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MicroRNAs 在乳腺癌发生、发展和转移中的作用

佘为为[1,2],黄清荣[1],李延敏[1],张桂春[1],周菊华[1]

(1. 鲁东大学 生命科学学院;肿瘤免疫研究院,山东 烟台 264039;2. 上海农林职业技术学院,上海 201699)

摘要:MicroRNAs(miRNAs)为真核生物中具有组织特异性和高度保守性的一类非编码调控的单链 RNAs,长度约为 20~24 个核苷酸,其通过与靶标 mRNA 完全或不完全互补配对导致 mRNA 降解或抑制转录后翻译从而导致基因的沉默。随着研究的不断深入,证实 miRNAs 的异常表达与乳腺癌之间存在很大的相关性。miRNAs 在肿瘤的产生、分化、侵袭以及转移等过程中都发挥着促进或抑制的作用。本文对近年来与乳腺癌相关的 miRNAs 及其作用机制的研究进行分析和展望,以期可以利用特异的 miRNAs 作为乳腺癌的早期诊断、预后指标和治疗的靶向目标。

关键词:miRNA;乳腺癌;作用机制;诊断;治疗

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乳腺癌是妇女最常见的恶性肿瘤。近年来,我国乳腺癌的发病率急速上升。研究表明,microRNAs(miRNAs)的异常表达与乳腺癌的发生紧密相关,在肿瘤的产生、分化、侵袭以及转移等过程中都发挥着重要的作用[1—2]。因此,本文对 miRNAs 在乳腺癌发生中的作用和机理研究作一总结分析。结果显示,特异的 miRNAs 有希望可以作为乳腺癌的早期诊断指标,也可以作为乳腺癌治疗的有效靶点。

1 miRNAs 的特性和功能

miRNAs 于 1993 年在秀丽隐杆线虫中发现,为小片段遗传物质,有助于在特定时间打开或关闭某一基因。经历两次剪切合成成熟的 miRNA,通过与靶基因序列的完全或不完全互补配对,致使靶序列降解或抑制转录后翻译,最终诱导基因沉默。大多数的 miRNA 具有高度的保守性、时序性及组织特异性,是正常细胞功能的重要部分,但表达不正常也能促发人类产生疾病。miRNA 在许多恶性肿瘤中扮演着重要的角色。近年来的研究发现与乳腺癌相关的 miRNAs,包括 let-7、miR-21、miR-10b、miR-17-5p、miR-155、miR-145 和 miR-520b 等,在乳腺癌组织中降低或升高,充当癌基因或抑癌基因样来发挥作用,从而促进或抑制肿瘤的发生、发展和转移(图 1)[3—4]。每个 miRNA 有多个靶基因,每个靶基因也是由多个 miRNA 来控制的,这是一种极度精确的调节网络。一旦打破了这种网络的平衡,就会出现无序性的表达,随之而来的是肿瘤或其他疾病的发生。为了更好的了解 miRNAs 的作用机理,就要知道哪一个 miRNA 作用于哪一个基因。目前,利用生物信息学技术比较容易预测 miRNA 的基因靶标[5]。

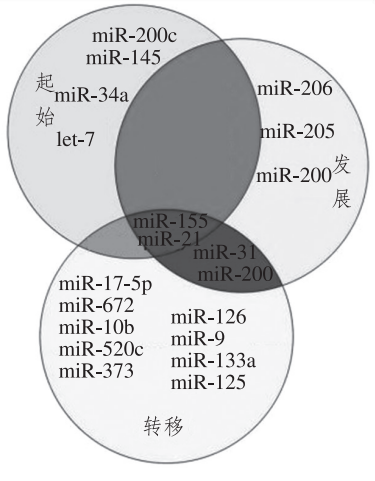

图 1 在乳腺癌发生的不同阶段所起作用的 microRNAs

Fig. 1 Role of microRNAs in the different stages of breast cancer development

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第一作者简介:佘为为(1990—),女,山东枣庄人,讲师,硕士,研究方向为肿瘤免疫。E-mail:272616927@qq.com

