doi: 10.3978/j.issn.2095-6959.2021.10.003
View this article at: https://dx.doi.org/10.3978/j.issn.2095-6959.2021.10.003

长链非编码RNA CRNDE对胰腺癌细胞增殖、迁移及侵袭的影响

刘向梅，许达峰，王春玲，符于正，王丹，武金才

(海南省人民医院，海南医学院附属海南医院肝胆胰外科，海口 570000)

[摘　要]　**目的：**探讨胰腺癌细胞系中长链非编码RNA CRNDE(LncRNA CRNDE)的表达及对细胞增殖、迁移和侵袭的影响。**方法：**通过real-time RT-PCR检测LncRNA CRNDE在胰腺癌细胞系和正常胰腺导管上皮细胞系中的表达。将胰腺癌细胞系Panc-1分成3组，LncRNA CRNDE沉默表达组(si-CRNDE组)、阴性对照组(si-NC组)及空白对照组(Blank组)，对si-CRNDE组及si-NC组采用Lipofectamine™ 3000分别转染LncRNA CRNDE沉默序列(si-CRNDE)及阴性对照序列(si-NC)，Blank组仅给予缓冲盐溶液对照。采用real-time RT-PCR验证沉默效率，CCK-8实验测定细胞增殖能力，细胞划痕实验测定细胞迁移能力，Transwell实验测定细胞侵袭能力，蛋白质印迹实验测定c-Myc和磷酸化细胞外信号调节激酶(p-ERK)蛋白的表达。**结果：**胰腺癌细胞系Panc-1(P<0.01)、AsPC-1(P<0.01)、HPAC(P<0.05)、BxPC-3(P<0.05)中LncRNA CRNDE相对表达量高于HPDE6-C7细胞系。转染siRNA 48 h后，si-CRNDE组LncRNA CRNDE相对表达量低于si-NC组(P<0.01)。CCK-8实验示细胞铺板后在0、24、48 h，si-CRNDE组与si-NC组的$OD_{450\ nm}$值差异无统计学意义(P>0.05)，在72和96 h，二者差异有统计学意义(分别P<0.05和P<0.01)；Blank组与si-NC组差异无统计学意义(P>0.05)。细胞划痕实验结果示si-CRNDE组细胞划痕愈合率低于si-NC组[(26.3±2.8)% vs (52.1±3.7)%，P<0.05]。Transwell实验示si-CRNDE组侵袭细胞数少于si-NC组(108±15 vs 319±21，P<0.05)。蛋白质印迹结果示si-CRNDE组c-Myc蛋白质表达量低于si-NC组(0.47±0.04 vs 1.02±0.03，P<0.05)。si-CRNDE组p-ERK蛋白质表达量低于si-NC组(0.27±0.04 vs 1.04±0.05，P<0.01)。**结论：**LncRNA CRNDE在胰腺癌细胞系中高表达，沉默LncRNA CRNDE表达可抑制胰腺癌细胞的增殖、迁移和侵袭，机制可能与c-Myc、p-ERK蛋白下调表达有关。

[关键词]　长链非编码RNA CRNDE；胰腺癌；增殖；迁移；侵袭

Effects of long-chain non-coding RNA CRNDE on proliferation, migration and invasion of pancreatic cancer cells

LIU Xiangmei, XU Dafeng, WANG Chunling, FU Yuzheng, WANG Dan, WU Jincai

(Department of Hepatobiliary Pancreatic Surgery, Hainan Hospital Affiliated to Hainan Medical College, Hainan People's Hospital, Haikou 570000, China)

Abstract　**Objective:** To investigate the expression of long-chain non-coding RNA CRNDE (LncRNA CRNDE) in

收稿日期 (Date of reception)：2020–06–26

通信作者 (Corresponding author)：武金才，Email: jincaiwu73@sina.com

基金项目 (Foundation item)：海南省自然科学基金 (819QN356, Hnky2019-53)。This work was supported by the Natural Science Foundation of Hainan Province, China (819QN356, Hnky2019-53).

