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敲低 HMGN2 可抑制肺腺癌细胞的增殖、迁移和侵袭

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摘要 目的 探究高迁移率蛋白 N2(HMGN2)对肺腺癌细胞的影响及作用机制。方法 通过TCGA数据库分析HMGN2与肺腺癌组织之间的关联。收集肺腺癌组织及其相邻正常组织,比较HMGN2的表达水平差异。利用定量逆转录聚合酶链反应(qRT-PCR)、Western blot检测肺腺癌细胞株A549和NC-H1299中HMGN2 mRNA的表达情况。通过si-RNA技术敲低HMGN2表达,分为对照组(转染同剂量NC-siRNA片段)和si-RNA组。根据si-RNA敲低效率构建稳定转染的细胞株。采用CCK-8、Transwell实验、划痕实验、单克隆形成实验以及EdU实验等方法,评估HMGN2敲低后对肺腺癌细胞增殖、迁移和侵袭能力的影响。转录组测序分析揭示HMGN2与肿瘤发生的相关通路。Western blot检测敲低HMGN2后,MAPK通路蛋白的相对表达情况。结果 HMGN2的mRNA在肺癌组织和肺腺癌细胞株中表达量明显升高($P < 0.05$)。抑制HMGN2表达后,细胞增殖、迁移和侵袭等功能显著下降($P < 0.05$),MAPK信号通路的磷酸化水平明显降低($P < 0.05$)。结论 HMGN2在肺腺癌细胞中具有促进增殖、迁移、侵袭的作用,其机制可能与MAPK通路的磷酸化激活水平密切相关。

关键词 肺腺癌; HMGN2; 增殖; 迁移; 侵袭; MAPK信号通路

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肺腺癌(lung adenocarcinoma, LUAD)是肺癌最常见的组织学类型,目前整体生存期仍未显著提高^[1]。因此,临床迫切需要深入了解LUAD的发病机制,探寻影响LUAD进展的关键分子并分析其生物学功能和作用机制,为临床治疗LUAD提供新的参考。高迁移率族N(high mobility group nucleosomal proteins, HMGNs)是一类非组蛋白的染色体蛋白^[2]。已有研究^[3]显示敲低HMGN2能够抑制乳腺癌细胞的增殖和促进其凋亡。然而,HMGN2是否能够影响肺腺癌的进展目前尚不清楚。因此,该研究通过实验验证以及转录组学测序分析探究HMGN2对肺腺癌的作用及其具体途径,为临床治疗LUAD提供新的思路。

1 材料与方法

1.1 实验试剂 人类正常支气管上皮细胞株BE-AS-2b及人类支气管非小细胞肺癌细胞株A549和

NCI-H1299(武汉普诺赛生命科技)。细胞培养液中含有10%的胎牛血清(武汉普诺赛生命科技),使用的培养基为RPMI-1640和DMEM(北京Gibco生物)。细胞生长条件设置为37℃及5%CO₂。实验所需PCR引物、小干扰RNA(si-RNA)(北京擎科生物)、RNA快速提取试剂盒(北京聚合美生物)、逆转录及荧光定量PCR试剂盒(上海近岸蛋白)及CCK8试剂(安徽华晓基因科技)。HMGN2和GAPDH一抗(ABclonal)、ERK、P-ERK、MEK和β-actin一抗及对应二抗(上海埃必威生物)。实验使用基质胶(Corning)和Transwell板(Labselect)。

1.2 标本来源 8对配对肺腺癌标本和癌旁正常组织标本均来源于蚌埠医科大学第一附属医院胸外科,癌组织取自肿瘤中心处,癌旁组织取自癌组织边缘5cm以上,标本使用-80℃冰箱保存。肺癌诊断均经两名病理科医师确诊,收集标本均已签署知情同意书,并且已得到蚌埠医科大学伦理委员会审批(伦科批字(2024)第224号)。

1.3 实验方法

1.3.1 细胞培养 细胞在含10%胎牛血清的1640培养基中进行培养,置于37℃、5%CO₂培养箱中。当细胞密度达到80%~90%时,使用胰酶进行适当时间的消化处理后进行离心,以便于进行下一代传

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代。

1.3.2 si-RNA 转染 首先将待转染细胞种植在 6 孔板中,当细胞生长至 70% ~ 80% 密度时,移除旧培养液并添加 2 ml 无血清培养基(opti-minimal essential medium, Opti-MEM)。接着准备两个 1.5 ml 的无菌 EP 管,每个中加入 125 μ l 的无血清 Opti-MEM 随后分别向每个管中加入 5 μ l 的 Lip6000 和 siRNA。两管内容物在室温下静置 5 min 后混合,再静置 5 min。然后将混合后的培养液加入 6 孔板,将板放回培养箱中孵育 4 ~ 6 h。弃掉培养液,换入含 10% 胎牛血清的完全培养基,继续培养 48 h 后进行后续实验。

1.3.3 慢病毒转染 选取生长状态良好的细胞株,消化后接种在 6 孔板中,保证转染前细胞生长到 60% ~ 80%。弃去原培养基,PBS 进行清洗。根据 6 孔板每孔细胞的生长密度、状态以及病毒滴度添加适量的病毒到 40 μ l 病毒转染试剂中,用完全培养基将转染体系补到 1 ml 后充分摇匀,放入培养箱中培养 6 ~ 8 h。再向 6 孔板中加 1 ml/孔的完全培养基继续培养 24 ~ 48 h,直至细胞长满。用含 5 ~ 10 μ g/ml 嘌呤霉素的完全培养基对转染细胞进行筛选,筛选后的细胞进行扩增,以及细胞实验,此外还需保留冻存部分稳转株以备后续实验使用。

1.3.4 实时荧光定量 PCR (quantitative real-time polymerase chain reaction, qRT-PCR) 根据试剂盒说明书从目标细胞中提取总 RNA,并将其逆转录成相应的 cDNA。随后,使用 PCR 方法进行扩增,以 Actin 作为内部对照。实验中,表达量的计算采用 $2^{-\Delta\Delta C_T}$ 方法。荧光定量 PCR 的典型热循环条件一般为 95 $^{\circ}$ C 1 min 95 $^{\circ}$ C 20 s 60 $^{\circ}$ C 20 s 72 $^{\circ}$ C 30 s 40 次循环。引物序列见表 1。

表 1 HMG2、Actin 引物序列

Tab. 1 Primer sequences of HMG2 and Actin

Gene	Sequence (5' - 3')
HMG2-F	CTGAAAGTCAGGTCGGCTT
HMG2-R	GCAGAAGTACCTGTTCCA
Actin-F	CATGTACGTTGCTATCCAGGC
Actin-R	CTCCTTAATGTCACGCACGAT

F: Forward primer; R: Reverse primer.

