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Chondroadherin binds to type II collagen

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Keywords

Articular cartilage, binding assay, chondroadherin, protein extraction, type II collagen

Context

Chondroadherin belongs to a family of small leucine-rich repeat (LRR) proteoglycans that is a major component of the cartilage matrix. This family also includes biglycan, decorin, fibromodulin, and lumican. Type II collagen (CII) is the major collagenous component in cartilage; previous studies have demonstrated binding of CII with several LRR proteins, as well as to cartilage oligomeric matrix protein. This study tested the hypothesis that chondroadherin binds to CII.

Significant findings

Chondroadherin was 36 kDa in monomeric form, and 67 kDa in dimeric form. CII and chondroadherin were found to co-fractionate and were detected in tightly associated complexes. Chondroadherin was bound to specific sites on the collagen fibrils, at 185 nm and 267 nm from the C-terminal end of the collagen. These associations were similar in both extracted complexes from *in vivo* materials, and in reconstituted complexes from pure proteins. The equilibrium dissociation constant for this interaction was 40 nM.

Comments

This report demonstrated definitively that chondroadherin binds to CII. Furthermore, based on extraction from biological materials, and the intactness of the extracted complexes, this report provided strong evidence that binding may also occur *in vivo*. The most significant implication from this study is that as chondroadherin is a territorial component, its binding to CII suggests that this complex may have

cell regulatory function, in addition to structural functions. The cell regulatory function may be mediated by the complexes in association with a2-?1 integrins that are expressed on the cell surface of chondrocytes. Chondroadherin is localized in a restrictive manner in the late proliferative cells of the growth plate, and to the developing articular cartilage (see Additional information [1]). This further suggests that the interactions between chondroadherin and collagen may regulate chondrocyte growth and proliferation. In addition to chondroadherin, several other LRR proteins are also bound to collagen fibrils. Targeted disruption of biglycan in mice leads to loss of integrity of the collagen network and an osteoporosis-like phenotype (see Additional information [2]). Altered levels of biglycan, decorin and fibromodulin were detected in an experimental osteoarthritic model (see Additional information [3]). Therefore, another significant implication from the current study is that chondroadherin contributes to the integrity of collagen network by regulating the assembly. Deregulation of chondroadherin may then lead to congenital skeletal disorder, or cartilage degenerative diseases such as arthritis. The biochemical interactions of chondroadherin and collagen may represent yet another mechanism for collagen homeostasis.

Methods

Molecular cloning, sequencing, expression of recombinant chondroadherin, generation of antibodies, biochemical extraction and purification, ion exchange chromatography, zonal rate centrifugation in glycerol gradients, SDS-PAGE, western blotting, transmission electron microscopy, surface plasmon resonance

Additional information

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