The molecular profile of colon cancer cells

Apostolou P.[1], Ntanovasilis D. [1], Papadimitriou M. [1] , Hatzidaki E. [1] ,
Pantopikou K. [1], Parsonidis P. [1] , Papasotiriou I.[1]

[1] Research Genetic Cancer Centre S.A.. (R.G.C.C. S.A.). Industrial Area of Florina GR53100, Florina, Greece

Background: Colon cancer is the third most commonly diagnosed cancer in both women and men, while it accounts for approximately 10-15% of all cancer deaths each year. People diagnosed with colon cancer at its earliest stage have higher survival (five-year or more) than those diagnosed at latest stages. Therefore the identification of new biomarkers, which constitute in early detection, is of primary importance for scientists. The present study aimed to analyze the gene expression profile of colon circulating tumor cells and compare it with profiles of other cancer types.

Methods: Blood samples were collected from 8 colon cancer patients in different stages of the disease and CTCs were isolated using enrichment isolation protocols. RNA was extracted from the above cells as well as from commercial cell lines representing the same type of cancer, provided by ECACC. The RNA was used as template for microarray experiments in the Human MI ReadyArray platform, while a universal reference RNA was used as a reference. The microarray data were normalized using background subscription and analysis of variance was performed. Genes with Log2ratios >2 and repeatable results were selected for clustering analysis. The above data were then compared with data from other cancer types.

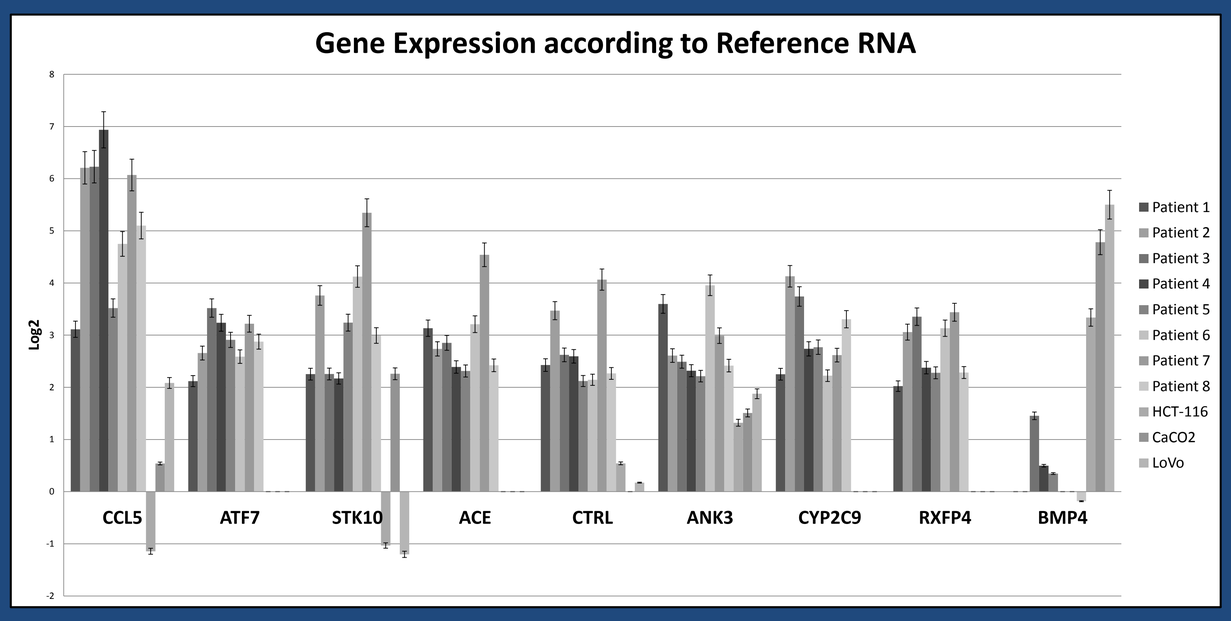

Figure 1: Relative gene expression analysis of colon cancer according to Reference RNA sample

Results: The microarray experiments in colon CTCs revealed more than 50 genes that were overexpressed, included transcription factors (ATF7), cytokine ligands (CCL5), kinases (STK10) and genes involved in other procedures. In addition over expression was observed for other genome regions including transposable elements (LINE-1), tRNAs or snRNAs. The clustering analysis including the commercial cell lines did not revealed common gene expression patterns. In commercial cell lines there was observed over expression mainly in genes correlated with cell adhesion (CDH3, ANXA3 etc.). Genes correlated with cell adhesion, cell motility and cell invasion, were also overexpressed in other types of cancer (prostate, breast).

Conclusions: The present study demonstrated that in colorectal cancer, the gene expression profile is different between CTCs and established colon cells. Furthermore, in colon CTCs there was observed over-expression in genes, which were not detected in other cancer types. Therefore, the above genes should be used as potential biomarkers or after evaluation as drugable targets. Further studies, in more samples, are imperative to confirm all the above and be able to use at clinical level.

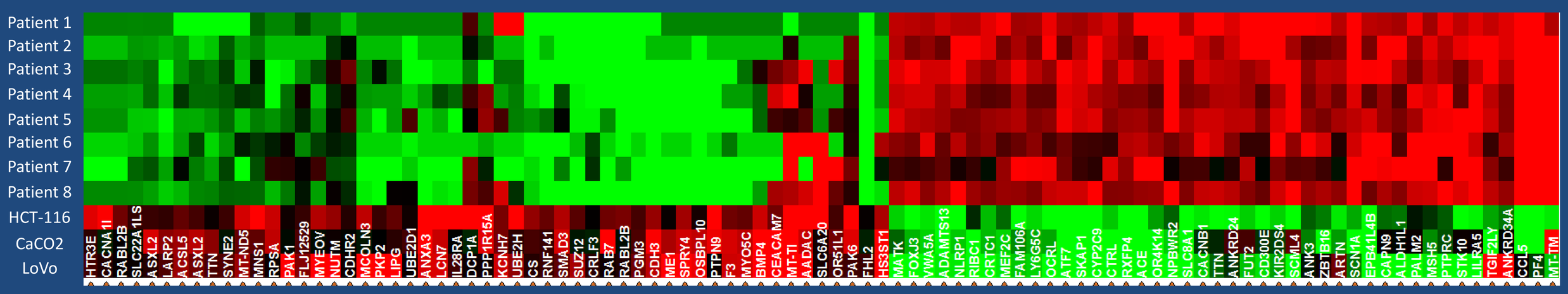

Figure 2: Heat map of genes among all samples. Negative values (green) indicate down-regulation, while positive values (red) indicate over-expression of gene expression. On the left is presented the scale diagram.

Selected References:
• Meropol NJ. The significance of circulating tumor cells as prognostic markers for colon cancer. Clin Adv Hematol Oncol 2009; 7:247-8.
• Bertucci F, Salas S, Eysteries S, Nasser V, Finetti P, Ginestier C, et al. Gene expression profiling of colon cancer by DNA microarrays and correlation with histoclinical parameters. Oncogene 2004; 23:1377-91.

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