·论 著·

CBX3在肺腺癌中的表达、预后相关性及对癌细胞生物学行为的影响

侯清华[1, 2]，钟燕凤[3]，刘林壮[2]，吴柳盛[2]，刘继先[2]

1. 潍坊医学院临床医学院，山东 潍坊 261053；
2. 北京大学深圳医院胸外科，广东 深圳 518036；
3. 北京大学深圳医院中心实验室，广东 深圳 518036

［摘要］ **背景与目的：**作为异染色质重要组分的染色体盒3（chromobox 3，CBX3）参与多种癌症的发生、发展过程，而*CBX*3基因在肺腺癌中的表达情况和作用尚不清楚。探讨CBX3在肺腺癌中的表达与肺腺癌患者预后的关系，并研究CBX3对A549肺腺癌细胞增殖、迁移和侵袭能力的影响。**方法：**下载癌症基因组图谱（The Cancer Genome Atlas，TCGA）中的肺腺癌转录组数据和对应的临床数据，应用R软件分析CBX3在肺腺癌中的表达差异和免疫浸润相关性，采用受试者工作特征（receiver operating characteristic，ROC）曲线和Kaplan-Meier分析CBX3在肺腺癌中的预后意义；收集北京大学深圳医院智能化生物样本库-80 ℃新鲜冻存的2020年8月—2021年1月行肺癌姑息性切除术或根治性切除术的肺腺癌样本20例（已获得知情同意），采用实时荧光定量聚合酶链反应（real-time fluorescent quantitative polymerase chain reaction，RTFQ-PCR）检测20例冻存的肺腺癌组织及配对正常肺组织中CBX3的表达；应用小干扰RNA（siRNA）转染A549细胞以沉默CBX3的表达，并根据siRNA转染的类型将A549细胞分为沉默组（si-CBX3组）和阴性对照组（si-NC组），通过用细胞计数试剂盒（cell counting kit-8，CCK-8）实验、克隆形成实验、划痕实验和transwell实验分别研究CBX3对A549肺腺癌细胞增殖、迁移和侵袭能力的影响。**结果：**基于TCGA肺腺癌数据的差异分析与采集的肺腺样本RTFQ-PCR实验的结果显示，CBX3在肺腺癌中呈显著的高表达，差异有统计学意义（$P<0.05$）；辅助型T细胞2的浸润与CBX3表达呈正相关，相关系数（r）＝0.437，而肥大细胞（$r=-0.444$）、嗜酸性粒细胞（$r=-0.380$）等免疫细胞与CBX3表达呈负相关；ROC曲线下面积（area under curve，AUC）值为0.912，表明CBX3对肺腺癌具有很好的诊断价值，Kaplan-Meier分析结果显示，CBX3高表达组生存期更短，提示预后较差；沉默CBX3在A549细胞中的表达后，CCK-8实验和克隆形成实验结果表明，A549细胞的增殖能力显著降低（$P<0.01$）；划痕实验结果表明沉默后的A549细胞的迁移率为（22.68±3.44）%，较阴性对照组迁移能力明显降低（$P<0.05$）；Transwell实验结果表明A549细胞的相对侵袭率为（53.94±5.39）%，侵袭能力显著降低（$P<0.01$）。**结论：**CBX3在肺腺癌中显著高表达并提示肺腺癌预后不良，可作为肺腺癌的预后标志物，且CBX3的高表达促进了A549细胞的增殖、迁移和侵袭能力。

［关键词］ CBX3；肺腺癌；免疫浸润；预后；细胞功能实验

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Expression, prognostic value of CBX3 in lung adenocarcinoma and its effect on biological behavior of cancer cells

HOU Qinghua[1, 2], ZHONG Yanfeng[3], LIU Linzhuang[2], WU Liusheng[2], LIU Jixian[2] (1. School of Clinical Medicine, Weifang Medical College, Weifang 261053, Shandong Province, China; 2. Department of Thoracic Surgery, Shenzhen Hospital, Peking University, Shenzhen 518036, Guangdong Province, China; 3. Central Laboratory of Shenzhen Hospital, Peking University, Shenzhen 518036, Guangdong Province, China)

Correspondence to: LIU Jixian E-mail: 252110465@qq.com

［**Abstract**］ **Background and purpose:** Chromobox 3 (CBX3), an important component of chromatin, is involved in the development and progression of various cancers. However, the expression and role of CBX3 in lung adenocarcinoma are still unclear. This study aimed to investigate the relationship between the expression of CBX3 in lung adenocarcinoma and prognosis of lung

