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Long noncoding RNA EPIC1 interacts with YAP1 to regulate the cell cycle and promote the growth of pancreatic cancer cells

Peng Xia [a, b], Pan Liu [a, b], Qiang Fu [a], Chuanjiang Liu [a], Qiankun Luo [a], Xu Zhang [a], Liyou Cheng [a], Tao Qin [a], Hongwei Zhang [a, *]

[a] Department of Hepato-Biliary-Pancreatic Surgery, People's Hospital of Zhengzhou University, Henan Provincial People's Hospital, Zhengzhou, People's Republic of China

[b] Translational Research Institute Integrative Research Hub, Henan Provincial People's Hospital, Zhengzhou, People's Republic of China

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ABSTRACT

Pancreatic cancer (PC) is a fatal disease; most patients are asymptomatic before the disease enters the advanced stage, but molecular mechanisms of early PC that can be exploited for diagnosis are not clear. Long noncoding RNAs (lncRNAs) play key roles in the progression of PC. In this study, we found that the expression of the lncRNA EPIC1 (Lnc-EPIC1) is high in PC and closely related to tumor size, TNM staging and lymph node metastasis status. Silencing Lnc-EPIC1 by siRNA targeting could significantly inhibit the cell growth and colony formation ability of PC cells and induced G1/S cell cycle arrest and apoptosis in PC cells. Lnc-EPIC1-specific siRNAs could downregulate the expression of cyclins and CDKs, such as CDC20, CDK4 and Cyclin A1. Knocking out YAP1 with the CRISPR/Cas-9 gene editing method recapitulated the effects of the Lnc-EPIC1-specific siRNAs on cell growth, colony formation ability and apoptosis in PC cells. In addition, the Lnc-EPIC1-specific siRNAs did not further inhibit cell growth or promote apoptosis in YAP1-knockout (YAP1-KO) cells. RNA immunoprecipitation (RIP) results showed that there was a direct interaction between Lnc-EPIC1 and YAP1. An Lnc-EPIC1-overexpressing lentiviral vector promoted the growth of PC cells. The results show that Lnc-EPIC1 interacts with YAP1 to promote the progression of PC.

1. Introduction

The incidence and mortality of pancreatic cancer (PC) are increasing annually and PC is expected to be the second leading cause of cancer deaths in some countries [1,2]. The prognosis of PC patients ranked last among all cancer patients, with patients exhibiting a 5-year survival rate below 2%–9% [2]. The increase in incidence is more pronounced in developed countries than in developing countries, which may be associated with smoking and obesity [3,4]. Although progress has been made in surgical treatment with chemotherapy or radiotherapy, there has been no significant improvement in the survival rate of patients with PC [3,5]. The main reason for the low overall survival rate is the lack of an understanding of the complex molecular mechanisms involved in the progression of PC, including cell physiological changes, cell growth and apoptosis signaling dysfunction [6,7]. At present, there is no screening method for PC. It is very important for the prevention and treatment of PC to elucidate the biological and molecular mechanisms of initiation, occurrence and antiapoptotic signaling in PC [8].

Long noncoding RNAs (lncRNAs) are stable noncoding RNAs that have a length greater than 200 nucleotides and play important roles in promoting and suppressing cancer [9]. Increasingly in-depth study has found that various lncRNAs form a very large regulatory network and directly regulate various life processes at various levels, such as the epigenetic and pre-and post-transcriptional levels [10]. In the occurrence and development of tumors, lncRNAs can be used as a special target or marker. The lncRNA EPIC1 (ENSG00000224271, Lnc-EPIC1) is highly expressed in human PC cells [11]. Recently, the roles of Lnc-EPIC1 in lung cancer, cholangiocarcinoma and osteosarcoma have been proven, providing us with the theoretical basis of the function of Lnc-EPIC1 [12–14]. However, the carcinogenic role of Lnc-EPIC1 in PC is still unclear. In this study, we investigated for the first time how Lnc-

* Corresponding author. Department of Hepato-Biliary-Pancreatic Surgery, People's Hospital of Zhengzhou University, Henan Provincial People's Hospital, No. 7 Weiwu Road, Jinshui District, Zhengzhou, 450000, Henan, People's Republic of China.
E-mail address: hwzhang666@126.com (H. Zhang).

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