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DECIPHERING THE ROLE OF A2B5 IN GLIOBLASTOMAS

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Patterns of ganglioside expression are characteristic of a particular cell type, tissue or tumour. This reflects their functional roles and their involvement in biological functions such as adhesion, cell-cell interaction and proliferation. In glioblastoma (GBM), not much has been explored. Our interest ingliomagenesis led us to focus on A2B5, a monoclonal antibody specific of polysialogangliosides and to a lesser extend of polysialoproteins. Our previous results suggested that A2B5+ cells isolated from human GBM had properties of GBM cancer stem like cells (CSLC) (1, 2, 3). To go further, it is now essential to establish the relationship between gliomagenesis and A2B5 immunoreactivity. A2B5 IgM specifically recognizes trisialogangliosides from the c-series (mainly GT3 and its acetylated form, but also GQ1c and GP1c) at the membrane. As little is known about glycosyltransferases involved in ganglioside biosynthesis, in a first step we focused on the ST8 alpha-N-acetyl-neuraminide α-2,8-sialyltransferase 3 enzyme (ST8sia3), reported to add a third sialic acid on GD3 by an α2-8 liaison to produce GT3. We developed GBM cell lines with various levels of A2B5 reactivity by overexpressing/suppressing ST8sia3 enzyme and tested for stem cell properties. To achieve this goal, we introduced the ST8sia3 coding sequence into U87-MG and U251-MG GBM cell lines which are not considered as GBM CSLC but are highly proliferative and aggressive *in vivo*. Thus the overexpression of ST8sia3 resulted in a huge increase of A2B5 immunoreactivity and ST8sia3 and A2B5 were detected in the same cells by flow cytometry and immunofluorescence. The increase of A2B5 immunoreactivity induced deep changes in cell behavior. As compared to control cells, the overexpression of ST8sia3 (thus increase of A2B5) triggered cellular migration and proliferation but no difference in their clonogenic potential was measured. Moreover, the survival of mice orthotopically injected with ST8sia3+-overexpressing U87-MG cells was slightly reduced when compared to mice injected with U87-MG control cell line. At this stage, these results showed that A2B5 expression is positively correlated with a more aggressive cellular behavior.

Note:

BIOGRAPHY

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