262nd American Chemical Society National Meeting
Biotechnology Division
August 22-26, 2021, Atlanta, GA
Abstracts

Cartilage Extracellular Matrix: Macromolecular Architecture and Biological Function

Ferenc Horkay[1], Emilios Dimitriadis[2], Iren Horkayne-Szakaly[1], Peter J. Basser[1]

[1]Section on Quantitative Imaging and Tissue Sciences, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, 13 South Drive, Bethesda, MD 20892, USA

[2]Laboratory of Bioengineering and Physical Science, National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, 13 South Drive, Bethesda, MD 20892, USA

The extracellular matrix of cartilage is a viscoelastic material composed of fluid components (water containing dissolved electrolytes) embedded in a collagen gel matrix, which contains chondrocytes (cartilage cells), proteoglycans (PGs), noncollagenous proteins and glycoproteins. Collagen forms a resilient mesh-like network *i*n which highly charged PGs and their assemblies are enmeshed. In healthy cartilage the collagen (primarily type II) content is about 15 % to 20 % and the proteoglycan content is about 4 % to 7 % of the relative wet mass.

The most abundant PG in cartilage is the bottlebrush shaped aggrecan molecule. It consists of an extended protein core to which many glucosaminoglycan (GAG) chains (mainly chondroitin sulfate and keratin sulfate) are attached. These GAG chains act as bristles oriented randomly around the protein chain. Aggrecan molecules form complexes by binding to long hyaluronic acid (HA) chains, creating a secondary bottlebrush structure. In vivo, aggrecan-HA complexes are stabilized by a link protein. In normal cartilage, these complexes provide load-bearing resistance in joints, transmitting large external loads with minimum friction and wear. With increasing age, however, both the concentration and size of the PGs decrease. Failure of cartilage function leads to osteoarthritis, which ranks among one of the most costly health care problems facing the developed world.

Our goal is to determine the properties of proteoglycan assemblies at their different hierarchical levels. Complementary techniques, including static and dynamic light scattering (SLS and DLS), small angle neutron scattering (SANS) and osmotic swelling pressure measurements are used to probe the structure of the solutions of individual components (aggrecan, HA, collagen) at different length and time scales. In cartilage, the next level of hierarchy is the aggrecan-HA complex. We investigate how complexation affects the behavior of aggrecan assemblies. These high molecular weight aggregates provide the hydration of cartilage and its load-bearing function. The structure of aggrecan-HA complexes is determined by SANS and Atomic Force Microscopy. In cartilage tissue engineering better understanding of the structure-function relationship is essential for developing procedures to regenerate damaged tissues.