

MiR-155 can be responsible for genomic instability and cell immortalization by targeting the shelterin component TRF1 in localized prostate cancer.

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Introduction and objectives

Telomeres are responsible for controlling the number of cell divisions and maintenance of genomic stability, being telomere dysfunction one of the hallmarks of cancer. In prostate cancer (PC) reactivation of telomerase and severe telomere shortening are considered a primary step of the disease, and both phenotypes may be related with TRF1. TRF1 is part of shelterin, a complex of six proteins which binds the telomere, maintaining its homeostasis. TRF1 inhibits telomerase activity and protects the telomeres. MicroRNAs are small molecules that control gene expression in post-transcriptional level. MiR-155 has been related to telomere dysfunction by targeting TRF1 in breast cancer. Our aim was to investigate the expression of TRF1 and miR-155 in PC clinical samples and cell lines

Methods

Expression levels of TRF1 and miR-155 was evaluated in 50 surgical specimens of localized PC and in the metastatic PC cell lines LNCaP, DU145 and PC3 by qRT-PCR. Ten samples of benign prostatic hyperplasia (BPH) were used as control. T test was used to compare two groups and one way ANOVA with Bonferroni correction for three groups.

Results

The patients' data are illustrated in figure 1A. There was no expression of TRF1 in all samples of localized PC, while the expression of miR-155 was higher compared with the control group ($p=0.0348$). In cell lines, TRF1 expression was present, being higher in LNCaP, a castration-sensitive cell line and progressively lower in DU145 and PC3 ($p=0.0327$), with no difference in miR-155 expression.

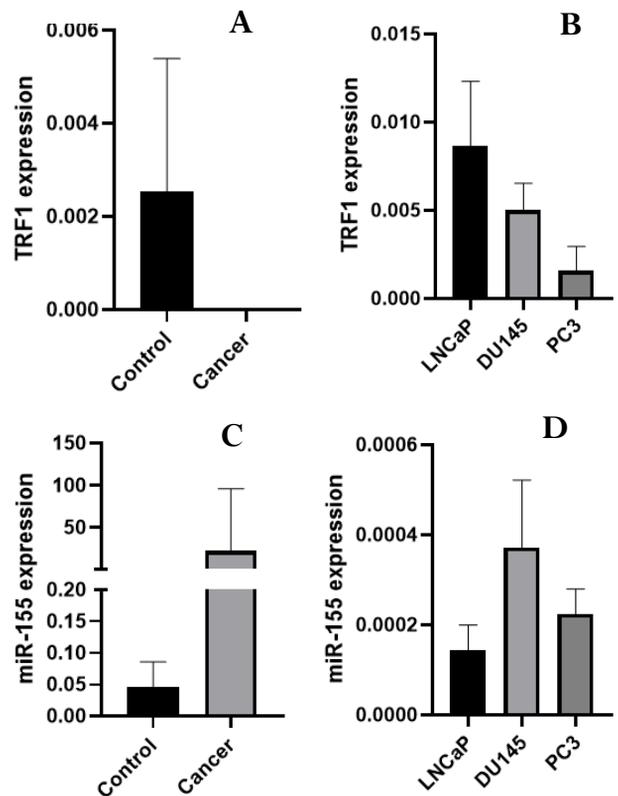


Figure 1. Expression of TRF1 and miR-155 in prostate cancer. A) TRF1 gene expression in tissue samples. B) TRF1 gene expression in cell lines. C) miR-155 expression in tissue samples. D) miR-155 expression in cell lines

Conclusion

Our hypothesis is that miR-155 has a role in the first stages of PC, having as target TRF1, a key element involved in the telomere homeostasis, contributing with cell immortalization and genomic instability. In cell lines we observed a progressive reduction of TRF1 expression related with their aggressiveness, but probably not dependent of miR-155.