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通信作者：刘继先 E-mail: 252110465@qq.com

adenocarcinoma, and to study the effects of CBX3 on proliferation, migration and invasion of A549 lung adenocarcinoma cells. **Methods:** Transcriptome data of lung adenocarcinoma and corresponding clinical data were downloaded from the Cancer Genome Atlas (TCGA), and R software was used to analyze the expression difference of CBX3 and the correlation of immune infiltration in lung adenocarcinoma. The prognostic significance of CBX3 in lung adenocarcinoma was analyzed by receiver operating characteristic (ROC) curve and Kaplan-Meier analysis. Twenty lung adenocarcinoma samples from patients (with informed consent obtained) who underwent palliative or radical lung cancer resection from August 2020 to January 2021 were collected from the intelligent Biobank of Peking University Shenzhen Hospital at −80 ℃. Real-time fluorescent quantitative polymerase chain reaction (RTFQ-PCR) was used to verify the expression of CBX3 in 20 frozen lung adenocarcinoma tissue samples and paired normal lung tissues. A549 cells were transfected with small interfering RNA (siRNA) to silence the expression of CBX3, and A549 cells were divided into silent group (si-CBX3 group) and negative control group (si-NC group) according to the type of siRNA transfection. The effects of CBX3 on proliferation, migration and invasion of A549 cells were investigated by cell counting kit-8 (CCK-8) assay, clone formation assay, scratch assay and transwell assay, respectively. **Results:** The difference analysis based on TCGA lung adenocarcinoma data and RTFQ-PCR results of lung adenocarcinoma samples showed that CBX3 was significantly overexpressed in lung adenocarcinoma (P <0.05). The infiltration of T helper 2 (Th2) cells was positively correlated with the expression of CBX3 [correlation coefficient (r)=0.437], while mast cells (r=−0.444), eosinophils (r=−0.380) and other immune cells were negatively correlated with the expression of CBX3. The area under ROC curve (AUC) value was 0.912, indicating that CBX3 has a good diagnostic value for lung adenocarcinoma. Kaplan-Meier analysis showed that the survival period of the group with high expression of CBX3 was shorter, suggesting a poor prognosis. After the expression of CBX3 was silenced in A549 cells, significantly decreased proliferation ability of A549 cells was detected by CCK-8 and clone formation assays (P<0.01). The results of scratch assay showed that the mobility of A549 cells was (22.68±3.44)% after silencing, which was significantly lower compared with the control group (P<0.05). Transwell assay results showed that the relative invasion rate of A549 cells was (53.94±5.39)%, and the invasion ability was significantly decreased (P<0.01). **Conclusion:** CBX3 is significantly overexpressed in lung adenocarcinoma, which predicts poor prognosis of lung adenocarcinoma and can be used as a prognostic marker of lung adenocarcinoma, and the high expression of CBX3 promotes the proliferation, migration and invasion of A549 cells.

[**Keywords**] CBX3; Lung adenocarcinoma; Immune infiltration; Prognosis; Cell function experiment

根据2020年公布的数据显示，肺癌是全球最致命和第二常见的癌症[1]，肺癌根据细胞学类型分为小细胞肺癌和非小细胞肺癌，非小细胞肺癌最常见的亚型是肺腺癌[2]。肺腺癌患者早期缺乏肿瘤特异性临床症状，中晚期肺癌发生局部浸润甚至远处转移，疗效较差，5年总生存率不足20%[3]。靶向治疗和免疫治疗为肺腺癌治疗的主要方法之一，虽然目前均取得了良好的临床疗效[4-6]，但临床上受益人群仍有限[7-8]。染色体盒3（chromobox 3，CBX3）基因编码的蛋白是异染色质蛋白1（heterochromatin protein 1，HP1）家族中的一员，参与癌细胞的多种信号转导通路，在许多恶性肿瘤中发挥着重要的调控作用[9]，其被认为在转录激活或抑制、表观遗传修饰和细胞生长与分化中发挥重要作用[10]。本研究探讨CBX3在肺腺癌中的表达、作用并分析与免疫细胞浸润的关系，研究其表达水平对A549肺腺癌细胞生物学行为的影响，判断其作为肺腺癌诊断和治疗靶点的可行性。

1 材料和方法

1.1 材料

1.1.1 数据来源

数据来自肿瘤基因组图谱数据库（The Cancer Genome Atlas，TCGA），去除重复和不含临床信息的样本后包含513例肺腺癌样本和59例正常样本。

1.1.2 标本来源

收集北京大学深圳医院智能化生物样本库-80 ℃新鲜冻存的2020年8月—2021年1月行肺癌姑息性切除术或根治性切除术的肺腺癌样本20例（已获得知情同意），其中男性8例，女性12例，年龄（61.3±10.9）岁，每例样本都包含对应的正常肺组织。肺腺癌细胞系A549由北京大学深圳医院中心实验室提供。

1.1.3 试剂材料

胎牛血清（fetal bovine serum，FBS）购自美国Gibco公司，Opti-MEM减血清培养液、Lipofectamin™2000转染试剂和TRIzol提试剂均购自美国Invitrogen公司，实时荧光定量聚合酶链反应（real-time fluorescent quantitative polymerase chain reaction，RTFQ-PCR）所用的试剂盒ReverTra Ace qPCR RT Kit和SYBR Green Realtime PCR Master Mix购自东洋纺（上海）生物科技有限公司，96孔PCR板购自荷兰BIOplastics公司，磷酸盐缓冲生理盐水（phosphate-buffered saline，PBS）、DMEM培养基和4%多聚甲醛（paraformaldehyde，PFA）固定液购自国药集团化学试剂公司，细胞计数试剂盒（cell counting kit-8，CCK-8）购自北京索莱宝科技有限公司，结晶紫购自上海碧云天生物技术有限公司，*CBX3*基因引物以及特异性针对*CBX3*基因的小干扰RNA（si-CBX3）及其阴性对照（si-NC）由武汉金开瑞生物工程有限公司设计并合成。

