RP3-439F8.1

Nuclear Receptor Subfamily 5 Group A Member 2 (NR5A2, LRH-1) is an oncogene in a wide range of cancer types. Bioinformatics analysis on glioblastoma multiforme (Glioblastoma) tumors has revealed that the miR-139-5p-NR5A2 axis may be putatively regulated by the long non-coding RNA (lncRNA) RP3-439F8.1. This led Qi et al. to hypothesize the existence of a RP3-439F8.1-miR-139-5p-NR5A2 regulatory axis in Glioblastoma cells.

Gene expression analysis was performed in Glioblastoma tumor samples and normal controls from the hospital, the Cancer Genome Atlas Glioblastoma Multiforme (TCGA-Glioblastoma) cohort, and the Gene Expression Omnibus (GEO) database (GSE7696). Cell proliferation, apoptosis, Matrigel Transwell, colony formation, and cell cycle assays were performed in T98G and U251 cells in vitro. An orthotopic U251 xenograft murine model was employed to test the effects of RP3-439F8.1 knockdown in vivo.

NR5A2 was upregulated in the three independent Glioblastoma tumor cohorts. In vitro, NR5A2 overexpression enhanced Glioblastoma cell proliferation, colony formation, invasiveness, and G0-G1 cell cycle phase shift via co-activating β-catenin/TCF4 signaling, with no apparent effect upon apoptosis. In contrast, RP3-439F8.1 knockdown produced the opposite effects. RP3-439F8.1 knockdown reduced tumor progression in vivo, increasing overall survival in model mice. Further in vitro experiments revealed that RP3-439F8.1 acts as a competing endogenous RNA (ceRNA) to regulate NR5A2 by sponging the microRNA miR-139-5p. These findings were clinically validated by a positive correlation between RP3-439F8.1 and NR5A2 and a negative correlation between RP3-439F8.1 and miR-139-5p in Glioblastoma tumors.

The study supports a tumorigenic role for RP3-439F8.1 in Glioblastoma through the RP3-439F8.1/miR-139-5p/NR5A2 axis [1)]

1)
Qi J, Pan L, Yu Z, Ni W. The lncRNA RP3-439F8.1 promotes Glioblastoma cell proliferation and progression by sponging miR-139-5p to upregulate NR5A2. Pathol Res Pract. 2021 Jan 2;223:153319. doi: 10.1016/j.prp.2020.153319. Epub ahead of print. PMID: 33991848.