Whole Transcriptome Sequencing Reveals Molecular Prognostic Markers in Pancreatic Adenocarcinoma

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Context Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy with few effective therapies. Although next-generation sequencing (NGS) further clarified the genomic complexity of PDAC, genes or pathways that specifically drive tumour progression or metastasis are not well understood. Objective Our challenge is to implement a whole transcriptome massively parallel sequencing (RNASeq) study to better understand the PDAC molecular biology for diagnosis and prognosis of PDAC. Methods We collected a total of 17 PDAC samples by ultrasound-guided biopsy or by surgical specimen for RNA extraction. Fourteen samples were analyzed by RNASeq, performed at 75x2 bp on a HiScanSQ Illumina platform. To study gene expression profiling related to poor outcome, we first studied differentially expressed genes between “poor” (overall survival <3 months; n=3) and “good” (overall survival >36 months; n=3) prognosis in a total of 6 PDAC sample. Results The relative presence of tumor cells in the sample was evaluated based on the presence of KRAS mutation. A total of 211 genes were differentially expressed. Genes involved in the p53 signalling pathway (CSNK1G1, TGFA), the Wnt/β-catenin (DKK1, WNT7B, WNT10A), insulin-like growth factor system (IGF2) and EGF receptor signalling pathway (EGF) were highly upregulated in “poor” PDAC samples. Interestingly, we found a strong overexpression of CA125/MUC16, recently demonstrated to be involved in PDAC and ovarian cancer invasion by stimulating matrix metalloproteinases. Conclusion Components of p53 signalling pathway, Wnt/β-catenin pathways, insulin-like growth factor system and MUC16 might be useful molecular markers in PDCA as their overexpression seems to be related with cancer growth, invasion and prognosis. Further validation of the role of these genes is necessary for translation in clinical practice.