ROBO1

Roundabout homolog 1 is a protein that in humans is encoded by the ROBO1 gene

Function

Bilateral symmetric nervous systems have special midline structures that establish a partition between the two mirror-image halves. Some axons project toward and across the midline in response to long-range chemoattractants emanating from the midline. The protein encoded by ROBO1 is structurally similar to a Drosophila integral membrane protein which is encoded by the Drosophila roundabout gene (a member of the immunoglobulin gene superfamily) and is both an axon guidance receptor and a cell adhesion receptor, known to be involved in the decision by axons to cross the central nervous system midline. Two transcript variants encoding different isoforms have been found for ROBO1.

MicroRNA-588 and its potential target Roundabout-directed receptor 1 (ROBO1) have been reported to promote tumor invasion and proliferation in diseases such as gastric, pancreatic, and hepatocellular carcinoma, while their function in GBM and response to hypoxic states remain elusive.

A microarray was leveraged to identify differentially expressed microRNAs in U251 glioma cells cultured under normoxic and hypoxic conditions. The expression of miR-588 was assessed using quantitative real-time PCR (qRT–PCR). Gain- and loss-of-function studies were used to evaluate the role of miR-588 under hypoxic and normoxic conditions. Cell invasion, migration, proliferation, and vasculogenic mimicry (VM) formation experiments were performed. The relationship between miR-588 and ROBO1 was confirmed using western blot and luciferase reporter assays. Intracranial xenograft tumor mouse models were used to study the function of miR-588 in vivo.

Results: The expression of miR-588 was significantly upregulated in hypoxic glioma cells relative to normoxic glioma cells. miR-588 inhibited the invasive, migratory, and VM-forming abilities of glioma cells in vitro and in vivo. Mechanistically, roundabout guidance receptor 1 (ROBO1) is a direct, functionally relevant target of miR-588 in glioma. ROBO1 knockdown suppressed the expression of matrix metallopeptidase 2 (MMP2) and matrix metallopeptidase 9 (MMP9), thereby inhibiting the invasive, migratory, and VM-forming abilities of glioma.

Conclusions: MiR-588 regulated the behaviors of hypoxic glioma cells by targeting ROBO1. miR-588 can be used as a prognostic marker for glioma and has potential implications in glioma gene therapy [1].

1)
Yu R, Zhao R, Sun X, Zhang Z, Wang S, Gao X, Sun Z, Xue H, Li G. MicroRNA-588 regulates the invasive, migratory and vasculogenic mimicry-forming abilities of hypoxic glioma cells by targeting ROBO1. Mol Biol Rep. 2022 Dec 2. doi: 10.1007/s11033-022-08063-z. Epub ahead of print. PMID: 36459288.