Nature Reviews Rheumatology | Published online 4 Feb 2016; doi:10.1038/nrrheum.2016.12

OSTEOARTHRITIS

Galectin-1 damages cartilage via inflammation

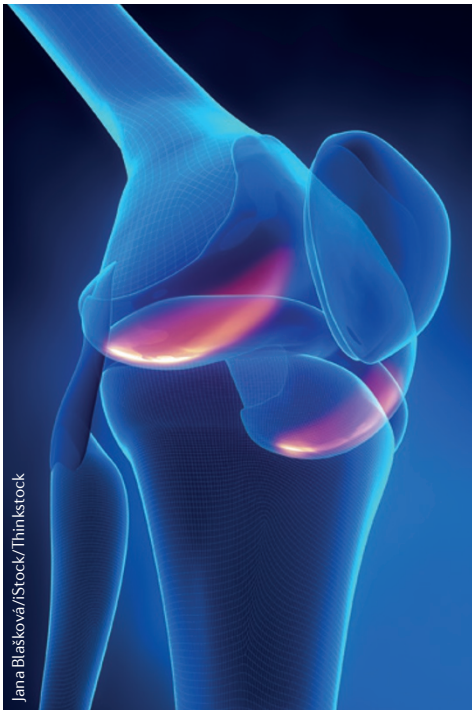
> "...galectin-1 promotes the proinflammatory process in osteoarthritic chondrocytes..."

Galectin-1 serves as coordinator, or master regulator, of the degeneration of osteoarthritic chondrocytes by stimulating NFκB-mediated inflammation, according to a new study.

Galectins, a family of lectins, bind to glycans at the cell surface and regulate cell adhesion and growth. Galectin-1, which acts as a bridge between cells and between distinct cell-surface glycoconjugates (the switch for outside-in signalling), has a protective anti-inflammatory role in rheumatoid arthritis. Paradoxically, galectin-1 and two other galectins have also been associated with cartilage degeneration in patients with osteoarthritis (OA).

The study researchers performed immunohistochemistry in samples of articular knee cartilage from 29 patients with OA. The expression of galectin-1 correlated with the degree of cartilage degeneration, with the protein being present specifically at sites of damage. Cell culture, followed by immunofluorescence analysis, revealed that galectin-1 binds to the cell surface of osteoarthritic chondrocytes via a glycan-dependent mechanism. Gene and protein expression analyses showed that galectin-1 significantly upregulated the expression of enzymes involved in matrix degradation (such as matrix metalloproteinases) *in vitro*. Conversely, expression of matrix components was downregulated. Treatment of osteoarthritic chondrocytes with lactose inhibited binding of galectin-1 to the cell surface and decreased the expression of galectin-dependent genes in a dose-specific manner. These observations suggest that binding of galectin-1 is glycan-dependent and contributes to the pathogenesis of OA.

Treatment of osteoarthritic chondrocytes with recombinant galectin-1 triggered strong expression of a gene signature enriched in genes involved in the NFκB signalling pathway. This relationship was unidirectional, as treatment of the cells with pro-inflammatory cytokines did not lead to increased expression of galectin-1. Targeted blockade of the NFκB pathway at different levels decreased expression of *IL1B*, a target of galectin-1-mediated transcription. These findings indicate that galectin-1 promotes the proinflammatory process in osteoarthritic chondrocytes through mechanisms involving the NFκB pathway. This effect contrasts with the anti-inflammatory action of galectin-1 in other diseases and shows that the role of galectin-1 is cell-dependent.



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Future work in this area is likely to focus on investigating the upstream mechanisms that lead to increased production of galectin-1 in OA cartilage and on clarifying the roles of other galectins in this process. According to the authors, interfering with the action of galectin-1 might lead to the development of new therapeutic approaches for OA.

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ORIGINAL ARTICLE(S) Toegel, S. *et al.* Galectin-1 couples glycobiology to inflammation in osteoarthritis through the activation of an NF-κB-regulated gene network. *J. Immunol.* http://dx.doi.org/10.4049/jimmunol.1501165 (2016)