**The impact of pancreatic cancer cell exosomes on the phenotype of pancreatic cancer cells**

**Background**

Exosomes vesicles measuring up to 100nm in size and play key roles in cell-to-cell communication. They are particularly rich sources of miRNA and are a means by which one cell can impact on the phenotype of neighbouring cells.

PSC’s are a key stromal component in pancreatic cancer. The aim of this study is to characterise PSC exosomes and their impact on pancreatic cancer cell phenotype.

**Methods**

Exosomes were isolated from conditioned media of PSC’s. Their miRNA cargo was identified using the nanostring system.

MiaPACA2 and PANC1 cells were exposed to exosomes in 2D and 3D culture. RNA was isolated from hanging drop cells and used for next generation RNAseq. Data was analysed with MonkSeq and Ingenuity Pathway Analysis software.

**Results**

The top 15 miRNA’s identified in exosomes were implicated in a variety of cancer associated KEGG pathways e.g. proteoglycans in cancer (p<0.0001), pancreatic cancer (p<0.0001), p53 signalling (p<0.0001), pathways in cancer (p<0.0001).

MiaPACA2 cells treated with exosomes demonstrate a 27% reduction in proliferation (p<0.05). This wasn’t replicated in PANC1 cells.

MiaPACA2 cells do not form spheroids in hanging drop culture however in the presence of exosomes do form 3D structures. PANC1 formed more compact spheroids in the presence of exosomes (p<0.001). Both cell lines demonstrated increased cytotoxicity in 3D culture in the presence of exosomes.

Next generation sequencing of RNA isolated from MiaPACA2 cells cultured in 3D either with or without PSC exosomes revealed changes in several key cell signalling pathways including ER Stress, circadian rhythm, metabolic control and ARE binding proteins.

**Conclusion**

PSC exosomes contain miRNA’s implicated in a variety of cancer related cell signalling processes and impact on the phenotype of pancreatic cancer cells.