HIGHLIGHT ARTICLE

Biomarkers in Pancreatic Neuroendocrine Tumors

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Summary

The aim of biomarkers is to identify patients most likely to benefit from a therapeutic strategy. Pancreatic neuroendocrine tumors are rare neoplasms that arise in the endocrine tissues of the pancreas. Pancreatic neuroendocrine tumors represent 3% of primary pancreatic neoplasms and their incidence has risen. The *SMAD4* gene is located on chromosome 18q and someday the *SMAD4* gene status may be useful for prognostic stratification and therapeutic decision. The cells respond to environmental signals by modulating the expressions of genes contained within the nucleus, when genes are activated are transcribed to generate messenger RNA (mRNA). The examination of multiple expressed genes and proteins provides more useful information for prognostication of individual tumors. Here we summarize and discuss findings presented at the 2014 ASCO Gastrointestinal Cancers Symposium. Anna Karpathakis *et al*. (Abstract #212) reported data about the role of DNA methylation in gastrointestinal neuroendocrine tumors. Christina Lynn Roland *et al*. (Abstract #250) looked the impact Of *SMAD4* on oncologic outcomes. Bong Kynn Kang *et al*. (Abstract #251) investigated prognostic biomarker using microRNA array technology.

What We Knew Before the 2014 ASCO Gastrointestinal Cancers Symposium

Pancreatic tumors present many times with advanced disease and limited treatment effect. The most used biomarker is a neurosecretory peptide chromogranin A and is of limited value as a predictor of treatment efficacy. Gene expression profiling is very promising. Changes in biomarkers may be associated with disease progression and response to treatment [1, 2].

Pancreatic neuroendocrine tumor loss by immunohistochemistry and loss of PAX8 is associated to a worse survival. The predictive biomarkers are somatostatin receptors, mammalian target of rapamycin (mTOR) pathway molecule, thymidylate synthase, and activated p-Akt [3].

Key words Biological Markers; MicroRNAs, Neuroendocrine Tumors; Smad4 Protein

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What We Learned at the 2014 ASCO Gastrointestinal Cancers Symposium

Genome-Wide DNA Methylation Profiling of Gastrointestinal Neuroendocrine Tumors to Identify Hypermethylation of mTOR, Notch Pathways in GI NET Pathways (Abstract #212) [4].

Anna Karpathakis *et al*. made the first comprehensive analysis of the epigenetic profile and they identify that increasing *RASSF1* promoter hypermethylation was associated with higher tumor grade. They also identified methylation of multiple cancer related pathways (including the Wnt, mTOR and Notch pathways) as a feature of hepatic metastases.

Loss of SMAD4 and Effect on Overall Survival in Resected Gastrointestinal Neuroendocrine Tumors (Abstract #250) [5].

Christina Lynn Roland *et al*. investigated the role of SMAD4 expression and overall survival. It was classified in three categories (negative-low-high). Thirty-three tumors were examined and differences in *SMAD4* expression result in important differences in overall survival without statistically significant difference.

MicroRNA 27b as a Prognostic Marker in Pancreatic Neuroendocrine Tumors (Abstract #251) [6].

Bong Kynn Kang *et al*. used the microRNA array technology to elucidate prognostic biomarker and they found that microRNA 27b would be a prognostic marker of recurrence in resected pancreatic neuroendocrine tumors.

DISCUSSION

We reported some important abstracts presented at the 2014 ASCO Gastrointestinal Cancers Symposium. The molecular markers are very useful, but we need larger studies. All of the above suggests that sequencing might provide many therapeutic targets or involved pathways for prediction. We must access prognostic and predictive biomarkers. Novel biomarkers must be explored and there are data regarding the potential role. Studies utilizing proteomics and tissue arrays are useful to provide insight into tumor biology. Biomarkers must be discovered to be sensitive and specific. Another era is early diagnosis, as well as circulating cell tumors. Because of the nature of these tumors, well designed studies are needed and promising results of therapy targeting pathways (mTOR and Notch).

Conflict of interest The authors have no potential conflict of interest

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