1.3.5 Western blot 当细胞贴壁密度达到 80% ~ 90% 时,加入蛋白裂解液并充分混匀,随后置于冰上冷藏 30 min。之后离心收集总蛋白,并通过 BCA 法确定蛋白浓度。使用 12% SDS-PAGE 进行电泳,初

始设定电压 80 V 运行 30 min,接着提高至 110 V 继续电泳 90 min。电泳完毕后进行蛋白转移至 PVDF 膜,该膜需用甲醇预激活。转膜过程中使用 200 mA 的恒定电流。转膜后,用封闭液处理并在 4 $^{\circ}$ C 下过夜孵育一抗,次日洗膜 3 次,每次 8 min。随后在室温下孵育二抗 1 h,再进行 3 次洗膜,每次 8 min,最后进行曝光。

1.3.6 CCK-8 检测细胞活性 敲低 HMG2 的肺癌细胞与对照组的正常肺癌细胞以 1×10^3 个/孔的密度分别种植在 96 孔板中,每组设 6 个重复孔,共使用 5 块板,分别于 24、48、72、96、120 h 后进行实验。实验前,每孔加入 10 μ l CCK-8 试剂,轻轻震荡使其混合均匀,然后将板放回细胞培养箱中孵育 1 h 随后进行光度计检测。

1.3.7 划痕实验检测细胞迁移能力 将细胞种植在 6 孔板中,当细胞覆盖率达到满盘时,使用 200 μ l 的枪头沿着培养盘的直径划开一条直线,用 PBS 清洗掉划线区域的细胞残片。接着更换为无血清的培养基,并在开始时(0 h)及 24 h 对划痕进行拍照记录。

1.3.8 Transwell 实验检测细胞迁移能力 当细胞生长密度达到 80% ~ 90% 时,进行消化并重新悬浮细胞。之后,将细胞悬液转移到 Transwell 的上室,下室加入含血清的培养基。细胞在培养箱中孵育 36 h 后,取出 Transwell 板并使用干棉签清除上室内的细胞。接着用多聚甲醛固定细胞 30 min,用结晶紫进行染色并晾干 30 min,最后使用倒置显微镜进行细胞观察和拍照记录。

1.3.9 Transwell 实验检测细胞侵袭能力 首先将培养基与基质胶按比例混合,在每个小室中添加 50 μ l 混合好的基质胶,混匀后放入培养箱使其凝固,约需 2 h。细胞生长至覆盖整个表面后,进行消化和离心,然后用无血清培养基重新悬浮细胞。将此细胞悬液转入 Transwell 的上室,下室则添加含血清的培养基。将装置放回培养箱中继续培养 36 h。完成后,移除 Transwell 板,用干棉签轻轻擦去上室的基质胶,随后用多聚甲醛固定 30 min。使用结晶紫染色并晾干 30 min,最后用倒置显微镜进行观察和拍照记录。

1.3.10 单克隆形成实验 取 1 000 个细胞接种于 6 孔板中,加入 2 ml 完全培养基培养 1 ~ 2 周。观察细胞数目,当有肉眼可见细胞团时,弃培养基,PBS 清洗,加固定液 10 ~ 15 min。弃固定液,加结晶紫染色 15 min,冲洗晾干。拍照统计结果。

1.3.11 EdU 实验 将稳转细胞株接种于 24 孔板中。制备 EdU 培养基,当细胞密度达到 70% 左右时。用含 EdU 试剂的培养基孵育 2 h,弃培养基。PBS 清洗 2 次细胞。加入预冷过的 4% 多聚甲醛室温孵育 30 min,弃固定液。加入甘氨酸,脱色摇床孵育 5 min,弃甘氨酸液。加入 PBS,脱色摇床清洗 5 min,弃 PBS。加入渗透液,室温孵育 10 min,离心。弃上清液,PBS 清洗,弃上清液。向样本中添加染色反应液后,将其置于室温避光条件下并在摇床上振荡 30 min。之后进行离心,丢弃上清液。接着加入渗透剂,并在室温下清洗 3 次,每次 10 min,离心弃上清液,PBS 清洗 3 次后在倒置荧光显微镜下成像并保存。

1.3.12 细胞转录组测序 取敲低 HMGN2 和空白组的 H1299 病毒稳转株各 3 组,送往美吉生物公司进行转录组测序。

1.4 统计学处理 实验数据采用 Image J 和 Graph-Pad Prism 9 软件进行统计分析,结果以 $\bar{x} \pm s$ 形式展示。对两组数据进行独立样本 *t* 检验,而多组数据则通过单因素方差分析进行比较。 $P < 0.05$ 为差异

有统计学意义。所有实验均独立进行 3 次重复。

2 结果

2.1 HMGN2 在肺腺癌中的表达情况及预后关系

利用 TCGA 数据库,分析肺腺癌组织和正常组织中的 HMGN2 表达,结果显示 HMGN2 在肿瘤组织中高表达,见图 1A,且在肺癌 5 年生存率方面差异有统计学意义,见图 1B ($P < 0.05$)。随后为了验证上述结果,通过 Western blot 分析比较了肺腺癌细胞系 NC-H1299 与 A549 和人类正常支气管上皮细胞 BEAS-2B 中 HMGN2 蛋白的表达。结果表明,NC-H1299 和 A549 细胞中 HMGN2 的表达水平显著高于 BEAS-2B 细胞,见图 1C,差异有统计学意义 ($P < 0.01$)。最后对 8 对肺腺癌的临床标本进行 Western blot 检测,结果显示肺腺癌患者组织中 HMGN2 的表达量与癌旁正常组织表达量存在统计学差异。见图 1D、E ($P < 0.01$)。

