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Published: 25 April 2014

Citation: Journal of Extracellular Vesicles 2014, **3**: 24214 - <http://dx.doi.org/10.3402/jev.v3.24214> **Oral Presentations**

O4A-143

miR-134 transported in extracellular vesicles reduces triple-negative breast cancer aggression
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Introduction: Previously, we reported that extracellular vesicles (EVs) from triple-negative breast cancer (TNBC) cell line, Hs578T, and its more aggressive variant, Hs578Ts(i)₈, increase the aggression of recipient cells in a manner mirroring the cells of EV origin. This observation was clinically validated using EVs from TNBC sera. Here, we have globally profiled the cellular and EV miRNAs contents, aiming to identify and assess those of potential therapeutic value. **Methods:** miRNA profiling was performed by TaqMan low density array on RNA from Hs578T and Hs578Ts(i)₈ cells and their respective EVs. Direct miRNA transfections were performed with lipofectamine. EVs from the transfected cells were isolated and phenotypic (invasion, migration and drug response) alterations they conferred were analysed; comparing the effects of direct cellular transfection to effects of EV exposure in inducing phenotypic alterations. Publically available miRNA datasets of breast cancer patients confirmed *in vitro* observations. miRNA levels in EVs from TNBC patients' sera were analysed by qPCR. miRNA protein targets predicted *in silico* were confirmed by immunoblotting. **Results:** Most (79%) of the miRNAs detected in Hs578T cells were identified in their EVs; similarly, 75% of those in Hs578Ts(i)₈ cells were identified in Hs578Ts(i)₈ EVs. Sixty-eight miRNAs were commonly down-regulated in Hs578Ts(i)₈ cells and EVs compared to Hs578T cells and EVs, respectively. A number of miRNAs were validated by qPCR with miR-134 emerging as potentially important. Both direct transfection of miR-134 into Hs578Ts(i)₈ cells and Hs578Ts(i)₈ cell treatment with miR-134-enriched EVs reduced the expression levels of STAT5B and Hsp90, subsequently reducing TNBC aggression. **Summary/conclusion:** miR-134 loss plays a functional role in increasing TNBC aggression. Encapsulating miR-134 in EVs may provide a therapeutic strategy by reducing oncoprotein levels to thus reduce TNBC aggression.