**MAGOH Proteins in Cancer**

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**Abstract**

*Introduction:* MAGOH, a homologue of the *mago nashi* protein of Drosophila, is a part of the exon junction complex (EJC) in humans and has a major role in splicing and mRNA transport. A second copy of MAGOH, namely MAGOHB, is also present in humans, which differs from MAGOH only by two amino acids. MAGOHB has the same functions as MAGOH with respect to the EJC and can compensate for the absence of MAGOH. Apart from splicing, MAGOH has also been found to play a part in neuronal development in zebrafish and downregulation of MAGOH and/ or MAGOHB could attenuate the progression of gastric cancer. Glioblastoma multiforme (GBM) is a highly heterogeneous malignant brain tumor which exhibits a high recurrence rate and chemoresistance, even after trimodal therapy (surgery, radiotherapy, and chemotherapy). In this study, we investigate the effect of MAGOH/ MAGOHB silencing in GBM progression and signalling. We also aim to study the effect of temozolomide, a DNA alkylating agent and the most widely used drug for GBM treatment, on the disease progression in MAGOH/ MAGOHB silenced cells.

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*Materials and Methods:* MAGOH or MAGOHB were silenced using shRNA in the GBM cell line U87MG, to generate stable cell lines and experiments such as colony formation assay, scratch wound assay, western blot analysis and neuroglial differentiation were performed to check the effect of MAGOH proteins on transduced cells. The concentration of temozolomide (TMZ) to be used was determined by a concentration curve and further experiments were performed accordingly.

*Results and inference:* Silencing of MAGOHB increased the colony forming ability. Colonies were larger in size compared to those obtained with shMAGOH and control cells. However, shMAGOH had higher migration ability than control or shMAGOHB cells. Gene expression analysis showed an upregulation of pERK1/2 level when MAGOH or MAGOHB were silenced compared to control cells. When cultured as spheroids, the upregulation of pERK1/2 was more pronounced in shMAGOHB cells. So, silencing of MAGOHB increases the proliferation of GBM cells, whereas MAGOH silencing increased the migration ability. These effects might be mediated by the MAPK/ ERK pathway. Treatment with TMZ led to formation of smaller and fewer colonies in all conditions and western blot showed increase in pERK1/2 level in control cells compared to shMAGOH/ shMAGOHB conditions.

*Conclusion:* It is established that the MAPK/ERK pathway has an essential role in GBM progression. From our results, we find that MAGOH might play a role in GBM progression as a tumor suppressor, where loss of either MAGOH/ MAGOHB led to increased ERK signaling.

**Keywords:** MAGOH, MAGOHB, glioblastoma, U87MG, MAPK/ERK