THE GLOBAL MICRORNA EXPRESSION PROFILE OF IRRADIATED THYROID CELLS

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INTRODUCTION

Ionizing Radiation (IR) is a well-known risk factor for papillary thyroid cancer[1], and it has been reported to alter microRNA expression[2], which is important to thyroid carcinogenesis[3].

OBJECTIVE

Therefore, we have evaluated the impact of IR on microRNA expression profile of the normal thyroid cell line (FRTL-5 CL2) and as well as its effect on radiosensitivity of thyroid cancer cell lines, especially the human anaplastic thyroid carcinoma cell line (8505c).

HYPOTHESIS

IR could alter the expression of microRNAs important to repair double-strand DNA breaks (DSB) in thyroid cells.

METHODOLOGY

- Global small RNA sequencing of irradiated thyroid cells;
- Validation of miR-10b-5p and miR-199a-3p predicted targets by western blot, q-RT-PCR and luciferase target assays;
- The effects of miR-199a-3p and miR-10b-5p on DNA repair were determined by: 1) assessing the activation of ATM and the expression of ATR and γH2AX (indirect measure of DSB) in irradiated FRTL-5 CL2 cells; 2) evaluating homologous recombination DNA repair activity in Hela cells;
- The impact of miR-10b-5p on radiosensitivity was analyzed by cell counting and MTT assays in FRTL-5 CL2, v-RAS-Ki-transformed FRTL-5 CL2 (FRTL KiKi) and 8505c cell lines.

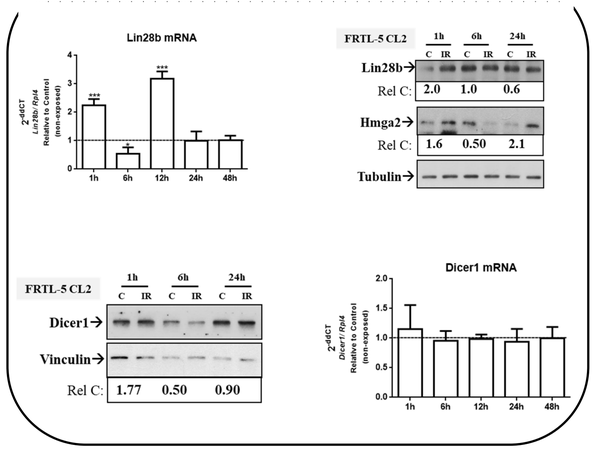
RESULTS

Differential miR expression in irradiated FRTL-5 CL2 cells

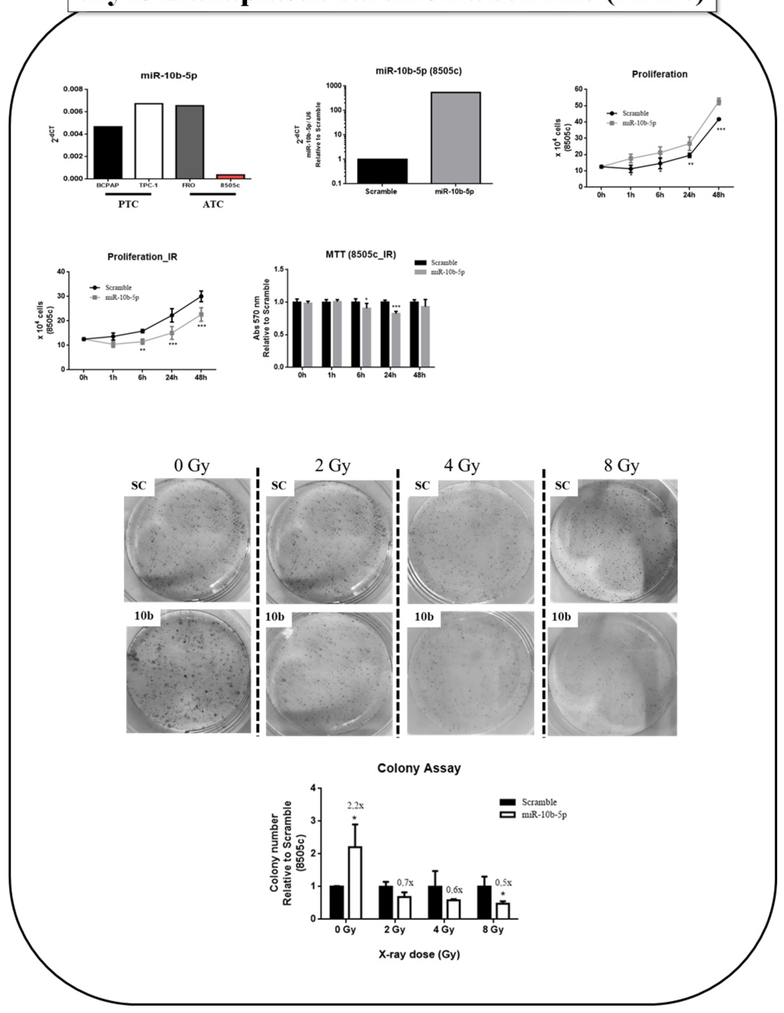
FRTL-5 CL2 wt IR *versus* CTRL (1H)		
miR	**Fold-change**	**prob**
rno-miR-541-5p	-8.54	0.72
rno-miR-199a-3p	-7.00	0.73
rno-miR-434-3p	-6.37	0.70
rno-miR-127-3p	-5.05	0.70
rno-miR-411-5p	-4.41	0.70
rno-miR-33-5p	-2.55	0.70
rno-miR-10b-5p	-2.41	0.70

