Poster ID: P-348
Category: Basic
Colon Cancer

The contribution of circulating tumor cells' gene expression in treatment response

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Background: Colorectal cancer, constitutes one of the most prevalent types of cancer. Despite the various treatment options, the mortality rate is extremely high. Chemotherapy and/or radiotherapy might be beneficial for patients, however "indicators" which could predict response to the above treatment protocols, would be helpful. Study of circulating tumor cells (CTCs), in combination with high-sensitivity assays, might contribute to more successful treatment protocols. In this study, we performed gene expression analysis in CTCs derived from patients with colorectal cancer and compared the outcome with the established protocols.

Methods: Blood sample was isolated from 54 patients with colorectal cancer at different stages of the disease. CTCs detected and isolated with Fluorescence-Activated Cell Sorting (FACS). RNA Isolated and qRT-PCR followed for more than 90 tumor related genes. The genes included growth factors receptors, self-repair mechanisms, angiogenesis, cell cycle regulation, apoptosis, metastasis, drug metabolism as well as specific biomarkers. Gene expression analysis performed also in non-cancer samples, and relative quantification followed.

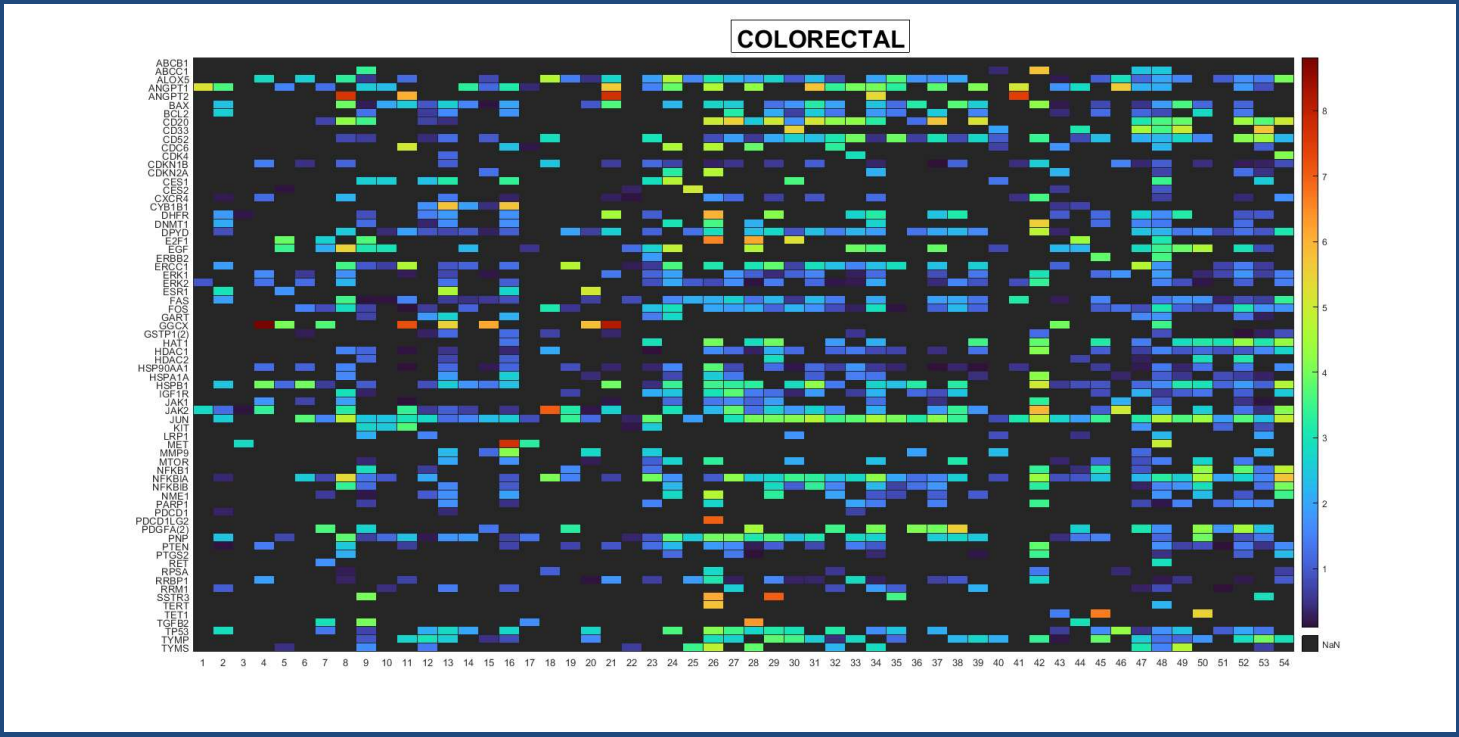

Figure 1: Gene Expression Heat-map in colorectal cancer. (Data presented in logarithmic scale, compared to normal samples)

Results: Among the genes which were overexpressed, were transcription factors involved in signal transduction pathways (FOS, JUN, JAK2), genes related with apoptosis (FAS, BAX), drug metabolism (TYMS, PNP, DPYD), and genes involved in cell cycle regulation (CDKN1B). On the contrary, genes encoding for heat shock proteins were downregulated (HSP90AA1, HSPA1A, HSPB1).

Conclusions: These preliminary data indicate that not all cases exhibit the same behavior, as it was expected. There are overexpressed genes, whose expression associated with response to chemotherapeutic drugs, like fluorouracil, oxaliplatin, irinotecan, monoclonal antibodies, such as nivolumab, cetuximab etc. However, these genes are not upregulated in all cases, since there is a percentage of approximately 30% with different expression profile. On the contrary, almost in all cases, showed sensitivity to radiotherapy and hyperthermia. Concluding, it has been demonstrated that the gene expression analysis is important for a comprehensive tumor analysis and might contribute to design of more effective treatment protocols.

Selected References:

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