

The analysis of the expression pattern of the intracellular and extracellular miRNAs in prostate tumor cell lines exposed to cytotoxic drugs.

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It has been recently discovered that microRNAs are stably expressed in body fluids of several organisms and that the expression patterns in the plasma/serum of cancer patients could represent a diagnostic/predictive tool of the disease. Extracellular miRNAs have been also found in the growth medium of cells in culture and this prompted us to verify whether prostate tumor cell lines release miRNAs specific of prostate tumor patients and whether anticancer drugs affect the expression patterns of the extracellular miRNAs. First of all we determined the expression of either prostate specific (PS-miRNA) or non prostate specific (NPS-miRNA) miRNAs in the growth medium of PC3 and DU-145 cells (prostate metastatic tumor cell lines) in comparison to PNT1A (immortalized prostate cell line). We found that the levels of both the intracellular and extracellular PS-miRNAs were higher in PC3 and DU-145 tumor cell lines in comparison to the immortalized cell line PNT1A and that a positive correlation exists between the intracellular and the extracellular levels suggesting that the release of miRNA in the growth medium may be a manner to maintain the intracellular miRNAs at physiological level. Thereafter, we investigated whether the release of miRNAs is affected in cells upon their exposure to a cytotoxic drug. To address the point, PC-3 and DU-145 cells were exposed to a cytotoxic concentration of either fludarabine (10 $\mu\text{g/mL}$) or taxotere (30 nM) for 48 hours. At the end of the treatment both the intracellular and extracellular PS-miRNAs and NPS-miRNAs were quantified. Data showed that i) those miRNAs that were up regulated in cells surviving to either fludarabine or taxotere were not released and that ii) the up regulated miRNAs found in fludarabine- or in taxotere-surviving cells were not the same. Overall data indicate for the first time a possible involvement of miRNAs in the survival/resistance of tumor cells to cytotoxic drugs and suggest that the expression pattern of the intracellular and extracellular miRNAs could be an useful tool to identify in tumor cell lines miRNAs responsible of survival/resistance to cytotoxic drugs and in plasma/serum of cancer patients the efficacy of an anticancer treatment.