1.2 方法

1.2.1 数据处理与分析

应用R软件对下载的TCGA数据库肺腺癌转录组数据和相应的临床病理学数据进行处理，评估不同分组之间不同临床变量的构成比差异，不同分组中缺失临床变量数据未在列联表中进行展示（表1）。应用“DESeq2”[11]软件包分析*CBX*3基因在肺腺癌与正常肺组织间的表达差异情况。使用R包“GSVA”[12]中的ssGSEA算法富集24种常见的免疫细胞类型[13]，并采用Spearman检验探究*CBX3*高表达与免疫细胞浸润的关系。采用受试者工作特征（receiver operating characteristic，ROC）曲线分析*CBX3*基因在肺腺癌诊断中的价值。采用Kaplan-Meier分析其预后价值。

1.2.2 RTFQ-PCR验证CBX3在肺腺癌中的表达差异

使用TRIzol从肺腺癌组织和配对的正常组织中研磨提取RNA，NanoDrop 2000c测定RNA浓度，保留吸光度（*D*）值$D_{260\ nm}/D_{280\ nm}$比值为1.9～2.1的RNA样品。采用ReverTra Ace qPCR RT试剂盒进行反转录，采用SYBR Green Realtime PCR Master Mix和RTFQ-PCR仪（罗氏LightCycler 480）进行相对定量分析。*CBX3*有义链为5’-AGAGATGCTGCTGACAAACCAAG-3’，反义链为5’-GGACACTTCATATTTGCCTCTTTCG-3’。*β-actin*有义链为5’-TGGACTTCGAGCAAGAGATG-3’，反义链为5’-GAAGGAAGGCTGGAAGAGTG-3’。反应条件：95 ℃ 1 min，95℃ 15 s，60 ℃ 30 s，循环40次，数据结果采用$2^{-\triangle\triangle CT}$法进行分析。

1.2.3 A549细胞培养与转染

使用含10%FBS及1%青霉素、链霉素双抗的DMEM培养液，将A549细胞置于37 ℃、CO_2体积分数为5%的培养箱中培养，处于对数生长期后，通过Lipofectamine™2000分别将si-CBX3和si-NC转入A549细胞中，分为si-CBX3组和si-NC组。细胞板置于37 ℃、CO_2体积分数为5%的培养箱，转染4～6 h后更换新鲜双抗培养基，在培养箱中培养48～72 h。si-CBX3有义链为5’-UCAGAAAGCUGGCAAAGAATT-3’，反义链为5’-UUCUUUGCCAGCUUUCUGATT-3’；si-NC有义链为5’-UUCUCCGAACGUGUCACGUTT-3’，反义链为5’-ACGUGACACGUUCGGAGAATT-3’。转染完成后采用RTFQ-PCR检测siRNA沉默效率，取转染后的细胞，通过TRIzol分别提取si-CBX3组和si-NC组的RNA，反转录、RTFQ-PCR操作和数据处理同方法1.2.2。

1.2.4 CCK-8分析

将si-CBX3组和si-NC组的细胞胰酶消化后计数，接种1 000个细胞至96孔板，将培养板置37 ℃、CO_2体积分数为5%培养箱中培养0、24、48和72 h，每孔加入10 μL CCK-8溶液后在细胞培养箱内继续温育0.5 h，用酶标仪在450 nm测定*D*值。

1.2.5 克隆形成实验

取对数生长期的单层培养细胞制备单细胞悬液，每皿接种500个细胞，置于37 ℃、CO_2体积分数为5%培养箱中，静置培养2～3周，当培养皿中出现肉眼可见的克隆时终止培养并应用4%PFA固定，加适量结晶紫染色液染色，空气干燥后Image J分析染色面积。

表 1 CBX3表达差异的肺腺癌患者临床病理学特征分析

Tab. 1 Clinicopathological features of lung adenocarcinoma with differential expression of CBX3

Characteristic*	Low expression of CBX3	High expression of CBX3	*P* value
T stage *n* (%)			0.031
T_1	97 (19.0)	71 (13.9)	
T_2	126 (24.7)	150 (29.4)	
T_3	25 (4.9)	22 (4.3)	
T_4	6 (1.2)	13 (2.5)	
N stage *n* (%)			0.005
N_0	179 (35.7)	151 (30.1)	
N_1	42 (8.4)	53 (10.6)	
N_2	26 (5.2)	48 (9.6)	
N_3	0 (0.0)	2 (0.4)	
M stage *n* (%)			0.342
M_0	165 (44.7)	179 (48.5)	
M_1	9 (2.4)	16 (4.3)	
Pathologic stage *n* (%)			0.102
Ⅰ	148 (29.3)	126 (25.0)	
Ⅱ	60 (11.9)	61 (12.1)	
Ⅲ	34 (6.7)	50 (9.9)	
Ⅳ	10 (2.0)	16 (3.2)	
Gender *n* (%)			0.504
Female	142 (27.7)	134 (26.1)	
Male	114 (22.2)	123 (24.0)	
Age/year *n* (%)			0.024
≤65	105 (21.3)	133 (26.9)	
>65	140 (28.3)	116 (23.5)	
Smoker *n* (%)			0.368
No	41 (8.2)	33 (6.6)	
Yes	208 (41.7)	217 (43.5)	

Some variable data were missing.

