THE GENETIC BACKGROUND OF PANCREATIC CANCER: GENES THAT MIGHT BE BIOMARKERS OR INDICATORS OF METASTASIS TO THE LUNG

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Introduction: Pancreatic cancer is the fourth leading cause of cancer deaths, being responsible for 6% of all cancer-related deaths. Pancreatic cancer is difficult to be diagnosed in its early stages. One major problem is that it metastasizes to regional lymph nodes and later to the liver or to the peritoneal activity and other organs, like lungs. The discovery of new biomarkers for early prognosis, or for predicting metastasis to lungs is essential. The present study aims to determine genes that are correlated with pancreatic cancer, as well as their correlation with other types of malignancies, including lung cancer.

Methods: DNA Microarrays were performed in a human Caucasian pancreatic cell line (PANC-1) and in a human primary pancreatic adenocarcinoma cell line (BxPC-3). PBMCs from a control sample (non-cancer) were used as reference. Then, RT-qPCR experiments, with specific primers, were performed for the genes that were over-expressed in both cell lines (LogRatio >7) to confirm the above data (microarray). The expression of the these genes was also studied in cancer stem cells representing lung, colon and breast cancer, as well as in differentiated cell lines, representing the same types of cancer (COLO699N, HCT-116 and T47D respectively). Mann-Whitney U tests were performed on qPCR data, which were then analyzed according to Livak method.

Results: The microarray experiments demonstrated 9 different genes that are over-expressed in pancreatic cancer. Among them, the TLR8, LYZ and PF4 are expressed only in pancreatic and differentiated lung cancer cell lines. The QPCT, PLEK and CELF2 genes are expressed in all cell lines as well as in normal samples. The MNDA gene is expressed only in primary pancreatic cancer and in T47D cell line. Furthermore, the C3AR1 is expressed in all cases apart from breast and lung CSCs. Finally, SH2D1A is not expressed in colorectal cancer, lung CSCs and in normal samples.

Conclusion: According to literature and experimental data, there are many biomarkers for pancreatic cancer. PF4 and LYZ are two of them. It has been shown that among toll-like receptors, many of them have been correlated with this type of cancer. However there is no correlation with TLR8. It is remarkable that the above genes are expressed only in pancreatic and differentiated lung cancer cells, demonstrating the common features displaying both types of cancer, as well as the common therapeutic approaches. It is also noteworthy that the above genes are not classified as lung cancer biomarkers. Therefore, they might be considered not only as pancreatic cancer biomarkers, but as potential indicators of metastasis to the lung. It is essential to perform further studies in other cancer cell lines and in more samples, so as to be used clinically. However the first results are quite encouraging.