Preliminary Results Characterizing the Role of Megakaryocytes in Pain Behavior and Fractured Healing

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Introduction: Bone is a heterogeneous tissue regulated by both a complex interconnected biological and mechanical response. Megakaryocytes play an integral role in the biological signaling of this response by increasing bone formation through osteoblast upregulation and osteoclast downregulation. Megakaryocytes may also have a significant role in pain amplification through the release of platelet derived growth factor. The aim of this study is to characterize the role of megakaryocytes in fractured healing and pain behavior.

Methods: PF4Cre;iDTR male and female mice were separated into two groups. One group received diphtheria toxin (DT), adjusted for weight, every four to five days to ablate the natural megakaryocyte population. The control group received isovolumetric saline injections at the same time points. A complete, nondisplaced fracture was created in the right hind femoral shaft. Weekly saphenous blood samples and twice weekly in vivo x-rays were collected. Weekly behavior testing, including Von-Frey mechanical sensitivity test, was conducted. At twenty-two days post fracture, the mice were euthanized. Surgical and contralateral femurs were collected for later analysis.

Results: DT mice had a significantly lower body platelet count compared to the control group. Body weight remained constant in both treatment groups. Preliminary pain and radiographic results did not show a difference in pain behavior response or healing. However, this was a small sample size (n = 5-6 per group), and only two analyses were completed at this point in the study.

Future Direction: In addition to doubling the current sample size, we plan to analyze blood samples, μCT scans, biomechanical torsional testing, and four different behavior responses. Through gaining a greater understanding of the extent of megakaryocyte involvement in fracture healing signaling, we may discover new targets for pain management and methods to improve fracture outcomes.