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Opinion

Metabotropic glutamate receptors: new targets for the control of tumor growth?

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Cancer stem cells are currently a target for the treatment of malignant tumors. Transformed neural stem–progenitor cells of the brain subventricular zone and the external granular layer of the cerebellum are the putative cells of origin of malignant gliomas and medulloblastomas, which are the most frequent malignant brain tumors in adults and children, respectively. The proliferation of neural stem–progenitor cells is regulated by metabotropic glutamate (mGlu) receptors, which are G-protein-coupled receptors that are activated by glutamate, the major excitatory neurotransmitter of the CNS. At least two receptor subtypes – mGlu₃ and mGlu₄ receptors – control the proliferation of brain tumor cells, whereas mGlu₁ receptors have been implicated in the development of melanomas. We believe that individual mGlu receptor subtypes represent new potential targets for the treatment of several malignant tumors, including brain tumors.

Glossary

Allosteric modulators

drugs that bind to a site that is different from the glutamate-binding site, which is usually located in the heptahelical domain of mGlu receptors.

Astrocytes

glial cells in the CNS that express glial fibrillary acidic protein.

Blastocyst

structure formed in early mammalian embryogenesis before implantation. The inner cell mass of a blastocyst is formed by pluripotent cells that give origin to the embryo.

Excitotoxicity

a mechanism of neuronal death that is triggered by an excessive activation of glutamate receptors.

Gliomas

intracranial tumors of presumed astrocytic, oligodendroglial or ependymal lineage. Glioblastoma multiforme (grade IV astrocytoma) is the most aggressive glial tumor and the most frequent primary brain tumor in the elderly.

Orthosteric agonists

agonists that bind to the glutamate-binding site in the N-terminal region of mGlu receptors.

Subventricular zone (SVZ)

- New perspectives for the development of selective metabotropic agonists
European Journal of Pharmacology
- Changes in metabotropic glutamate receptor 1–8 gene expression
Neuropharmacology

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a region that lines the lateral ventricles of the forebrain. The SVZ comprises three main cell types: Type-B astrocytes, which probably correspond to neural stem cells, give rise to transit-amplifying type-C precursors – which, in turn, generate type-A neuroblasts.

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