Altered collagen expression in the cornea of a child with Ehlers-Danlos syndrome type VI

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Purpose: Ehlers-Danlos syndrome is a systemic disease caused by collagen deficiency, with type VI being characterized by its ocular complications. We have now examined the pattern of collagen expression in the cornea of a child with Ehlers-Danlos syndrome type VI.

Methods: An 8-year-old boy diagnosed with Ehlers-Danlos syndrome type VI developed retinal detachment and congenital corneal leukoma in his right eye. He was treated by pars plana vitrectomy with penetrating keratoplasty, and frozen sections were prepared from the excised corneal tissue. The expression of collagen types I, III, IV, and V in the sections was examined by immunohistochemical techniques.

Results: Nomarski images revealed Bowman's membrane to be intermittent in the cornea of the proband. Collagen types I and V were detected in Bowman's membrane and throughout the corneal stroma, whereas collagen type IV was apparent in the corneal epithelial basement membrane and in the portion of Descemet's membrane facing the endothelium. The expression patterns of these three types of collagen in the subject were virtually identical to those in the normal cornea. Collagen type III was expressed only in the anterior stroma and the portion of Descemet's membrane facing the endothelium in the normal cornea. In contrast, it was detected in association with the corneal epithelial basement membrane, its abundance in the anterior stroma was reduced, and it was not detected in Descemet's membrane in the patient.

Discussion: We have shown that the pattern of expression of collagen type III is altered in the cornea of an individual with Ehlers-Danlos syndrome type VI. The changes in the expression pattern of this collagen likely result from the congenital abnormality in collagen synthesis and chronic corneal epithelial disorders.

Expression of ATF5 in the Developing Limbs

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The multistep process of endochondral bone formation begins with the condensation of mesenchyme cells followed by their differentiation into chondrocytes. We recently developed a new system to identify genes specifically activated in the early phase of chondrogenic differentiation using a clonal cell line, ATDC5. ATF5 (activating transcription factor 5) is one of the transcription factors identified in this system. We report here in vivo expression pattern of ATF5 in the developing limbs.

Materials and Methods: ICR mice were obtained at selected time-points for analysis: these included embryos (E12.5-E18.5), newborn mice (postnatal day 1, 7, 14, and 28), and adult mice (3 month old). The forelimbs were harvested, fixed in 4% paraformaldehyde and embedded in paraffin. Thin sliced tissue sections at each time-points were prepared for in situ hybridization study. Digoxigenin-labeled cRNA probes were prepared using a DIG RNA labeling kit.

Results: In E12.5 forelimb buds, ATF5 transcripts were initially detected in condensed mesenchymal cells. In E14.5 forearm bones, ATF5 was expressed in the reserve and proliferative chondrocytes, but not in hypertrophic chondrocytes. Furthermore, in E15.5 forelimbs, the expression of ATF5 was detected in osteoblast like cells of bone tuberculae, in cells of perichondrium and periosteum. In the newborn mice at postnatal day 7, the expression of ATF5 was down-regulated in the reserve and proliferative chondrocytes, whereas it was still at high level in the cells of periosteum, and bone marrow. ATF5 transcripts were detected in articular cartilage in the newborn mice at postnatal day 14, but its expression level became low at postnatal day 28. In 3-month-old adult mice, ATF5 was expressed in epiphyseal growth plate and bone marrow.

Discussion: ATF5 was transiently activated in the developing limbs, which was similar pattern as seen in differentiating ATDC5 cells. Our observation suggests that ATF5 is closely associated with cartilage development and differentiation.

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