doi: 10.3978/j.issn.2095-6959.2018.11.007
View this article at: http://dx.doi.org/10.3978/j.issn.2095-6959.2018.11.007

miR-129通过靶向调控HMGA2抑制卵巢癌细胞侵袭迁移的作用机制

邓艳蕾[1]，赵琴[1]，李明明[2]

(十堰市妇幼保健院 1. 妇科；2. 超声科，湖北 十堰 442000)

[摘　要]　**目的：**研究miR-129在高级别浆液性卵巢癌(high-grade serous ovarian cancer，HGSOC)组织及细胞系中的表达，并探讨其对卵巢癌细胞侵袭迁移的影响及作用机制。**方法：**实时荧光定量PCR(real-time quantitative PCR，qRT-PCR)检测miR-129，HMGA2在70例HGSOC组织和30例正常输卵管组织中的表达，以及miR-129在人卵巢癌细胞系和人正常卵巢上皮细胞系中的表达；Pearson相关分析评估HGSOC组织中miR-129与HMGA2表达的相关性；将miR-129 mimic和对照转染卵巢癌细胞CAOV后，用Transwell小室法检测细胞侵袭情况，细胞划痕试验检测细胞迁移情况、HMGA2 mRNA和蛋白表达变化；采用生物信息软件及荧光素酶报告基因试验。分析miR-129对HMGA2基因的靶向性作用；转染HMGA2过表达质粒，观察HMGA2对miR-129 mimic CAOV细胞侵袭和迁移的影响。**结果：**miR-129在HGSOC组织和细胞系中的表达均显著低于正常输卵管组织和正常卵巢上皮细胞(均$P<0.05$)；HMGA2在HGSOC组织中的表达显著高于正常输卵管组织(均$P<0.05$)，与miR-129的表达呈负相关($r=-0.712$，$P<0.05$)；与对照组相比，miR-129 mimic组CAOV细胞侵袭迁移能力下降，HMGA2 mRNA和蛋白表达减少(均$P<0.05$)；生物信息软件预测和荧光素酶报告基因实验显示HMGA2为miR-129的靶基因；与miR-129+对照组相比，miR-129 mimic+HMGA2组细胞侵袭迁移能力明显升高(均$P<0.05$)。**结论：**miR-129在HGSOC组织中低表达，可能通过靶向下调HMGA2抑制卵巢癌细胞的侵袭迁移。

[关键词]　高级别浆液性卵巢癌；miRNA-129；HMGA2；侵袭；迁移

Mechanism of miR-129 inhibiting invasion and migration of ovarian cancer cells by targeting HMGA2

DENG Yanlei[1], ZHAO Qin[1], LI Mingming[2]

(1. Department of Gynaecology; 2. Department of Ultrasound, Maternal and Child Health Hospital of Shiyan, Shiyan Hubei 442000, China)

Abstract　**Objective:** To investigate the expression of miR-129 in high-grade serous ovarian cancer (HGSOC) tissues and cell lines, and to explore its effect on the invasion and migration of ovarian cancer cells and its mechanism. **Methods:** Real-time quantitative PCR (qRT-PCR) was used to detect the expression of miR-129 and HMGA2 in 70 HGSOC tissues and 30 normal fallopian tubes, and the expression of miR-129 in human ovarian cancer cell

收稿日期 (**Date of reception**)：2018–08–06
通信作者 (**Corresponding author**)：邓艳蕾，Email: 1186677898@qq.com

lines and human normal ovarian epithelial cells. Pearson correlation analysis evaluated the correlation between miR-129 and HMGA2 expression in HGSOC tissues. After transfection of ovarian cancer cells CAOV with a miR-129 mimic and control, cell invasion was detected by Transwell microscopy, cell migration was detected by cell scratch test, and HMGA2 mRNA and protein expression changes were detected. Bioinformatics software and luciferase reporter gene assay were used to analyze the targeting effect of miR-129 on HMGA2 gene. HMGA2 overexpression plasmid was transfected to observe the effect of HMGA2 on the invasion and migration of miR-129 mimic CAOV cells. **Results:** The expression of miR-129 in HGSOC tissues and cell lines were significantly lower than that in normal fallopian tubes and normal ovarian epithelial cells (P<0.05). HMGA2 was significantly higher in HGSOC tissues than in normal fallopian tubes (P<0.05), negatively correlated with the expression of miR-129 (r=−0.712, P<0.05). Compared with the control group, the invasion and migration ability of CAOV cells in miR-129 mimic group decreased, and the expression of HMGA2 mRNA and protein decreased (P<0.05); bioinformatics software prediction and luciferase reporter gene experiments confirmed that HMGA2 is a target gene of miR-129; compared with miR-129+ control group, miR-129 mimic+HMGA2 group has significantly increased invasion and migration ability (all P<0.05). **Conclusion:** MiR-129 is lowly expressed in HGSOC tissues, and it can inhibit the invasion and migration of ovarian cancer cells by targeting down-regulation of HMGA2.