2.2 敲低 HMGN2 后,肺腺癌的生物功能变化情况

通过设计 HMGN2 敲低小干扰 (si-#1、si-#2、si-#3) 对 NC-H1299 和 A549 的 HMGN2 进行敲低处

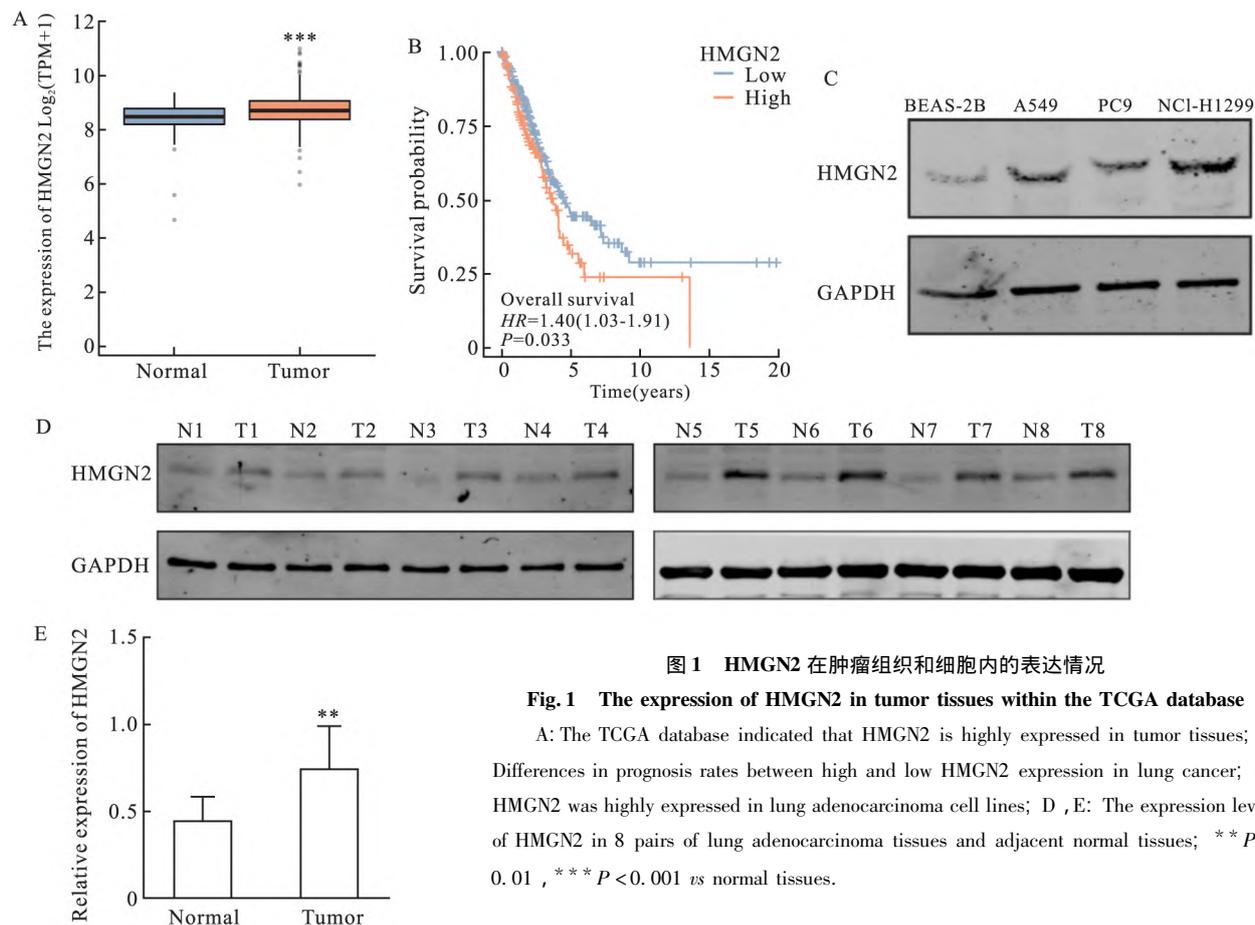


图 1 HMGN2 在肿瘤组织和细胞内的表达情况

Fig. 1 The expression of HMGN2 in tumor tissues within the TCGA database

A: The TCGA database indicated that HMGN2 is highly expressed in tumor tissues; B: Differences in prognosis rates between high and low HMGN2 expression in lung cancer; C: HMGN2 was highly expressed in lung adenocarcinoma cell lines; D, E: The expression levels of HMGN2 in 8 pairs of lung adenocarcinoma tissues and adjacent normal tissues; ** $P < 0.01$, *** $P < 0.001$ vs normal tissues.

理。结果 si-#1 和 si-#2 的小感染敲降效率最高,见图 2($P < 0.01$)。根据它们的序列进行了敲低慢病毒的制备,并且在后续实验中均用细胞稳转株进行。

2.2.1 敲低 HMGN2 后,肺腺癌的增殖功能变化情况 为探究 HMGN2 敲低后对肺腺癌细胞增殖功能的影响,本研究进行了单克隆形成实验和 CCK-8 实验。单克隆形成实验结果显示,与对照组相比,HMGN2 敲低组形成的克隆细胞团更少,见图 3A、B。此外,连续 6 d 测定稳转株细胞活力时,HMGN2 敲低稳转株的增殖能力明显减弱,见图 3C、D。

课题组检测了当 HMGN2 敲低后 NC-H1299 和 A549 的荧光强度变化。如图 4 所示,与对照组相比,HMGN2 敲低稳转株的荧光强度明显降低,并且差异有统计学意义($P < 0.05$)。

