Polymer Networks 2016 Invited Lecture
June 18-23, 2016,
Stockholm, Sweden

Gel-like Properties of Cartilage Proteoglycans

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Cartilage extracellular matrix (ECM) can be considered a network of large molecules that provides structural strength to the tissue by maintaining a complex hierarchical architecture. ECM is composed of two main components that define its biomechanical properties: proteoglycan assemblies, which give articular cartilage its ability to resist compressive loads, and a collagenous network, which is responsible for the tensile strength of the tissue. The most abundant proteoglycan is aggrecan, a bottlebrush shaped molecule that possesses over 100 sulfated glycosaminoglycan (chondroitin sulfate and keratan sulfate) chains. The side-chains are long, linear carbohydrate polymers that are negatively charged under physiological conditions. Aggrecan interacts with hyaluronic acid (HA) to form large aggregates. The aggregation between aggrecan and hyaluronic acid is essential for the biomechanical function of cartilage. The negatively charged aggrecan/HA complexes interspersed in the collagen matrix provide a high osmotic pressure that defines the compressive resistance of the tissue. The other proteoglycans (decorin, fibromodulin, etc.) are much smaller than aggrecan. They interact with collagen and help maintain the structural integrity. The collagen matrix counterbalances the osmotic swelling pressure of the embedded proteoglycan assemblies. The biomechanical properties of cartilage strongly vary with age, injury and disease.

Bone formation, i.e., the conversion of cartilage into bone requires several processes that involve different ECM components and ions, particularly divalent calcium ions. In charged polyelectrolyte systems [e.g., poly(acrylic acid), DNA] higher valence counter-ions often results in phase separation. It is unlikely that the aggrecan/HA assemblies could fulfill their biological functions if they exhibit similar ionic sensitivity.

Our objectives are to:

(i) determine the effect of complex formation between aggrecan and HA molecules on the osmotic pressure at different ratios of aggrecan to HA;

(ii) identify important differences between the static and dynamic properties of aggrecan and chondroitin sulfate solutions;

(iii) quantify the effect of calcium ions on the supramolecular organization and dynamic behavior of aggrecan assemblies.

Experimental results obtained by complementary techniques (small angle neutron and X-ray scattering, neutron spin echo, static and dynamic light scattering, osmotic pressure measurements) probing the structure and dynamics over a broad range of length and time scales will be discussed.

ACKNOWLEDGEMENT

This research was supported by the Intramural Research Program of the NICHD, NIH.