通信作者简介:周菊华(1963—),男,浙江东阳人,教授,博士,研究方向为肿瘤免疫。E-mail:juhuaz@hotmail.com

2　miRNAs 在乳腺癌发生中的变化

近年来,利用高通量芯片(High-throughput microarray)、第二代测序技术(Next-generation sequencing,NGS)、单细胞测序技术(Single-cell genomics)和荧光实时定量 PCR 等多种实验技术研究,发现多种肿瘤细胞中存在 miRNA 异常表达的现象。miRNAs 的异常表达与乳腺癌血管形成、肿瘤细胞的转移、侵袭及肿瘤耐药性等过程有密切的关系。这些看似不重要却异常表达的 miRNAs,将成为潜在的肿瘤治疗靶点。Toda 等利用 RNA 测序技术发现在乳腺癌患者中 miR-99a-5p/-3p、miR-101-5p/-3p、miR-126-5p/-3p、miR-143-5p/-3p 和 miR-144-5p/-3p 的表达显著降低,并且经证实这些 miRNAs 是抑癌基因,与乳腺癌的发生、侵袭和转移密切相关[6]。Wu 等利用 RNA 测序技术,发现在三阴性乳腺癌患者中有 34 种 miRNAs 的表达显著降低,而 20 种 miRNAs 的表达则显著增加[7]。综合近年来的研究发现,在乳腺癌病人中下调的 miRNAs 有 miR-34、miR-126 和 miR-335 等(详见表 1),而上调的 miRNAs 包括 miR-10b、miR-21 和 miR-155 等(详见表 2)。

表 1　在乳腺癌中表达下调的 miRNAs 及其功能

Tab. 1 Down-regulated miRNAs and their functions in breast cancer

miRNA	靶点	功能	参考文献
miR-27a	EGFR	抑制癌细胞增殖和侵袭	[8—9]
miR-30a	Snail	抑制癌细胞增殖和侵袭	[10—11]
miR-30b	NT5E	抑制癌细胞增殖、转移和侵袭	[9,12]
miR-30c	BCL9、SOX9	抑制癌细胞增殖和转移	[11,13—14]
miR-31	FZD3、ITGA5、M-RIP、MMP16、PDX、RhoA、SATB2	抑制癌细胞转移和侵袭	[15—17]
miR-34a	Bcl-2、SIRT1、Wnt1	抑制癌细胞增殖和转移	[18—20]
miR-107	HMGB1	抑制癌细胞增殖和转移	[21]
miR-126	VEGF-A、PIK3R2	抑制转移	[11,22—23]
miR-126-5p	Bcl2l2	诱导癌细胞凋亡	[24—25]
miR-133a	FSCN1	抑制转移	[26—27]
miR-136-5p	MTDH	抑制癌细胞增殖和诱导凋亡	[24,28]
miR-140	PD-L1	抑制癌细胞增殖	[11,29]
miR-145-3p	LMNB2	抑制癌细胞增殖、转移和侵袭	[30—31]
miR-145-5p	LMNB2	抑制癌细胞增殖、转移和侵袭	[30—31]
miR-146a	CDKN2A	抑制癌细胞增殖	[32]
miR-148a	IGF-IR	抑制癌细胞增殖、转移和侵袭	[9,33]
miR-148b-3p	RLBP1	抑制癌细胞增殖、转移和侵袭	[34—35]
miR-195	SOX4	抑制转移和侵袭	[36—38]
miR-200	ZEB1、ZEB2	抑制转移	[39—40]
miR-200b-3p	LIMK1	抑制癌细胞增殖、转移和侵袭	[41]
miR-205(miR-205-5p)	HER3、HMGB1	抑制癌细胞增殖、集落、侵袭和转移	[18,42—43]
miR-206	Cx43	抑制细胞增殖和侵袭	[11,44—45]
miR-221-3p	ARF4	抑制癌细胞增殖和转移	[46]
miR-335	c-Met	抑制转移和侵袭	[11,47—48]
miR-340	EZH2、c-Met、MYO10	抑制癌细胞增殖、转移和侵袭,诱导细胞死亡	[49—51]
miR-342	HER2Δ16	抑制耐药性乳腺癌细胞的生长	[52—54]
miR-429-5p	LIMK1	抑制癌细胞增殖、转移和侵袭	[41]
miR-451	c-Myc、MIF	抑制癌细胞增殖、转移、侵袭和血管生成	[9,55—56]
let-7	HMGA2、H-RAS	抑制乳腺癌干细胞增殖	[57—59]