Keywords high-grade serous ovarian cancer; miRNA-129; HMGA2; invasion; migration

卵巢癌是第三大常见女性生殖系统恶性肿瘤，其病死率占恶性妇科肿瘤的第一位[1]。虽然目前临床上多采用手术、放化疗和分子靶向等多个学科的联合治疗，但是我国卵巢癌的发病率和病死率仍居高不下[2-3]。由于卵巢癌具有早期症状不明显、无可靠的肿瘤生物学标志物、不断复发和缺乏有效治疗靶标等多个特征，使得卵巢癌的治疗进入瓶颈[4]，而局部和全身转移是卵巢癌患者病死率较高的主要原因[5]，但其转移的具体机制尚未明确。卵巢癌组织学类型90%为上皮性恶性卵巢癌，其中高级别浆液性卵巢癌(high-grade serous ovarian cancer，HGSOC)占2/3以上[6]。因此为改善卵巢癌患者预后，阐明潜在的肿瘤转移发展机制并发掘新的治疗靶点至关重要。

微小RNA(miRNA)是一组长约19~25个核苷酸的内源表达非编码小RNA，可通过与靶基因mRNA的3'非翻译区结合降低mRNA的稳定性负调节靶基因mRNA的表达[7]。MiRNA在生物学活动中起至关重要的作用[8-9]，且miRNA的失调与肿瘤的发生、发展密切[10]。MiRNA是参与卵巢癌起始和进展的重要因子。研究[11]表明：miR-129-5p可抑制卵巢癌细胞的增殖和存活，并且在卵巢癌细胞中miR-129-5p的下调与恶性进展和较差的预后有关，而其在卵巢癌侵袭迁移中的作用及机制尚未明确。因此本研究以卵巢癌细胞株CAOV为研究对象，旨在探究miR-129在卵巢癌细胞系侵袭迁移中发挥的作用及机制，为发掘卵巢癌治疗的新靶标提供实验依据。

1 对象与方法

1.1 对象

选取2016年1至12月首次于十堰市妇幼保健院治疗且并未进行治疗的卵巢癌患者，收集手术切除病理确诊的70例HGSOC组织标本以及30例因其他良性疾病切除子宫输卵管术标本，并立即保存于−80 ℃液氮中用于提取组织RNA。患者的临床病理学数据均保存可查，并签署知情同意书。本研究经十堰市妇幼保健院医学伦理委员会审核批准。

1.2 材料

人卵巢癌细胞系3AO，CAOV，HO8910和人正常卵巢上皮细胞IOSE80均购自美国ATCC细胞库；Transwell小室、蛋白裂解试剂购自上海碧云天生物技术有限公司；反转录试剂盒、实时荧光定量PCR(real-time quantitative PCR，qRT-PCR)试剂盒等均购自日本TaKaRa公司。HMGA2、内参GAPDH引物由上海捷瑞生物工程有限公司设计合成，兔抗人HMGA2抗体(ab52039)、鼠抗人GAPDH抗体(ab9485)、突变型和野生型HMGA2的3'-非翻译区(3'-UTR)荧光素酶报告载体(HMGA2-wt，HMGA2-

mut)、miR-129 mimics、HMGA2过表达质粒由上海吉凯基因公司包装合成。

1.3 方法

1.3.1 细胞培养及转染

将细胞培养在37 ℃，5% CO_2全湿度培养箱中，3AO，CAOV细胞培养基为10% FBS + RPMI1640，HO8910细胞培养基为10% FBS + DMEM-F12。CAOV细胞在呈对数生长期时铺至6孔板，贴壁24 h后，按说明书将脂质体2000与各组转染试剂转染至细胞中，分为miR-129 mimics与对照组，以及miR-129 mimic+HMGA2组，放至培养箱中培养。

