Glycosylated chondroitin sulfate proteoglycans (CSPGs), a major component of the extracellular matrix (ECM) in the brain, contribute to the physical structure of the local brain microenvironment but also induce or inhibit glioma invasion by regulating the dynamics of the CSPG receptor LAR as well as the spatiotemporal activation status of resident astrocytes and tumor-associated microglia. Using a multi-scale mathematical model, Kim et al. investigated a CSPG-induced switch between invasive and non-invasive tumors through the coordination of ECM-cell adhesion and dynamic changes in stromal cells. They showed that the CSPG-rich microenvironment is associated with non-invasive tumor lesions through LAR-CSGAG binding while the absence of glycosylated CSPGs induce the critical glioma invasion.

They illustrated how high molecular weight CSPGs can regulate the exodus of local reactive astrocytes from the main tumor lesion, leading to encapsulation of non-invasive tumor and inhibition of tumor invasion. These different CSPG conditions also change the spatial profiles of ramified and activated microglia. The complex distribution of CSPGs in the tumor microenvironment can determine the nonlinear invasion behaviors of glioma cells, which suggests the need for careful therapeutic strategies <sup>1)</sup>.

## 1)

Kim Y, Kang H, Powathil G, Kim H, Trucu D, Lee W, Lawler S, Chaplain M. Role of extracellular matrix and microenvironment in regulation of tumor growth and LAR-mediated invasion in glioblastoma. PLoS One. 2018 Oct 4;13(10):e0204865. doi: 10.1371/journal.pone.0204865. eCollection 2018. PubMed PMID: 30286133.

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