表2 在乳腺癌中表达上调的miRNAs

Tab. 2 Up-regulated miRNAs and their functions in breast cancer

miRNA	靶点	功能	参考文献
miR-9	E-钙黏蛋白、SOCS3	促进EMT和转移、MDSC产生	[60—62]
miR-10b(miR-10b-5p)	HOXD10	促进转移	[35,63—64]
miR-15b	MTSS1	促进转移和侵袭	[65]
miR-17-5p	RUNX3、PTEN、PIK3R1	促进癌细胞增殖、侵袭和抑制凋亡	[66—69]
miR-19a	RhoB、THBS1、PTEN	促进癌细胞增殖、转移和侵袭	[70—73]
miR-21(miR-21-5p)	PTEN、PDCD4、Maspin、FasL	癌基因,促转移、侵袭	[74—77]
miR-24	ZNF367、WWOX	促进癌细胞增殖、转移和侵袭	[73,78—79]
miR-96-5p	AK3、CAV1、CCDC67	促进癌细胞增殖、转移和侵袭	[80—83]
miR-106a-5p	TGFβR2	促进转移和耐药性	[84—85]
miR-130b-5p	RASAL1	促进癌细胞增殖、转移和侵袭	[86—87]
miR-135b-5p	KLF4、CMTM3、NR3C2	提高癌细胞活力,促进癌细胞增殖、转移和侵袭	[24,88—90]
miR-155	TSPAN5、SOCS1	抑制凋亡,促进癌细胞增殖、转移、耐药性和癌干细胞	[73,91—94]
miR-181b	PDCD4、Bim、AC9	促进癌细胞增殖和转移,抑制凋亡,增加耐药性	[73,95—97]
miRNA-182	PTEN、FBXW7	促进癌细胞增殖、转移和侵袭,抑制凋亡	[98—100]
miR-182-5p	CAMK2N1、FOXO3a	促进癌细胞增殖、转移和侵袭	[24,101—102]
miR-197	FUS1、p120 catenin	抑制抑癌基因、促进EMT	[93,103—104]
miR-205	APC、PTEN、SMAD4	促进癌细胞增殖和侵袭	[93,105—106]
miR-206	Neurokinin-1	促进癌细胞增殖、转移和侵袭	[87,107]
miR-221	SOCS3、PHF2、BMF	促进癌细胞增殖、抑制凋亡	[108—111]
miR-221/222	PTEN、TRPS1、GAS5	促进癌细胞生长、癌干细胞活性,抑制凋亡	[63,112—114]
miR-222-3p	BBC3、PPP2R2A、TIMP3	促进癌细胞增殖、转移和侵袭,抑制凋亡	[87,115—117]
miR-331(miR-331-3p)	ST7L	促进癌细胞增殖、转移、侵袭和EMT	[38,118]
miR-373	TXNIP	促进转移和侵袭	[119—121]
miRNA-375	SEC23A	促进癌细胞增殖	[100,122]
miR-720	E-cadherin、Rab35	促进癌细胞增殖、转移和侵袭,抑制凋亡	[123—125]
miR-nov3	ATRX	抑制抑癌基因	[126]
miR-nov7	CDH11、APC、SFRP2	抑制抑癌基因	[126]

