Plasma Biomarkers for Pancreatic Cancer

Object:

Pancreatic cancer (PCa) is a highly malignant tumor with a poor prognosis because of a lack of symptoms at the early stages and less than effective systemic therapies at advanced stages. Although surgical resection shows promise as an effective treatment for PCa, a lack of tools for diagnosis in early stages results in low 5-year survival rates. The survival rates drop rapidly from >50% in patients with stage I disease to <5% in patients with more advanced stages. Thus effective diagnostic tool was are in urgent need to improve PCa patients' survival.

We designed a study to look for valuable plasma diagnostic tools for pancreatic cancer. We selected 6 miRNAs which were elevated in the tissue of pancreatic cancer patients as reported. A candidate protein, macrophage inhibitory factor-1(Mic-1), was also investigated. The importance was that we included tissue specificity in our study. Several digestive system diseases, such as acute or chronic pancreatitis, colorectal cancer (CRC), gastric cancer (GC) and liver cancer were used to determine the specificity of our microRNA profile.

Progression:

So far we measured the expression of 6 miRNAs (miR-21, miR-210, miR-155, miR-20a, miR-25, miR-196a）and a candidate protein, Mic-1 in plasma samples of 64 PCa patients, 20 acute or chronic pancreatitis patients and 67 normal controls as our Training Group. All of 6 miRNAs and Mic-1 were significantly upregulated in the PCa group compared with the normal group and the pancreatitis group ($p<0.05$). Mic-1 was also elevated in pancreatitis group compared with the normal group ($p<0.05$). Mic-1, miR-21, miR-25 and miR-155 also have better diagnostic value than other microRNAs when used as a diagnostic marker alone to distinguish PCa from normal control and pancreatitis.

To validate the expression and diagnostic value of miR-21, miR-25, miR-155 and Mic-1, we further validated them in plasma samples of 38 PCa patients, 4 acute or chronic pancreatitis patients and 39 normal controls. Similar results were obtained.

The expression of the miR-21, miR-25, miR-155 and Mic-1 were further measured in 30 colorectal cancer（CRC） patients, 30 gastric cancer(GC) patients and 30 liver cancer patients to identify their tissue specificity. The result showed that Mic-1, miR-25 and miR-21, but not miR-155, can not only distinguish PCa from normal control and pancreatitis but also from other digestive system cancers.

Thus we established a diagnostic panel including Mic-1, miR-25 and miR-21 to screen for pancreatic cancer.

The correlation of this panel with the clinical characteristics was analyzed. No significant correlation was found to the patients' gender, sex, family history of pancreatic cancer, smoking, alcohol consumption or and tumor size. With MiR-155, miR-196a and miR-210 it may be possible to distinguish pancreatic cancer patients staged Ⅰ/Ⅱ from those staged Ⅲ/Ⅳ. 56 of 64 PCa patients' survival month data were collected via an overall survival follow-up. The expression levels of all six

miRNAs and Mic-1 has no significant relationship to the survival rate of PCa patients.

We hope our selected biomarkers can be evaluated with US samples by Michael A. (Tony) Hollingsworth's group.

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Future plan:

1. Recruit more patients into validation group.
2. Conduct a double blind screening study in a group of patient samples with different diseases.
3. Validate the microRNA profile in US patients. Compare the results in two populations.
4. Compare the diagnostic value of microRNA with CA19.9 and CEA.
5. Validate biomarkers from EDRN in Chinese pancreatic cancer patients.

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