ARTICULAR CARTILAGE COLLAGEN: AN IRREPLACEABLE FRAMEWORK?

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INTRODUCTION: Collagen provides the tensile fabric and two-thirds of the dry weight of mature articular cartilage [1]. The collagen is highly cross-linked and its turnover is at best extremely slow and the articular chondrocytes appear incapable of repairing any overt damage. It is still unclear, however, to what extent molecular remodeling, fibril growth and repair or other metabolic changes to the collagen framework are essential features of joint cartilage biology and functional longevity.

METHODS: By dissecting the collagen fabric proteolytically, determining the structure of cross-linked peptides and identifying the sites of interaction of the various gene products, steps in the molecular assembly and inherent heteropolymeric nature and tissue-specific differences in the collagen polymer can be defined. Using the latest methods in protein mass spectrometry, this type of work has been greatly facilitated and is allowing us to define in more detail the post-translational phenotype that characterizes articular cartilage collagen.

RESULTS: The basic polymeric fabric begins as a cross-linked copolymer of types II, IX and XI collagens [2]. Other types of collagen including collagens VI, XII and XIV are present in the pericellular space (type VI) or associated with fibril surfaces (types XII and XIV), but these molecules are extractable by protein denaturants not part of the covalently bonded polymer [1]. The placement of covalent intermolecular bonds between collagens II, IX and XI suggests a hierarchical assembly, with a collagen XI filament providing a scaffold for collagen II and collagen IX covalently bonding to the surface of the nascent fibril network [3,4]. As the tissue matures, much of the collagen IX disappears, presumably by proteolysis, to allow the collagen II fibrils to grow laterally but the mechanism, whether by fusion of thin fibrils or incremental addition of more collagen monomers, is unclear. With maturity, collagen III appears as a significant component of adult articular cartilage. Our recent findings reveal that collagen III molecules are extensively cross-linked to type II collagen, primarily in the form of pN-type III molecules attached to the surface of collagen II fibrils (Fig. 1). This appears to be an addition imposed metabolically on the existing collagenous matrix by the articular chondrocytes, and can be considered a form of matrix repair response.

DISCUSSION & CONCLUSIONS: In summary, as we continue to dissect the molecular details of collagen hierarchical assembly, cross-linking and chain isoform usage, for example in the collagen V/XI subfamily, it becomes clear that articular cartilage collagen has acquired distinctive molecular properties that presumably have evolved with the tissue's adaption for a load-bearing function and longevity. The results also indicate that new monomers (in this case collagen III) can become covalently added to the surface of an existing fibrillar network (collagen II). This has implications for collagen fibril growth and remodeling in tissues in general.

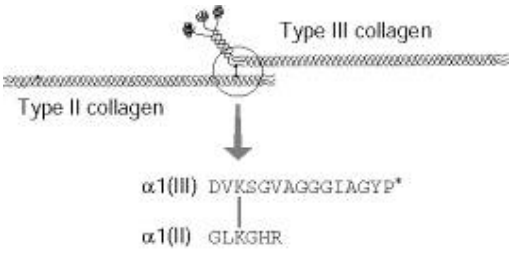

Fig. 1 Structure of a cross-linked peptide from articular cartilage originating from the interaction of pN-type III collagen with type II collagen**.**

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