pancreatic cancer cell lines and its effect on cell proliferation, migration, and invasion. **Methods:** The expression of LncRNA CRNDE in pancreatic cancer cell lines and normal pancreatic duct epithelial cell lines was detected by real-time RT-PCR. PANC-1 cell line was divided into a LncRNA CRNDE silence expression group (Si-CRNDE group), a negative control group (Si-NC group) and a Blank control group (Blank group). In the Si-CRNDE group and Si-NC group, lipofectamine™ 3000 was used to transfect LncRNA CRNDE silence sequence (Si-CRNDE) and negative control sequence (Si-NC). The Blank group was only given buffer salt solution. Real-time RT-PCR was used to verify the silencing efficiency. CCK-8 was used to measure cell proliferation. Cell scratch assay was used to measure cell migration ability. Transwell assay was used to measure cell invasion ability. Western blotting was used to measure the expression of c-myc and p-ERK proteins expression. **Results:** The relative expression of LncRNA CRNDE in PANC-1 (P<0.01), AsPC-1 (P<0.01), HPAC (P<0.05), BXPC-3 (P<0.05) was higher than that in HPDE6-C7. After 48 hours of siRNA transfection, it was found that the relative expression of LncRNA CRNDE in Si-CRNDE group was lower than that in Si-NC group (P<0.01). The results of CCK-8 showed that at 0, 24, 48, 72 and 96 hours after the cell laying, the OD450 nm values of the Si-CRNDE group vs the Si-NC group were 0.33±0.04 vs 0.32±0.04 (P>0.05), 0.49±0.05 vs 0.52±0.06 (P>0.05), 0.72±0.07 vs 0.74±0.08 (P>0.05), 0.97±0.09 vs 1.28±0.10 (P<0.05), and 1.25±0.10 vs 1.97±0.14(P<0.01), respectively. There was no significant difference between the Blank group and the Si-NC group (P>0.05). The results of cell scratch test showed that the cell scratch healing rate of the Si-CRNDE group was lower than that of Si-NC group (26.3%±2.8% vs 52.1%±3.7%, P<0.05). The transwell experiment showed that the invasive cell number of si-CRNDE group was significantly less than that in the si-NC group (108±15 vs 319±21, P<0.05). Western blot showed that the expression of c-Myc protein in the Si-CRNDE group was lower than that in the Si-NC group (0.47±0.04 vs 1.02±0.03, P<0.05). The expression of p-ERK protein in Si-CRNDE group was lower than that in the Si-NC group (0.27±0.04 vs 1.04±0.05, P<0.01). **Conclusion:** LncRNA CRNDE is highly expressed in pancreatic cancer cell lines. Silencing the expression of LncRNA CRNDE can inhibit the proliferation, migration, and invasion of pancreatic cancer cells. The mechanism may be related to the down-regulation of c-Myc and p-ERK protein.

Keywords LncRNA CRNDE; pancreatic cancer; proliferation; migration; invasion

胰腺癌是一种高度致死性的恶性肿瘤，主要起源于胰腺导管上皮，具有高度侵袭性和易转移的特点[1]。胰腺癌预后较差，1年生存率为26%，5年生存率为8%[2]，在被明确诊断时往往已是中晚期。长链非编码RNA(long non-coding RNA，lncRNA)是一类在基因调控、细胞分化和发育等细胞生理过程中起重要作用的RNA分子，其并不能编码蛋白质分子[3]。lncRNA在癌症、神经系统疾病等疾病中表达失调，调控多种疾病的发生及病理变化过程[4]。LnRNA CRNDE是近年来发现的在细胞增殖、凋亡、侵袭等细胞生物学行为中起关键作用的lncRNA分子[5]。在结直肠癌[6]、胆囊癌[7]、非小细胞肺癌[8]等肿瘤中，lncRNA CRNDE表达水平较高，且参与促进癌细胞增殖、迁移、化疗耐药等生物学过程。然而，lncRNA CRNDE在胰腺癌中功能研究尚且不足。本研究旨在研究lncRNA CRNDE在胰腺癌细胞系中的表达及对增殖、迁移及侵袭的影响。

1 材料与方法

1.1 材料

正常胰腺导管上皮细胞系HPDE6-C7及胰腺癌细胞系Panc-1、AsPC-1、HPAC、BxPC-3均购自广州吉妮欧生物科技有限公司，Eagle细胞培养基购自武汉博士德生物科技有限公司，TRIzol RNA提取试剂盒、real-time RT-PCR试剂盒、Transwell小室及基质胶Matrigel购自美国Invitrogen公司，PCR扩增仪购自美国BD公司，细胞增殖检测试剂盒Cell Counting Kit-WST-8购自美国Abcam公司，c-Myc、磷酸化细胞外信号调节激酶(phosphorylated extracellular signal-regulated

kinase，p-ERK)及GAPDH一抗购自美国Cell Signaling公司，二抗羊抗兔及Lipofectamine™ 3000购自美国Invitrogen公司，蛋白质检测试剂盒购自武汉谷歌生物科技有限公司，LncRNA CRNDE沉默序列(si-CRNDE)及阴性对照序列(si-NC)均由广州锐博生物科技有限公司合成。