FRTL-5 CL2 wt IR versus CTRL (6H)		
miR	**Fold-change**	**prob**
rno-miR-10a-5p	2.02	0.79
rno-miR-328a-3p	2.05	0.83
rno-miR-1249	2.21	0.74
rno-miR-30c-2-3p	2.23	0.89
rno-miR-193b-3p	2.28	0.77
rno-miR-451-5p	2.63	0.75
rno-miR-296-5p	2.78	0.73
rno-miR-128-1-5p	3.28	0.75
rno-miR-10b-5p	4.28	0.91
rno-miR-199a-3p	10.04	0.92

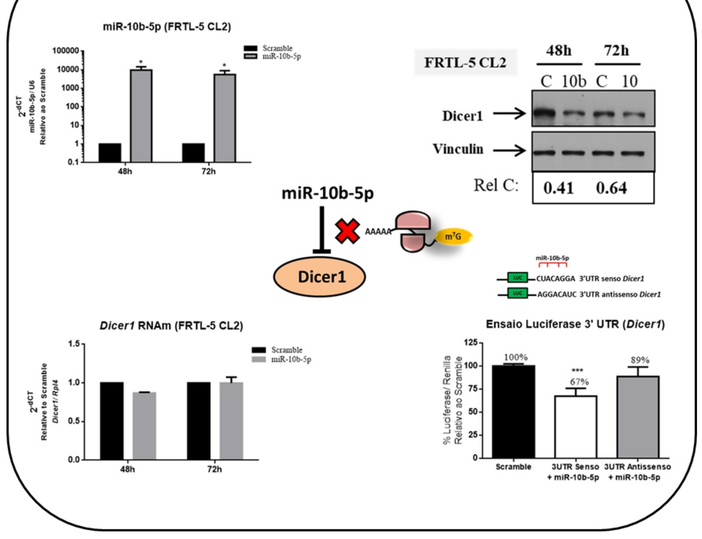
miR expressions correlates to targets expression levels



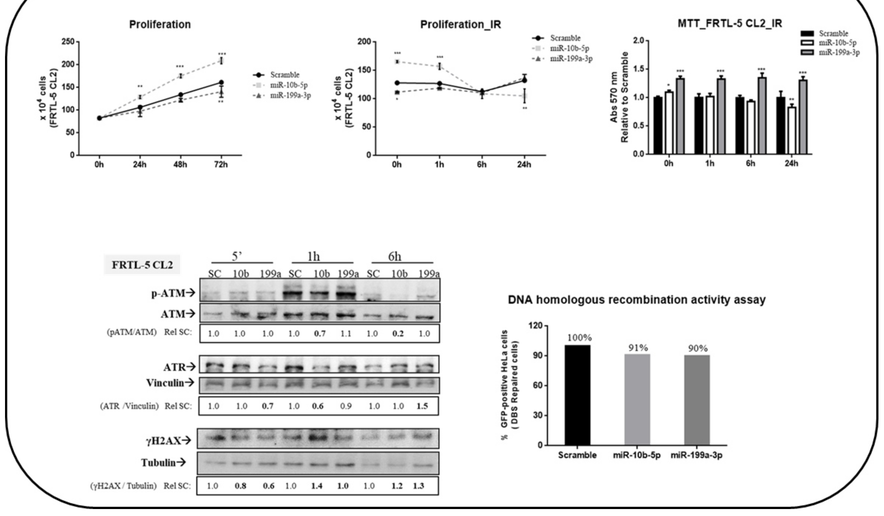
miR-10b-5p overexpression sensitizes thyroid anaplastic carcinoma cell line (8505c)