1.2.6 划痕实验

接种约5×10^5个细胞至6孔板，次日贴壁后用移液器吸嘴在孔中划线，用PBS清去划下的细胞后加入新鲜的培养基，放入培养箱中培养，在显微镜下拍照记录，Image J分析0、24和48 h的划痕面积。

1.2.7 Transwell实验

将transwell小室放入24孔板中，加入稀释的Matrigel基质胶后放入培养箱4～5 h，上室胶凝固吸取残余液体，加入DMEM培养基再次放入培养箱，水化20 min，消化细胞后用无血清DMEM重悬制备成细胞悬液，血球计数板计数，取上述1×10^4个细胞接种至上室，下室接种含有10%FBS的DMEM培养基，置于37 ℃、CO_2体积分数为5%的培养箱中进行培养，24 h后吸干孔板的培养基，用4%PFA固定后结晶紫染色，在显微镜下拍照计数。

1.3 统计学处理

应用R软件（3.6.3版本）和GraphPad（primer6）进行数据统计分析和可视化分析，免疫细胞浸润相关性分析采用Spearman检验，采用Kaplan-Meier生存曲线进行预后分析，采用*t*检验分析北京大学深圳医院样本库肺腺癌样本的CBX3表达差异，细胞实验均独立重复3次；采用*t*检验进行数据分析，结果以$\bar{x}\pm s$表示。$P<0.05$为差异有统计学意义。

2 结　果

2.1 CBX3在肺腺癌组织中高表达

在TCGA数据的基础上分析了CBX3 mRNA在不同类型肿瘤中的表达（图1），33种肿瘤中有21种肿瘤CBX3表达明显升高，尤其是在胃肠道肿瘤和肺肿瘤中。基于TCGA数据的肺腺癌组中，Mann-Whitney *U*检验结果显示，CBX3在肿瘤组织的表达显著高于正常组织，差异有统计学意义（$P<0.001$，图1）。

2.2 CBX3高表达影响肺腺癌中免疫细胞的浸润

采用ssGSEA算法分析了肺腺癌中24种免疫细胞的浸润情况。结果显示，仅辅助型T细胞2的浸润与CBX3表达呈正相关（$r=0.437$，$P<0.001$），而肥大细胞（$r=-0.444$，$P<0.001$）、嗜酸性粒细胞（$r=-0.380$，$P<0.001$）和未成熟树突状细（$r=-0.346$，$P<0.001$）等免疫细胞浸润与*CBX3*表达呈负相关（图2）。

