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Abstracts

Extracellular matrix: macromolecular organization and function

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The extracellular matrix (ECM) provides physical support to cells and plays role in various cellular processes including cell proliferation, and differentiation The ECM consists of several components that form a complex network in which the macromolecules are organized in a tissue-specific manner. For example, the ECM of the brain is mainly composed of glycosaminoglycans (e.g., hyaluronan), proteoglycans (e.g., neurocan, versican and aggrecan), and small quantity of fibrous proteins (e.g. collagen). Components of the ECM form a stable composite that accounts for approximately 20% of the total volume in the adult brain. In the brain ECM regulates certain neural processes and plays a role in physiological and pathological conditions, including neurite outgrowth, synaptic stabilization, etc. Structurally, the ECM acts as a physical barrier to reduce the diffusion of soluble and membrane-associated molecules and cell migration and contributes to the mechanical properties of tissues. The latter is particularly important in load bearing tissues such as cartilage.

The organization of the ECM has a significant impact on disease (e.g., cancer) development and progression. We propose a multiscale experimental approach to determine the structure and interactions among the major macromolecular components of the ECM. We combine small-angle neutron scattering and osmotic pressure measurements to determine the static properties of well-defined model systems (hyaluronan and aggrecan complexes) at microscopic and macroscopic length scales. The dynamic behavior of the systems is characterized by dynamic light scattering and rheological measurements. Our approach has the potential to advance therapies (e.g.; targeted immunotherapy), providing new strategies for drug delivery, etc.