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Role of hyaluronan in maintaining brain extracellular space structure

Hyaluronan (HA) is a ubiquitous matrix molecule found in the extracellular space (ECS) of all tissues of the body, including brain. HA has been established as a 'structural support' molecule in tissues like skin, vitreous humor and synovial fluid. However, our understanding of the structural role of HA in the brain is poor. HA's unique physical property of occupying large volume and its scaffold like arrangement in the narrow gaps of brain ECS suggest that it could be important in maintaining the brain ECS structure. Previous literature shows that when HA content was changed in the brain ECS, it caused a change in the volume occupied by the ECS in brain tissue. The objective of this project is to explore this relationship between the HA content and ECS structure in detail, and to answer the central question: Does HA have a role in maintaining the brain extracellular space structure? Based on our understanding of the molecule, we hypothesize that HA does indeed have an important role in maintaining ECS structure. We will test this hypothesis by studying how acute changes in the HA content affect the structural parameters of ECS, using diffusion studies as a tool. Since HA content is known to change in various physiological and pathological conditions, this project will help us understand how those changes affect not just the structure of ECS, but also diffusive transport of substances through the spaces. Moreover, this project will explore the mechanisms that HA can potentially use to maintain ECS structure. Thus, this project aims at understanding how HA affects the biophysics of brain ECS.