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ARE-binding factors TTP and HUR reveal antagonistic relationships within glioma-related gene networks

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Statement of the Problem: Glioma is a heterogeneous group of primary brain tumors with poor prognoses. Effective treatment strategies for glioma have yet to be developed. This requires better understanding of molecular mechanisms involved into pathology, determining promising drug targets. Recently, it has become clear that mRNA stability regulation by Adenine-Uridine Rich Element (ARE) binding factors plays crucial role in cancer biology. This study aimed to unravel participation of ARE-binding factors TTP, HUR, BRF1, BRF2, KSRP, AUF1 in gene networks of gliomas.

Methodology & Theoretical Orientation: Data on gene expression in 276 glioma samples and 8 samples of healthy brain tissue were downloaded from Gene Omnibus (ID: GSE16011). Differential expression of the ARE-binding factors; correlations in expression patterns of the ARE-factors and other genes; biological functions of genes with associated expression patterns were analyzed.

Conclusion & Significance: Among ARE-binding factors TTP, BRF1, BRF2, KSRP but not HUR were upregulated at an mRNA level in brain tumors. Genes, correlating with ARE-factors by their expression patterns, split into two large subgroups: those that positively correlated with TTP and negatively correlated with HUR and vice versa. Interestingly, TTP-positive/HUR-negative genes were enriched in innate immune response mediators and TTP-negative/HUR-positive genes were enriched in RNA binding factors. Moreover, TTP associated genes were previously recognized as glioma survival prognosis markers. The obtained data demonstrate that ARE-binding factors are involved into glioma biology on a transcriptome level, reveal antagonistic relations between TTP and HUR and indicate that an ARE-mediated mRNA stability control pathway represents a promising target for tumor treatment strategies development. The research was supported by RFBR grant №16-34-01085 mol_a.

Fig. 1. Relationships between ARE-binding factors and genes, forming networks in glioma transcriptome. Red arrows determine positive and green arrows depict negative correlation on a transcription level between ARE-binding factors and genes forming group with distinguished biological functions.

Biography

Dmitryi V Chistyakov has his expertise in cell signaling pathways controlling inflammatory responses within the central nervous system. His scientific interests concern mechanisms that control innate immune response within nervous tissue on cellular level. Investigations within this field have brought him to the question about mRNA stability control during inflammatory response on the level of cells. These two processes – activation of innate immune response and post-transcriptional gene expression regulation turned out to be crucial for glioma development as well. Understanding their interaction during tumor development is one of the attractive directions of his research development.

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