1.2 细胞培养和分组

所有细胞系，即正常胰腺导管上皮细胞系HPDE6-C7及胰腺癌细胞系Panc-1、AsPC-1、HPAC、BxPC-3均培养于37 ℃、5%的CO_2培养箱中，培养基为含10%胎牛血清的Eagle细胞培养基，细胞培养至对数期行传代培养，并分成3组，即LncRNA CRNDE沉默表达组(si-CRNDE组)、阴性对照组(si-NC组)及空白对照组(Blank组)。

1.3 细胞转染

对si-CRNDE组及si-NC组采用Lipofectamine™ 3000分别转染LncRNA CRNDE沉默序列(si-CRNDE)及阴性对照序列(si-NC)，转染序列如下：si-CRNDE正向引物为5'-GGGUAUUCCUGUUUAUAGATT-3'；反向引物为3'-UCUAUAAACAGGAAUACCCTT-3'；si-NC正向引物为5'-UGUGGUAGGAAAGAGAAAUGAAUGG-3'；反向引物为5'-CCAUUCAUUUCUCUUUCCUACCACA-3'。Blank组仅给与缓冲盐溶液。

1.4 Real-time RT-PCR测定LncRNA CRNDE的表达

si-CRNDE组、si-NC组及Blank组3组细胞系经培养至对数生长期后，采用TRIzol提取细胞总RNA后，采用反转录酶试剂盒反转录成cDNA，并行PCR扩增反应，以GAPDH为内参序列。引物序列如下：CRNDE正向引物为5'-AAATCAAAGTGCTCGAGTGGT-3'，反向引物为5'-ACCTTCTTCTGCGTGACAAC-3'；GADPH正向引物为5'-CTATAAATTGAGCCCGCAGCC-3'，反向引物为5'-GCGCCCAATACGACCAAATC-3'。相对表达量计算公式采用$2^{-\Delta\Delta Ct}$法计算。

1.5 CCK-8实验测定细胞增殖能力

对si-CRNDE组、si-NC组及Blank组细胞系接种于96孔板后，再经培养0、24、48、72及96 h，加入CCK-8试剂盒，然后在Bio-Rad酶标仪上测定吸光度$OD_{450\ nm}$，以时间为横坐标，OD450 nm值为纵坐标画细胞增殖曲线。

1.6 细胞划痕实验测定细胞迁移能力

将si-CRNDE组、si-NC组及Blank组细胞置于细胞培养皿经培养至融合后，用无菌注射枪在3组细胞中央画痕，待培养24 h后，观察细胞划痕愈合情况，计算愈合面积和愈合率。愈合率越高表示迁移能力越强。

1.7 Transwell实验测定细胞侵袭能力

将si-CRNDE组、si-NC组及Blank组细胞经培养后，以每组1×10^5细胞数量加入200 μL的培养基后置于24孔板的Transwell小室的上室，上室膜为8 μm孔径膜并用Matrigel预涂覆盖。经培养48 h后，观察细胞从上室穿入到下室的细胞数，经100%甲醇固定和结晶紫染色后，在10个视野下计算穿膜细胞数，取均值。

1.8 蛋白质印迹测定c-Myc和p-ERK蛋白的表达

采用蛋白质印迹法测定si-CRNDE组、si-NC组及Blank组c-Myc、p-ERK及GAPDH蛋白的表达。简单步骤如下：将si-CRNDE组、si-NC组及Blank组细胞提取总蛋白质后定量，经浓缩胶和分离胶电泳后，纤维素膜转膜，加入c-Myc(1:100)和p-ERK(1:100)一抗4 ℃孵育过夜，经漂洗后，加入二抗于37 ℃孵育2 h，漂洗后经显影液曝光，计算蛋白质灰度值和蛋白质相对表达量。

1.9 统计学处理

数据用均数±标准差($\bar{x}\pm s$)表示，多组间的比较采用单因素方差分析，在有意义的基础上再行两组间的比较，采用LSD-t检验，$P<0.05$为差异有统计学意义。

