

The exon-Junction Complex Proteins MAGOH and MAGOHB are pro-tumorigenic factors in glioblastoma

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Abstract

Glioblastoma multiforme (GBM) is the most aggressive tumor of the central nervous system. In spite of advances in science and medicine, the average life expectancy remains about 18 months after diagnosis and the current treatment are becoming obsolete. Therefore, the search for more effective GBM therapeutic targets is urgently needed. To look for new therapeutics targets, here we investigated, through computation tools and next-generation sequencing data, the role of exon junction complex (EJC) components MAGOH/B, key genes of the post-transcriptional gene regulation mechanism, in low-grade gliomas and GBM. Our results show that a higher expression of MAGOH/B is: i) positively correlated to more aggressive gliomas; ii) significantly related to lower overall survival of GBM patients and iii) with GBM showing worst responses to treatments. We also find that the knockdown of MAGOH/B decreases the GBM cell lines viability and proliferation, but increase their apoptosis. Additionally, we find that MAGOH/B knockdown changes the expression of genes associated with splicing, RNA transport, translation, and cell cycle affected, suggesting an auto-regulation. Interestingly, genes that were alternatively spliced by MAGOH/B KD were linked to RNA stability/processing/metabolism, DNA repair, and stress response, Gene Ontology pathways commonly deregulated in cancer. Furthermore, we have shown MAGOH/B KD reaches RS exons and leads to stop-codon gain and frame change in genes commonly deregulated in GBM. In summary, we believe that MAGOH/B are key genes involved in GBM, which would be investigated as new markers for the disease or novel targets for therapy in the near future.

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