3 miRNAs在乳腺癌发生中的作用及其作用机理

不同的miRNAs在乳腺癌发生中的作用及其作用机理不同(表1、表2和图2)。例如,miR-9能够直接作用于E钙黏蛋白[60,127],而miR-200和miR-205通过ZEB1、ZEB2作用于E钙黏蛋白(E-cadherin),从而调控上皮细胞—间充质细胞转换(Epithelial-mesenchymal transition,EMT)的作用影响肿瘤细胞的侵袭[128—129];而miR-205又可以作用于HER3,通过影响PI3K/Akt信号通路调控肿瘤细胞的增殖[130—131]。以下着重讨论几种研究比较深入的miRNAs在乳腺癌发生中的作用及其作用机理。

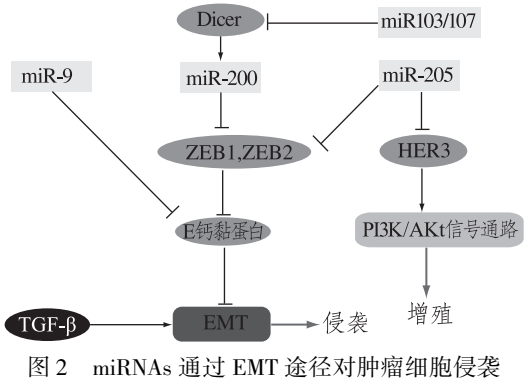

图2 miRNAs通过EMT途径对肿瘤细胞侵袭以及增殖的影响

Fig. 2 Effects of microRNAs on the proliferation, EMT and invasion of breast cancer cells

3.1 miR-10b

miR-10b(也称为miR-10b-5p)在具有明显的转移侵袭能力的乳腺癌细胞中表达上调[132]。

转录因子 Twist 可结合到 miR-10b 的启动子区进而促进其表达[133]。表达上调的 miR-10b 将会结合到靶基因 HOXD10 的 3'UTR 区,抑制其翻译,继而增强了 RhoC 的表达量[134]。RhoC 是一种小分子 GTP 酶,可促使细胞骨架蛋白肌动球蛋白的重建并调节细胞形态,并通过下调 E 钙黏蛋白的表达影响细胞的黏附性和迁移性[135]。由此,miR-10b 具有促进乳腺癌细胞转移和侵袭的能力[132]。

3.2　miR-17-5p

与正常乳腺组织相比,乳腺癌组织中 miR-17-5p 表达水平明显上调[136]。miR-17-5p 除了通过 CyclinD1 影响细胞增殖外,还可以通过抑制 RUNX3、PTEN 和 PIK3R1 来影响 PI3K/AKT 信号通路的激活能力进而获得癌细胞增殖能力,促进癌症的发生[66—68,137]。另外,Li 等早期研究发现 miR-17-5p 可以通过抑制下游靶基因 HBP1 进而导致乳腺癌细胞的转移侵袭能力的增强[138]。

3.3　miR-34

miR-34 家族包括 miR-34a、miR-34b 和 miR-34c 三个成员[139]。miR-34(通常指的是 miR-34a)在三阴性乳腺癌细胞中的表达降低[20]。miR-34 在乳腺癌组织中下调可能是由多种因素造成的,其中包括 miR-34 在基因组中的缺失、启动子区域的甲基化以及某些转录因子 P53 和 ELK1 的活性水平[140]。研究指出,有些 miRNA 在乳腺癌发生中充当了抑癌基因的作用。例如 miR-34 通过下调其下游靶基因 Fra-1、Myc、SIRT1、Notch1、Wnt1 及细胞凋亡调节因子 Bcl-2 来抑制肿瘤细胞的扩增和侵袭,并诱导凋亡[18—19,141]。Notch1 是跨膜蛋白受体,细胞通过其来调控细胞的生长,而 miR-34 则可通过对 Notch1 的调节来影响乳腺癌细胞对阿霉素的敏感性[142]。已有研究表明,Fra-1 能激活肿瘤相关巨噬细胞的 IL-6/JAK/Stat3 通路,导致这些细胞释放促血管生成因子,从而促进乳腺癌细胞的浸润[143]。因此,miR-34 可能通过调节多种靶基因在乳腺癌的发生中起着重要的作用(图 3)。

