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Antagonism between miR-21 and 338-3p in prostate cancer invasion through regulation of matrix metalloproteinase 9

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Introduction & Objectives: Matrix metallo-proteinases (MMPs) are important in physiopathology of many tumors. MicroRNAs are new agents that control many processes and studies report MMPs regulation through them. MiRNA-21 and 338-3p may play a role in MMP-9 control. We evaluated prostate cancer cell invasion *in vitro* through the regulation of MMP-9 with these miRNAs.

Methods: LNCap, DU 145 and PC3 cells were transfected with miR-338-3p, miR-21 or their antagonists. A co-transfection (miR-21+antagomiR-338-3p and antagomiR-21+miR-338-3p) in DU145 was done. The MMP-9 mRNA expression was evaluated by qRT-PCR relative quantification (2-ΔΔ ct). Matrigel assays were done 48 hours after transfection with 3x105 cells. Those which have invaded were counted under optical microscope.

Results: We previously reported that miR-21 regulates MMP-9 through RECK protein in DU145. In the present study, miR-21 in PC3 cells reduced RECK expression (p=0.00), increased MMP-9 mRNA (p=0.003), MMP9 protein (ELISA detected, p=0.60) and Matrigel invasion (p = 0.01). Also in PC3, miR-338-3p decreased MMP-9 mRNA (p=0.04), MMP-9 protein (p=0.06) and invasion in DU145 (p=0.002), LNCap (p=0.007) and PC3 (0.058). Transfecting two different miRNAs at the same time is a feasible method but only the transfection of anti-miR-21 together with miR-338-3p could significantly reduce the expression of MMP 9 mRNA. (p=0.05). With this combination, less cells invaded the Matrigel chamber (mean 304 x 114,87 cells, p=0.13).

Conclusions: MiR-21 and miR-338-3p regulate MMP-9 in opposite ways affecting cell invasion ability. The co-transfection of miR-21 antagonist+miR-338-3p reduces the MMP-9 expression.

Biography

Renato Ivanovic has completed Residency Program in Urology in São Paulo University. Currently he is a pursuing his Post graduation at the same institution.

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