

Uncovering the Role of Growth Hormone in Aging Associated Hip Osteoarthritis

Anna Miller^{1,2,3*}, Siqi Ren^{1,3}, Abhijit Sukul^{1,3}, Huanhuan Liu^{1,3}, John J. Kopchick¹, Shouan Zhu^{1,3}

Heritage College of Osteopathic Medicine¹, Athens, OH, Ohio University Honors Tutorial College², Ohio Musculoskeletal & Neurological Institute (OMNI)³, Athens OH; *am646021@ohio.edu

INTRODUCTION: Osteoarthritis (OA) of the hip affects about 1 in 4 people over 60. Patients with acromegaly, caused by excess growth hormone (GH), show higher rates of hip OA. Our lab previously demonstrated that GH excess in bGH transgenic mice accelerates knee OA, while blocking GH signaling protects against age-related degeneration. Although GH's role in the knee is established, its impact on the hip remains unclear. Muñoz-Guerra et al. reported increased femoral head pathology in bGH mice but did not assess intact hip joints or mechanisms. Here, we aim to evaluate hip joint degeneration in aging bGH mice and identify underlying mechanisms, hypothesizing that GH excess drives greater OA pathology in the hip

METHODS: In-tact left hip joints from male and female ~13-month-old mice overexpressing bGH and WT were collected and processed for histological analysis using standard methods. The acetabulum and femoral head of the samples were scored separate and averaged using OARSI and Mankin OA scoring systems. An additional 10 left in-tact hips from each group have been collected for later micro-CT analysis and will then be processed using standard methods for histological review. Finally, all right in-tact hip joints were collected and stored at -80°C in RNA-Later for later bulk RNA-sequencing.

RESULTS SECTION: Both WT male and females showed similar phenotypes with only mild degeneration of the femoral head and acetabulum (Figure 1A). Additionally, there was no significant difference between males and females in the OARSI and Mankin scores of the femoral head and acetabulum of WT mice (Figure 1D, Figure 1E). Male and female bGH mice show more pronounced joint degeneration compared to WT groups as characterized by increased joint space narrowing, severe degradation of the acetabulum and larger femoral head (Figure 1B). When compared to WT groups, the total hip joint of bGH mice had a significantly higher OARSI and Mankin score ($p < 0.05$) with males having a slightly higher overall OA score compared to female counterparts. Interestingly, when comparing OARSI and Mankin scores of the femoral head alone, there was no significant difference between bGH and WT groups except between male Mankin scores, with bGH mice having a significantly higher Mankin Score than WT mice (Figure 1D). Additionally, bGH mice had significantly higher OARSI and Mankin scores of the acetabulum compared to WT across all groups suggesting that the acetabulum has increased OA pathologies compared to the femoral head (Figure 1E).

DISCUSSION: This study seeks to investigate the impact of excess growth hormone on the development of OA in the hip joint, addressing a significant gap on basic hip OA research compared to the knee joint. While these results are preliminary, they do support our hypothesis that bGH transgenic mice exhibit greater hip joint degeneration. The differences in OARSI and Mankin scores of the individual components of the hip joint show the need to score the total hip joint rather than just the femoral head and has also shown us an interesting phenotype in the acetabulum which has been missed in previous studies. Future directions of this study include micro-CT analysis of in-tact joints to further characterize joint pathologies and bulk RNA sequencing to identify a mechanism leading to the observed phenotype.

SIGNIFICANCE: Hip OA in basic research is vastly understudied when compared to knee OA. There is a significant need to specifically study the hip joint in conjunction with the knee joint to ensure that all patients receive the highest care for their different forms of OA.

Figure 1

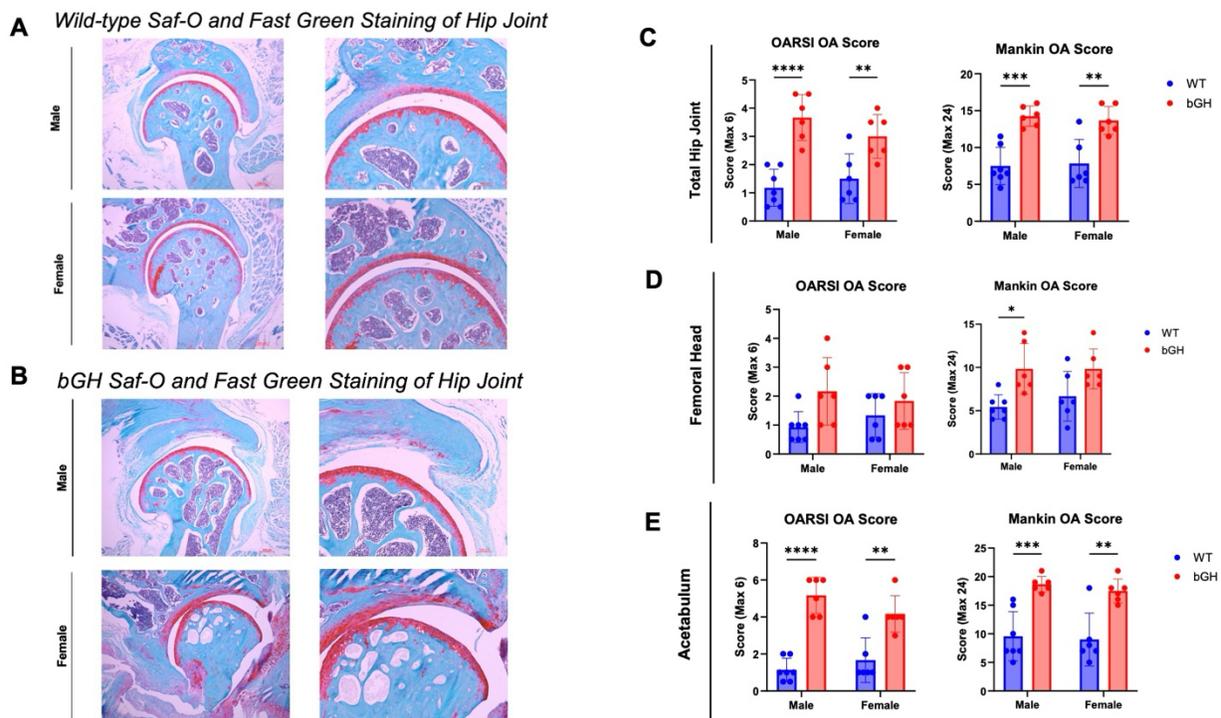


Figure 1. bGH mice show increased joint degeneration compared to WT mice. Representative images of Safranin-O and Fast Green of (A) WT male (n=7) and female hip joints (n=6) and (B) bGH male (n=6) and female hip joints (n=6). OARSI and modified Mankin OA scores of (C) total hip joint (acetabulum and femoral head), (D) femoral head alone and, (E) acetabulum alone.