2 结果

2.1 LncRNA CRNDE在胰腺癌细胞系中高表达

Real-time RT-PCR示：LncRNA CRNDE在正常胰腺导管上皮细胞系HPDE6-C7中相对表达量为1.03±0.04，LncRNA CRNDE在胰腺癌细胞系Panc-1、AsPC-1、HPAC、BxPC-3中相对表达量分别为5.78±0.26、4.35±0.21、3.63±0.13及2.41±0.12，经方差检验，差异有统计学意义($F=13.762$，$P=0.024$)，胰腺癌细胞系Panc-1($P<0.01$)、AsPC-1($P<0.01$)、HPAC($P<0.05$)、BxPC-3($P<0.05$)中LncRNA CRNDE相对表达量高于HPDE6-C7细胞系(图1)。

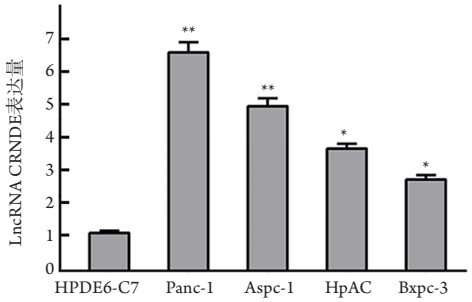

图1 LncRNA CRNDE在胰腺癌及正常胰腺导管上皮细胞系中的表达

Figure 1 Expression of LncRNA CRNDE in pancreatic carcinoma and normal pancreatic ductal epithelial cell lines

与HPDE6-C7比较，*P<0.05，**P<0.01。

Compared with HPDE6-C7, *P<0.05, **P<0.01.

2.2 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞增殖

转染siRNA 48 h后，用real-time RT-PCR验证沉默效率，发现si-CRNDE组中LncRNA CRNDE相对表达量为0.22±0.03，si-NC组为1.04±0.02，Blank组为1.03±0.04，经方差分析，差异有统计学意义(F=9.387，P=0.037)，si-CRNDE组LncRNA CRNDE相对表达量低于si-NC组(P<0.01，图2A)；CCK-8法测定细胞增殖，细胞铺板后在0、24、48 h，si-CRNDE组与si-NC组$OD_{450\ nm}$值比较差异均无统计学意义(P>0.05)，在72和96 h，二者差异均有统计学意义(分别P<0.05和P<0.01)；Blank组与si-NC组$OD_{450\ nm}$值差异无统计学意义(P>0.05，图2B)。

2.3 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞迁移

细胞划痕实验测定沉默LncRNA CRNDE表达后细胞迁移情况，示si-CRNDE组划痕愈合率为(26.3±2.8)%，si-NC组为(52.1±3.7)%，Blank组为(53.2±2.9)%，经方差分析，3组差异有统计学意义(F=16.387, P=0.017)，si-CRNDE组划痕愈合率低于si-NC组(P<0.05，图3)。

2.4 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞侵袭

Transwell实验测定沉默LncRNA CRNDE表达后细胞侵袭情况，100×视野下，si-CRNDE组侵袭细胞数为108±15个，si-NC组为319±21个，Blank组为325±27个，经方差分析，三组差异有统计学意义(F=37.287，P<0.001)，si-CRNDE组侵袭细胞数少于si-NC组(P<0.05，图4)。

2.5 沉默LncRNA CRNDE表达对c-Myc和p-ERK蛋白质表达的影响

si-NC组c-Myc蛋白质相对表达量为1.02±0.03，Blank组c-Myc蛋白质表达量为1.04±0.03，si-CRNDE组c-Myc蛋白质表达量为0.47±0.04，经方差分析，三组c-Myc蛋白质表达量差异有统计学意义(F=8.387，P=0.042)，si-CRNDE组c-Myc蛋白质表达量低于si-NC组(P<0.05)。

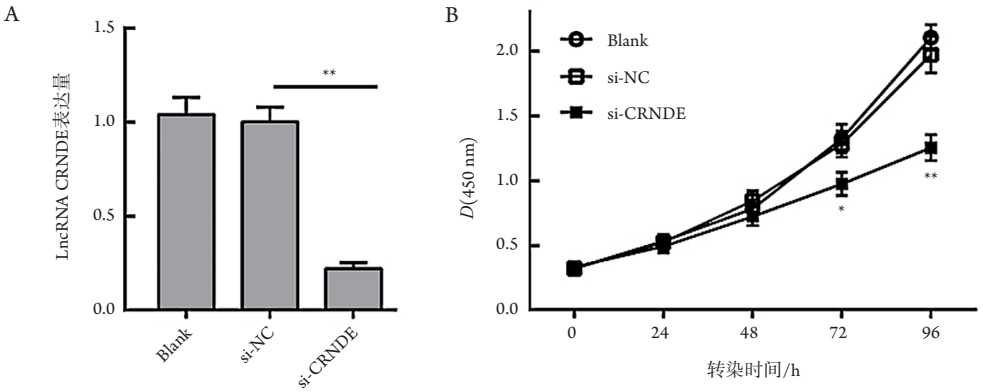

图2 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞增殖

Figure 2 Silencing LncRNA CRNDE expression inhibits the proliferation of PANC-1 cell line

(A)转染效率测定；(B)si-CRNDE组、si-NC组及Blank组细胞增殖曲线。与si-NC组比较，*P<0.05，**P<0.01。

(A) Determination of transfection efficiency; (B) the proliferation curve of the si-CRNDE group, the si-NC group, and the Blank group. Compared with the si-NC group, *P<0.05, **P<0.01.