2.2.2 敲低 HMGN2 后,肺腺癌的伤口愈合能力变化情况 为了检测敲低 HMGN2 后对肺癌细胞的伤口愈合能力的影响,课题组进行了划痕实验,图 5 结果显示,与对照组相比,HMGN2 敲低的 NC-H1299 和 A549 稳转株的伤口愈合能力明显下降,差异有统计学意义($P < 0.01$)。

2.2.3 敲低 HMGN2 后,肺腺癌的迁移和侵袭能力变化情况 上述结果证明敲低 HMGN2 后,肺腺癌细胞的增殖和伤口愈合能力减弱,而侵袭和迁移能力也是肿瘤发生恶性生物学行为的体现。对 NC-H1299 和 A549 稳转株进行了 Transwell 实验。图 6 显示,与对照组相比,HMGN2 敲低后,NC-H1299 和

A549 细胞的迁移和侵袭能力明显下降,差异有统计学意义($P < 0.01$)。

2.3 敲低 HMGN2 后,转录组水平的变化情况 为了探究 HMGN2 敲低后,肺腺癌生物学功能减弱的可能机制,对 NCI-H1299 稳转株进行转录组测序,火山图(图 7A)显示,表达上调基因 269 个,表达下调基因 112 个。随后对差异基因进行了 KEGG 注释和 GO 富集分析,结果显示差异基因与信号通路传导和癌症有关(图 7B、D)。为了将差异基因聚焦在信号通路上,课题组进行了 KEGG 富集分析,结果显示差异基因富集在 MAPK 信号通路上,如图 7C 所示。

2.4 HMGN2 通过 MAPK 信号通路对癌症的影响

MAPK 信号通路是常见的与肿瘤发生发展密切相关的信号通路之一。Western blot 实验结果显示,HMGN2 敲低后,MEK 和 ERK 的总蛋白水平没有明显改变,而发挥作用的 P-MEK 和 P-ERK 蛋白的表达明显减弱,表明 HMGN2 是通过 MAPK 信号通路发挥其促癌作用,差异有统计学意义($P < 0.01$)。见图 8。

3 讨论

本研究通过构建病毒来敲低肺腺癌细胞系 A549 和 H1299 中的 HMGN2 表达,细胞的增殖、侵袭和迁移能力有明显下降。实验表明,HMGN2 对于调控肺腺癌细胞系的增殖、侵袭和迁移能力有着重

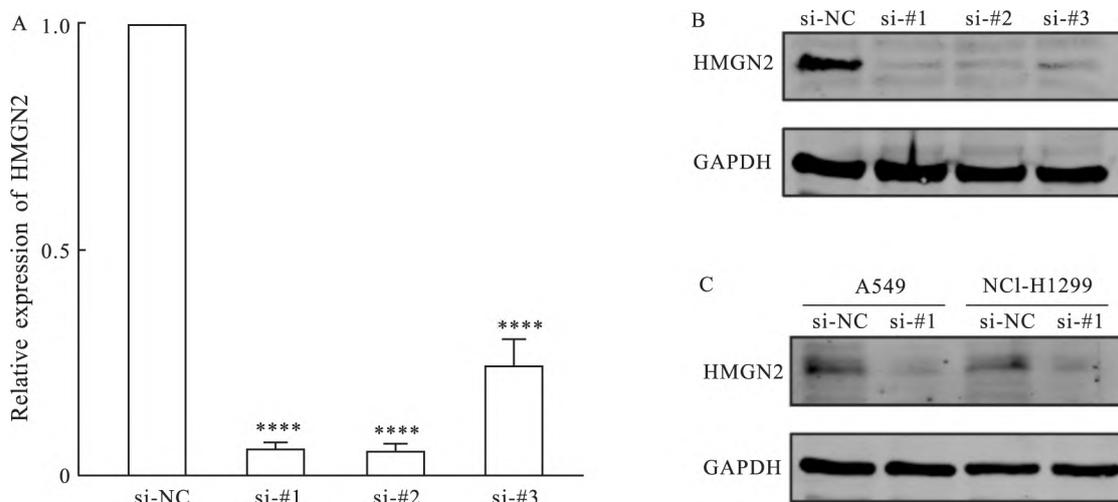


图2 RT-qPCR 分析 HMGN2 在细胞内表达水平,Western blot 分析敲低效率

Fig. 2 RT-qPCR analysis of the expression levels of HMGN2 within cells. Western blot results showed the efficiency of the knockdown

A: RT-qPCR analysis of HMGN2 mRNA expression in A549 cells; B: Western blot was used to detect the efficiency of HMGN2 knockdown by si-RNA; C: Western blot was used to detect the efficiency of stable cell line establishment using the si-#1 sequence; **** $P < 0.0001$ vs si-NC.