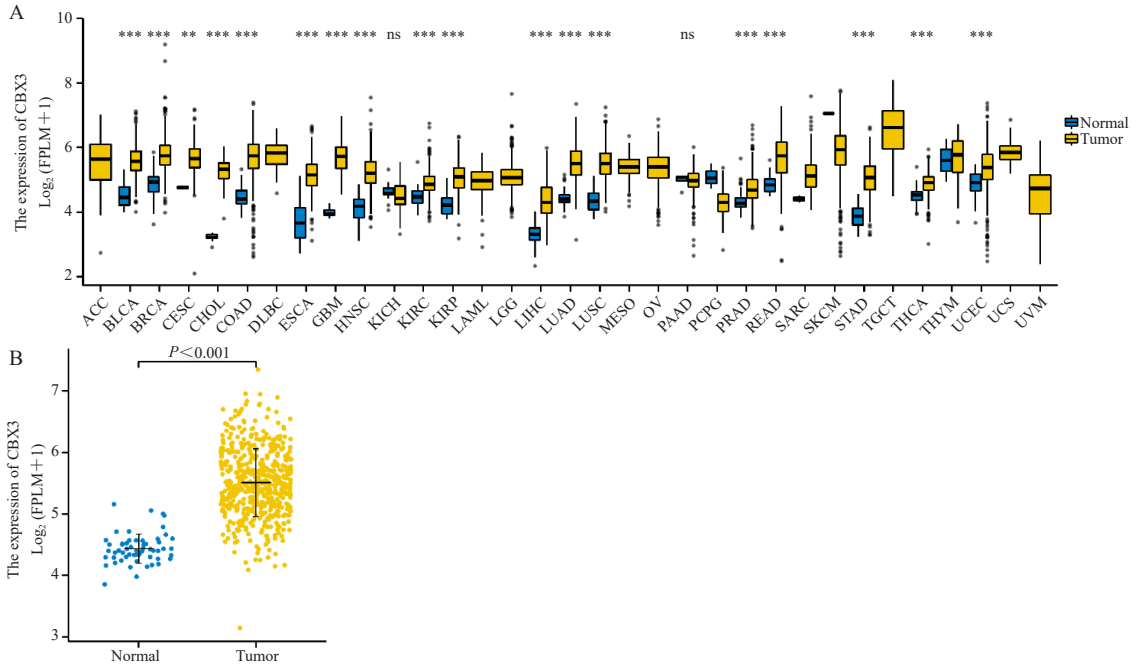

图 1 CBX3差异表达分析

Fig. 1 Differential expression analysis of CBX3

A: The expression of CBX3 in generalized carcinoma was analyzed based on TCGA data; B: The expression of CBX3 in LUAD was analyzed based on TCGA data. ns: $P>0.05$, compared with each other; *: $P<0.05$, compared with each other; **: $P<0.01$, compared with each other; ***: $P<0.001$, compared with each other.

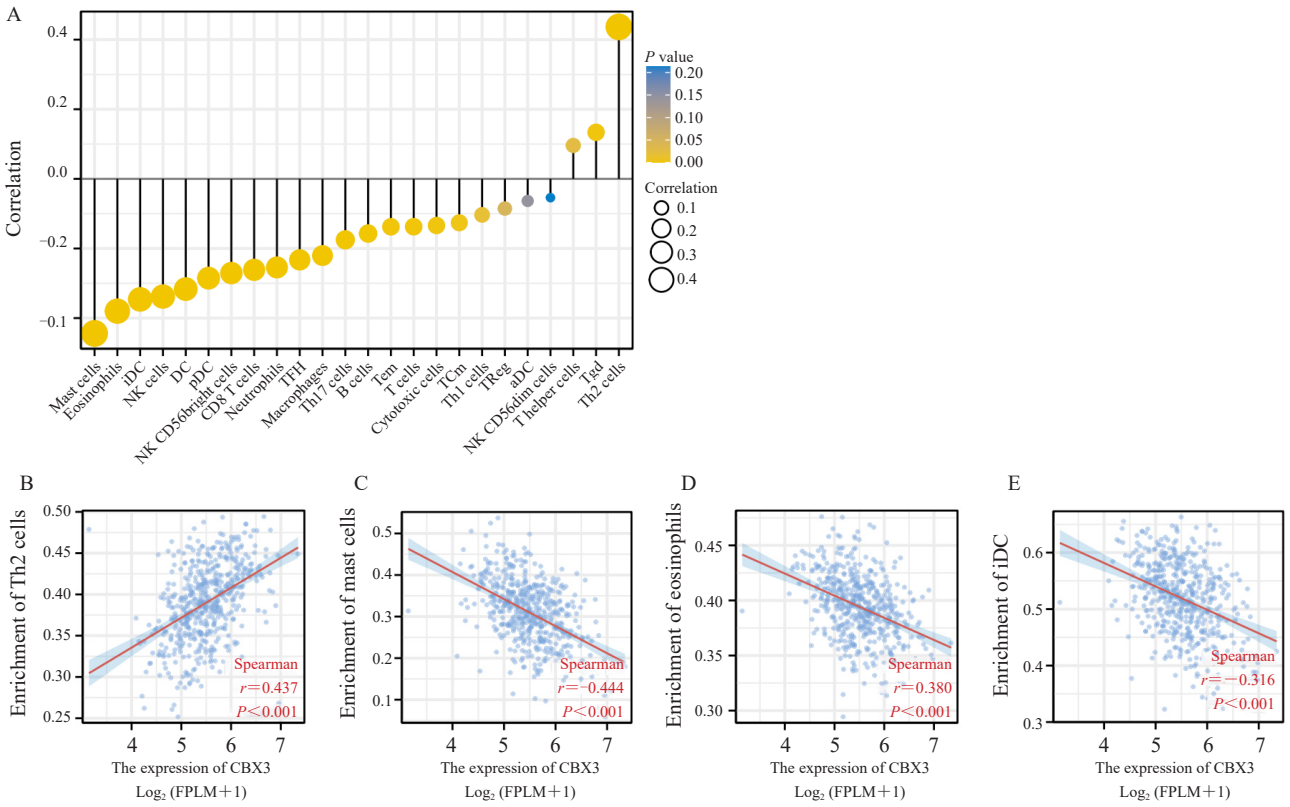

图 2 CBX3过表达与免疫浸润情况与CBX3相关性得分前4名的免疫细胞免疫浸润情况

Fig. 2 CBX3 overexpression and immune infiltration and immune cell infiltration of the top 4 immune cells with CBX3 correlation score A

A: Correlation between different cells; B-E: The enrichment of helper T cell 2 cell (Th2) cells, mast cells, eosinophils, and iDC cells with *CBX3* correlation score.

