Molecular profiling of gastrointestinal cancer

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Background: Gastro-intestinal cancer (GI) include a variety of cancers that affect esophagus, gallbladder, liver, pancreas, stomach, intestine and other organs involved in digestive system. The above types of cancers appear higher mortality rates in comparison with cancers in other systems. Therefore, it is essential the optimization of treatment management. Even though great achievements have been performed the last years in prediction of cancer therapy, treatment is based in specific markers, avoiding genes that affect or affected through signaling transduction pathways. The present study aimed to analyze the gene expression in cancer cells, representing different GI cancer types and compare them with circulating tumor cells (CTCs) from patients and cells from normal donors.

Methods: RNA was extracted from commercial cell lines representing gastric (MKN45, 23132/37), liver (Huh 7D-12), colon (CaCO2, HCT15, HCT116) and pancreatic (PANC-1) cancer. Blood was collected from two healthy donors as well as two colon cancer patients. PBMCs in healthy individuals and CTCs in cancer samples were isolated and RNA was extracted. qRT-PCR was performed including reference RNA as positive control. Primer pairs were designed for exon-exon amplification of genes involved in signaling pathways, invasion, receptors, cell cycle regulation, resistance etc. ACTB was used as housekeeping genes and DeltaCt analysis was followed. Experiments were performed in triplicates including appropriate controls. Hierarchical clustering was performed to identify gene expression patterns.

Results: The genes ERK1, ERK2, CDC6, JAK1, JAK2, FAS, NRAS, BCL2, NME1 and HSPB1 were not expressed in normal samples. In CTCs there was not observed expression for JUN, ERCC1, RRM1, HRAS, MAP2K kinases, as well as TGFB2, TGFB3, CDKN2A, TP53, KIT, GART, DPYD and TYMS. On the contrary, patients-derived cells' gene expression was higher for ERK2, PTEN, RPSA, JAK1, JAK2, FAS, KRAS, TGFB1 and NANOG. The clustering method efficiently discriminated cancer cells from normal samples, while it categorized in different clusters the commercial colon cancer cells from colon CTCs.
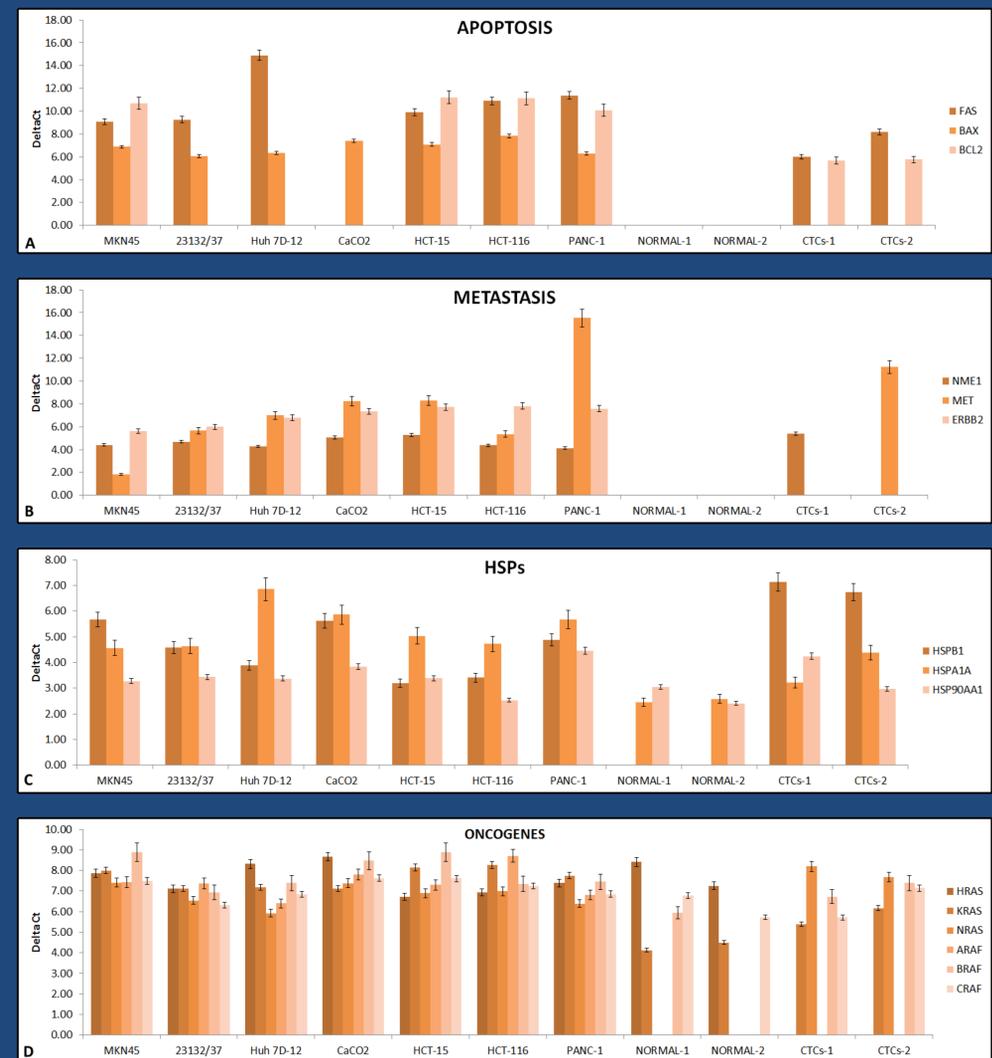
Figure 1: Delta Ct qPCR Data among all samples. The higher the DeltaCt the lower the gene expression. Absence of bar indicates no expression in the appropriate sample.
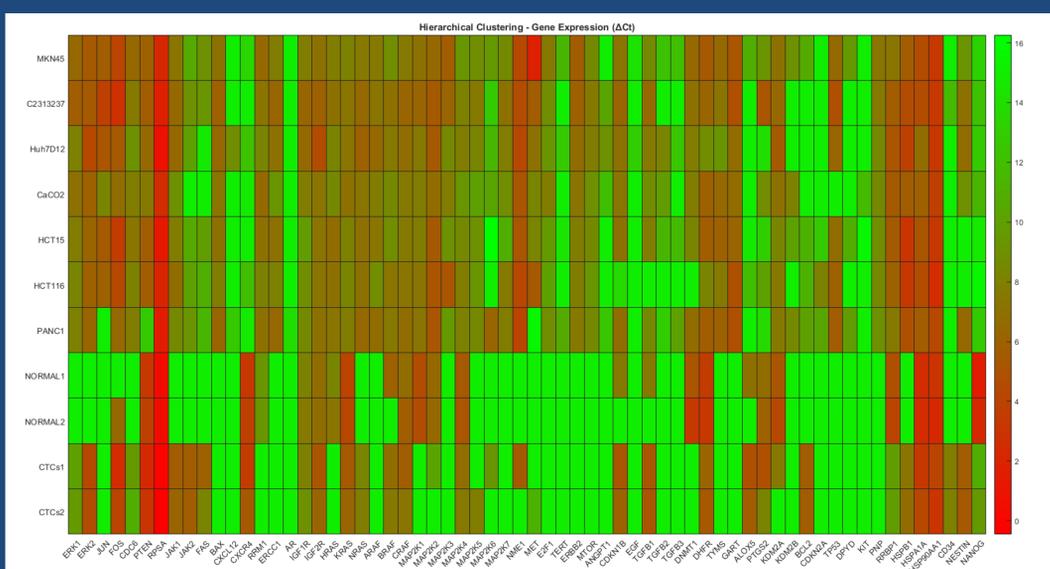

