

# The genetic profile of pancreatic circulating tumor cells

Apostolou P.<sup>1</sup>, Toloudi M.<sup>1</sup>, Papadimitriou M.<sup>1</sup>, Papasotiriou I.<sup>1</sup>

<sup>1</sup> Research Genetic Cancer Centre Ltd. (R.G.C.C. Ltd). Industrial Area of Florina GR53100, Florina, Greece

**Background:** Pancreatic cancer is one of the types of cancer with poor prognosis, and pancreatic tumors are hard to detect in locally advanced stage. Furthermore, the progression from stage I to II is very fast, therefore, the improvement of early detection methods is essential. Circulating tumor cells (CTCs) that flow into the blood or lymphatic circulation, might contribute to the detection of cancer at earlier stages. CTCs genetic profile might be useful for detection of new biomarkers or new prognostic tools. In addition, specific genes could be used as new drug-able targets. The present study aimed to identify the gene expression profile of CTCs in pancreatic cancer and compare them with the gene expression among breast, colon, lung and prostate CTCs.

**Methods:** Blood samples were collected from 24 patients suffered from pancreatic (4), breast (5), colon (5), lung (5) and prostate (5) cancer in different stages of the disease. CTCs were isolated using enrichment isolation protocols and RNA was extracted from the above cells. The RNA was used as template for microarray experiments in the Human MI ReadyArray platform, while a universal reference RNA was used as reference. The microarray data were normalized using background subtraction and analysis of variance was performed. Genes with Log2ratios >2 and repeatable results were selected for clustering analysis.

**Results:** The analysis revealed more than 2,500 genes that were overexpressed in all pancreatic samples. These were categorized according to their function and included the genes BAK1, CASP4 and TNFSF8, correlated with apoptosis, the genes LAMA3, TTN and PPFIBP1, which involved in cell adhesion, the ACTN4, DCX, DNAH9 and OCRL genes that implicated in cytoskeleton. Furthermore, different kinases like ATM, PTK2B, TAOK2 and PIK4CA and finally the genes RUNX1T1, ELAVL4, POLR2A and PPARD that correlated with transcription regulation. The genes correlated with transcription and apoptosis were not only over-expressed in pancreatic CTCs but also were not expressed in all samples on the rest types of cancer.

