Nuclear Receptor Subfamily 5 Group A Member 2

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 T98 G 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.