

## THE ROLE OF NIDOGEN-1 AND NIDOGEN-2 IN THE PATHOGENESIS OF OSTEOARTHRITIS

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**Introduction:** We have already demonstrated that nidogen-1 and nidogen-2 are components of healthy as well as osteoarthritic cartilage of the human knee joint. We recently investigated differences in the mRNA and protein amounts between the cells in the intact area (type 1 cells) in Osteoarthritis (OA) and the fibroblast-like cells in the defect area (type 2 cells) in OA. Further investigations were done to detect possible functions of nidogen-1 and -2 in articular cartilage and OA. **Materials and Methods:** With the help of in situ-hybridization and immunohistochemistry the mRNA and protein amounts of type 1 and type 2 cells in human OA cartilage were electron microscopically elucidated. The adhesion of OA cells to both proteins was observed in vitro by cell attachment and cell inhibition assays. Differences between nidogen-1 knockout, nidogen-2 knockout and heterozygous mice were studied. **Results:** In OA cartilage, strongest staining for nidogen-1 and -2 mRNA was found for type 2 cells in the defect area. The same was true for the pericellular protein amount for both nidogens. In vitro, the cell assays showed a distinct adhesion to nidogen-1 and nidogen-2 for cells taken from the defect area. The adhesion could be inhibited by nidogen-1 or -2 antibodies. Type 1 cells, taken from the intact area, did not attach. The knee joints of 8-week-old nidogen-1 and -2 knockout mice did not differ from the normal appearing knee joints of heterozygous mice. However, nidogen-1 knockout mice exhibited a loss of proteoglycans, in the interterritorial matrix. Nidogen-2 knockout mice showed a total loss of proteoglycans, pericellularly and interterritorially. **Conclusion:** Nidogen-1 and nidogen-2 are involved in the pathogenesis of OA, since they may be important for the maintenance of proteoglycans in articular cartilage of the knee joint. They are secreted in increased amounts by type 2 cells, especially around deep surface fissures, maybe as a sign of regeneration efforts. Furthermore, the in vitro data for the 2 different cell types in OA cartilage show different binding kinetics to both nidogens, and, therefore, a different integrin receptor repertoire. These findings could be used to further characterize these 2 cell types. The different binding kinetics could help to separate these cells in vitro.