Metabolomics analysis of human pancreatic cancer tissue and paired adjacent tissue samples.

Dong Ouyang*, Qingyue Dai
Department of General Surgery, Armed Police Corps Hospital in Fujian, Fuzhou, PR China

Abstract

Background/aims: This study aimed to apply $^1$H spectrum Nuclear Magnetic Resonance spectroscopy (1H-NMR) to detect the metabolites in pancreatic cancer tissue and paired adjacent tissue samples.

Methods: 48 samples were taken from cancer tissues of 24 pancreatic cancer patients and paired adjacent tissues. The samples were subjected to $^1$H-NMR and principle component analysis to compare endogenous small-molecule metabolites.

Results: Leucine and isoleucine levels were significantly higher in pancreatic cancer tissues than in control tissues. Lactate, betaine, choline, α-glucose and α-hydroxybutyrate levels were significantly lower in pancreatic cancer tissues than in control tissues.

Conclusions: $^1$H-NMR-based metabolomics is an effective method to identify small-molecule metabolites in pancreatic cancer tissues. These metabolites can be used as the metabolic markers of pancreatic cancer for early diagnosis.

Keywords: Metabolomics, 1H-NMR, Extracted liquid, Pancreatic cancer, Metabolic markers.
Discussion

Because of unnoticeable symptoms and deep location, pancreatic cancer often develops silently without symptoms at early stage. At present, the diagnosis methods of pancreatic cancer include: (1) Tumor markers: current markers lack sensitivity and specificity for early lesions. (2) Gene detection: current clinical trials have not yet found a specific gene for pancreatic cancer. (3) Imaging diagnosis: ultrasonic gastroscopy and Endoscopic Ultrasonography guided Fine Needle Aspiration biopsy (EUS guided FNA), Positron Emission Computed Tomography (PET-CT) and Multislice Spiral Computed Tomography (MSCT) and Magnetic Resonance Imaging (MRI). Imaging technologies lack the sensitivity and specificity of the tumor with a diameter smaller than 2 cm.

Hydrogen spectrum based nuclear magnetic resonance is a new approach for qualitative and quantitative analysis of metabolomics of the organism or cell. The present study was to explore the use of hydrogen spectrum nuclear magnetic resonance spectroscopy to identify low molecular weight metabolites in pancreatic cancer tissue. Using principal component analysis, we found that leucine and isoleucine levels were significantly higher while lactate, betaine, choline, alpha-glucose, alpha-hydroxybutyrate levels were significantly lower in pancreatic cancer tissues compared to adjacent non-tumor pancreatic tissues.

Leucine and isoleucine are essential amino acids. Leucine and isoleucine play an important role in the metabolism of glucose in the liver by downregulating gluconeogenesis and inhibiting the expression of rate limiting enzyme for gluconeogenesis [10]. Pancreatic carcinoma tissues had high levels of leucine and isoleucine compared with adjacent tissues which had active glucose metabolism. Furthermore, alpha-glucose level was lower in tumor tissues than the paired adjacent tissues, consistent with the results of leucine and isoleucine.

Several studies have suggested the link of betaine intake and reduced risk of nasopharyngeal carcinoma and colorectal cancer [11,12]. This is in agreement with our results that the level of betaine in pancreatic cancer tissue was significantly lower than that in the adjacent tissues.

Serum alpha hydroxy acid levels increased in diabetes. Varvel et al. found that the potential cause of the rapid increase in the serum levels of alpha hydroxy acid was the damage of insulin secretion [13]. Many studies have found a correlation between pancreatitis, pancreatic cancer and diabetes. In this study, the level of alpha hydroxy acid in pancreatic cancer tissue was significantly lower than that in the adjacent tissues.

Lactic acid is the product of anaerobic fermentation. Tumor tissue is prone to hypoxia, ischemia and blood supply deficiency, and the level of lactic acid increased significantly in many tumor tissues [14,15]. However, in the present study we found that the level of lactate in the extract of pancreatic cancer tissue did not increase. Further studies are needed to understand the underlying mechanism.

In conclusion, this study showed that endogenous small molecule metabolites of pancreatic cancer tissue and paired adjacent tissue samples were significantly different. Application of hydrogen spectrum NMR metabolic group method to explore the characteristics of low molecular metabolites in the tissue extracts of pancreatic cancer patients with pancreatic carcinoma tissues and paired adjacent tissue can provide a new approach for early diagnosis of pancreatic cancer.

References


*Correspondence to*

Dong Ouyang

Department of General Surgery

Armed Police Corps Hospital

PR China