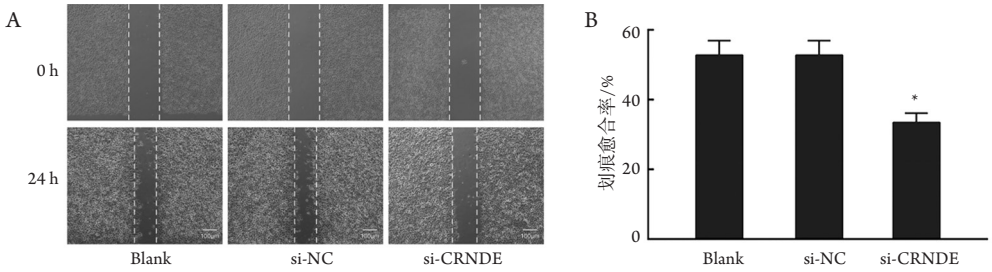

图3 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞迁移

Figure 3 Silencing LncRNA CRNDE expression inhibits cell migration of PANC-1 cell line

(A)细胞划痕实验；(B)划痕愈合率比较。与si-NC组比较，*P<0.05。

(A) Cell scratch test; (B) Comparison of wound healing rate. Compared with the si-NC group, *P<0.05.

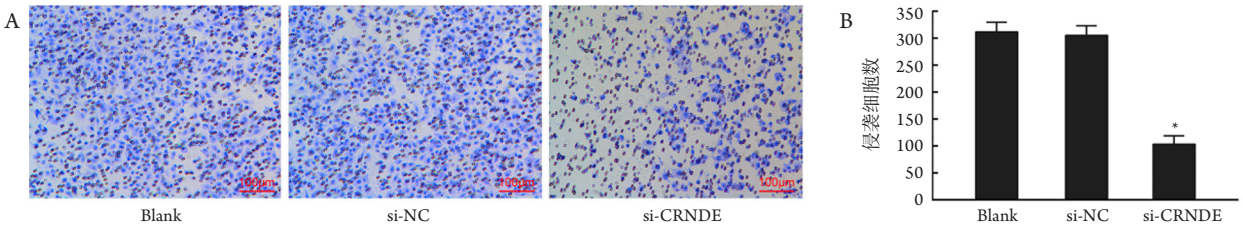

图4 沉默LncRNA CRNDE表达抑制Panc-1细胞系细胞侵袭

Figure 4 Silencing LncRNA CRNDE expression inhibits cell invasion in PANC-1 cell line

(A)Transwell图比较(结晶紫染色)；(B)侵袭细胞数比较。与si-NC组比较，*P<0.05。

(A) Transwell plot comparison (crystal violet staining); (B) Comparison of invasive cell number. Compared with the si-NC group, *P<0.05.

si-NC组p-ERK蛋白质相对表达量为1.04±0.05，Blank组p-ERK蛋白质表达量为1.02±0.05，si-CRNDE组p-ERK蛋白质表达量为0.27±0.04，经方差分析，3组p-ERK蛋白质表达量差异有统计学意义(F=16.413，P=0.027)，si-CRNDE组p-ERK蛋白质表达量低于si-NC组(P<0.01，图5)。

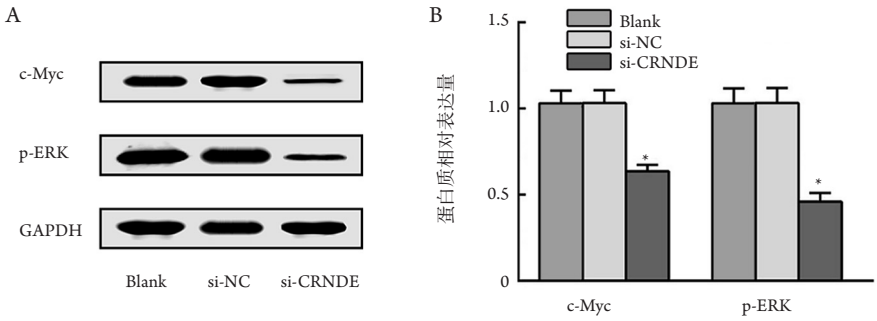

图5 沉默LncRNA CRNDE表达对c-Myc和p-ERK蛋白质表达的影响

Figure 5 Effects of silencing LncRNA CRNDE expression on c-Myc and p-ERK protein expression

