

A32 MATRIX METALLOPROTEINASE 3 IS REGULATED BY THE LAMININ LAMA4 IN HUMAN OSTEOARTHRITIS

F C Fuerst,¹ S M Kielhauser,¹ G Gruber,¹ M H Stradner,¹ H Angerer,¹ M L Kremser,¹ D Setzgel,¹ W B Graninger¹ ¹Department of Rheumatology and Immunology, Medical University Graz, Graz, Austria

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Background Osteoarthritis (OA) is characterised by a loss of cartilage extracellular matrix and chondrocyte hypertrophy. Syndecan 4 was shown to regulate ADAMTS5 and matrix metalloproteinase 3 (MMP3) which is crucial for cartilage breakdown. Syndecans have a binding site for laminins like LAMA4. Therefore the authors examined the expression and function of LAMA4 in OA cartilage.

Methods The authors collected osteoarthritic cartilage specimen (n=20) from patients undergoing total knee replacement and performed immunohistochemistry for Syndecan 4 and LAMA4. Furthermore human chondrocytes cultures were treated with the LAMA4 blocking antibody 2A3 and gene expression of MMP3, MMP13, ADAMTS5, LAMA4 and Syndecan 4 was measured using RT-PCR.

Results LAMA4 and Syndecan 4 are specifically co-expressed in hypertrophic chondrocyte clusters. Compared to sections from low-grade OA LAMA4 staining is significantly stronger in high-grade OA. Blocking LAMA4 in vitro leads to a significant ($p<0.03$) suppression of MMP3 expression.

Conclusion LAMA4 is expressed selectively in high-grade OA and regulates expression of MMP3 presumably via syndecan 4.