1.3.2 qRT-PCR检测基因mRNA的表达

收集研磨的组织粉末和转染48 h后的各组细胞，采用TRIzol法裂解细胞提取总RNA。采用在线软件miRBase(http://www.mirbase.org/)分析miR-129 mimics序列。采用Premier 5在线软件设计引物序列，HMGA2基因引物序列：正向引物为5'-ACCCAGGGGAAGACCCAAA-3'，反向引物为5'-CCTCTTGGCCGTTTTTCTCCA-3'；GAPDH基因引物序列：正向引物为5'-GGAGCGAGATCCCTCCAAAAT-3'，反向引物为5'-AGCGAGCATCCCCCAAAGTT-3'，由上海捷瑞生物工程有限公司设计合成。将RNA反转录成cDNA并进行荧光定量PCR。以GAPDH为内参基因。每个样品设置3个反应复孔，按两步法进行反应，分析各样品的循环阈值(cycle threshold，Ct)，用$2^{-\Delta\Delta Ct}$法分析各组实验数据。实验重复3次。

1.3.3 Transwell小室法检测细胞侵袭能力

接种细胞前用50 μL无血清培养基湿润Transwell小室聚碳酸酯微孔膜，取转染48 h后的各组细胞无血清培养基洗3次，以每孔1×10^5个细胞、100 μL培养基接种于Transwell小室的上室，下室加500 μL的完全培养基作为趋化因子，放至培养箱中培养，12 h后于显微镜下观察下室穿过5个细胞的时候终止培养，取出聚碳酸酯微孔膜，PBS洗3次后中性甲醛固定10 min，苏木精染色。显微镜下随机计数5个视野计数，取其均值代表细胞侵袭能力。

1.3.4 细胞划痕试验检测细胞迁移能力

取转染48 h后的各组细胞，以每孔1×10^6个细胞、12 mL接种于6孔板中，将其置于培养箱中，待细胞贴壁后约12 h，用10 μL的无菌枪头在6孔板正中沿直线画1条划痕，PBS冲洗3次后，加入无血清培养基培养。于倒置显微镜下每24 h记录1次细胞迁移情况。

1.3.5 荧光素酶报告基因实验

实验分4组：HMGA2-wt与miR-129 mimics共转染组(HMGA2-wt+miR-129)；A20-wt与scramble共转染组(HMGA2-wt+scramble)；HMGA2-mut与miR-129 mimics共转染组(HMGA2-mut+miR-129)；HMGA2-mut与scramble共转染组(HMGA2-mut+scramble)，分别转染上述4组到CAOV细胞中，48 h后收集细胞，按照双荧光素酶活性检测试剂盒的说明书进行操作，检测荧光素酶活性，实验重复3次。

1.3.6 蛋白提取及Western印迹

收集细胞，每孔加入500 μL的蛋白裂解液(含有5 μL蛋白酶抑制剂和5 μL磷酸酶抑制剂)，震荡裂解20 min，4 ℃，12 000 r/min离心30 min后，BCA试剂盒检测蛋白浓度，变性后，每孔30 μg蛋白进行SDS-PAGE电泳，蛋白经湿转至PVDF膜，5%脱脂牛奶封闭1 h，加入一抗4 ℃孵育过夜，TBST洗3次后，二抗室温孵育1 h，ELC化学发光法曝光条带，显影定影。采用Image J软件进行蛋白条带灰度值的分析，结果重复3次。

1.4 统计学处理

采用SPSS 17.0统计软件进行数据分析，数据均以均数±标准差($\bar{x}\pm s$)表示，两组间比较采用配对t检验，多组间比较采用单因素方差分析，$P<0.05$为差异有统计学意义。

2 结果

2.1 MiR-129在HGSOC组织和细胞系中的表达

MiR-129在HGSOC组织中的表达显著低于正常输卵管组织，差异有统计学意义($P<0.05$，图1A)。与正常卵巢上皮细胞IOSE80相比，miR-129在卵巢癌细胞系3AO，CAOV，HO8910中表达下调，且在CAOV中表达最低，差异均有统计学意义(均$P<0.05$，图1B)，即miR-129在卵巢癌组织和细胞系中低表达。

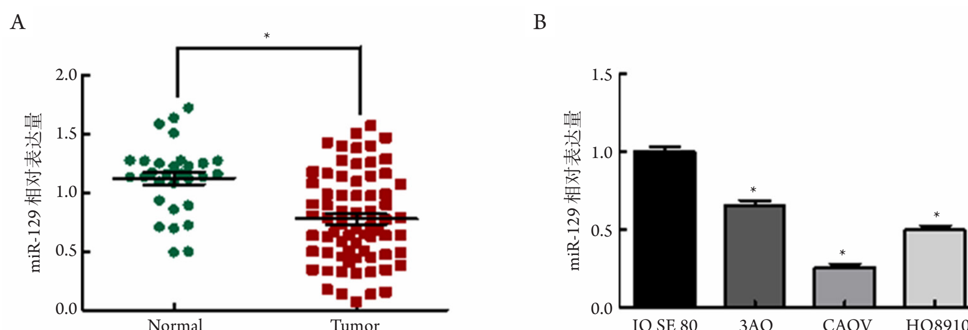

图 1 qRT-PCR 法检测 miR-129 的表达

Figure 1 Expression of miR-129 was detected by qRT-PCR

(A)HGSOC 组织和正常输卵管组织中 miR-129 的表达水平，miR-129 在 HGSOC 组织中低表达 (*P<0.05)；(B)miR-129 在 3 株卵巢癌细胞系 3AO，CAOV，HO8910 中的表达显著低于正常卵巢上皮细胞 IOSE80(*P<0.05)。