(A)蛋白质印迹法示si-CRNDE组、si-NC组及Blank组c-Myc和p-ERK蛋白质表达；(B)si-CRNDE组、si-NC组及Blank组c-Myc和p-ERK蛋白质相对表达量比较。与si-NC组比较，*P<0.05。

(A) Western blotting showed c-Myc and p-ERK protein expression in the si-CRNDE group, the si-NC group and the Blank group; (B) Comparison of c-Myc and p-ERK protein relative expression levels among the si-CRNDE group, si-NC group and Blank group. Compared with the si-NC group, *P<0.05.

3 讨论

研究[9]发现，胰腺癌的发病机制与基因突变、抑癌基因表达下调和促癌基因被激活相关。LncRNAs是一类转录本长度超过200 nt的RNA分子，不具有开放阅读框等多种mRNA所具有的特征[10]。LncRNA CRNDE在调控基因表达、转录后修饰、表观遗传学等方面引起人们的高度关注，被证实作为抑癌或促癌基因在肿瘤细胞增殖、转移和侵袭等方面起重要作用[11]。Han等[6]采用real-time RT-PCR技术对64例结肠癌患者肿瘤组织和癌旁组织分析lncRNA CRNDE表达，发现lncRNA CRNDE在结肠癌组织中高表达，且可通过调控miR-181a-5p介导的Wnt/β-catenin信号途径促进肿瘤细胞增殖和化疗耐药性。相比正常肝组织和细胞系，lncRNA CRNDE在肝癌组织和细胞系中表达较高，并可通过抑制miR-384促进肝癌细胞增殖、迁移和侵袭[5]。在神经胶质瘤中，lncRNA CRNDE同样呈高表达，参与调控mTOR信号途径并诱导肿瘤细胞生长和转移[12]。在肝内胆管癌细胞系[13]中，LncRNA CRNDE呈上调表达，且LncRNA CRNDE高表达与分化程度、淋巴结转移、TNM分期、肿瘤大小及预后不佳等恶性生物学特征相关，LncRNA CRNDE高表达可促进细胞增殖，并通过促进上皮间质转化促进细胞迁移和侵袭。在皮肤黑色素瘤[14]中，LncRNA CRNDE可促进细胞迁移和侵袭。

本研究分析了lncRNA CRNDE在四种胰腺癌细胞系和正常胰腺导管上皮细胞中的表达，发现lncRNA CRNDE在4种胰腺癌细胞系中均呈高表达状态，而在正常胰腺导管上皮细胞系中表达较低。通过转染技术，在胰腺癌细胞系Panc-1中沉默lncRNA CRNDE表达，发现Panc-1细胞增殖、迁移及侵袭能力显著抑制，提示沉默lncRNA CRNDE的表达可起抑癌的作用，lncRNA CRNDE在胰腺癌中扮演着促癌基因的角色。这与LncRNA CRNDE在其他肿瘤[5,12-13]中所扮演的作用类似。

转录因子家族myc成员c-myc过度表达与人类70%的癌症发生发展高度相关，包括胰腺癌[15]。为研究lncRNA CRNDE沉默是否影响c-myc表达水平，本研究采用蛋白质印迹法测定si-CRNDE组、si-NC组及Blank组中c-myc蛋白质表达，结果显示lncRNA CRNDE沉默表达显著下调c-myc蛋白质表达水平。c-myc作为一种重要的转录调控因子，具有核定位序列、DNA结合域、螺旋-环-螺旋二聚结构域、转录调控域，在多种生理学过程中扮演重要角色，包括蛋白质合成、细胞黏附、细胞存活、细胞周期调控等[16]。肿瘤细胞无限制增殖与细胞周期失调有关，而细胞周期受细胞周期复合体调控。研究[17]发现：c-myc通过绑定E-box促进调控细胞周期进程的关键因子细胞周期素D2转录，并抑制细胞周期蛋白质依赖性激酶抑制剂p21和p27的表达。c-myc可直接激活细胞周期素E的表达，而细胞周期素E高表达对细胞周期S期有关键促进作用，而且与肿瘤患者预后不良有一定关联[18]。此外，细胞分裂周期素25A(cell division cycle 25 homolog A，CDC25A)被证实为c-myc的直接靶点，CDC25A能产生刺激细胞周期素依赖性激酶2(cyclin-dependent kinase 2，CDK2)、细胞周期素依赖性激酶4(cyclin-dependent kinase 4，CDK4)激活的磷酸酶[19]。在本研究中，lncRNA CRNDE表达下调抑制c-myc蛋白质表达，可能直接或间接影响到与细胞周期过程相关的调控因子的表达，阻碍细胞周期进程，因而抑制胰腺癌细胞增殖。另有研究[20]发现：c-myc对靶基因的调控影响到肿瘤细胞迁移。我们推测，lncRNA CRNDE敲低后，可能通过调控c-myc影响细胞迁移相关基因的表达，进而参与抑制胰腺癌细胞迁移，但是哪些细胞迁移相关基因与c-myc相关还有待进一步挖掘。

