ABSTRACT

Collagen IX is a cartilage specific extracellular matrix protein and belongs to the family of FACIT- (*fibril associated collagens with interrupted triple helices*) collagens. It is known that humans carrying polymorphisms in the collagen IX gene develop early onset disc degeneration. In order to investigate the role of collagen IX in the development and degeneration of the spine, the lumbar spine of collagen IX deficient mice was systematically analyzed. The first part of this thesis focused on newborn animals. It was found that collagen IX deficiency causes the loss of a number of other proteins from the extracellular matrix. In contrast, ectopic accumulations of these proteins could be observed in the intervertebral disc. Further, an increased amount of the matrix protein COMP could be detected in the serum of collagen IX deficient mice. Investigation of the expression at RNA level did not show any differences. In contrast, a reduced anchorage of the proteins could be demonstrated. Measurement of the biomechanical properties of the extracellular matrix showed a reduced stiffness of collagen IX deficient tissue. Furthermore, collagen IX deficient mice exhibited an increased bone mineral density in the vertebral bodies as well as a smaller nucleus pulposus. Analysis of adult animals showed early signs of disc degeneration and deformations of the spine. However, bone parameters as well as nucleus pulposus size returned to normal with age. Since collagen IX deficient mice revealed morphological differences of the spine already at birth, embryonic stages were analyzed. Already at E12.5 morphological changes in the developing vertebral bodies could be observed. A reduction in nucleus pulposus size was first seen at E18.5. In addition, the vertebral bodies showed an increased number of hypertrophic chondrocytes at E15.5. Analysis of the PTHrP-Ihh- as well as the TGFß signaling pathway revealed an increased Ihh- and TGFß- and a reduction of PTHrP activity. This leads to a shift towards terminal differentiation. Therefore, collagen IX deficiency leads to a disturbed differentiation already at an embryonic stage. This early maldevelopment promotes early onset disc degeneration.