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Prognostic significance of microRNA-141 expression and its tumor suppressor function in human pancreatic ductal adenocarcinoma

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Abstract Increasing evidence shows that dysregulation of microRNAs is correlated with tumor development. This study was performed to determine the expression of miR-141 and investigate its clinical significance in pancreatic ductal adenocarcinoma (PDAC). Taqman quantitative RT-PCR was used to detect miR-141 expressions in 94 PDAC tissues and 16 nontumorous pancreatic tissues. Correlations between miR-141 expression and clinicopathologic features and prognosis of patients were statistically analyzed. The effects of miR-141 expression on growth and apoptosis of PDAC cell line (PANC-1) were determined by MTT, colony formation, and flow cytometry assays. Potential target genes were identified by luciferase reporter and Western blot assays. The expression level of miR-141 in PDAC tissues was significantly lower than that in corresponding nontumorous tissues. Downregulation of miR-141 correlated with poorer pT and pN status, advanced clinical stage, and lymphatic invasion. Also, low miR-141 expression in PDAC tissues was significantly correlated with shorter overall survival, and multivariate analysis showed that miR-141 was an independent prognostic factor for PDAC patients. Further, functional researches suggested that miR-141 inhibits growth and colony formation, and enhances caspase-3-dependent apoptosis in PANC-1 cells by targeting Yes-associated protein-1 (YAP1). Therefore, miR-141 is an independent prognostic factor for PDAC patients, and functions as a tumor suppressor gene by targeting YAP1.

Keywords MicroRNA-141 · Pancreatic ductal adenocarcinoma · YAP1 · Prognosis

Introduction

Pancreatic cancer is one of the most aggressive human malignant tumors and a leading cause of cancer-related mortality around the world [1]. Of these, pancreatic ductal adenocarcinoma (PDAC) accounts for ~90 % of all the cases. Despite advances in surgery, chemotherapy, and other therapies, the overall survival of patients with PDAC is quite low [2]. Therefore, a better understanding of the biology of PDAC will be helpful for the identification of novel molecular markers to predict the prognosis of the patients.

Extensive researches have characterized the complex genetic networks and transcriptomics alterations underlying the progression of PDAC [3]. Recently, the discovery of a new class of microRNAs (miRNAs) has provided additional insights, potentially explaining the gap that exists between tumor genotype and phenotype [4, 5]. MiRNAs can downregulate gene expression by inducing the degradation or impairing the translation of target mRNAs. Increasing evidences have shown that miRNAs

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