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Quercetin-induced microRNA regulation of Pancreatic Ductal Adenocarcinoma

Promotionsfach: Molecular and Cellular Biology (Tumor Biology)

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The anti-oncomirs let-7c and miR-200b-3p that are induced by quercetin are down-regulated in Pancreatic Ductal Adenocarcinoma (PDA). Herein, they both have been shown to actively regulate Notch signaling.

Let-7c directly targets Numbl and activating it via the post-transcriptional increase of its mRNA levels and antagonizing Notch in the process in a feedback mechanism. The overall outcome is the inhibition of tumor growth, increase in apoptosis, inhibition of clonogenicity, migration and expression of progression markers. The injection of a let-7c/lipofectamine mixture or of quercetin into the vessels of the Chorioallantoic membrane (CAM) of fertilized chicken eggs xenotransplanted with PDA cells reduced the tumor size and induced an expression pattern in tumor tissue similar to those observed *in vitro*.

MiR-200b-3p on the other hand, directly targets Notch, inhibiting it and activating Numb in the course. It influences cell fate decisions in PDA by modulating by reversing the elevated Notch levels/ decreased Numb levels, thereby inhibiting self-renewal and decreasing proliferation and ultimately switching SCD to ACD. Hence, miR-200b is proposed as a cell fate determinant miRNA in PDA.

Restoration of let-7c and miR-200b functions in cancer cells may represent an important therapeutic strategy for future cancer treatment. In addition, this study introduces the injection of a miRNA/liposome mixture into the CAM of chick eggs harboring xenograft tumors as a new model for easy-to-perform and cost-effective *in vivo* miRNA studies in cancer research. The fact that quercetin regulates several miRNAs in the same pathway, two (let-7c and miR-200b-3p) of which have been studied here, raises the possibility of synergistic miRNA treatments. This is a key issue for the future.