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Pancreatic Cancer: Specific Problems of Genetic Profiling

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Pancreatic cancer is the fourth leading cause of cancer death in the United States and Europe [1]. The prognosis of patients with pancreatic cancer remains extremely poor, with five-year survival being less than 5% [2]. The most serious problems of pancreatic cancer are: i/ late diagnosis due to absence tests allowing early detection of the tumor, ii/ poor prognosis, which does not correlate with classic clinical factors and iii/ very limited efficacy of chemotherapy, which usually works in other tumor types. From existing data, it is evident that molecular factors such as genetic profiles, proteins expression and their activity exist and need to be validated and additional ones discovered for use in more precise division of patients into prognostic subgroups as well as it is imperative to identify subgroups of patients who may benefit from specific biological agents and "tailor" therapy to their "tumor profile".

Gene expression profiles are commonly used for an identification of groups of genes involved in specific functional aspects of tumor biology and for the development of candidate biomarkers [3]. A number of methods have been developed to study gene expression. The relative quantification by real-time PCR method (qPCR) is adequate strategy for most purposes where investigation of physiological changes in gene expression levels is conducted [4-6]. There are several essential requirements for successful expression analysis.

The first and crucial problem in pancreatic cancer gene profiling is a correct sample collection, handling and preparation [7]. More than 80% of the patients who present with the disease cannot be cured by surgical resection [8]. Thus, sampling in large specialized centers rather than in numerous smaller surgical departments is necessary for practical reasons. Because of lack of samples obtained from metastatic patients studies are always limited to pancreatic cancer patients with early stage of the disease who underwent surgery. It remains to be determined whether the observed associations would have the same prognostic significance in patients with advanced or metastatic tumors.

The second problem is associated with the histological characteristic of pancreatic tumors. The pancreatic adenocarcinomas have a low neoplastic cellularity and a predominance of nonneoplastic fibrous (or desmoplastic) stroma. This is rather unique to duct adenocarcinomas of the pancreas; in contrast to infiltrating carcinomas arising in other organs. To overcome this obstacle potentially leading to spurious results, two approaches are generally used. First, microdissection or other methods of purification of the epithelial component are utilized. Second, differences between macrodissected pancreatic tumors and non-neoplastic control tissues and eventually specimen from patients with chronic pancreatitis as an intermediate group are analyzed with stable cell lines as correctors [9].

Next in pancreatic tissues specifically, high-quality RNA preparation as the prerequisite condition for successful analysis presents an extremely difficult challenge. Subsequent assessment of RNA quality and quantity is the next critical step in expression analysis. Pancreatic tissues contain a large amount of endogenous RNAses. RNAses are a major secretory product of normal pancreatic acinar cells and cause extensive degradation of mRNA in pancreatic tissues. Moreover, there is a frequent loss of acinar cells during development of infiltrating pancreatic cancers due to atrophy or destruction of the gland by the tumor growth [9]. The content of RNAse secreting cells thus may vary among tumors. Thus for laboratories aiming at expression profiling of pancreatic cancer, it is essential to introduce specific protocol for the handling of a pancreatic specimen, RNA isolation procedure and rigorous control of RNA and cDNA quality and quantity.

The last but not least question in pancreatic cancer gene profiling is the appropriate choice of internal standards (reference genes) is for qPCR performance. Ideally, the internal standards should be constitutively expressed in all cell types under study. Internal standards should also be independent of experimental conditions and unaffected by human disease conditions. Formerly, a number of housekeeping genes, which are necessary for basic cell survival, like glucose-6-phosphate dehydrogenase (GAPDH), ribosomal RNA subunits (18S and 28SrRNA), β-actin or cyclophilins were used as reference genes. However, it has become clear that these highly popular reference genes show distinct differences in gene expression in certain tissue types and considerably vary between normal and malignant tissues [10-12]. EIF2B1, ELF1, MRPL19, and POP4 have been identified as the most stable and suitable reference genes for future expression studies in pancreatic carcinoma [13].

It is clear that, as well as the diagnosis and the therapy of pancreatic cancer, the research of molecular biology of pancreatic tumors is more difficult and has specific problems when compared to other types of solid tumors. It has managed to overcome obstacles during the last several years and gene profiling of pancreatic tumors became the common method in studying the molecular biology of pancreatic cancer. The complex analysis of candidate genes can help to reveal the mechanism of their action in pancreatic cancer progression in context with evidence-based medicine, which is needed for reasonable subsequent exploitation of the results. The identification of genes connected with progression of pancreatic cancer would improve common knowledge about molecular targets to be addressed for better outcome of the treatment of this disease.

References

1. Jemal A, Siegel R, Xu J, Ward E (2010) Cancer statistics, 2010. CA Cancer J Clin 60: 277-300.
2. Hidalgo M (2010) Pancreatic cancer. N Engl J Med 362: 1605-1617.
3. Rosty C, Ueki T, Argani P, Jansen M, Yeo CJ, et al. (2002) Overexpression of S100A4 in pancreatic ductal adenocarcinomas is associated with poor differentiation and DNA hypomethylation. Am J Pathol 160: 45-50.
4. Fleige S, Walf V, Huch S, Prgomet C, Sehm J, et al. (2006) Comparison of

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relative mRNA quantification models and the impact of RNA integrity in quantitative real-time RT-PCR. Biotechnol Lett 28: 1601-1613.

5. Hubackova M, Vaclavikova R, Mrhalova M, Kubackova K, Kodet R, et al. (2009) NAD(P)H:quinone oxidoreductase 1 Pro187Ser polymorphism and expression do not cosegregate with clinico-pathological characteristics of human mammary tumors. Pharmacogenet Genomics 19: 505-512.
6. Hubackova M, Vaclavikova R, Ehrlichova M, Mrhalova M, Kodet R, et al. (2012) Association of superoxide dismutases and NAD(P)H quinone oxidoreductases with prognosis of patients with breast carcinomas. Int J Cancer 130: 338-348.
7. Bustin SA, Benes V, Garson JA, Hellemans J, Huggett J, et al. (2009) The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. Clin Chem 55: 611-622.
8. Sharma C, Eltawil KM, Renfrew PD, Walsh MJ, Molinari M (2011) Advances in diagnosis, treatment and palliation of pancreatic carcinoma: 1990-2010. World J Gastroenterol 17: 867-897.
9. Vilardell F, Iacobuzio-Donahue CA (2010) Cancer gene profiling in pancreatic cancer. Methods Mol Biol 576: 279-292.
10. Zhong H, Simons JW (1999) Direct comparison of GAPDH, beta-actin, cyclophilin, and 28S rRNA as internal standards for quantifying RNA levels under hypoxia. Biochem Biophys Res Commun 259: 523-526.
11. Blanquicett C, Johnson MR, Heslin M, Diasio RB (2002) Housekeeping gene variability in normal and carcinomatous colorectal and liver tissues: applications in pharmacogenomic gene expression studies. Anal Biochem 303: 209-214.
12. Mane VP, Heuer MA, Hillyer P, Navarro MB, Rabin RL (2008) Systematic method for determining an ideal housekeeping gene for real-time PCR analysis. J Biomol Tech 19: 342-347.
13. Mohelnikova-Duchonova B, Oliverius M, Honsova E, Soucek P (2012) Evaluation of reference genes and normalization strategy for quantitative real-time PCR in human pancreatic carcinoma. Dis Markers 32: 203-210.