Growth hormone promotes joint degeneration and chondrocyte metabolic dysfunction in mice

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Objective: Many patients with acromegaly, a hormonal disorder with excessive growth hormone (GH), report pain in joints. The objective of this study is to characterize the joint pathology of mice with over-expression of either bovine GH (*bGH*) or a GH receptor antagonist (*GHa*). We also investigate the effect of GH on regulation of chondrocyte cellular metabolism.

Methods: Knee joints from mice over-expressing *bGH* or *GHa* and WT were histologically and µCT analyzed for OA pathologies. Additionally, cartilage from *bGH* mice was used for metabolomics. Mouse primary chondrocytes treated with bGH and with or without Pegvisomant (Peg) were used for Seahorse Respirometry and Q-PCR analysis.

Results: Both male and female *bGH* mice at ~13 months had increased knee joint degeneration, which is characterized by loss of cartilage structure, expansion of hypertrophic chondrocytes, synovitis, and subchondral plate thinning. The joint pathologies were also demonstrated by significantly higher OARSI and Mankin scores in *bGH* compared with WT mice. Metabolomics revealed changes of a wide range of metabolic pathways in *bGH* mice including beta-alanine metabolism, tryptophan metabolism, lysine degradation, and ascorbate and aldarate metabolism. Also, chondrocytes treated with bGH upregulated fatty acid oxidation (FAO) and increased expression of *Col10a*. Joints of *GHa* mice are remarkably protected from developing age-associated joint degeneration with smooth articular joint surface.

Conclusions: These studies uncover that an excessive amount of GH promotes joint degeneration in mice, while antagonizing GH action through a *GHa* protects mice from OA development, which is associated with chondrocyte metabolic dysfunction and hypertrophic changes.
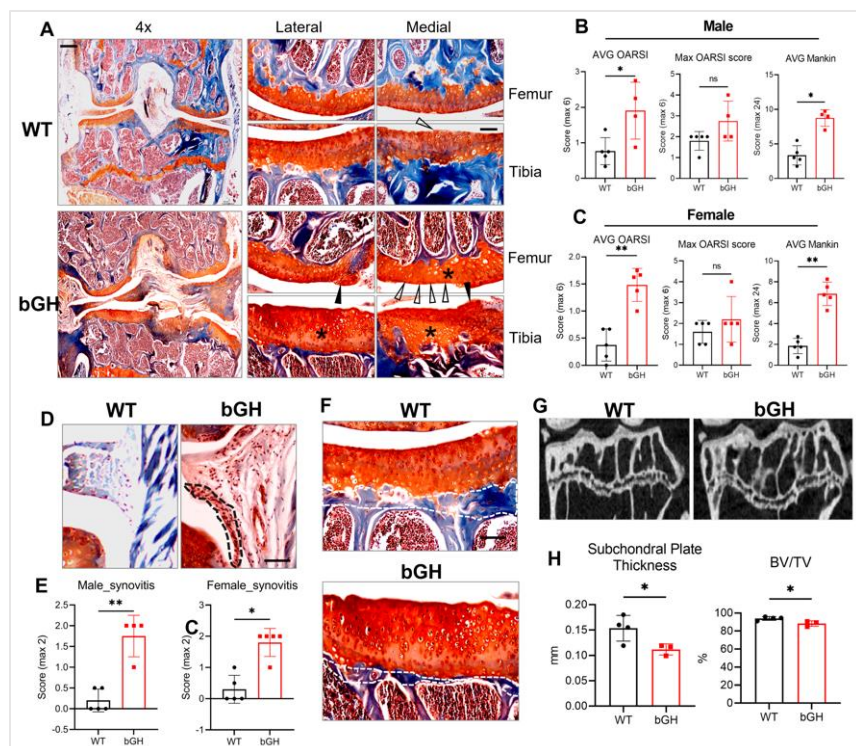
Figure 1

Figure 2