3.4　miR-126

Kawaguchi 和 Li 等研究发现 miR-126 在乳腺癌病灶中表达降低[11,23]。miR-126 的下游靶基因为 VEGF-A 和 PI3R2,所以,miR-126 抑制与癌细胞的存活密切相关的 VEGF/PI3K/AKT 信号通路[22]。AKT 下游非常多,包括 NF-κB 和 FOXO 等等,多是促增殖抑凋亡的因子[144—145]。由此可见,miR-126 在乳腺癌病灶中表达降低的结果是促进癌细胞的增殖和存活。

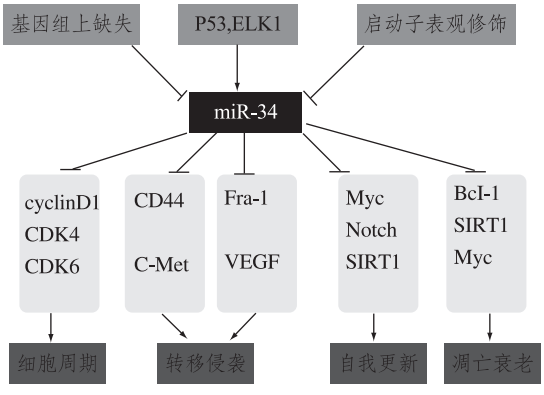

图 3　miR-34 的表达调控因子、作用靶基因和生物学功能

Fig. 3 Transcription factors, gene targets and biological functions of miR-34

3.5　miR-145

癌症是一种细胞周期性的疾病。细胞周期的调控是细胞周期蛋白 Cyclin 和周期蛋白依赖性激酶 CDK 等多种调节因素相互作用的结果。因此,任何一种调节因素的表达失衡都会影响细胞周期的正常运转。miR-145,包括 miR-145-5p 和 miR-145-3p,在乳腺癌组织中表达下调[31]。miR-145-5p 的靶基因之一为 CDK6,阻止癌细胞分裂停留在 G1 期[146]。miR-145-5p 可以直接作用于 SOX2 靶基因,从而抑制乳腺癌细胞的增殖[147]。miR-145-5p 也能够作用于其它靶基因,例如 c-Myc、MUC1 和 MMP11,因而抑制癌细胞的转移和侵袭,阻止肿瘤的发生[148]。miR-145-5p 和 miR-145-3p 都可以作用于 LMNB2 靶基因,抑制癌细胞的增殖、转移和侵袭[30]。因此,miR-145 通过作用于多个靶基因,抑制乳腺癌细胞的增殖、转移和侵袭;miR-145 表达的下调则促进了乳腺癌细胞的增殖、转移、侵袭和癌症的发生。

3.6　miR-155

许多研究证实,miR-155 在乳腺癌病人的血清中含量显著增加[73,93—94]。miR-155 的靶基因包括抑癌基因 SOCS1,miR-155 负调控 SOCS1 以及增强 MMP16 的表达,因此促进乳腺癌细胞的

增殖和转移[92]。miR-155 作用于 TP53INP1 (tumor protein 53-induced nuclear protein 1)靶基因,所以,能够促进乳腺癌细胞的增殖和抑制细胞凋亡[149]。miR-155 抑制靶基因 TSPAN5 的表达,从而增加三阴性乳腺癌细胞的干细胞特性和地西他滨的耐药性[91]。另有研究表明,miR-155 作用于 TRF1 靶基因,增加染色体端粒的不稳定性,从而促进乳腺癌的发生[150]。所以,miR-155 本身是一种癌基因,抑制乳腺癌癌细胞凋亡,促进癌细胞增殖、转移、耐药性和癌干细胞形成。

