Title: The Role of GPNMB in Osteoarthritic Bone Remodeling

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Objectives: Inflammatory factors lead to osteoclast differentiation, so increased inflammation should theoretically be associated with a higher osteoclast count. In addition, previous studies have demonstrated that osteoactivin has anti-inflammatory properties. Understanding the role of osteoactivin in the osteoarthritis disease process may be useful in developing novel therapies to combat this debilitating disease.

Abstract: Osteoclasts are integral to the process of remodeling in bone. They function by reabsorbing the bone and are associated with debilitating bone diseases such as osteoporosis and osteoarthritis. In this study, we performed destabilization medial meniscus (DMM) surgery to model osteoarthritis in mice. We utilized DBA/2J mice, which harbor a natural mutation in the osteoactivin gene, yielding a truncated nonfunctioning protein. As a control, we used the DBA/2J Osteoactivin+ wild-type (OAR) mice. Following the DMM surgery, knee joints were dissected and stained with Fast Green dye and TRAP (tartrate-resistant acid phosphatase) stain. Fast Green was used to visualize the cartilage in the joints while TRAP stain was used to visualize the osteoclasts. In order to have quantifiable data, the osteoclasts in the subchondral area of the bone in both the tibia and the femur were counted by using Osteocount. Previous studies have indicated that osteoactivin has anti-inflammatory properties, thus we hypothesized that there would be a higher osteoclast count in the right side of each joint, where the DMM surgery was performed. In addition, we expect that the DBA/2J mice will have a higher osteoclast count overall, due to their natural mutation in the osteoactivin protein. Thus, our results suggest that the DBA/2J mice exhibited more inflammation than the DBA/ 2J Osteoactivin+ wild-type (OAR) mice. In addition, these results associate a greater number of osteoclasts with an increased amount of inflammation, which also demonstrates the role of osteoclasts in osteoarthritis.