2.3 CBX3的高表达预示肺腺癌患者预后不良

ROC曲线验证了CBX3在肺腺癌诊断中的应用价值，曲线下面积（area under curve，AUC）为0.912，表明CBX3对诊断肺腺癌具有较高的敏感性和特异性。之后采用Kaplan-Meier分析CBX3在肺腺癌临床预后预测中的作用，总生存期［风险比（hazard ratio，HR）=1.43，*P*=0.010］、无进展间期（HR=1.59，*P*=0.001）和疾病特异性生存期（HR=1.49，*P*=0.038）在*CBX3*高表达组的情况均明显低于*CBX3*低表达组（图3）。

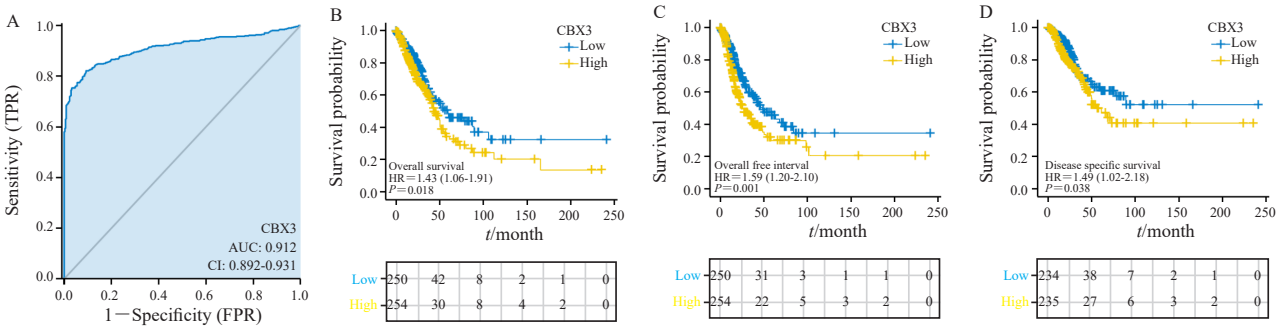

图 3 CBX3的表达对肺腺癌患者诊断和临床预后的预测价值Kaplan–Meier

Fig. 3 The predictive value of CBX3 expression in diagnosis and clinical prognosis of patients with lung adenocarcinoma

A: Receiver operating characteristic (ROC) curve analysis of CBX3 in diagnosis of lung adenocarcinoma; B: Kaplan-Meier analysis of disease-specific survival of overall survival, between the high and low expression groups of CBX3; C: Progression-free survival; D: Disease-specific survival.

2.4 冻存肺腺癌样本中CBX3显著高表达

20例配对肺腺癌样本RTFQ-PCR实验结果显示，肺腺癌组织中的CBX3相对于配对的正常肺组织呈显著高表达，差异有统计学意义（*P*＜0.05，图4）。此结果与基于TCGA数据库的差异分析一致。

2.5 siRNA对*CBX*3基因沉默效果显著

RTFQ-PCR结果显示，CBX3在si-CBX3组的表达量明显低于si-NC组，差异有统计学意义（*P*＜0.001，图5）。转染后的A549细胞系可用于后续实验。

2.6 CBX3高表达促进A549肺腺癌细胞的增殖

CCK-8分析结果显示，si-CBX3组细胞的增殖能力与si-NC组相比明显减弱，在24、48和72 h的*D*值分别为0.35±0.01、0.48±0.01和0.72±0.01，与si-NC组相比差异有统计学意义（*P*＜0.01，图6）；克隆形成实验结果显示，si-CBX3组的相对克隆形成率为0.65±0.05，与si-NC组相比A549细胞的克隆形成率明显降低（*P*＜0.001，图7）。

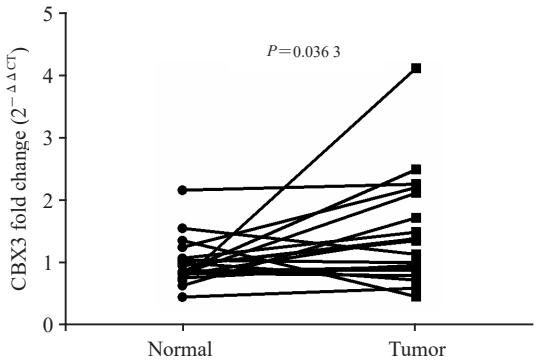

图 4 RTFQ–PCR检测肺腺癌与癌旁组织中CBX3的表达

Fig. 4 The expressions of CBX3 in adenocarcinoma tissues and normal para-cancerous tissues detected by RTFQ-PCR

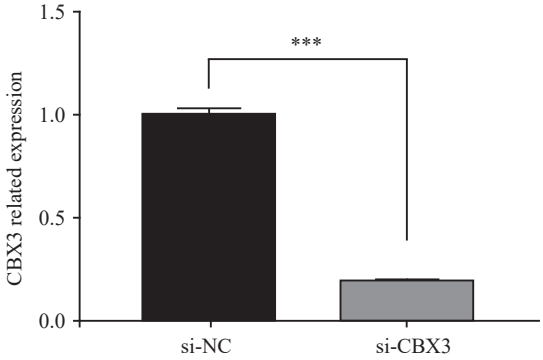

图 5 siRNA对*CBX3*基因的沉默效率

Fig. 5 Silencing efficiency of siRNA on *CBX3* gene

***: *P*＜0.001, compared with each other.

2.7 CBX3高表达促进A549肺腺癌细胞迁移能力

划痕实验结果得出，在24 h时间点，si-CBX3组迁移率为（9.46±1.14）%，较si-NC组有降低趋势，而在48 h时间点si-CBX3组的迁移率为（22.68±3.44）%，显著低于si-NC组，差异有统计学意义（$P<0.05$，图8）。

