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Emerging role of plexins signaling in glioma progression and therapy

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Abstract

Gliomas are highly invasive brain tumors with increased resistance to chemotherapy and high recurrence rate. Neoplastic cells commonly infiltrate into the surrounding tissue even at low grade tumors. Cell migration is often ceased at white and grey matter junctions indicating the involvement of tropic and axon guidance molecules in glioma growth and invasion. Emerging evidence implicates plexin-semaphorin signaling in the pathobiology of gliomas. Plexins are transmembrane receptors divided into four subfamilies (Plexins-A to -D) with differential specificity and functionality. They are involved in cell adhesion and motility, vascular growth and organogenesis, as well as tumor progression.

In gliomas, plexins-A serve as coreceptors of neuropilins and transduce signals of class 3 semaphorins to PI3K/Akt pathway promoting cell growth, migration and invasion. Plexins-B1 and -B2 bind class 4 semaphorins to regulate RhoGTPases and induce glioma invasiveness and angiogenesis while, plexins-B3 interact with class 5 semaphorins to inhibit cell invasion and promote astrocytic cell differentiation via glial fibrillary acidic protein (GFAP) regulation.

This review focuses on the biological roles of plexin-semaphorin signaling in glioma pathogenesis and discusses their potential as prognostic biomarkers and therapeutic targets.