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Cartilage Hierarchy and Function

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Abstract

The biochemistry of cartilage has been extensively studied in the last couple of decades. The major proteoglycan component of catilage extracellular matrix is the high molecular weight ($1x10^8 < M < 3x10^6$) bottlebrush shaped aggrecan. In the presence of hyaluronic acid (HA) and link protein, aggrecan self- assembles into a supramolecular structure with as many as 100 aggrecan molecules attached as side chains on a filament of HA. This supramolecular array yields a hydrated, viscous gel that provides the osmotic properties necessary for the cartilage to resist deswelling under compressive load. In cartilage these complexes are interspersed in the collagen matrix. Imaging techniques (electron microscopy, atomic force microscopy, etc) have revealed the size and structural pattern of large distinct aggrecan-HA acid complexes. Such methods yield detailed information on the morphology within a selected area of the sample. However, the interactions that govern the morphology and dynamics of aggrecan-HA assemblies in solution remained poorly understood. Owing to the complexity of the aggrecan-HA system the determination of the relationship between its structure and function requires a range of experimental approaches combining both physical and biochemical techniques. We investigate the spatial organization both in solutions of aggrecan and aggrecan-HA complexes over a length scale range between 1 and 500 nm. The static properties are studied by small angle neutron scattering (SANS) and static light scattering (SLS), while the dynamics are probed by dynamic light scattering (DLS). The length scale range probed by scattering methods detects changes in the architecture on the supramolecular scale. Changes at the molecular level are detected by virtue of the average effect that they exert on the larger scale structures. Better understanding of the organization of aggrecan assemblies and their effect on cartilage mechanical properties is essential to advance our knowledge of arthritis and develop treatment strategies.