2.8 CBX3高表达促进A549肺腺癌细胞侵袭能力

Transwell实验结果显示，si-CBX3组A549细胞穿过基底膜的数目明显低于si-NC组，相对侵袭率为（53.94±5.39）%，差异有统计学意义（$P<0.01$，图9）。

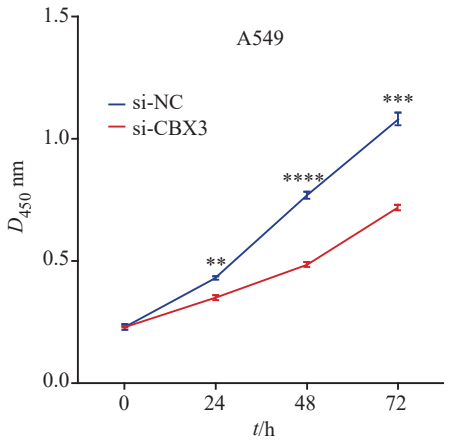

图 6 CCK-8实验结果，分别在24、48和72 h实验组si-CBX3和对照组si-NC的增殖情况

Fig. 6 Results of CCK-8 experiment, proliferation of si-CBX3 in experimental group and si-NC in control group at 24, 48 and 72 h, respectively

**: $P<0.01$, compared with each other; ***: $P<0.001$, compared with each other; ****: $P<0.000\ 1$, compared with each other.

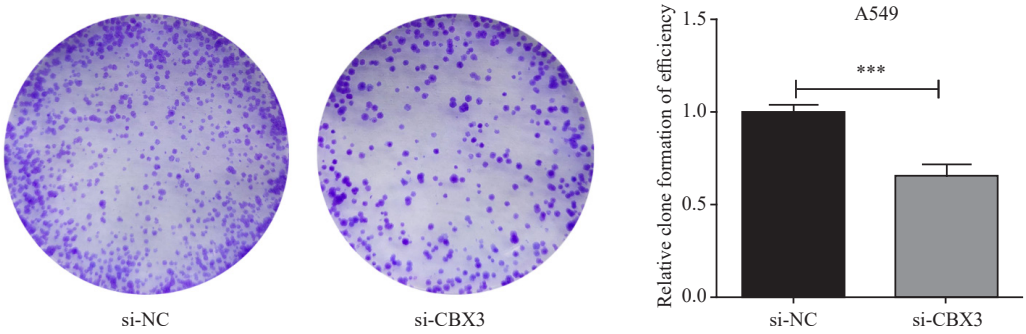

图 7 克隆形成实验检测沉默CBX3对A549细胞增殖的影响

Fig. 7 The effect of silencing CBX3 on A549 cell proliferation was detected by clonal formation assay

***: $P<0.001$, compared with each other.

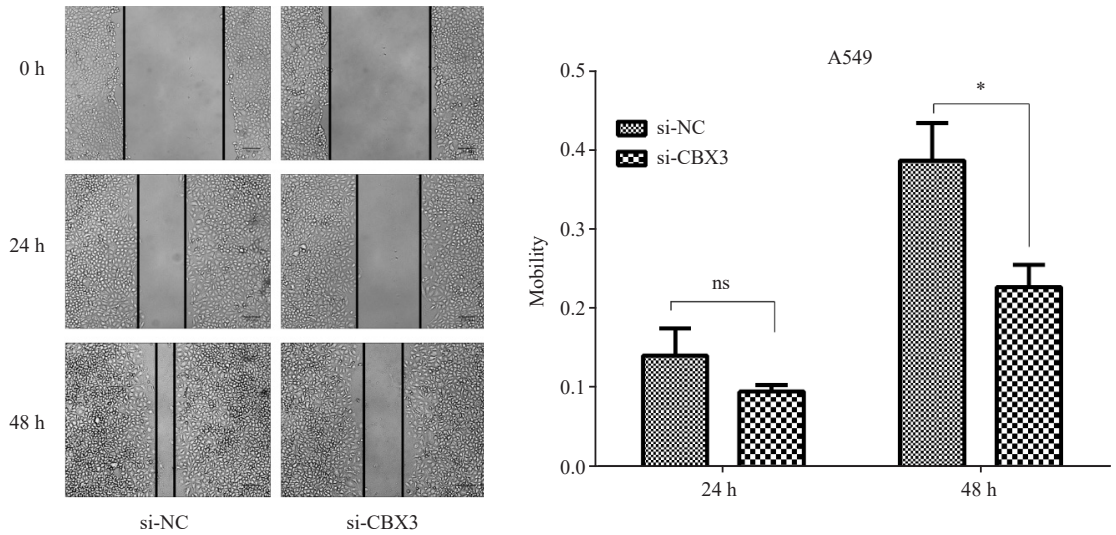

图 8 划痕实验检测沉默CBX3对A549细胞迁移能力的影响

Fig. 8 The effect of silencing CBX3 on A549 cell migration was detected by scratch assay

ns: $P>0.05$, compared with each other; *: $P<0.05$, compared with each other.

