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Mini Review

The Emerging Role of miRNA in Pancreatic Adenocarcinoma: Mechanisms, Diagnostics, and Therapeutic Potential

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Abstract

miRNAs were first identified in *Caenorhabditis elegans* in the early 1990s, but have since been reported in a wide variety of organisms ranging from single-cell algae to humans, suggesting that miRNA-mediated biological function is an ancient and critical cellular regulatory system and microRNAs (miRNAs) are small non-coding RNAs that are crucial regulators of carcinogenesis. The deregulation of miRNAs in prostate cancer was investigated. miRNA microarray profiling was performed in fresh frozen prostate cancer and matched normal adjacent tissues. Differentially expressed miRNAs were subsequently validated by real-time quantitative PCR (RT-qPCR). Fifteen miRNAs differentially regulated in prostate cancer in comparison with normal tissue. Expression of 5 miRNAs was correlated with the pathological stage and the Gleason score. MicroRNAs (miRNAs) are small noncoding RNAs (18-25 nucleotides) that regulate gene expression post-transcriptionally. MicroRNAs (miRNAs) are small non-coding, endogenous, single-stranded RNAs. MiRNAs have been implicated in different areas such as the immune response, neural development, DNA repair, apoptosis, oxidative stress response and cancer.

Keywords: *miRNA; Pancreatic Carcinoma; miRNA Signatures; Cancer*

Introduction

Cancer cells are characterized by self-sufficiency in growth signalling and resistance to anti-growth signals [1]. MiRNA-expression profiling of human tumours has identified signatures associated with diagnosis, staging, progression, prognosis and response to treatment. In addition, profiling has been exploited to identify miRNA genes that might represent downstream targets of activated oncogenic pathways, or that target protein coding genes involved in cancer [2]. Recent therapeutic strategies not only have focused on the regulation of miRNA function but also have tried to improve existing therapies. For example, glioma cells can be sensitized to treatment with 5-fluoroacyl if it is simultaneously delivered to cells with miR-21 [3]. Cancer initiation and progression can involve microRNAs (miRNA), which are small noncoding RNAs that can regulate gene expression. Their expression profiles can be used for the classification, diagnosis, and prognosis of human malignancies [2]. microRNAs (miRNAs) are evolutionarily conserved, endogenous, small, noncoding RNA molecules of about 22 nucleotides in length that function as posttranscriptional gene regulators. They are deemed to play a crucial role in the initiation and progression of human cancer, and those with a role in cancer are designated as oncogenic miRNAs (oncomiRs) [4].

miRNA signatures

miRNA expression profiling followed by differential expression analysis and target prediction suggested numerous miRNA signatures in AML and CML cell lines. Some miRNAs may act as either tumor suppressors or oncomiRs in AML and CML by targeting key genes in AML and CML pathways [5]. In fact, evidence that miRNAs represent new diagnostic and prognostic factors in human cancers is rapidly accumulating. In BCLL, a unique miRNA signature is associated with prognostic factors and with the time from diagnosis to initiation of therapy [6]. miRNA expression profiling is gaining popularity because miRNA signatures have been associated with the diagnosis and prognosis of diseases such as leukemias [7,8]. MicroRNAs are a class of small noncoding RNAs that are abnormally expressed in different cancer cells. Molecular signature of miRNAs in different malignancies suggests that these are not only actively involved in the pathogenesis of human cancer but also have a significant role in patient's survival [9-11]. One of the most unexpected and fascinating discoveries in oncology over the past few years is the interplay between abnormalities in protein-coding genes and noncoding RNAs (ncRNAs) that is causally involved in cancer initiation, progression, and dissemination10. MicroRNAs (miRNAs) are involved in cancer pathogenesis, apoptosis and cell growth, thereby functioning as either tumor suppressors or oncogenes [2,12]. MicroRNA expression profiles can be used to distinguish normal B cells from malignant B cells in patients with chronic lymphocytic leukemia (CLL). A unique microRNA signature is associated with prognostic factors and disease progression in CLL. Mutations in microRNA transcripts are common and may have functional importance [13].

