HYALURONIC ACID IN THE EXTRACELLULAR MATRIX OF THE BRAIN

Summary

Hyaluronic acid (HA) is a non-branched polysaccharide of various size, with repeats of a disaccharide unit consisting of D-glucuronic acid and N-acetyl-D glucosamine. It is synthesized by three synthases, HAS1-3, at the plasma membrane, and degraded partially at the same localization by hyaluronidase Hyal-2, endocytosed and directed to lysosomes, where final degradation by Hyal-1 and exoglycosidases takes place. Despite its chemical simplicity, hyaluronic acid exhibits an array of functions in the brain, depending on molecular size of the molecule. High molecular weight HA is abundantly expressed in the embryonic brain extracellular matrix (ECM) and also in adults, where, on the surface of selected neurons, together with other constituents, it forms perineuronal nets, the structures that impede synaptic plasticity. In developing brain it promotes neuronal migration and in adult brain it is abundant in neurogenic niches, where it plays the same role. Both high and low molecular weight HA interacts with various proteins and proteoglycans to organize the ECM, binds with cell surface receptors and activates signaling pathways which regulate axonal and dendritic growth, as well as regulates astrocyte migration, inflammation and healing in the injured brain. It is up regulated in gliomas and involved in tumor progression and metastasis. Although extensively studied in other tissues, the function and the molecular basis of action of hyaluronic acid in the brain is far from understood. A deeper knowledge of the mechanisms underlying the roles of HA in various physiological processes can provide new insights and tools for intervening therapies in case of brain injury or cancer.