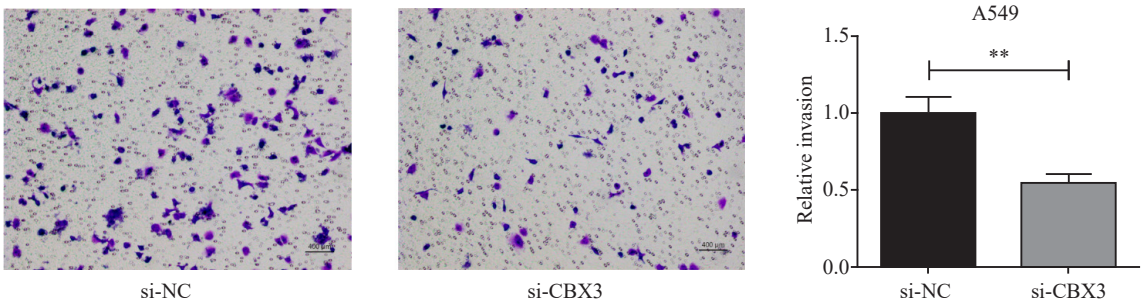

图9 Transwell实验检测沉默CBX3对A549细胞侵袭能力的影响

Fig. 9 Transwell assay was used to detect the effect of silencing CBX3 on invasion ability of A549 cells

**: $P<0.01$, compared with each other.

3 讨 论

肺癌易发生转移和耐药[14-15]，且不同的肺癌亚型具有不同的临床特征和预后，因此探讨肺腺癌特异性的预后标志物至关重要。

*CBX3*基因编码异染色质蛋白1（heterochromatin protein 1，HP1）蛋白家族的成员之一HP1γ[10]，是异染色质中最保守的核心蛋白[16]，该蛋白家族的功能包括转录激活和延伸、姐妹染色单体凝聚、染色体分离、端粒维护、DNA修复和RNA剪接[17-22]。Eguchi等[23]研究表明*CBX3*/HP1γ与热激蛋白（heat shock protein，HSP）70’B mRNA的转录有关，并与HSP70’B mRNA对应的蛋白血红素样重复结构域共同作用，并在启动子区域组装DNA。*CBX3*在多种癌症中高表达[24]，Wang等[25]研究证实，*CBX3*在胶质母细胞瘤中高表达，其沉默可通过阻断细胞周期G_2/M期，抑制胶质瘤U373细胞系增殖，并提示胶质母细胞瘤患者预后不良。Chang等[9]的研究发现，*CBX3*基因在非小细胞肺癌中有显著的上调，且*CBX3*高表达与*EGFR*基因突变之间有很强的相关性。此外，Han等[26]利用全基因组RNA测序转录88个非小细胞肺癌样本，发现*CBX3*、*GJB2*、*CRABP2*和*DSP*基因差异表达最显著，后续免疫组织化学检测结果显示，*CBX3*在组织中阳性率最高（>90%）。上述研究结果表明，*CBX3*可以通过多种机制促进多种类型癌症的发生、发展并影响癌症的预后。本研究通过TCGA数据库分析了*CBX3*在肺腺癌中的表达谱，结果显示，*CBX3*在肺腺癌中的表达高于与其匹配的正常组织，并且通过医院样本库样本RTFQ-PCR实验也证实了这一结论。免疫细胞浸润分析中，肥大细胞与*CBX3*呈负相关且相关程度最大。肥大细胞浸润于正常组织和肿瘤之间的边界并表达多种血管生成因子，这可能在肿瘤发生的早期发挥促血管生成作用[27]。肿瘤细胞通常会产生干细胞因子，这会导致肥大细胞的募集和激活[28]。此外，Kaplan-Meier分析显示*CBX3*的高表达提示肺腺癌患者的预后不良。以上分析均提示*CBX3*在肺腺癌的发生、发展中发挥重要作用，因此，我们对*CBX3*基因进行细胞功能实验来探究其在肺腺癌发生、发展过程中的作用，结果表明，沉默A549肺腺癌细胞中的*CBX3*表达，细胞的增殖、迁移和侵袭能力明显低于对照组的肺腺癌细胞，说明*CBX3*参与肺腺癌细胞的发生、发展过程，其高表达可促进A549肺腺癌细胞的增殖、迁移和侵袭。本研究存在的不足之处在于未对*CBX3*参与的信号转导通路进行研究，且有待扩大样本量进一步研究。

综上所述，*CBX3*在肺腺癌中显著高表达，影响了辅助型T细胞2、肥大细胞等免疫细胞在肺腺癌组织中的浸润情况，对临床预后有一定的预测价值，*CBX3*高表达可促进A549肺腺癌细胞的增殖、迁移和侵袭能力，提示*CBX3*可作为肺腺癌的潜在治疗靶点。

利益冲突声明：所有作者均不存在利益冲突。

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