

Mir-145-5p Functions As A Tumor Suppressor In Nonfunctioning Pituitary Adenoma By Regulating TPT1-Mcl-1/Bcl-XI/Bax Pathway

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Objectives

Nonfunctioning pituitary adenomas (NFPAs) are among the most common intracranial tumors, however, the molecular background remains largely unknown. In one of our previous microRNA array study, miR-145-5p was found to be down-regulated in the NFPAs specimens, compared to the normal pituitary tissues. Thus, we aimed to explore the role of miR-145-5p in the pathogenesis of NFPAs.

Methods

In vitro and in vivo experiments were applied to evaluate the suppression effect of miR-145-5p on NFPAs cell lines, PDFS and a primary NFPA cell line. The underlining potential mechanisms were also explored with western blot, RT-PCR, western blot and flow cytometry.

Results

Our results showed that miR-145-5p was markedly decreased in NFPAs samples and cell lines, and negatively associated with the invasiveness of NFPAs. Overexpression of miR-145-5p resulted in a significant reduction of cell proliferation, migration, invasion, colony formation, and in vivo tumor growth. Through bioinformatics analysis and dual luciferase assays, translationally controlled tumor protein (TPT1) was identified as a novel direct target of miR-145-5p. Concurrent experiments demonstrated that miR-145-5p induced cell apoptosis by targeting TPT1, sequentially downregulating Mcl-1/Bcl-xL and upregulating Bax.

Conclusion

Taken together, these data suggested a potential tumor suppressor role of miR-145-5p in NFPA, by regulating TPT1-Mcl-1/Bcl-xL /Bax signaling pathway.