CLINICAL IMPACT OF THE KIT ISOFORMS IN PATIENTS WITH GLIOBLASTOMA

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Glioblastoma is the most common adult brain tumor and one of the deadliest human malignancies, being urgent to develop novel therapeutic strategies. The success of specific small molecule inhibitors for KIT oncogene made this protein a key molecular therapeutic target in cancer. Importantly, due to mRNA alternative splicing, KIT is expressed by two different functional isoforms (GNNK+/GNNK-), that were shown to display different tumorigenic transforming activities depending on cell type and tumor context. KIT protein is reported to be expressed in normal and tumor brain tissue; hitherto, there are no reports assessing KIT GNNK isoforms expression and its relation with clinicopathological features. The aim is to correlate the isoforms predominance with clinicopathological characteristics, thus leading to a predictive biomarker to anti-KIT therapy response. In the present work, we firstly determined by RT-PCR the expression levels of KIT isoforms in patient’s derived samples (tumor and normal) and glioblastoma cell lines. Sixty five patients samples were correlated with their respective clinicopathological information. In addition to correlate the expression levels of isoforms, the KIT protein expression by immunohistochemistry will be assessed. Curiously, the normal brain tissues, the tumor paraffin-derived samples and frozen tissue presented a predominance of GNNK+ isoform expression. By contrast, GNNK- isoform was highly expressed in glioblastoma cell lines, suggesting that this isoform could play a role in glioblastoma tumorigenesis. No statistically significant difference was found between the groups of isoforms predominance. However, compared to the survival curves patients, there was difference in survival between those with a predominance of isoforms, GNNK+ shows better survival compared to GNNK-. In conclusion we found that KIT mRNA isoforms are differentially expressed in normal and tumor samples versus cell lines. We believe that the project results will determine whether glioblastoma patients exhibiting KIT may benefit from therapy with anti-KIT inhibitors treatment.

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