ABSTRACT

The extracellular matrix (ECM) represents a complex alloy of different members of diverse protein families, the composition of which defines structural integrity and various physiological functions. Collagen IX is a quantitatively minor component in all hyaline cartilages, always occurring together with collagen II. Due to its periodical localisation along the collagen II fibril, collagen IX is thought to act as a macromolecular bridge between collagen fibrils and other ECM molecules. However, the exact function in matrix organisation and bone development still needs to be elucidated.

As a first step, the effect of collagen IX deficiency on the deposition of matrix proteins into cartilage tissues was investigated. Newborn collagen IX deficient mice showed significantly decreased matrilin-3 amounts in most cartilaginous tissues, while the biosynthesis was not affected. In the absence of collagen IX, a substantial amount of matrilin-3 was released into the medium of cultured chondrocytes instead of being integrated into the cell layer as in cultures of wildtype cells. This points to a direct interaction of matrilin-3 with collagen IX, a notion that could be confirmed by *in vitro* experiments.

The mild skeletal defects in mice deficient for collagen IX, COMP or matrilin-3 might result from redundancy between these ECM proteins. To reduce redundancy and to further study the role of collagen IX, a mouse model lacking both collagen IX and COMP was generated. Mice deficient in both proteins exhibited shortened and widened long bones as well as an altered bone structure. They displayed severe growth plate abnormalities with large hypocellular areas in the central parts of the tibia. In addition, the typical columnar arrangement was disturbed. Surprisingly, mice lacking only collagen IX exhibited similar growth plate disturbances. These phenotypical traits were not observed in mice deficient only in COMP. Hence, the contribution of COMP to the phenotype of mice deficient in both collagen IX and COMP appears minor. However, comparing collagen IX and double deficient mice, we could detect differences in the deposition of matrilin-3, pointing to a role of COMP in matrix organisation.