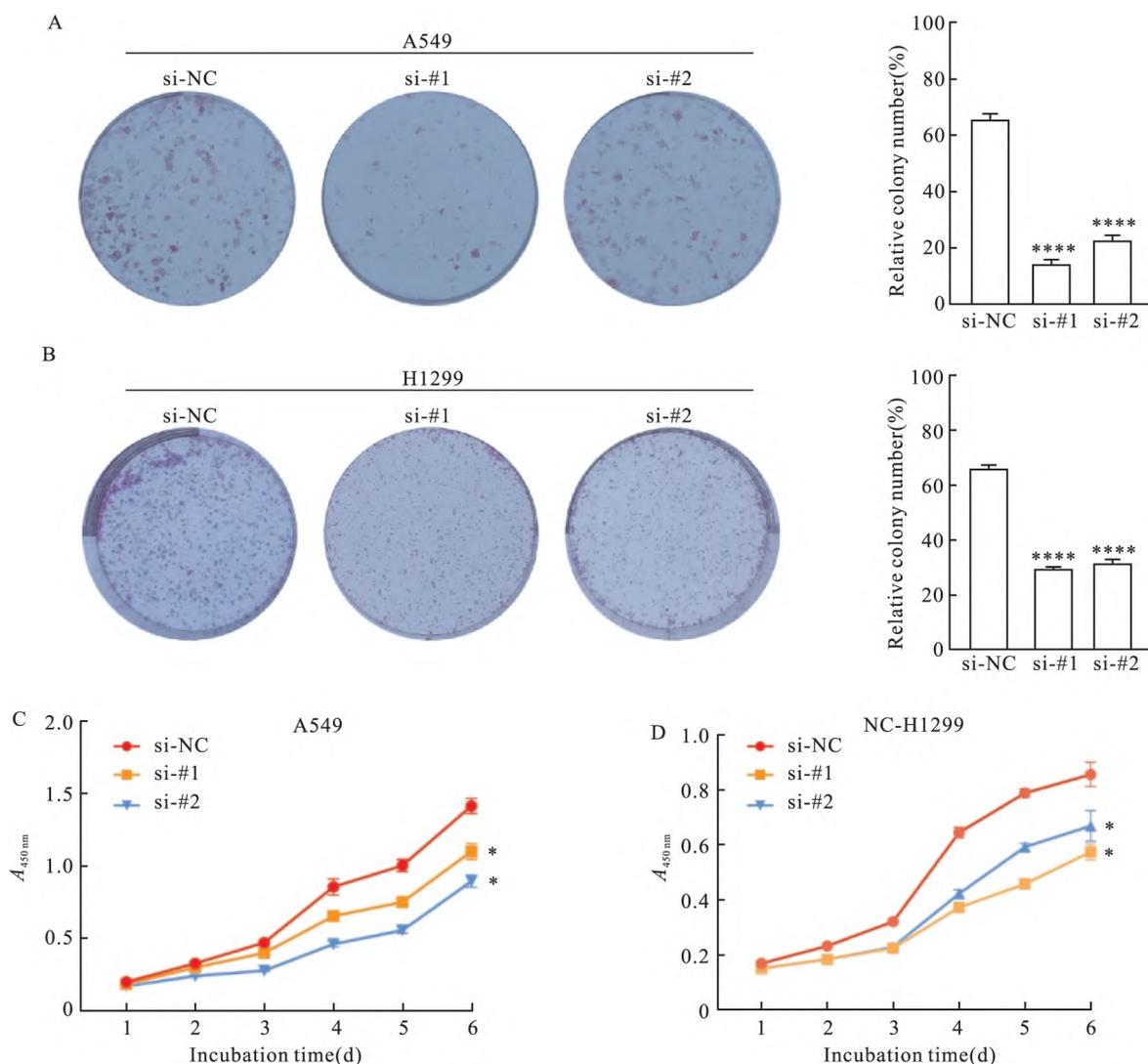


图3 单克隆实验检测细胞、CCK-8 实验检测细胞活性

Fig. 3 Colony formation results showed cell clonogenicity and CCK-8 assay results showed cell viability

A, B: Detection of the impact of different HMG2 expression levels on the clonogenic ability of A549 and H1299 cells through a colony formation assay; C, D: The effect of HMG2 knockdown on the proliferation ability of lung adenocarcinoma cells; * $P < 0.05$, **** $P < 0.0001$ vs si-NC.

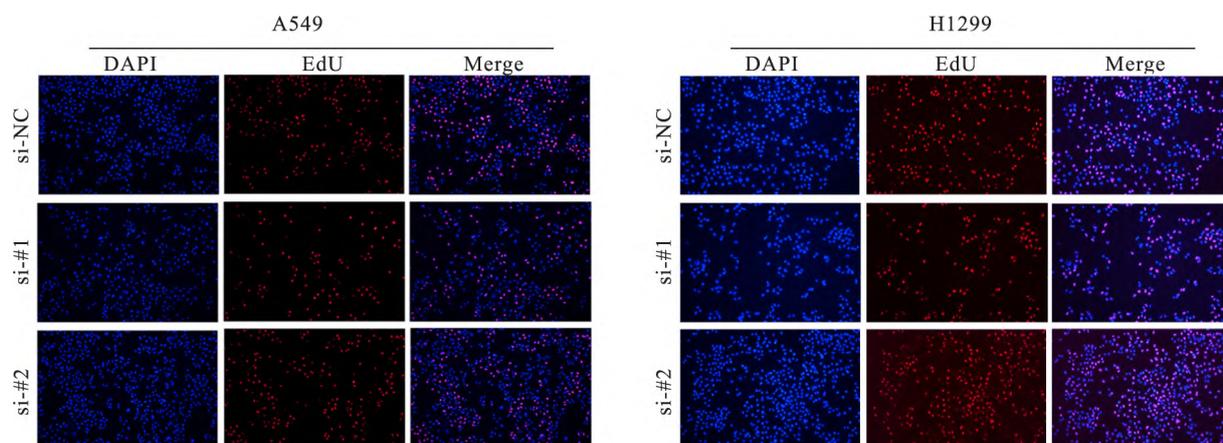


图4 EDU 实验表明不同 HMG2 表达量与细胞增殖能力有关 ×10

Fig. 4 The EDU assay indicated that different HMG2 expression levels were associated with cellular proliferation capacity ×10

Blue: the cell nucleus; red: cells that have proliferated within 2 h.