促分裂原活化蛋白质激酶(mitogen-activated protein kinase，MAPK)/ERK信号途径是也是诱导细胞周期信号转导、细胞增殖和分化的关键途径[21]。本研究[22]发现MAPK途径的组成分子p-ERK表达水平受lncRNA CRNDE基因沉默影响而表达下调。p-ERK也是细胞骨架调节效应受体，能够促进上皮间质转化，进而促进肿瘤细胞迁移和侵袭。Wu等[23]指出肺腺癌合并肺腺癌转录1(metastasis associated lung adenocarcinoma transcript 1，MALAT1)通过激活ERK/MAPK信号通路促进胆囊癌细胞增殖和转移。在此，本研究认为lncRNA CRNDE沉默抑制p-ERK表达下调，可能也是通过调控细胞周期进程，同时抑制上皮间质转化而抑制胰腺癌细胞增殖、迁移及侵袭能力。

虽然lncRNA CRNDE在调控胰腺癌细胞增殖、迁移及侵袭能力中发挥了重要作用，但本研究中western blot实验尚不能说明lncRNA CRNDE与c-myc和p-ERK之间的相互作用是直接还是间接，未来我们将对lncRNA CRNDE调控c-myc和p-ERK的作用机制，及与细胞周期进程、迁移及侵袭有关的分子机制进一步探索。

