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Exosomes—potential regulators and biomarkers of prostate cancer progression

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Hormone-refractory prostate cancer treatment remains hindered by inevitable progression of resistance to first-line treatment with docetaxel. To help determine the complexity of this problem, in vitro cell line models of docetaxel resistance were established representative of the clinical situation. This study aimed to (i) isolate exosomes from medium conditioned by these cell line models and investigate their effects on motility, invasion, proliferation and docetaxel resistance of secondary cells; (ii) perform a proof-of-principle translational investigation of the clinical relevance of exosomes isolated from prostate cancer serum; and (iii) perform microRNA profiling on cells and their corresponding exosomes to determine intracellular and extracellular biomarkers predictive of response to docetaxel. Exosomes expelled from DU145 docetaxel-resistant variant (DU145RD) conferred docetaxel resistance to both DU145 and 22Rv1 cells, which may be partly due to exosomal MDR-1/P-gp transfer. Furthermore, exosomes from prostate cancer patient sera increased cell proliferation and invasion, compared with age-matched controls. Finally, miRNA profiling studies revealed a panel of miRNAs common between cells and exosomes that may offer potential as biomarkers predictive of response to docetaxel. Our in vitro observations and preliminary clinical studies indicate that exosomes play an important role in prostate cancer and may offer potential as vehicles containing predictive biomarkers and new therapeutic targets.

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