Figure 2: Heat map of genes among all samples. On the right is presented the scale diagram.

Conclusions: Taking everything into consideration it is well understood that personalized treatment is essential, since different expression profiles are observed among samples with the same type of cancer. The more genes that are studied, the more information are collected for the cancer; therefore a treatment with greater success can be achieved. In addition, the study of genes should not limited in receptors and/or pathways, but also to include genes involved in various cell processes. Further studies, in more samples, are imperative to confirm all the above and be able to use at clinical level.

Selected References:
• Lin, I.H., Chen, D.T., Chang, Y.F., Lee, Y.L., Su, C.H., Cheng, C., Tsai, Y.C., Ng, S.C., Chen, H.T., Lee, M.C., et al. (2015). Hierarchical clustering of breast cancer methylomes revealed differentially methylated and expressed breast cancer genes. PLoS One 10, e0118453.
• Jiang, H.B., Yang, T.J., Lu, P., and Ma, Y.J. (2014). Gene expression profiling of gastric cancer. Eur Rev Med Pharmacol Sci 18, 2109-2115.
• Marimuthu, A., Jacob, H.K., Jakharia, A., Subbannayya, Y., Keerthikumar, S., Kashyap, M.K., Goel, R., Balakrishnan, L., Dwivedi, S., Pathare, S., et al. (2011). Gene Expression Profiling of Gastric Cancer. J Proteomics Bioinform 4, 74-82.

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