综上，本研究发现lncRNA CRNDE沉默表达可抑制胰腺癌细胞增殖、迁移和侵袭，其机制可能与c-myc和p-ERK表达下调有关，该基因在胰腺癌

中调控网络的初步揭示对于未来寻求更为有效的治疗方法提供了一定的理论基础。

参考文献

1. Tsujita E, Ikeda Y, Kinjo N, et al. Postoperative neutrophil-to-lymphocyte ratio as a predictor of long-term prognosis after pancreatectomy for pancreatic carcinoma: a retrospective analysis[J]. Am Surg, 2017, 83(6): 610-616.
2. 杨永超, 李宜雄. 胰腺癌外科治疗的历史和现状[J]. 中国普通外科杂志, 2018, 27(3): 269-283.
   YANG Yongchao, LI Yixiong. The surgical treatment of pancreatic cancer: history and present state[J]. Chinese Journal General Surgery, 2018, 27(3): 269-283.
3. Bhan A, Mandal SS. LncRNA HOTAIR: A master regulator of chromatin dynamics and cancer[J]. Biochim Biophys Acta, 2015, 1856(1): 151-164.
4. Ayana R, Singh S, Pati S. Decoding crucial LncRNAs implicated in neurogenesis and neurological disorders[J]. Stem cells Dev, 2017, 26(8): 541-553.
5. Chen Z, Yu C, Zhan L, et al. LncRNA CRNDE promotes hepatic carcinoma cell proliferation, migration and invasion by suppressing miR-384[J]. Am J Cancer Res, 2016, 6(10): 2299-2309.
6. Han P, Li JW, Zhang BM, et al. The lncRNA CRNDE promotes colorectal cancer cell proliferation and chemoresistance via miR-181a-5p-mediated regulation of Wnt/β-catenin signaling[J]. Mol Cancer, 2017, 16(1): 9.
7. Shen S, Liu H, Wang Y, et al. Long non-coding RNA CRNDE promotes gallbladder carcinoma carcinogenesis and as a scaffold of DMBT1 and C-IAP1 complexes to activating PI3K-AKT pathway[J]. Oncotarget, 2016, 7(45): 72833-72844.
8. Liu XX, Xiong HP, Huang JS, et al. Highly expressed long non-coding RNA CRNDE promotes cell proliferation through PI3K/AKT signalling in non-small cell lung carcinoma[J]. Clin Exp Pharmacol Physiol, 2017, 44(8): 895-902.
9. Kamisawa T, Wood LD, Itoi T, et al. Pancreatic cancer[J]. Lancet, 2016, 388(10039): 73-85.
10. Hu G, Niu F, Humburg BA, et al. Molecular mechanisms of long noncoding RNAs and their role in disease pathogenesis[J]. Oncotarget, 2018, 9(26): 18648-18663.
11. Yang G, Lu X, Yuan L. LncRNA: a link between RNA and cancer[J]. Biochim Biophys Acta, 2014, 1839(11): 1097-1109.
12. Wang Y, Wang Y, Li J, et al. CRNDE, a long-noncoding RNA, promotes glioma cell growth and invasion through mTOR signaling[J]. Cancer Lett, 2015, 367(2): 122-128.
13. Xia XL, Xue D, Xiang TH, et al. Overexpression of long non-coding RNA CRNDE facilitates epithelial-mesenchymal transition and correlates with poor prognosis in intrahepatic cholangiocarcinoma[J]. Oncol Lett, 2018, 15(4): 4105-4112.
14. Xu L, Zhang Y, Zhao Z, et al. The long non-coding RNA CRNDE competed endogenously with miR-205 to promote proliferation and metastasis of melanoma cells by targeting CCL18[J]. Cell Cycle, 2018, 17(18): 2296-2308.
15. Chen BJ, Wu YL, Tanaka Y, et al. Small molecules targeting c-Myc oncogene: promising anti-cancer therapeutics[J]. Int J Biol Sci, 2014, 10(10): 1084-1096.
16. Stine ZE, Walton ZE, Altman BJ, et al. MYC, Metabolism, and Cancer[J]. Cancer Discov, 2015, 5(10): 1024-39.
17. Gordan JD, Thompson CB, Simon MC. HIF and c-Myc: sibling rivals for control of cancer cell metabolism and proliferation[J]. Cancer Cell, 2007, 12(2): 108-113.
18. Tu K, Zheng X, Zhou Z, et al. Recombinant human adenovirus-p53 injection induced apoptosis in hepatocellular carcinoma cell lines mediated by p53-Fbxw7 pathway, which controls c-Myc and cyclin E[J]. PLoS One, 2020, 15(3): e0231287.
19. Unger C, Popescu R, Giessrigl B, et al. An apolar extract of Critonia morifolia inhibits c-Myc, cyclin D1, Cdc25A, Cdc25B, Cdc25C and Akt and induces apoptosis[J]. Int J Oncol, 2012, 40(6): 2131-2139.
20. Zhou W, Feng X, Ren C, et al. Over-expression of BCAT1, a c-Myc target gene, induces cell proliferation, migration and invasion in nasopharyngeal carcinoma[J]. Mol Cancer, 2013, 12(1): 53.
21. Sun Y, Liu WZ, Liu T, et al. Signaling pathway of MAPK/ERK in cell proliferation, differentiation, migration, senescence and apoptosis[J]. J Recept Signal Transduct Res, 2015, 35(6): 600-604.
22. Li W, Cao L, Han L, et al. Superoxide dismutase promotes the epithelial-mesenchymal transition of pancreatic cancer cells via activation of the H2O2/ERK/NF-κB axis[J]. Int J Oncol, 2015, 46(6): 2613-2620.
23. Wu XS, Wang XA, Wu WG, et al. MALAT1 promotes the proliferation and metastasis of gallbladder cancer cells by activating the ERK/MAPK pathway[J]. Cancer Biol Ther, 2014, 15(6): 806-814.

本文引用： 刘向梅, 许达峰, 王春玲, 符于正, 王丹, 武金才. 长链非编码RNA CRNDE对胰腺癌细胞增殖、迁移及侵袭的影响[J]. 临床与病理杂志, 2021, 41(10): 2239-2245. doi: 10.3978/j.issn.2095-6959.2021.10.003

Cite this article as: LIU Xiangmei, XU Dafeng, WANG Chunling, FU Yuzheng, WANG Dan, WU Jincai. Effects of long-chain non-coding RNA CRNDE on proliferation, migration and invasion of pancreatic cancer cells[J]. Journal of Clinical and Pathological Research, 2021, 41(10): 2239-2245. doi: 10.3978/j.issn.2095-6959.2021.10.003