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miR-34a is an intracellular and exosomal predictive biomarker for response to docetaxel with clinical relevance to prostate cancer progression

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Introduction: Resistance to docetaxel (RD) can limit the success of treatment for castration-resistant prostate cancer (CRPC). We have previously demonstrated that exosomes derived from conditioned media (CM) of resistant cell lines can induce resistance when applied to secondary cells. Here we investigated the intracellular and extracellular miRNA expression in a panel of cell line models of RD *versus* their parent, sensitive cell lines. **Methods:** We performed global miRNA profiling on the cells and corresponding extracellular vesicles (EVs) from 3 cell line models of RD. The expression of several identified miRNAs was assessed in 4 publicly available clinical datasets, representing tissues and urine from prostate cancer *versus* benign patients, as well as prostate tissues from patients with biochemical recurrence *versus* non-recurrence and also from patients experiencing metastatic disease *versus* primary disease and benign tissue. Transfection of miR-34a mimics and inhibitors was used to manipulate miR-34a levels in cells to assess effects on response to docetaxel and target protein expression. **Results:** TEM and western blotting suggested that the vast population of EVs isolated were exosomes. On average 76.5% of miRNAs detected in cells was also present in EVs while on average 9.8% were detected in EVs only. Linear regression analysis demonstrated a strong correlation in the detection of miRNAs in EVs and their corresponding cells of origin. Decreased miR-34a expression showed substantial clinical relevance and so was chosen for further functional assessment. Our knockdown and over expression studies confirmed that miR-34a directly regulates BCL-2 and may, in part, regulate response to docetaxel. **Summary/conclusion:** This study confirms that EVs derived from the media conditioned by a panel of prostate cancer cell lines do represent the cells of origin. Furthermore, our functional assessment of miR-34a supports its role as a predictive biomarker for RD in CRPC.