3.7 miR-335

研究表明,miR-335 在乳腺癌病灶中的表达降低[48]。miR-335 作用于 c-Met 靶基因,因而抑制乳腺癌细胞的转移[47]。miR-335 也可以作用于 OCT4 和 PAX6 等靶基因,抑制癌细胞的增殖、转移和肿瘤发生[151—152]。miR-335 可通过直接作用于细胞转录因子 SOX4 [Sex determining region Y(SRY)-box4,Sox4]和肌腱蛋白 C(也叫细胞粘合素 C,tenascin C)而使细胞的形态发生改变,最终癌细胞的转移和侵袭能力受到影响[153—154]。SOX4 广泛调控与肿瘤细胞的转移有密切联系的 Wnt、TGF-β、Notch 和 Hedgehog 等信号通路[155—157]。因此,miR-335 可能通过参与这些信号通路的调控而影响乳腺癌细胞的转移和癌症的发生。

3.8 let-7

let-7 在乳腺癌肿瘤组织中低表达,其通过抑制癌基因 HMGA2 和 H-Ras 的表达来抑制乳腺癌干细胞的增殖和自我更新(图 4)[57—59]。HMGA2 为致癌基因高迁移率族蛋白(high mobility group AT-hook 2、HMGA2),基因定位于 12q13-15,胚胎发育早期表达,但在胚胎发育大约 15 天后表达即被关闭,只有在肿瘤组织中才重新被打开。HMGA2 蛋白的 AT 钩区会特异的结合在 DNA 双螺旋结构的小沟中,其结果是导致了 DNA 发生剧烈的弯折,从而大大促进了转录因子复合体的结合,进而调节转录和修复[158]。最近有研究证明,TET1 和 HOXA9 对乳腺癌的产生和迁移起到抑制作用,HMGA2 的靶基因为 TET1 和 HOXA[15]。HMGA2 通过抑制 TET1 介导的脱甲基和 HOXA 基因的表达,进而促进了乳腺癌细胞的迁移[15]。

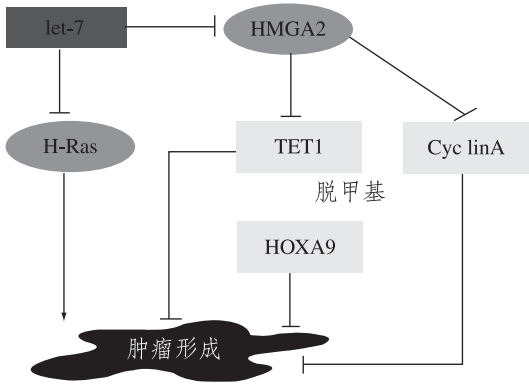

图 4 let-7 对肿瘤形成的影响

Fig. 4 Effects of let-7 on the formation of breast cancer

4 miRNAs 在肿瘤发生中作用的研究意义

多种 miRNAs 在乳腺癌中的差异表达以及不同的 miRNAs 通过调控各自不同的靶基因在乳腺癌发生、发展和转移进程中可能起着重要的作用(表 1、表 2 和图 5),为研究乳腺癌的发生、增殖、转移以及诊断、治疗、预后研究提供了很好的方向[159]。此外,合成特定药物来特异性抑制某些促进乳腺癌增殖和转移的 miRNAs,有希望达到治疗癌症的目的[160]。因此,一些特定的 miRNAs 可以用于乳腺癌的诊断、治疗和预后评估。

4.1 诊断

大量的研究表明,miRNAs 可以用于乳腺癌的早期诊断指标[161—162]。ZHAO 等研究指出,血浆中的 miRNA 异常表达可作为早期乳腺癌诊断的标志物[163]。李雪峰等应用荧光定量 PCR 技术检测乳腺癌患者血清中 miRNA-21 的含量,发现荧光定量 RCR 检测血清 miR-21 的方法,是一种比较敏感、稳定的方法,这种方法对乳腺癌的诊断具有很大的价值[164]。

