miR 375

The functional role of microRNA-375 (miR-375) in the development of prostate cancer (PCa) remains controversial. Previously, Gan et al. found that plasma exosomal miR-375 is significantly elevated in castration-resistant PCa (CRPC) patients compared with castration-sensitive PCa patients. They aimed to determine how miR-375 modulates CRPC progression and thereafter to evaluate the therapeutic potential of human umbilical cord mesenchymal stem cell (hucMSC)-derived exosomes loaded with miR-375 antisense oligonucleotides (e-375i). We used miRNA in situ hybridization technique to evaluate miR-375 expression in PCa tissues, gain- and loss-of-function experiments to determine miR-375 function, and bioinformatic methods, dual-luciferase reporter assay, qPCR, IHC and western blotting to determine and validate the target as well as the effects of miR-375 at the molecular level. Then, e-375i complexes were assessed for their antagonizing effects against miR-375. We found that the expression of miR-375 was elevated in PCa tissues and cancer exosomes, correlating with the Gleason score. Forced expression of miR-375 enhanced the expression of EMT markers and AR but suppressed apoptosis markers, leading to enhanced proliferation, migration, invasion, and enzalutamide resistance and decreased apoptosis of PCa cells. These effects could be reversed by miR-375 silencing. Mechanistically, miR-375 directly interfered with the expression of phosphatase nonreceptor type 4 (PTPN4), which in turn stabilized phosphorylated STAT3. Application of e-375i could inhibit miR-375, upregulate PTPN4 and downregulate p-STAT3, eventually repressing the growth of PCa. Collectively, they identified a novel miR-375 target, PTPN4, that functions upstream of STAT3, and targeting miR-375 may be an alternative therapeutic for PCa, especially for CRPC with high AR levels [1)].

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Gan J, Liu S, Zhang Y, He L, Bai L, Liao R, Zhao J, Guo M, Jiang W, Li J, Li Q, Mu G, Wu Y, Wang X, Zhang X, Zhou D, Lv H, Wang Z, Zhang Y, Qian C, Feng M, Chen H, Meng Q, Huang X. MicroRNA-375 is a therapeutic target for castration-resistant prostate cancer through the PTPN4/STAT3 axis. Exp Mol Med. 2022 Aug 30. doi: 10.1038/s12276-022-00837-6. Epub ahead of print. PMID: 36042375.