Do Megakaryocytes Regulate Mechanical Loading Induced Bone Formation?

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Background and Hypothesis:

Megakaryocytes are known to play a role in stimulating bone formation and recent studies from our laboratory show higher numbers of megakaryocytes in mice subjected to mechanical loading. Whether megakaryocytes play a role in mechanical induced bone formation was the primary aim of this study.

Experimental Design and Results:

Mice were generated in which megakaryocytes could be selectively ablated. Briefly, we crossed PF4-Cre mice (megakaryocyte-specific promoter) with iDTR mice carrying the inducible diptheria toxin (DT) receptor. Next, we determined a treatment regimen to reduce megakaryocytes and their resulting platelets. PF4-Cre;iDTR and PF4-cre mice were treated with DT (16μg/kg) and 6 days after treatment a significant, greater than 15 fold reduction in platelet number (complete blood count with differential) was observed in PF4-Cre;iDTR mice as compared to that observed in PF4-cre mice. Likewise, an almost 2 fold reduction in megakaryocytes was observed using flow cytometry. With these conditions in place, we then completed strain gage testing on the tibias of these mice to determine the proper loading regimen to subject the mice to. We have recently begun the mechanical loading studies in the DT treated PF4-Cre;iDTR and PF4-cre mice and once completed we will use microCT and histomorphometric analyses to determine if depletion of megakaryocytes reduces the ability of mechanical loading to increase bone formation.

Conclusions and Potential Impact:

While this study is ongoing, we would predict that mechanical loading of the mice tibias will show an elevated number of megakaryocytes and bone formation in the tibias from the PF4-Cre mice as opposed to the PF4-Cre;iDTR mice. If the microCT analysis shows the difference in bone formation between the control and experimental groups, this would indicate that megakaryocytes do in fact play a role in mechanical loading induced bone formation.