

Oral Abstract

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BMP3 is a candidate for modulating focal bone erosion in rheumatoid arthritis

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Focal articular bone erosion is a common feature of rheumatoid arthritis (RA). Despite treatment, repair of erosions with adequate formation of new bone is uncommon. We have demonstrated using the serum transfer arthritis (STA) model of inflammatory arthritis that osteoblast function is compromised at bone surfaces adjacent to inflammation with inadequate formation of mineralised bone. Osteogenic BMP activity is critical for the early commitment of mesenchymal precursor cells to osteoblast-lineage cells. In this study, we demonstrate that BMP3, an inhibitor of osteogenic BMP activity, is expressed within arthritic tissues and that it may contribute to focal bone erosion. In situ hybridization and quantitative RT-PCR demonstrated that BMP3 mRNA expression is upregulated late in the time course of STA in C57Bl6/J mice, with maximal 15-fold induction at day 15 in tissues obtained from erosion sites compared with non-arthritic tissues. A 2-fold induction within arthritic synovium and soft tissues was also observed. BMP3 protein was observed in inflamed synovial tissues, particularly within synovial-lining cells, and in cells that were consistent morphologically with osteoblast-lineage cells lining bone surfaces. Preliminary STA studies using BMP3 knockout mice (BMP3 KO) demonstrated that BMP3 deficiency attenuates focal bone erosion. Despite developing robust inflammation similar to wildtype littermates, a significant reduction in bone erosion scores in the forefoot bones ($p = 0.0022$) was observed in BMP3 KO mice. Our data demonstrates that BMP3 expression is upregulated within arthritic tissues, and is a novel candidate factor that may contribute to focal bone loss in inflammatory arthritis.