原位杂交技术研究临床标本后发现,miR-145 只在正常乳房导管和小叶的肌上皮细胞中正常表达,而在与之对应的肿瘤组织中低表达甚至不表达。此外,miR-145 在肿瘤处的表达明显异常[26]。这些结果表明,miR-145 可作为乳腺癌早期诊断标志物。

报道显示,miR-221/222 在三苯氧胺(tamoxifen)耐药的乳腺癌细胞中过度表达[165]。因而,miR-221/222 的表达水平可作为预测乳腺癌患者对三苯氧胺化疗效果的有效指标。

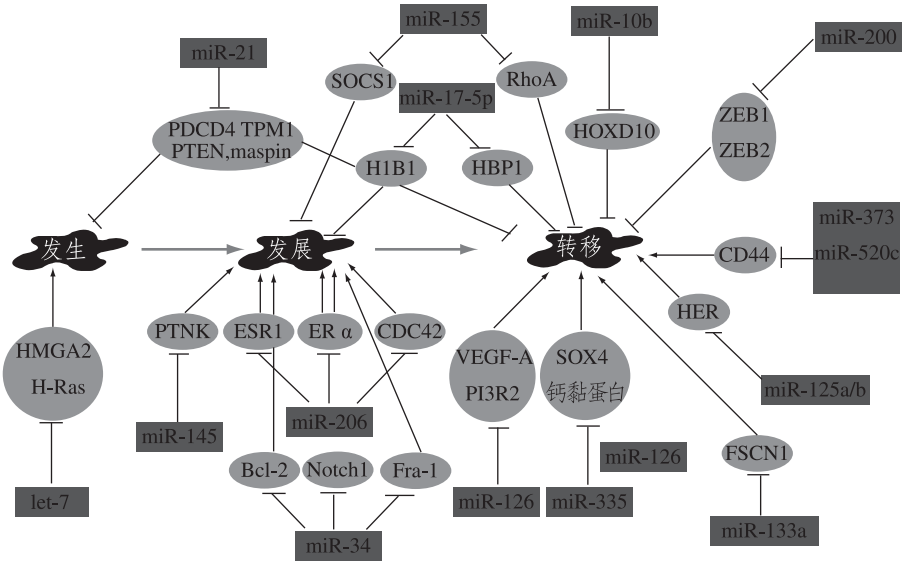

图 5　miRNAs 对肿瘤细胞发生、发展和转移影响的作用机理

Fig. 2 Mechanisms of microRNAs in the initiation, progression and metastasis of breast cancer cells

4.2　治疗

miRNAs 有希望成为用于乳腺癌的有效治疗药物[166—167]。miR-21 是目前研究较为深入的 miRNA 之一,在包括乳腺癌在内的大多数恶性肿瘤中表达都会发生上调[168—169]。Yan 等研究发现,下调乳腺癌细胞 MDA-MB-231 中 miR-21 的表达水平,会明显抑制乳腺癌细胞的侵袭能力和肺转移[170]。学者们对 miR-21 的作用机理进行深入的研究,发现 miR-21 的作用靶点除了 PDCD4 外,还有 maspin、PTEN、SCOS1 和 TPM1 等,即 miR-21 可通过多种途径促进乳腺癌的侵袭和转移[169,171-173]。因此,以 miR-21 为靶点的靶向治疗,可以高效、快捷地为干预肿瘤侵袭、转移提供思路。

研究表明,miR-155 是一种癌基因,在乳腺癌病人中的表达显著增加,促进乳腺癌的发生、转移和耐药性[73,91—94]。因此,miR-155 也是一种乳腺癌治疗的靶点。开发降低 miR-155 表达的措施和方法,可以用于乳腺癌的治疗。

另外,miR-126 发现是一种抑癌基因,在乳腺癌病灶中表达显著降低[11,23]。miR-126 能够抑制乳腺癌细胞增殖、转移和侵袭[174—175]。因此,miR-126 可能是一种有效的药物,可以用于乳腺癌的治疗。