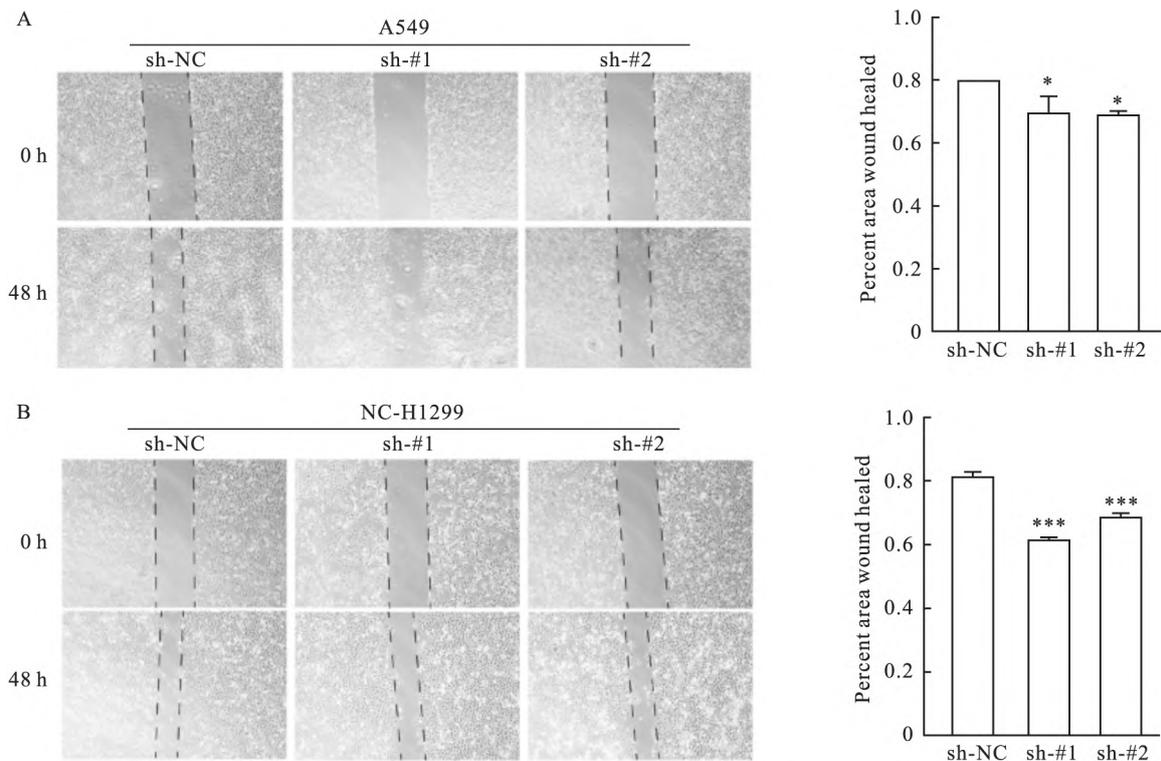


图5 划痕实验检测细胞迁移能力

Fig.5 Wound healing assay results showed cell migration capability

A,B: Effect of HMG2 knockdown on the migration ability of A549 cells (A) and NC-H1299 cells (B), detected by wound healing assay $\times 4$; * $P < 0.05$, *** $P < 0.001$ vs sh-NC.

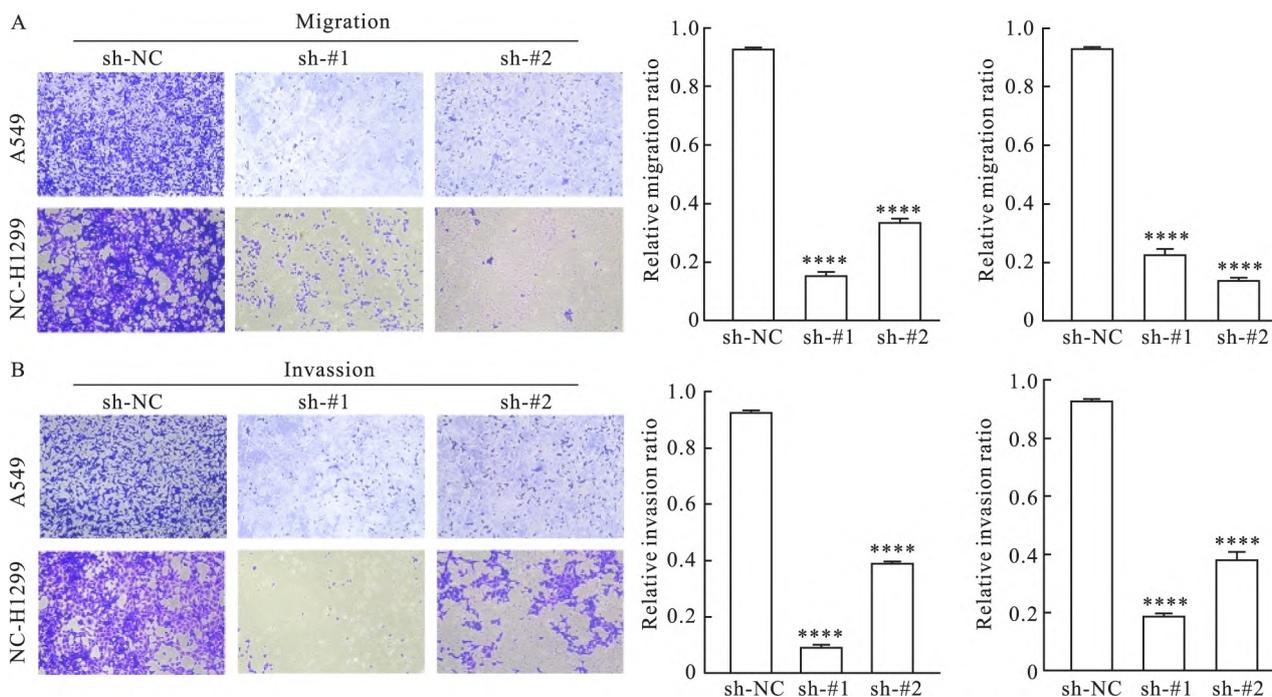


图6 Transwell 实验检测细胞迁移、侵袭能力

Fig.6 Transwell assay results showed cell migration and invasion capabilities

A: The effect of knocking down HMG2 expression on the migration ability of lung adenocarcinoma epithelial cells A549 and NC-H1299 $\times 10$; B: The effect of knocking down HMG2 expression on the invasion ability of lung adenocarcinoma epithelial cells A549 and NC-H1299 $\times 10$; **** $P < 0.0001$ vs sh-NC.

