Exosomal miRNAs are Associated with the Epithelial to Mesenchymal Transition in Ovarian Cancer

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Results

It’s All About the EMT!

CAOV-3 cells were chosen as target cells to determine EMT expression as they are representative of early stage ovarian disease. 100µg/mL of isolated exosomes were incubated with the CAOV-3 cells for 48 hours before RNA extraction. 48 hours was chosen as previous experiments showed that cells required approximately 24 hours to uptake exosomes.

Figure 1: CAOV-3 require 12 hours for exosome uptake. (A) Exosomes were labelled with a green fluorescent marker (PKH67), and uptake by CAOV-3 cells was determined overtime. (B) Fluorescent microscopy images of exosomes (green), and cell nuclei (blue). Expression of (C) E-Cadherin or (D) N-Cadherin in cells treated with either exosomes or TGF-β, compared to control cells.

Figure 2: Effect of exosomes on EMT. (A) Compared to control cells, Treatment of CAOV-3 cells with benign patient exosomes resulted in decreased expression of Matrix Metalloproteinase 9 (MMP9) and Frizzled 7 (FZD7) in the CAOV-3 cells and this was also seen when the cells were treated with cancer patient derived exosomes. Increased expression of SPARC (Secreted Protein Acidic and Rich in Cysteine) was also noted in both cases. (B) Interestingly, expression of CTNNB1 (β-Catenin) and WNT11 decreased in cells that were treated with cancer exosomes compared to cells treated with benign exosomes.

Cancer exosomes are able to induce changes characteristic of EMT, such as increased N-Cadherin expression and the expression of genes such as the WNT family. Further research is required to isolate cancer specific exosomes (e.g. through the use of antibody coated beads) and to examine their content (using MS/MS) for the potential use of exosomes as minimally invasive biomarkers. This may lead to earlier diagnosis and a better understanding of disease progression.