(A) Expression level of miR-129 was in HGSOC tissues and normal oviduct tissues, and miR-129 was lowly expressed in HGSOC tissues (*P<0.05); (B) Expression of miR-129 was significantly lower in three ovarian cancer cell lines 3AO, CAOV, HO8910 than that in normal ovarian epithelial cells IOSE80 (*P<0.05).

2.2 Transwell小室检测miR-129对细胞侵袭能力的影响

Transwell小室结果显示：与对照组相比，miR-129组细胞穿过的细胞显著减少，差异有统计学意义(P<0.05，图2)。表明miR-129具有抑制CAOV细胞的侵袭能力。

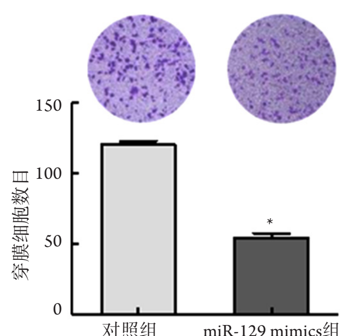

图2 Transwell小室检测转染CAOV细胞miR-129 mimics后细胞穿膜数量减少，细胞侵袭能力下降

Figure 2 Transwell chamber detected the number crossed-membrane of CAOV cells transfected with miR-129 mimics was reduced, and cell invasiveness ability was decreased

与对照组相比，*P<0.05。

Compared with the control group, *P<0.05.

2.3 划痕试验检测miR-129对细胞迁移能力的影响

划痕试验结果显示：与对照组相比，miR-129组细胞划痕愈合度显著降低，差异有统计学意义(P<0.05，图3)。表明miR-129具有抑制CAOV细胞的迁移能力。

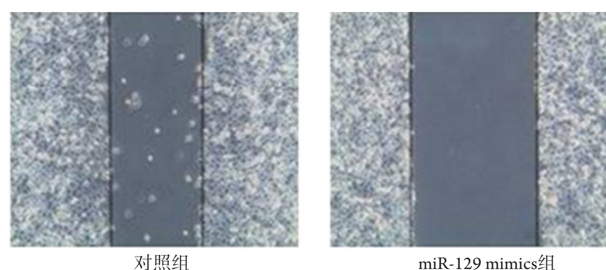

图3 划痕试验检测转染CAOV细胞miR-129 mimics后细胞划痕愈合度下降，细胞迁移能力下降

Figure 3 Scratch assay detected the scratch healing of CAOV cells transfected with miR-129 mimics was reduced, and cell migration ability was decreased

与对照组相比，*P<0.05。

Compared with the control group, *P<0.05.

2.4 MiR-129靶基因的预测和验证

与正常输卵管组织相比，HGSOC组织中HMGA2 mRNA表达明显升高(P<0.05，图4A)。Pearson相关分析表明HGSOC组织中miR-129表达与HMGA2 mRNA表达呈负相关(r=−0.712，P<0.05；图4B)。利用miRBase，Target Scan和mi Target等软件行生物学分析，结果表明miR-129与HMGA2的3'-UTR结合(图4C)。荧光素酶报告基因实验结果显示：与HMGA2-wt+scramble共转染组相比，HMGA2-Wt+miR-129共转染组的荧光素酶活性显著降低；而HMGA2-mut+scramble和HMGA2-mut+miR-129组之间的荧光素酶活性强度无显著差异(图4D)。qRT-PCR和Western印迹表明：与对照组相比，miR-129 mimics组HMGA2 mRNA和蛋白表达

均显著下降(P<0.05；图4E，4F)。说明miR-129在卵巢癌细胞中靶向调控HMGA2基因。

2.5 HMGA2对miR-129介导的CAOV细胞抑制侵袭迁移作用的影响

与miR-129 mimic+对照组相比，miR-129 mimic+HMGA2组CAOV细胞HMGA2 mRNA和蛋白表达均明显增加(P<0.05；图5A，5B)，Transwell小室穿膜细胞数和划痕愈合度均显著增加(P<0.05；图5C，5D)，说明miR-129通过下调HMGA2抑制卵巢癌细胞的侵袭和迁移。

