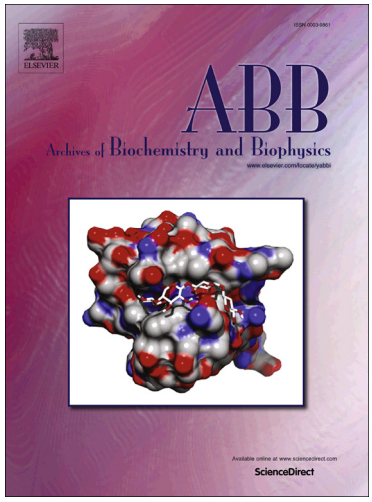

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Targeting strategies on miRNA-21and PDCD4 for glioblastoma

Gang Wang[1,2]*, Jun Jie Wang [1], Hong Ming Tang[2], Shing Shun Tony TO[3]

[1] Department of Pharmaceutics, Shanghai Eighth People's Hospital, Shanghai 200235, China.

[2] Shanghai East Hospital, Tongji University School of Medicine. Shanghai 200000, China.

[3] Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Hong Kong S.A.R., China.

Abstract

MicroRNAs (miRNAs) are often deregulated in glioblastoma multiforme (GBM). Downregulation of microRNA-21 (miR-21), especially in GBM, is responsible for increased apoptosis, decreased cell proliferation and invasion, increased G0/G1 cell cycle arrest, and reduced chemotherapeutic resistance to doxorubicin. Furthermore, it is a critical regulator of multiple downstream genes and signaling pathways involved in gliomagenesis. Programmed cell death 4 (PDCD4) is critical in mediating apoptosis in GBM, and is downregulated by miR-21, which may mediate the resistance of glioblastoma cells against chemotherapy or radiation via its target genes PDCD4. Evidence is mounting that how alterations of these miRNAs transcription factors provide initiation, maintenance, or progression of tumors. This review will focus on the roles of miRNAs family members (particularly miR-21 and its target gene PDCD4) in tumors like glioblastoma and new targeting strategies, as examples some new targeting therapeutic methods and molecular mechanisms of signal pathways in glioblstoma therapeutics, to give the reader the current trends of approach to target regulation of these miRNA and genes for future glioma therapies.

Abbreviations

GBM, glioblastoma multiforme; miRNAs, microRNAs; PDCD4, programmed cell death 4; EMT, epithelial-mesenchymal transition; JNK, Jun N-terminal protein kinase; PTEN, phosphatase and tensin homolog; PI3K/AKT, phosphatidylinositol-3 kinase/Akt; MAPK/ERK, mitogen-activated protein kinase/extracellular signal-regulated kinase; STAT3, signal transducer and activator of transcription 3; MMPs, matrix metalloproteinases; hnRNP, heterogeneous nuclear ribonucleoprotein C1/C2; mTOR, mammalian target of rapamycin; EGFR, epidermal growth factor receptor; TRCP, transducin repeats-containing proteins; TGF-β, transforming growth factor-β; TRAIL, tumor necrosis factor–related apoptosis-inducing ligand; MTAP, S-methyl-5'thioadenosine phosphorylase;hnRPK, heterogeneous nuclear ribonucleo protein K; FOS, v-fos FBJ murine osteosarcoma viral oncogene homolog; RECK, reverse-inducing cystine-rich protein with kazal motifs; PAMAM, poly-amidoamine dendrimer; PDGF, platelet-derived growth factor; TMZ, temozolomide; LRRFIP1, leucine-rich repeating flightless-interacting protein 1; GICs, glioblastoma initiating cells; SHH, suppressing the sonic hedgehog; TSCC, tongue squamous cell carcinoma cells; mAb, monoclonal antibody; VHL, von Hippel-Lindau; PPARα, peroxisome-proliferator-activated receptor α; VEGF, vascular endothelial growth factor; LNA, locked nucleic acid; UA, ursolic acid; RSV, resveratrol; MGMT , O^6-methylguanine-DNA methyl transferase.

Keywords

Glioblastoma; miRNA; oncogenes; apoptosis; resistance; signaling pathways

*Corresponding author: Gang WANG, MD, PhD, Department of Pharmaceutics, Shanghai Eighth People's Hospital, Shanghai 200235, China. Email: wangan139@163.com