickness with loading but exhibited a trend of lower trabecular bone formation rate due to DT ablation. Female mice in the control group displayed increased number of osteoclasts per bone perimeter due to mechanical loading. This was not the same for the group treated with DT. This suggests that MKs may play a role in bone remodeling due to mechanical loading. While more work is required to further elucidate these preliminary findings, it appears that reduced numbers of MKs for a short time minimally alters trabecular bone responses induced by mechanical stimuli. Importantly, dissecting the mechanisms responsible for skeletal changes may yield insights into potential therapeutic targets which could be developed to improve the bone mass and reduce osteoporotic related fractures in our aging demographic.