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Background and objectives Nuclear and cytoplasmic protein glycosylation by the addition of O-linked N-acetylglucosamine (O-GlcNAc) to serine and threonine residues is a widespread post-translational modification that has been implicated in the regulation of a variety of signal transduction pathways. This modification is catalysed by the O-GlcNAc transferase (OGT). Despite the important role that has been described for this system in degenerative and age-related diseases, such as Alzheimer's and diabetes, the role of O-GlcNAc-glycosylation in osteoarthritis (OA) has not been considered previously. The authors analysed the O-GlcNAc glycosylation levels in the articular cartilage of patients with OA and the expression of the different isoforms of OGT.

Materials and methods Human cartilage was extracted from patients with knee OA during the joint replacement surgery (n=6), while healthy cartilage was obtained from the knee of age and sex-matched donors (n=6). The hyaline cartilage from the medial tibia was isolated and immediately frozen. Cartilage levels of O-GlcNAc glycosylation and OGT expression were assessed by western blot analysis employing specific antibodies.

Results In human cartilage, OA was associated with a different level of O-NAcGlc in a variety of proteins with different molecular weights in comparison to the levels observed in the healthy cartilage. The authors have observed that human cartilage expressed at least three OGT isoforms that have been previously described in other tissues. OA was also associated with an altered expression of the OGT isoforms identified, in comparison to the expression observed in healthy cartilage. Surprisingly, the level of 110-KDa OGT isoform, that has been considered the most ubiquitous one, was not modified, while the 70 and the 85 kDa isoforms were differently regulated in human OA cartilage in comparison to healthy one.

Conclusions These results demonstrate that OA could be associated with a dysregulation in the hexosamine biosynthesis pathway that could lead to an alteration of the level of O-GlcNAc-glycosylation in a variety of proteins. Our data support the hypothesis that O-GlcNAc protein modification mediated by the different OGT isoforms may play an important role in degenerative and age-related diseases.

A201 PROTEIN O-LINKED N-ACETYLGLUCOSAMINE LEVELS IN THE CARTILAGE OF PATIENTS WITH KNEE OSTEOARTHRITIS

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