Finding new molecular markers for aggressive brain tumors

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Every year 7 out of 100,000 individuals are diagnosed with *Glioblastoma multiforme* (GBM) which is an aggressive brain tumor where the average survival of patients is usually less than a year despite treatment. It is important to increase our understanding of this disease so we can characterize it better to find new targets for improved treatments and perhaps diagnose it earlier.

The SOX proteins are gene expression-regulating factors that have been found to be expressed in the developing central nervous system (CNS). Some of them have been found to contribute to the formation of glial cells, the supporting cells in the CNS. One of the SOX proteins, SOX5, exists in a long (L-SOX5) and a short (S-SOX5) version. It has been shown earlier* that S-SOX5 can suppress brain tumor development in mice, and when engineered and overexpressed in GBM cells from patients, it can inhibit their growth.

In my study, I focused on establishing whether the activity of six different genes differed within human GBM cells and if these levels could vary due to SOX5. In other words, the *SOX5* gene´s potential as a molecular marker of human GBM cells was investigated. The genes tested included *S-SOX5/L-SOX5, SOX6* and *SOX9* along with genes called *platelet derived growth factor-A (PDGFRA), platelet derived growht factor-B (PDGFRB)* and *epidermal growth factor receptor (EGFR).* The latter three genes encode three cell surface receptors and PDGFRA and EGFR are commonly overactive in GBMs.

I performed quantitative real-time polymerase chain reaction (qPCR) measurements where gene expression in GBM cells from 27 different patients was measured with the so called $2^{-\Delta\Delta C_T}$ method. The results demonstrated how differently GBM tumors behave from patient to patient since the expression for each gene was often quite different between cells from different patients. Expression levels of S-SOX5 and L-SOX5 had the strongest positive correlation. In accordance with our earlier preliminary data, the expression of *S-SOX5*, as well as of *L-SOX5* had a positive correlationg with PDGFRA. This goes hand in hand with our earlier finding that in the "proneural" subclass of GBMs, where PDGFRA is upregulated, SOX5 expression was also increased.

In the future, it would be interesting to correlate these results with patient survival and relapse and to analyse more markers so it is possible to further divide the cell cultures into subclasses. The plan is also to construct an inducible system where lentivirus is used to infect and make human GBM cells overexpress *S-SOX5* in order to analyze how that affects the growth of these tumor-inducing cells.

* Tchougounova E, Jiang Y, Bråsäter D, Lindberg N, Kastemar M, AsplundA , Westermark B and Uhrbom L. 2009. Sox5 can suppress platelet-derived growth factor B-induced glioma development in Ink4a-deficient mice through induction of acute cellular senescence. Oncogene 28: 1537–1548.

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