Clinics in Oncology

Short Communication
Published: 17 Mar, 2017

Trends of Molecular Research for Pancreatic Cancer Diagnostics: Insights of Clinician

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Short Communication

Pancreatic cancer is an aggressive malignancy with very high negative impact for overall patients survival and non-reducing incidence rates in western countries [1,2]. In comparison to other solid tumors, pancreatic cancer has one of the highest rates of genetic alterations which lead to expression of large amount of various proteins and metabolites. Due to recent improvement and innovations of related technologies, research of pancreatic cancer proteome and metabolome is on the scope with promising results for improvement in diagnostics and treatment of this cancer type. A lot of efforts are being done worldwide searching for a sensitive, specific and cost-effective biomarkers which could be used for more effective early diagnostics and management of pancreatic cancer [3,4].

Galectins can regulate a wide variety of biological processes because of their ability to bind highly modifiable carbohydrate ligands. An over-expression of galectin-1 was discovered in Pancreatic Intraepithelial Neoplasia (PanIN), but not in healthy pancreas [5]. Since this form of neoplasia is recognized as the immediate precursor lesion of pancreatic cancer, galectin-1 could serve as a biomarker for improving early diagnostics. Upregulation of DJ-1, another multifunctional protein, previously has been identified in blood serum and pancreatic juicein individuals with pancreatic cancer compared to controls [6,7].

The S100 family is rich of clinically significant proteins. The expression of S100A6 was reported to be increased in pancreatic juice during pancreatic cancer progression. While this increase of expression appears at the early cancer stage it enables the possibility of early diagnostics. S100A6 proved to be highly sensitive biomarker when measured in endoscopic ultrasonography guided fine needle aspiration specimens reaching up to 97.06% diagnostic sensitivity. S100P, another member of this family, was suggested to be sensitive and specific biomarker with a potential to be identified in pancreatic intraepithelial neoplasia. It was recommended to be assessed in duodenal juice during routine upper endoscopy with the intention to become a screening tool for the pancreatic carcinoma [8].

Apolipoproteins form a lipoprotein family with a function to regulate metabolism of plasma lipoproteins. Changes in their expression were reported to correlate with pancreatic cancer.Findings ofPadoan et al. indicate that the expression of apolipoprotein A-I is reduced in patients with pancreatic carcinoma [9]. Likewise, reduction of this protein level was shown to be associated with an increased risk of colorectal cancer [10]. Research of recent years has shown that metabolomics could be used for more precise pancreatic cancer diagnostics [4]. Sugimoto et al. [11] identified forty eight metabolites as biomarker candidates in easily accessible sample sourceslike saliva. Investigation of urine metabolome was shown to be useful non-invasive technique for the pancreatic cancer detection [12]. Furthermore, this approach permits separation of patients with intermediate and advanced pathologic staging. Blood serum samples from patients with pancreatic carcinoma and healthy controls were analyzed and scientists identified that concentrations of taurine, choline and glucose plus triglycerides were significantly higher in the carcinoma group [13]. Another similar study concluded that metabolites have a higher accuracy than conventionally used tumor markers CA19-9 and CEA for differential diagnostics of pancreatic cancer [14].

In patients with pancreatic cancer, plasma amino acid concentrations are influenced by metabolism of cancerous tissues, systemic effects of cancer for body metabolism and dysfunctions of other organs including liver and kidney. Therefore, measurements of plasma amino acids during various stages of pancreatic cancer could be a valuable source of information for early diagnostics. Group of scientists performed amino acid profiling and multi-marker models of serum samples

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Received Date: *19 Dec 2016*
Accepted Date: *03 Jan 2017*
Published Date: *17 Mar 2017*

Citation:
Petrulionis M, Kurlinkus B, Sileikis A, Strupas K. Trends of Molecular Research for Pancreatic Cancer Diagnostics: Insights of Clinician. Clin Oncol. 2017; 2: 1223.

in pancreatic carcinoma patients, pancreatitis patients and healthy controls [15]. The results showed that combined amino acid-based metabolite panel is superior to CA19-9 alone in differentiating between these groups. Study with a large number of fasting plasma samples from pancreatic cancer patients, chronic pancreatitis patients and healthy controls was conducted at multi-institutions in Japan [16]. Concentrations of amino acids were measured and significant increases in Ser concentrations and significant decreases in the concentrations of 14 amino acids (Thr, Asn, Pro, Ala, Cit, Val, Met, Leu, Tyr, Phe, His, Trp, Lys and Arg) were observed in cancer patients compared with healthy subjects. In a prospective study, elevated branched-chain amino acid concentrations in prediagnostic plasma samples were associated with more than twofold increased pancreatic cancer risk, with the strongest prediction value observed in samples collected 2–5 years prior to pancreatic cancer diagnosis, isoleucine, leucine and valine being the most significant [17].

Results of overall survival are increasing in specialized pancreas surgery centres with relatively low postoperative complication rates after surgery [18]. Due to issues, radiologic assessment can hardly be applied as first step method for screening of pancreatic cancer in certain risk groups. Therefore, novel biological markers validated in easily accessible body fluids, complementing or substituting conventional CA19-9 and CEA, are considered as a necessity for further success improving treatment results of pancreatic cancer patients.

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