RNA-binding protein

RNA-binding proteins (often abbreviated as RBPs) are proteins that bind to the double or single-stranded RNA in cells and participate in forming ribonucleoprotein complexes. RBPs contain various structural motifs, such as RNA recognition motif (RRM), dsRNA binding domain, zinc finger protein and others.

RNA-binding proteins (RBPs) and circular RNAs (circRNAs) play important roles in glioblastoma. Aerobic glycolysis is a metabolic characteristic of Glioblastoma. However, the roles of RBPs and circRNAs in aerobic glycolysis in Glioblastoma remain unclear. The aim of this study is to explore the mechanisms by which RBPs and circRNAs regulate aerobic glycolysis in Glioblastoma cells.

RNA sequencing and circRNA microarray analysis were performed to identify RBPs and circRNAs for further study. Mass spectrometry validated the encoded protein and its interacting proteins. Quantitative reverse transcription PCR and western blot assays were used to determine the mRNA and protein expression, respectively. Furthermore, immunofluorescence and fluorescence in situ hybridization assays were used to determine the protein and RNA localization, respectively. Glucose and lactate measurement assays, Seahorse XF glycolysis stress assays and cell viability assays were conducted to investigate the effects on glycolysis and proliferation in Glioblastoma cells.

Results: We selected zinc finger CCHC-type and RNA-binding motif 1 (ZCRB1) and circRNA HEAT repeat containing 5B (circHEATR5B) as candidates for this study. These genes were expressed at low levels in Glioblastoma tissues and cells. Both ZCRB1 and circHEATR5B overexpression suppressed aerobic glycolysis and proliferation in Glioblastoma cells. ZCRB1 overexpression promoted the Alu element-mediated formation of circHEATR5B. In addition, circHEATR5B encoded a novel protein HEATR5B-881aa which interacted directly with Jumonji C-domain-containing 5 (JMJD5) and reduced its stability by phosphorylating S361. JMJD5 knockdown increased pyruvate kinase M2 (PKM2) enzymatic activity and suppressed glycolysis and proliferation in Glioblastoma cells. Finally, ZCRB1, circHEATR5B and HEATR5B-881aa overexpression inhibited Glioblastoma xenograft growth and prolonged the survival time of nude mice.

This study reveals a novel mechanism of regulating aerobic glycolysis and glioblastoma proliferation in Glioblastoma cells through the ZCRB1/circHEATR5B/HEATR5B-881aa/JMJD5/PKM2 pathway, which can provide novel strategies and potential targets for Glioblastoma treatment [1)]

Recent studies suggested that RNA binding proteins (RBPs) were related to the tumorigenesis and progression of glioma. This study was conducted to identify prognostic RBPs of glioblastoma (Glioblastoma) and construct an RBP signature to predict the prognosis of Glioblastoma. Univariate Cox regression analysis was carried out to identify the RBPs associated with overall survival of Glioblastoma in The Cancer Genome Atlas (TCGA), GSE16011, and Repository for Molecular Brain Neoplasia Data (Rembrandt) datasets, respectively. Overlapping RBPs from the TCGA, GSE16011, and Rembrandt datasets were selected. The biological role of prognostic RBPs was assessed by Gene Ontology, Kyoto Encyclopedia of Genes and Genomes, and protein-protein interaction analyses. The least absolute shrinkage and selection operator regression analysis and multivariate Cox regression analysis were used to constructing an RBP-related risk signature. The prognostic value of the RBP signature was measured by the Kaplan-Meier method and time-dependent receiver operating

characteristic curve. A nomogram based on independent prognostic factors was established to predict survival for Glioblastoma. The CGGA cohort was used as the validation cohort for external validation. This study identified 27 RBPs associated with the prognosis of Glioblastoma and constructed a 6-RPBs signature. Kaplan-Meier curves suggested that a high-risk score was associated with a poor prognosis. The area under the curve of 1-, 3-, and 5-year overall survival was 0.618, 0.728, and 0.833 for TCGA cohort, 0.655, 0.909, and 0.911 for the GSE16011 cohort, and 0.665, 0.792, and 0.781 for the Rembrandt cohort, respectively. A nomogram with 4 parameters (age, chemotherapy, O6-methylguanine-DNA methyltransferase promoter status, and risk score) was constructed. The calibration curve showed that the nomogram prediction was in good agreement with the actual observation. The 6-RBPs signature could effectively predict the prognosis of Glioblastoma, and the findings supplemented the prognostic index of Glioblastoma to a certain extent [2].

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Song J, Zheng J, Liu X, Dong W, Yang C, Wang D, Ruan X, Zhao Y, Liu L, Wang P, Zhang M, Liu Y. A novel protein encoded by ZCRB1-induced circHEATR5B suppresses aerobic glycolysis of Glioblastoma through phosphorylation of JMJD5. J Exp Clin Cancer Res. 2022 May 10;41(1):171. doi: 10.1186/s13046-022-02374-6. PMID: 35538499.
2)
Huang QR, Li JW, Pan XB. A novel risk signature with 6 RNA binding proteins for prognosis prediction in patients with glioblastoma. Medicine (Baltimore). 2021 Dec 3;100(48):e28065. doi: 10.1097/MD.0000000000028065. PMID: 35049227.