Association of Notch-1, osteopontin and stem-like cells in ENUglioma malignant process

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Notch-1 and osteopontin (OPN) mediate angiogenesis and glioma stem-like cell (GSLC) maintenance. However, the relationship between these molecules and GSLCs during the development of glioma is unknown. We investigate the expression of Notch-1, OPN and vascular endothelial growth factor (VEGF) associated to the stemness markers nestin and CD133 in three stages of murine gliomas induced by N-ethyl-N-nitrosourea (ENU). Notch-1 and OPN overexpress in the intermediate stage (II), which corresponds to the "angiogenesis switch". Nestin+ cells appear in all stages of ENU-glioma but CD133 only from stage II on. In stage III, neoplastic cells expressing nestin, CD133 and nestin/CD133 reside in spheroid-like aggregates (SAs) and in the neoangiogenic border. These aggregates show Notch-1 and VEGF+ surrounding cells and a significant size and density increase with respect to stage I (3.3 ± 1.5 to 22.4 ± 6.3 ?m2, no = 0.3 ± 0.1 to 4.2 ± 0.9, from stage I to stage III, respectively). OPN expression increases in correlation to the glioma malignancy from 4.5 ± 1.8% (I) to 12.3 ± 1.2% of OPN+ cells (III). It predominates in astrocyte-like cells of the neoangiogenic border, displaying co-location with VEGF and CD133. The OPN immunopositivity distribution correlates with the CD133 distribution. In conclusion, OPN co-expressing with CD133 contributes to the identification of GSLCs in the neoangiogenic border, while Notch-1 is present around SAs in advanced stages. The ENU-glioma, mainly in stage II, is a useful tool for assessing new antitumour therapies against these molecules. © Bulnes et al.

Angiogenesis

Glioma stem-like cells

N-ethyl-N-nitrosourea

Notch-1

Osteopontin

CD133 antigen

ethylnitrosourea

nestin

Notch1 receptor

osteopontin

vasculotropin

adult

animal cell

animal experiment

animal model

animal tissue

Article

astrocyte

cancer staging

cell aggregation

cell density

cell size

disease course

glioma cell

glioma stem cell

mouse

nonhuman

protein expression

protein localization

spheroid cell

tumor vascularization