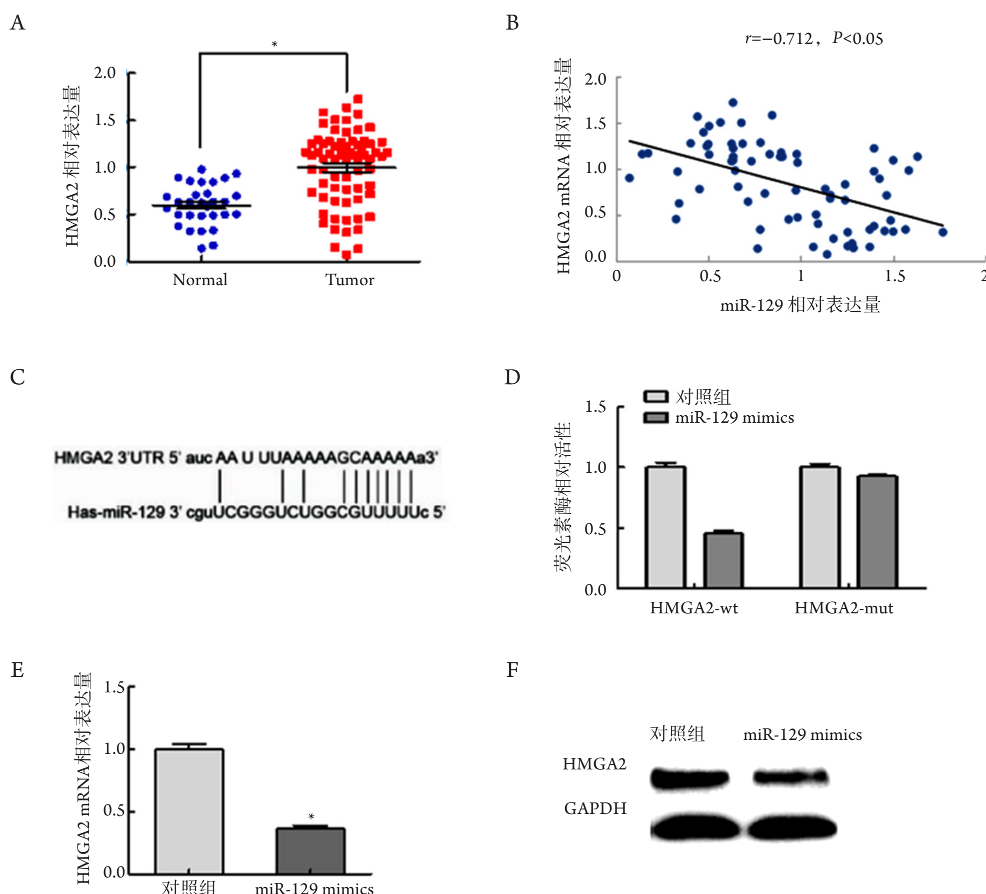

图 4 miR-129 靶基因的预测和验证

Figure 4 Prediction and validation of the miR-129 target gene

(A)HMGA2 在 HGSOC 组织中的表达显著高于正常输卵管组织；(B)Pearson 相关分析 HGSOC 组织中 miR-129 表达与 HMGA2 mRNA 表达呈负相关；(C) 生物信息学预测 miR-129 与 HMGA2 的结合位点；(D) 荧光素酶报告基因验证 HMGA2 为 miR-129 的靶基因；(E) 过表达 miR-129 抑制 HMGA2 mRNA 的表达；(F) 过表达 miR-129 抑制 HMGA2 蛋白的表达。与对照组相比，*P<0.05。

(A) Expression of HMGA2 in HGSOC tissues was significantly higher than that in normal fallopian tubes; (B) Pearson correlation analysis showed that miR-129 expression was negatively correlated with HMGA2 mRNA expression in HGSOC tissues; (C) Bioinformatics predicted the binding site between miR-129 and HMGA2; (D) Luciferase reporter gene verified that HMGA2 was a target gene of miR-129; (E) Overexpression of miR-129 inhibited HMGA2 mRNA expression; (F) Overexpression of miR-129 inhibited expression of HMGA2 protein. Compared with the control group, *P<0.05.