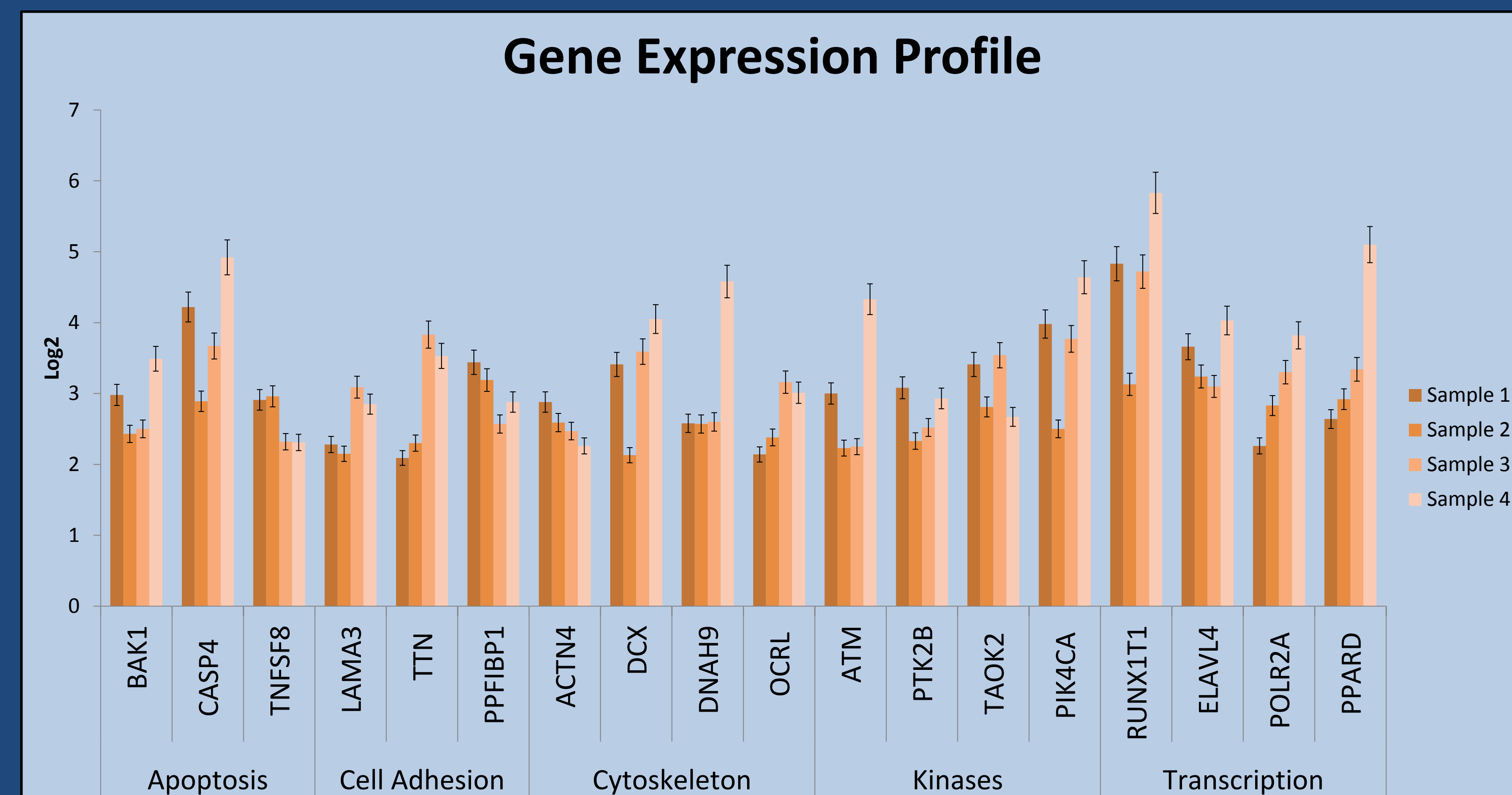


Figure 1: Relative gene expression analysis of pancreatic cancer according to Reference RNA sample

**Conclusions:** The present demonstrated that the pancreatic CTCs' gene expression may have some common patterns with the rest types of cancer CTCs, however the differences are more. First and foremost, it is noteworthy that genes involved in key-processes like apoptosis and transcription, were different for pancreatic CTCs. Therefore, the above genes could be used as potential biomarkers or might contribute to new drug-able targets discovery. Further studies, in more samples, are imperative to confirm all the above and be able to use at clinical level.

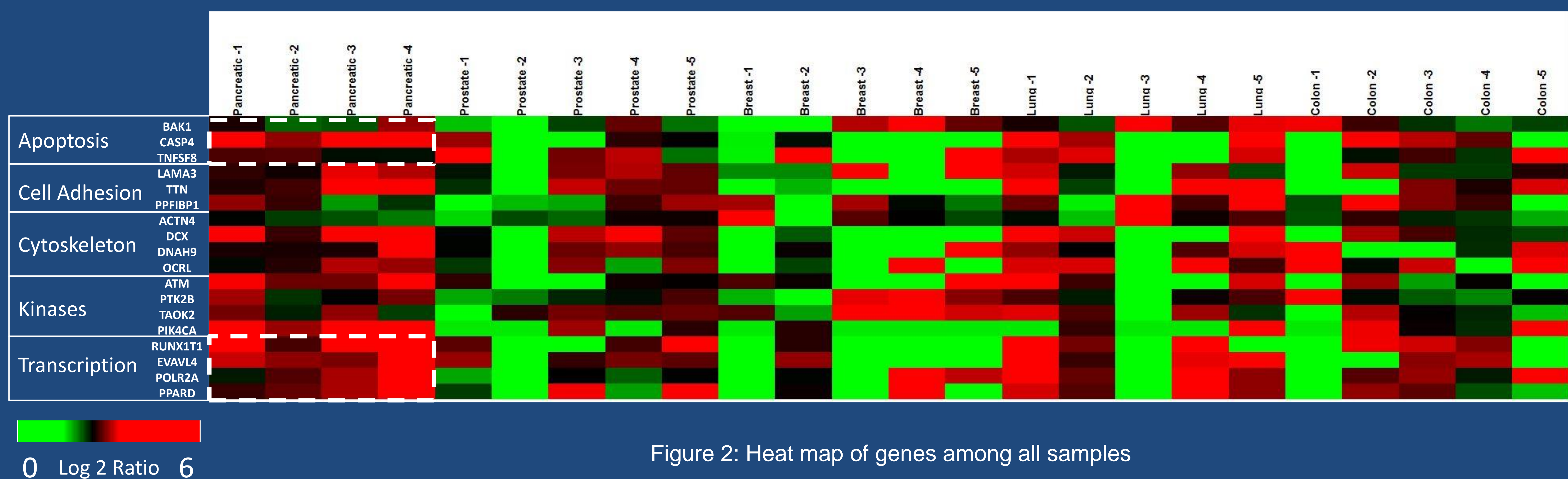


Figure 2: Heat map of genes among all samples