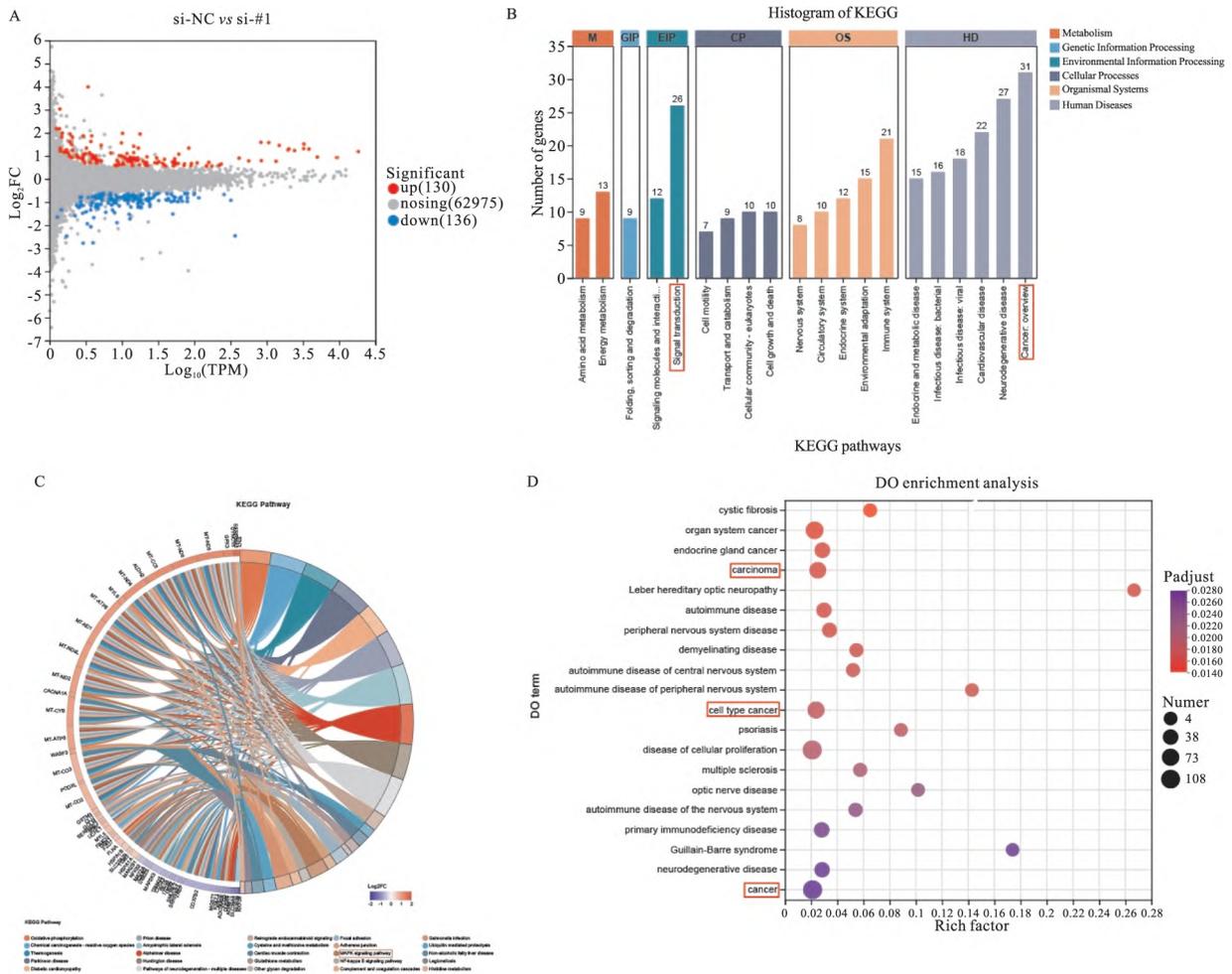


图7 转录组测序结果的火山图和 KEGG、GO 富集分析

Fig.7 Volcano plots of transcriptome sequencing results and KEGG , GO enrichment analysis

A: The volcano plot displays the differentially expressed genes between A549 si-NC and si-#1; The gray dots represented genes with no significant difference in expression levels; B ,D: Differential gene KEGG and GO enrichment analyses revealed that the differentially expressed genes are enriched in tumor-related pathways; C: The right side showed the information on the significantly enriched Terms/Pathways of differentially expressed genes/transcripts; The left side listed the genes/transcripts within those Terms/Pathways ,sorted by their log₂FC values; The MAPK signaling pathway was ultimately selected for experimental validation.

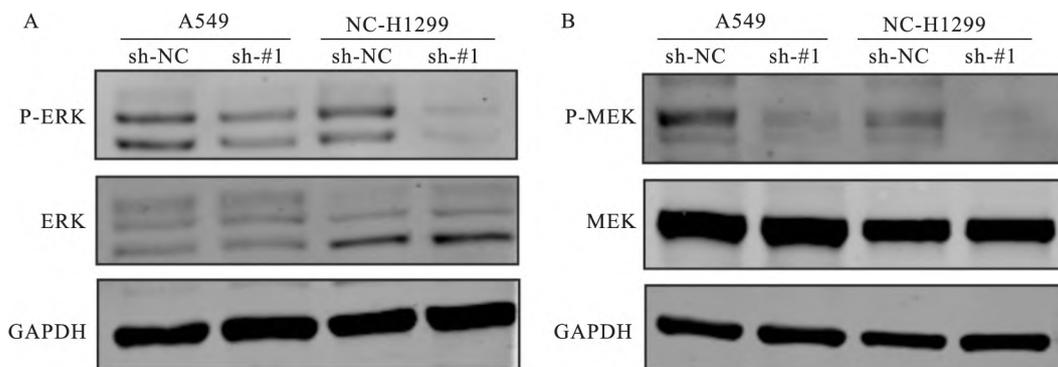


图8 敲低 HMG2 表达后 A549、NC-H1299 细胞 MAPK 通路的激活情况的变化。

Fig. 8 After knocking down HMG2 expression , the activation status of the MAPK pathway in A549 and NC-H1299 cells changed

A: The changes in total protein levels of P-ERK and ERK after knocking down HMG2 in A549 and NC-H1299 cells; B: The changes in total protein levels of P-MEK and MEK after knocking down HMG2 in A549 and NC-H1299 cells.