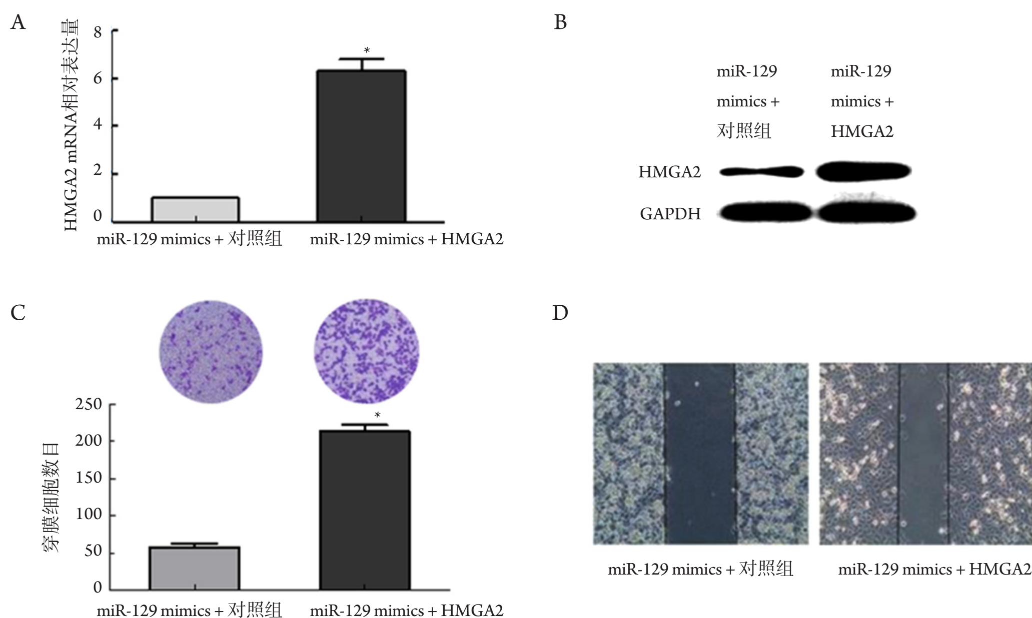

图5 HMGA2对miR-129介导的CAOV细胞抑制侵袭迁移作用的影响

Figure 5 Effect of HMGA2 on inhibition of miR-129 mediated CAOV cells invasion and migration

(A)HMGA2 mRNA在过表达mimics和HMGA2的CAOV细胞中的表达显著高于过表达mimics和对照的细胞；(B)HMGA2 蛋白在过表达mimics和HMGA2的CAOV细胞中的表达显著高于过表达mimics和对照的细胞；(C)Transwell小室检测转染CAOV细胞miR-129 mimics和HMGA2后细胞穿膜数量增多，细胞侵袭能力增加；(D)划痕试验检测转染CAOV细胞miR-129 mimics和HMGA2后细胞划痕愈合度增加，细胞迁移能力增加。与对照组相比，*P<0.05。

(A) HMGA2 mRNA expression in CAOV cells overexpressing mimics and HMGA2 was significantly higher than that in overexpressing mimics and control cells; (B) HMGA2 protein expression was significantly higher in CAOV cells overexpressing mimics and HMGA2 than overexpressing mimics and control cells; (C) Transwell chamber detected the number crossed-membrane of CAOV cells transfected with overexpressing mimics and HMGA2 was increased, and cell migration ability was increased; (D) Scratch assay detected the scratch healing of CAOV cells transfected with overexpressing mimics and HMGA2 was increased, and cell migration ability was increased. Compared with the control group, *P<0.05.

3 讨论

卵巢癌是最致命的妇科恶性肿瘤，其病死率高居女性生殖系统三大恶性肿瘤之首[12-13]。随着医学进步，患者的预后有所改善，但由于卵巢癌不断复发、耐药、早期转移致手术困难和缺乏有效的分子靶向治疗等问题的出现，使卵巢癌患者的5年存活率仍较低[14]。因此研究卵巢癌转移的机制，对寻找治疗卵巢癌新的治疗策略具有重大意义。近年来miRNA在肿瘤的早期诊断、发生发展、肿瘤细胞侵袭和迁移等方面发挥的重要作用引起了广大学者的密切关注[15]。Iorio等[16]首次比较了miRNA在卵巢癌及正常卵巢组织中全基因组范围内的表达情况，发现约30种表达失调的miRNA。

MiR-129是新近发现的miRNA，最早由Lagos-Quintana等[17]在斑马鱼、大鼠和人体等生物体内发现，目前是肿瘤研究的热点，在多个肿瘤中均显示出抑癌基因和抑癌因子的作用。Meng等[18]研究发现miR-129可靶向CBX4抑制乳腺癌细胞的增殖和侵袭。与正常胃组织比较，胃癌组织中miR-129表达下调，其低表达与胃癌患者的肿瘤大小和淋巴结侵袭以及预后不良密切相关，提示miR-129通过靶向调节ADAM9而抑制胃癌细胞的增殖和侵袭能力[19]。MiR-129作为抑癌因子，在多种肿瘤组织或细胞系中表达下调，而在卵巢癌中的表达及是否为抑癌因子未见有报道。HGSOC是卵巢癌的主要组织类型，本研究通过qRT-PCR发现：miR-129在70例HGSOC组织中的表达显著低于30例正常输卵管组织，在3株卵巢癌细胞系中的表达显著低于人正常卵巢上皮细胞系，miR-129低表达于HGSOC组织和卵巢癌细胞中，提示miR-129可能是抑癌因子，可发挥抑癌作用。因此本研究通过合成miR-