4.3　预后

miRNAs 也可以用于乳腺癌的预后诊断指标[176]。Camps 等对 219 例早期乳腺癌患者的预后发现,miR-210 的表达量与患者的无病生存率及总生存率呈显著负相关,表明 miRNA-210 的表达可成为乳腺癌预后的独立预测标志[177]。此外,miR-10b、miR-21 和 miR-210 等 miRNAs,也可以用于乳腺癌的预后诊断指标[76,178]。

5　结语与展望

综上所述,研究 miRNAs 在乳腺癌中的表达差异、功能和作用机理,对肿瘤产生机制的理解具有重大意义。同时,miRNAs 靶向治疗将有希望成为治疗肿瘤的有效手段。通常,一种 miRNA 有多个靶基因,以乳腺癌相关的 miRNA 为靶点的生物靶向治疗应用于临床中,则可能比针对单一靶基因进行治疗的效率要高很多。但是,每种 miRNA 调控基因表达的机制有所不同,各个具体机制的每一环节尚未完全阐明,靶基因的预测,各种转录因子、细胞因子等影响因素对通路中任一环节的调节作用等问题还需进一步研究。我们期待将不同信号通路通过共调基因相互联系在一起,进而对这一复杂的网络有更深入的了解。相信在不久的将来,我们会开拓乳腺癌治疗的新视野,为乳腺癌患者带来福音。此外,迫切需要、尽快实施通过临床试验来验证特定 miRNAs 在乳腺癌早期诊断、治疗和预后中的作用和临床意义。

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Role of MicroRNAs in Breast Carcinogenesis

SHE Weiwei[1,2], HUANG Qingrong[1], LI Yanmin[1], ZHANG Guichun[1], ZHOU Juhua[1]

(1. Institute for Tumor Immunology, School of Life Sciences, Ludong University, Yantai 264039, China;
2. Shanghai Vocational College of Agriculture and Forestry, Shanghai 201699, China)

Abstract: MicroRNAs (miRNAs) are a group of non-coding single-stranded RNAs, which are composed of 20 ~24 nucleotides. In eukaryotes, miRNAs are highly conservative and tissue-specific. miRNAs usually induce mRNA degradation or post-transcriptional inhibition by completely or incompletely complementary pairing with their target mRNAs, leading to target gene silencing. Recent studies have confirmed that the dysregulation of miRNA expression is associated with breast cancer development. miRNAs play an important role in tumor formation, differentiation, invasion and metastasis. Recent studies on the expression, function and underlying mechanisms of specific miRNAs in breast cancer pathogenesis are discussed. The results presented here will provide solid evidences for the development of novel effective diagnosis, prognosis and treatment for breast cancer.

Keywords: microRNAs; breast cancer; mechanism of action; diagnosis; therapy

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Effect of Anti-solvent on the Performance of Perovskite Thin Films and Solar Cells

JIA Xiangrui[1], BAI Fan[2], MAO Caixia[3], ZHANG Shufang[1,2]

(1. School of Physics and Optoelectronic Engineering, Ludong University, Yantai 264039, China;
2. School of Materials Science and Engineering, Nanjing University of Technology, Nanjing 210094, China;
3. School of Electronics and Information Engineering, Hubei University of Science and Technology, Xianning 437100, China)

Abstract: The efficiency of perovskite solar cells has increased rapidly in a few years, showing a great potential for application. As the most important part of this kind of battery, perovskite thin film is very important to the performance of the battery. Perovskite thin films prepared by traditional one-step solution method are prone to small grain size and poor coverage, which lead to low efficiency and poor stability of the battery and are not conducive to its commercial development. The quality of perovskite thin films can be effectively improved by introducing anti-solvent in the one-step solution method. In this paper, hydrophobic solvents (toluene, chlorobenzene, ethyl acetate) were used as anti-solvent to study the effect of different anti-solvents on the performance of perovskite thin film and battery.

Keywords: perovskite thin film; anti-solvent; one-step deposition method; photoelectric property; stability

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