要作用。

LUAD 发生过程复杂,已知与 LUAD 发生有关的信号通路包括: PI3K/AKT^[4-5]、NF-κB^[6]、wnt/β-catenin^[7]、Snail、Slug/E-cadherin^[8] 通路等。细胞外信号调节激酶(ERK) 通路,作为丝裂原活化蛋白激酶(MAPK) 家族中的一员,主要响应生长因子、激素和其他细胞外刺激^[9]。主要通过精确调节 ERK 的磷酸化状态,细胞能够传递信号至核内,影响特定基因的表达,进而调控细胞分裂、分化和存活等关键过程^[10]。有研究^[11]表明 Sugiol 通过抑制关键的 RAF/MEK/ERK 信号通路来影响卵巢癌 SKOV3 细胞系的生长。因此,深入理解 ERK 通路的调控机制对于发展肺腺癌新的靶向治疗策略至关重要。

本研究分析纳入患者的临床组织,HMGN2 在肺腺癌组织中的表达水平较癌旁组织呈高表达。敲低 HMGN2 表达后,与对照组相比,MAPK 信号通路的磷酸化水平显著下降。这表明在肺腺癌细胞系中,HMGN2 的降低会影响 MAPK 通路的磷酸化表达。

综上所述,本实验结果表明 HMGN2 可能通过调节 MAPK 信号通路的磷酸化活性来控制肺腺癌细胞的增殖、侵袭和迁移。HMGN2 表达的增加是肺腺癌细胞影响因素的关键机制之一,研究 HMGN2 的功能有助于开发治疗肺腺癌的新分子生物标志物。本实验已证实降低 HMGN2 表达能减少肺腺癌细胞中 MAPK 的磷酸化水平,但 HMGN2 如何精确调控 MAPK 的磷酸化还需要进一步探索。未来研究可探讨 HMGN2 在不同肿瘤分期(T 分期)和淋巴侵犯情况(N 分期)等临床病理参数中的相关性。

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Knocking down HMGN2 can inhibit the proliferation, migration, and invasion of lung adenocarcinoma cells

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Abstract Objective To investigate the effects and underlying mechanisms of high mobility group nucleosome- (下转第 487 页)

focus. Immunohistochemistry (Envision two-step method) was used to detect the expression levels of GPR15 and FOXP3 in CRC and adjacent tissues, and analyze their relationships with clinicopathological factors of colorectal cancer. Kaplan–Meier method was used to draw the survival curve to analyze the correlation between the expressions of GPR15 and FOXP3 and the survival prognosis of patients with CRC. The factors influencing prognosis of patients with colorectal cancer were analyzed by Cox regression. **Results** The immunohistochemistry showed that the expression levels of GPR15 and FOXP3 in CRC were significantly higher than those in normal colorectal mucosal tissues ($P < 0.05$). The expression of GPR15 in CRC tissues was correlated with location, nerve invasion and TNM stage; FOXP3 expression was correlated with sex ($P < 0.05$). Both expressions were not significantly correlated with the clinicopathologic features of age, tumor size, differentiation degree, tissue type, depth of invasion, tumor budding, vascular invasion and lymph node metastasis. Correlation analysis showed that there was no significant correlation between GPR15 and FOXP3 expression ($Kappa = -0.019$, $P > 0.05$). The survival prognosis of GPR15 positive group was significantly worse than that of negative group ($\log\text{-rank: } \chi^2 = 4.3$, $P = 0.039$); while the survival prognosis of FOXP3 positive group was significantly better than that of negative group ($\log\text{-rank: } \chi^2 = 7.3$, $P = 0.007$). Age ≤ 55 years, positive GPR15 and negative FOXP3 were independent risk factors for poor prognosis in patients with CRC ($P < 0.05$). **Conclusion** The expression levels of GPR15 and FOXP3 in CRC are significantly higher than those in paracancer tissues, GPR15 and FOXP3 are expected to become new tumor markers for early screening, accurate treatment and prognosis assessment of CRC.

Key words colorectal carcinoma; GPR15; FOXP3; immunohistochemistry; prognosis

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binding domain protein 2 (HMG2) on lung adenocarcinoma cells. **Methods** This work first analyzed the association between HMG2 and lung adenocarcinoma tissues using The Cancer Genome Atlas (TCGA) database. Lung adenocarcinoma tissues and adjacent normal tissues were collected to compare the differential expression levels of HMG2. The expression of HMG2 mRNA in lung adenocarcinoma cell lines A549 and NC-H1299 were detected by qRT-PCR and Western blot. HMG2 expression was knocked down using si-RNA technology, with the control group transfected with an equivalent amount of NC-siRNA, and the si-RNA group transfected with si-HMG2. Stable transfected cell lines were established based on si-RNA knockdown efficiency. The effects of HMG2 knockdown on the growth, movement, and spread of lung adenocarcinoma cells were assessed using CCK-8, Transwell assays, scratch assays, colony formation assays, and EdU assays. Transcriptome sequencing analysis revealed pathways related to tumorigenesis associated with HMG2. The relative expression levels of MAPK pathway proteins after HMG2 knockdown were detected by Western blot. **Results** HMG2 mRNA expression was significantly elevated in lung cancer tissues and lung adenocarcinoma cell lines ($P < 0.05$). After HMG2 knockdown, cell proliferation, migration, and invasion were significantly reduced ($P < 0.05$), and the phosphorylation levels of the MAPK signaling pathway markedly decreased ($P < 0.05$). **Conclusion** HMG2 enhances the proliferation, migration, and invasion of lung adenocarcinoma cells, and its mechanism may be closely related to the activation of the MAPK signaling pathway *via* phosphorylation.

Key words lung adenocarcinoma; HMG2; proliferation; migration; invasion; MAPK signaling pathway

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