129 mimics及其对照，并且转染至卵巢癌CAOV细胞株，Transwell小室和划痕试验检测结果显示过表达miR-129显著抑制CAOV细胞的侵袭和迁移，说明miR-129具有抑制卵巢癌细胞侵袭和迁移的抑癌功能。

每个miRNA通常有数个靶基因，通过调控靶基因发挥不同的生物学功能。本研究利用生物信息学预测到HMGA2 mRNA的启动子区有miR-129的结合位点，进一步双荧光素酶检测结果证实HMGA2为miR-129的靶基因，高迁移率族蛋白A2(high mobility group protein A2，HMGA2)是一种小的非组蛋白染色体蛋白，没有内在的转录活性，但可以通过改变染色质结构来调节转录[20]。HMGA2在胚胎发生中高度表达，而在大多数成熟和分化组织中其几乎不表达。研究[21]表明：HMGA2在许多人类恶性肿瘤中高表达，参与调节肿瘤不同的细胞活动，包括细胞周期调控、分化和衰老。HMGA2过度表达与许多人类肿瘤如乳腺癌和胰腺癌等肿瘤的发生、发展有关[22-23]。本研究发现HMGA2在HGSOC组织中的表达高于正常输卵管组织，与HMGA2在乳腺癌和胰腺癌等肿瘤中高表达的研究结果[22-23]一致。Pearson相关分析显示其与miR-129在HGSOC组织中的表达呈负相关，而荧光素酶报告基因实验结果显示miR-129直接靶向负调控HMGA2基因，而miR-129是否通过调控HMGA2发挥抑制卵巢癌细胞侵袭和迁移的功能尚不明确。

本研究结果显示：CAOV细胞转染miR-129 mimics后细胞侵袭和迁移能力下降，如miR-129通过负调控HMGA2基因抑制细胞侵袭和转移，HMGA2基因的过表达会削弱miR-129的抑制作用，而CAOV细胞同时转染miR-129 mimics和HMGA2后，Transwell小室和划痕试验显示细胞穿膜数量和划痕愈合度比同时转染miR-129 mimics和对照组增加，表明HMGA2可以减少miR-129对卵巢癌细胞侵袭和迁移能力的抑制作用，miR-129通过负调控HMGA2基因发挥抑制细胞侵袭和转移的功能，HMGA2具有促进细胞侵袭和迁移的作用，与Xia等[24]发现的下调HMGA2表达减少上皮间质转化来抑制胃癌细胞的增殖、侵袭能力的结果类似。

综上，miR-129在HGSOC组织和卵巢癌细胞中低表达，通过负调控HMGA2可抑制卵巢癌细胞的侵袭和迁移，本研究结果可为研究卵巢癌的恶性生物学行为侵袭和迁移的分子机制提供新的理论基础，为卵巢癌的治疗提供新的干预靶点。

