

Chondrocyte senescence in facet joint cartilage of adolescent idiopathic scoliosis and the therapeutic potential of senolytic drugs

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Introduction

Facet joint osteoarthritis (OA) is increasingly recognized in adolescent idiopathic scoliosis (AIS) and may contribute to curve progression through impaired control of axial rotation. While cellular senescence is a key driver of age-related OA, its role in adolescent OA and the therapeutic potential of senolytics remain unexplored. This study aimed to characterize cellular senescence in AIS-associated facet joint OA and to evaluate the senolytic potential of o-vanillin.

Materials and Methods

Facet joint cartilage was obtained from 72 AIS patients undergoing elective posterior spinal fusion and 18 non-scoliotic organ donors during multiorgan procurement procedures. Cellular senescence was assessed using RNA sequencing and p16INK4a immunostaining. Paired facet joints from the same spinal level were analyzed to examine side-to-side differences in degeneration and senescence burden by quantifying senescence-associated gene expression using qPCR. The effects of the senolytic compound o-vanillin were evaluated in patient-derived chondrocyte cell cultures and cartilage explant cultures by assessing senescence markers, SASP expression, matrix catabolism, and proteoglycan content.

Results

RNA-seq revealed significant enrichment of senescence-associated gene sets in AIS chondrocytes, with the SEN_MAYO signature exhibiting the strongest enrichment score (ES = 0.76). Consistently, AIS cartilage exhibited a higher proportion of p16-positive chondrocytes compared with non-scoliotic control cells (AIS: 15.28%, 95% CI 11.75–18.81; NSC: 5.22%, 95% CI 3.47–6.96; $p < 0.0001$). In paired facet joints, increased OA severity was associated with elevated expression of cell-cycle inhibitors, RB family members, and SASP factors, including P16, P21, RB1, RBL1, RBL2, ILs, CXCLs, CCLs and MMPs. O-vanillin treatment reduced senescence markers and SASP expression in *in vitro* chondrocyte culture, and further attenuated matrix catabolism and improved proteoglycan preservation in *ex vivo* cartilage explant culture.

Conclusion

Cellular senescence is a prominent feature of AIS-associated facet joint OA and correlates with OA severity. These findings provide a rationale for further investigation of senolytic strategies as potential disease-modifying approaches in AIS.