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Recombinant Progranulin Prevents the Loss of Proteoglycan in Surgically Induced Osteoarthritis Model

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Abstract

Osteoarthritis (OA) is a degenerative joint disease that affects more than 46 million people in the United States alone. Since mechanisms by which OA ensues are largely unknown, there are no therapeutic targets that effectively prevent and treat the disease. However, growth factors, cytokines and matrix-degrading enzymes are strongly implicated in initiating and aggravating OA lesions. Thus, a molecular understanding of these molecules will provide invaluable information toward the search for novel therapeutic targets for OA. Our genome-wide screen for novel, differentially expressed genes in OA led to the isolation of progranulin (PGRN) as a novel OA-associated growth factor [1]. In subsequent global screen for the binding proteins of PGRN, we found that PGRN bound to TNF Receptors (TNFR). In addition, PGRN blocks the binding of TNFα to TNFR and inhibits TNFα-induced ADAMTS cleavage of cartilage oligomeric matrix protein (COMP) [2]. These previous findings led us to determine whether recombinant PGRN prevents cartilage degradation in the progression of OA in vivo. For this purpose, we took advantage of PGRN knockout mice to generate *anterior cruciate ligament* (*ACL*) transection induced OA models which develop severe OA due to the deficiency of PGRN. Importantly, intra-articular injection of rPGRN growth factor significantly prevented the degeneration of cartilage in PGRN-deficient OA model. PGRN treated mice retained cartilage integrity and showed little or no degradation of cartilage matrix in comparison to highly degraded cartilage of non-treated mice (Figure).
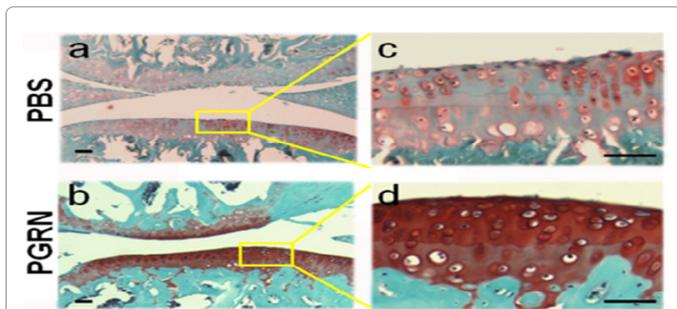
Figure 1: Recombinant progranulin (rPGRN) reduces the loss of proteoglycan in surgically induced osteoarthritis (OA) model. Intra-articular injection of rPGRN chondrogenic growth factor significantly prevented the degeneration of cartilage in PGRN-deficient OA model *induced* by *anterior cruciate ligament* (*ACL*) transection. PGRN treated mice retained cartilage integrity and showed little or no degradation of cartilage matrix in comparison to highly degraded cartilage of non-treated mice.

References

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