参考文献

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017[J]. CA Cancer J Clin, 2017, 67(1): 7-30.
2. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018[J]. CA Cancer J Clin, 2018, 68(4): 284-296.
3. Wang J, Li J, Chen R, et al. Contribution of lymph node staging method and prognostic factors in malignant ovarian sex cord-stromal tumors: a world wide database analysis[J]. Eur J Surg Oncol, 2018, 44(7): 1054-1061.
4. Zhao R, Liu Q, Lou C. MicroRNA-299-3p regulates proliferation, migration and invasion of human ovarian cancer cells by modulating the expression of OCT4[J]. Arch Biochem Biophys, 2018, 651: 21-27.
5. Liu DT, Yao HR, Li YY, et al. MicroRNA-19b promotes the migration and invasion of ovarian cancer cells by inhibiting the PTEN/AKT signaling pathway[J]. Oncol Lett, 2018, 16(1): 559-565.
6. Prat J. New insights into ovarian cancer pathology[J]. Ann Oncol, 2012, 23 Suppl 10(1): x111-x117.
7. Hausser J, Zavolan M. Identification and consequences of miRNA-target interactions--beyond repression of gene expression[J]. Nat Rev Genet, 2014, 15(9): 599-612.
8. Frith JE, Kusuma GD, Carthew J, et al. Mechanically-sensitive miRNAs bias human mesenchymal stem cell fate via mTOR signalling[J]. Nat Commun, 2018, 9(1): 257.
9. 李辉. miR-2135对P19细胞增殖及向心肌细胞分化的作用[J]. 中国组织工程研究, 2016, 20(45): 6814-6820.
   LI Hui. Effect of miR-2135 on the P19 cell proliferation and differentiation into cardiomyocytes[J]. Chinese Journal of Tissue Engineering Research, 2016, 20(45): 6814-6820.
10. Wang XZ, Hang YK, Liu JB, et al. Over-expression of microRNA-375 inhibits papillary thyroid carcinoma cell proliferation and induces cell apoptosis by targeting ERBB2[J]. J Pharmacol Sci, 2016, 130(2): 78-84.
11. Tan G, Cao X, Dai Q, et al. A novel role for microRNA-129-5p in inhibiting ovarian cancer cell proliferation and survival via direct suppression of transcriptional co-activators YAP and TAZ[J]. Oncotarget, 2015, 6(11): 8676-8686.
12. Liu J, Jiang Y, Wan Y, et al. MicroRNA-665 suppresses the growth and migration of ovarian cancer cells by targeting HOXA10[J]. Mol Med Rep, 2018, 18(3): 2661-2668.
13. Siegel RL, Miller KD, Fedewa SA, et al. Cancer statistics, 2017[J]. CA Cancer J Clin, 2017, 67(3): 177-193.
14. Cliby WA, Powell MA, Al-Hammadi N, et al. Ovarian cancer in the United States: contemporary patterns of care associated with improved survival[J]. Gynecol Oncol, 2015, 136(1): 11-17.
15. Qu X, Gao D, Ren Q, et al. miR-211 inhibits proliferation, invasion and

migration of cervical cancer via targeting SPARC[J]. Oncol Lett, 2018, 16(1): 853-860.
16. Iorio MV, Visone R, Di Leva G, et al. Micro RNA signatures in human ovarian cancer[J]. Cancer Res, 2007, 67(18): 8699-8707.
17. Lagos-Quintana M, Rauhut R, Meyer J, et al. New microRNAs from mouse and human[J]. RNA, 2003, 9(2): 175-179.
18. Meng R, Fang J, Yu Y, et al. miR-129-5p suppresses breast cancer proliferation by targeting CBX4[J]. Neoplasma, 2018, 65(4): 572-578.
19. Liu Q, Jiang J, Fu Y, et al. MiR-129-5p functions as a tumor suppressor in gastric cancer progression through targeting ADAM9[J]. Biomed Pharmacother, 2018, 105: 420-427.
20. Pallante P, Sepe R, Puca F, et al. High mobility group a proteins as tumor markers[J]. Front Med (Lausanne), 2015, 2: 15.
21. Zhang H, Tang Z, Deng C, et al. HMGA2 is associated with the aggressiveness of tongue squamous cell carcinoma[J]. Oral Dis, 2017, 23(2): 255-264.
22. Sgarra R, Pegoraro S, Ros G, et al. High Mobility Group A (HMGA) proteins: molecular instigators of breast cancer onset and progression[J]. Biochim Biophys Acta Rev Cancer, 2018, 1869(2): 216-229.
23. 王运良, 李翠. HMGA1和HMGA2在胰腺癌中的表达及临床意义[J]. 河北医药, 2017, 39(10): 1449-1452.
WANG Yunliang, LI Cui, Expression and clinical significance of HMGA1 and HMGA2 in pancreatic carcinoma[J]. Hebei Medical Journal, 2017, 39(10): 1449-1452.
24. Xia YY, Yin L, Jiang N, et al. Downregulating HMGA2attenuates epithelial-mesenchymal transition-induced invasion and migration in nasopharyngeal cancer cells[J]. Biochem Biophys Res Commun, 2015, 463(3): 357-363.

本文引用： 邓艳蕾, 赵琴, 李明明. miR-129通过靶向调控HMGA2抑制卵巢癌细胞侵袭迁移的作用机制[J]. 临床与病理杂志, 2018, 38(11): 2329-2336. doi: 10.3978/j.issn.2095-6959.2018.11.007

Cite this article as: DENG Yanlei, ZHAO Qin, LI Mingming. Mechanism of miR-129 inhibiting invasion and migration of ovarian cancer cells by targeting HMGA2[J]. Journal of Clinical and Pathological Research, 2018, 38(11): 2329-2336. doi: 10.3978/j.issn.2095-6959.2018.11.007