miRNA and pancreatic cancer

A miRNA based treatment of pancreatic cancer thereafter appears to be an important alternative towards cancer therapy as miRNAs can be directed against pancreatic cancer through various pathways, including the inhibition of overexpressed oncogenes, suppressor of tumour growth and enhancement of apoptosis [14-16]. Meanwhile, in recent years, researchers in a growing number of studies have suggested that microRNAs (miRNAs) play an important role in the diagnosis and prognosis of pancreatic cancers [17-19]. miRNAs inhibit the transcription levels of mRNA, induce degradation of the regulation of gene expression [20] and have been proved to be involved in many disease processes. Therefore, the identification of miRNA changes might explain the pathology of CP in another way and provide a new method for diagnosing CP. A number of miRNAs that have been studied have a role in pancreatic diseases. By comparing pancreatic cancer tissue to CP tissue and normal pancreas, Bloomston and colleagues identified 21 miRNAs with increased expression and 4 with decreased expression, which suggests that the miRNAs likely play an important regulatory role in pancreatic cancer [15]. MiRNAs are tiny, endogenously expressed noncoding RNAs (18-25 nucleotides in length) that act as crucial posttranscriptional regulators of gene expression [21]. Plasma miRNAs are ideal biomarkers for PCa diagnosis. Plasma miR-16 and miR-196a are both early markers for PCa, which can effectively be used with serum CA19-9 for PCa screening in early tumor stage [22]. Micro (mi) RNAs are small non-protein-coding RNA (_22 nucleotides) molecules that negatively regulate gene expression at the posttranscriptional level [23]. As well as being potentially useful in pancreatic cancer diagnosis, miRNAs may also be of value in predicting patient outcome. Six miRNAs were differentially overexpressed in patients with long-term survival compared with those who died within 24 months of diagnosis [15]. Current diagnostic tools for pancreatic cysts fail to reliably differentiate mucinous from nonmucinous cysts. Reliable biomarkers are needed. MicroRNAs (miRNA) may offer insights into pancreatic cysts [24]. Biomarkers for the early diagnosis of patients with pancreatic cancer are needed to improve prognosis. The discovery cohort demonstrated that 38 microRNAs in whole blood were significantly dysregulated in patients with pancreatic cancer compared with controls [25]. Pancreatic cancer may have a distinct miRNA expression pattern that may differentiate it from normal pancreas and chronic pancreatitis. miRNA expression patterns may be able to distinguish between long- and short-term survivors, but these findings need to be validated in other study populations[15]. MicroRNAs are small RNAs regulating various cellular processes and have recently been identified as possible markers of malignant diseases including pancreatic ductal adenocarcinoma [26]. Pancreatic ductal adenocarcinomas show differential expression of miRNAs compared to benign pancreatic lesions. A select panel of miRNAs aids the distinction between pancreatic lesions in cytology specimens [27]. The diagnostic and prognostic value of microRNA (miRNA) expression aberrations in pancreatic ductal adenocarcinoma (PDAC) has been studied extensively in recent years. However, differences in measurement platforms and lab protocols as well as small sample sizes can render gene expression levels incomparable [28].

miRNA and its regulation

Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal disease and is usually resistant to chemotherapy. MicroRNA181b (miR-181b) has been reported to be associated with chemoresistance in various types of cancer [16]. Mature microRNAs (miRNA) are small 19-23 nt regulatory RNAs that control gene expression at the posttranscriptional level and whose mis-regulation has been linked to many human cancers, including pancreatic carcinomas [29]. A microRNA signature in molecularly defined, high-risk, cytogenetically normal AML is associated with the clinical outcome and with target genes encoding proteins involved in specific innate-immunity pathways [30]. The measurement of miRNAs in blood offers an option for the non-invasive detection of chronic pancreatitis or pancreatic cancer [14]. MicroRNAs (miRNAs) are 21-24 nucleotide RNA molecules that regulate the translation and stability of target messenger RNAs. Abnormal miRNA expression is a common feature of pancreatic ductal adenocarcinoma [31]. The identified miRNAs may be used to develop a panel of diagnostic and prognostic biomarkers for PDAC with sufficient sensitivity and specificity for use in a clinical setting. Genome-encoded microRNAs (miRNAs) provide a post-transcriptional regulatory layer that is important for pancreas development [30]. MicroRNAs (miRNAs) are 21-24 nucleotide RNA molecules that regulate the translation and stability of target messenger RNAs. Abnormal miRNA expression is a common feature of diverse cancers. Several previous studies have classified miRNA expression in pancreatic ductal adenocarcinoma (PDAC), although no uniform pattern of miRNA dysregulation has emerged[32]. MicroRNAs (miRNAs) are RNA molecules that are involved in the regulation of many cellular processes, including those related to human cancers. The specific candidate miRNAs could be detected in fine-needle aspirate (FNA) biopsies of pancreatic ductal adenocarcinoma (PDAC) and could accurately differentiate malignant from benign pancreatic tissues [33]. MicroRNAs (miRNAs), small RNA molecules of approximately 22 nucleotides, have been shown to be up- or downregulated in specific cell types and disease states. These molecules have become recognized as one of the major regulatory gatekeepers of coding genes in the human genome [11].

Conflict of Interests

The authors declared no conflict of interests.

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