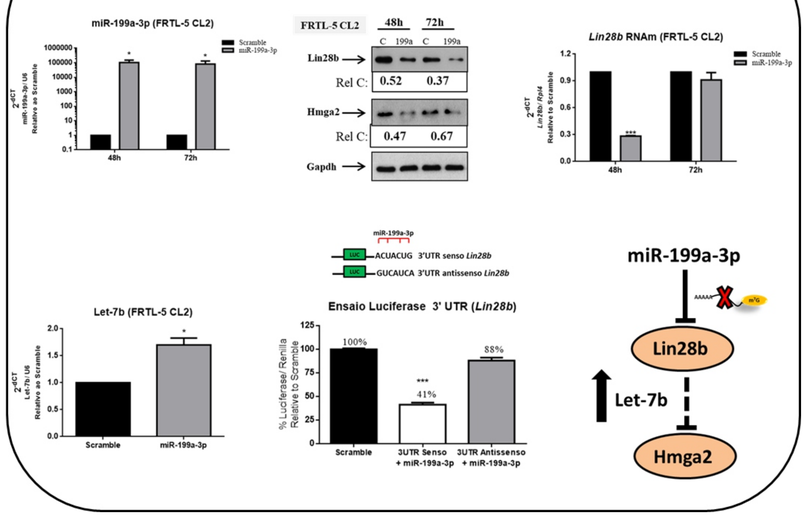
miR-10b-5p targets *Dicer1*



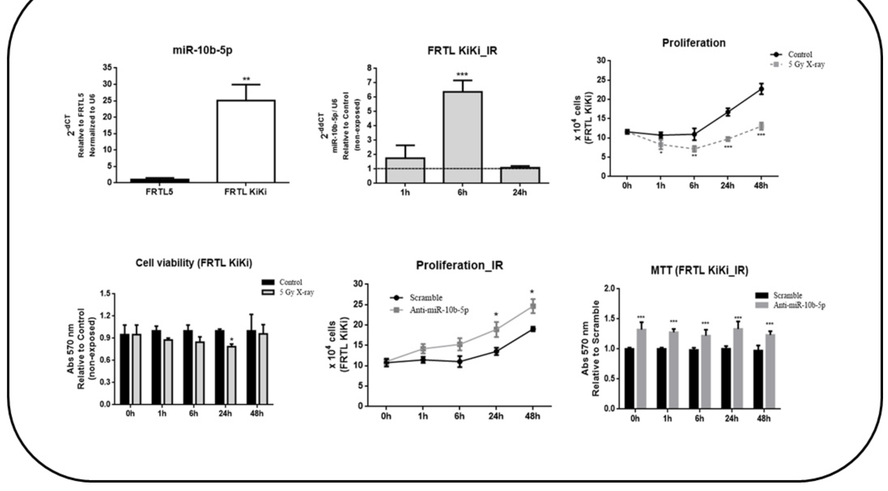
miR-10b-5p and miR-199a-3p impair HR repair



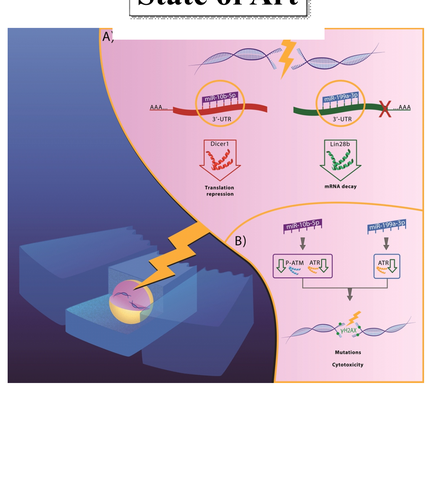
miR-199a-3p targets *Lin28b*



Inhibition of miR-10b-5p induces radioresistance



State of Art



CONCLUSION

These results demonstrate that IR deregulates microRNA expression, affecting the homologous recombination DNA repair efficiency of irradiated thyroid cells, and suggest that miR-10b-5p overexpression may be an innovative approach for anaplastic thyroid cancer therapy by increasing cancer cell radiosensitivity.

REFERENCES

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