

· 综 述 ·

## miRNA 和 lncRNA 在动物脂肪沉积中的研究进展

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**摘 要:** 微小 RNA (MicroRNA, miRNA) 是一类由 18–25 个核苷酸组成的高度保守的核苷酸序列, 它可以特异性结合信使 RNA (mRNA) 的 3'-非编码区域, 进而发挥降解 mRNA 或阻遏 mRNA 翻译的负调控作用。长链非编码 RNA (Long non-coding RNA, lncRNA) 是一类长度超过 200 个核苷酸、不能编码蛋白质或只能编码蛋白质肽段的核苷酸序列, 它可以在表观遗传、转录水平和转录后水平调控基因表达。脂肪作为一种重要的储能物质, 在调节动物体能量平衡过程中发挥着重要的作用, 并与动物产肉量、肉品质等产肉性状密切相关。而脂肪功能的紊乱可导致高血脂、II 型糖尿病以及一系列心血管疾病发生, 因此动物脂肪沉积的分子调控机制备受人们关注。近年来, 越来越多的研究发现 miRNA 和 lncRNA 在动物脂肪沉积中发挥重要作用。文中就现阶段 miRNA 和 lncRNA 在动物脂肪沉积中的研究进展进行综述, 以期为进一步揭示动物脂肪沉积的分子调控机制提供理论指导和新思路。

**关键词:** 脂肪沉积, 微小 RNA, 长链非编码 RNA, 脂肪细胞, 基因表达调控

## Role of miRNA and lncRNA in animal fat deposition-a review

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**Abstract:** MicroRNA (miRNA) is a type of highly conserved nucleotide sequence composed of 18 to 25 nucleotides, which can specifically bind to the 3'-noncoding regions of mRNA, and then play a negative regulatory role in degrading mRNA or inhibiting translation. Long non-coding RNA (lncRNA) is a type of nucleotide sequence that exceeds 200 nucleotides in length and cannot encode proteins or can only encode protein peptides. It regulates gene expression at the levels of epigenetic, transcriptional and post-transcriptional. As an important energy storage organ, fat plays an important role in regulating the energy balance of animals, and is closely related to meat production traits such as meat production and meat quality. And the disorder of fat function can lead to hyperlipidemia, type 2 diabetes and a series of cardiovascular diseases, so the molecular

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regulation mechanism of animal fat deposition has attracted more attention. In recent years, more and more studies have found that miRNA and lncRNA play a crucial role in animal fat deposition. We review here the current research progresses in the role of miRNA and lncRNA in animal fat deposition, to provide theoretical guidance and new ideas for further revealing the molecular regulation mechanism of animal fat deposition.

**Keywords:** fat deposition, miRNA, lncRNA, adipocyte, gene expression regulation

脂肪沉积是指机体将过多摄入的能量储存在脂肪组织中这一过程,脂肪组织可以在适宜的时候释放能量,用于维持机体能量代谢平衡。除此之外,脂肪也是机体中很多脂溶性维生素和类固醇激素的重要来源,还具有高度活跃的分泌功能,能分泌一系列脂肪细胞因子调节机体代谢<sup>[1]</sup>。同时,在畜牧业上,脂肪沉积还会影响畜禽的产肉量与肉品质<sup>[2-3]</sup>。而脂肪功能的异常不仅会引发一系列的代谢综合征,还会影响脂肪在体内的沉积,导致机体过瘦或过肥,增加患病风险。在过去的几年中,越来越多的研究表明,曾被认为是基因组“噪音”的 miRNA 和 lncRNA 可以通过参与脂肪沉积调控网络,介导脂肪沉积相关基因的表达遗传、转录水平和转录后水平调控<sup>[4-6]</sup>,因此研究脂肪沉积与 miRNA 及 lncRNA 的关系,可为探索动物脂肪沉积的分子调控机制提供新的思路 and 方向。

## 1 脂肪沉积过程及其调控因子

### 1.1 脂肪沉积过程概述

脂肪细胞作为脂肪组织的最小单位,动物的脂肪组织由大量的脂肪细胞不断聚集形成。脂肪细胞的分化过程分为定向分化和终末分化两个阶段<sup>[7]</sup>:第一阶段,多能干细胞经过定向分化形成前体脂肪细胞,前体脂肪细胞中开始出现少量的小脂滴;第二阶段,前体脂肪细胞进一步分化为球形或椭球形的多室脂肪细胞,多室脂肪细胞里有大量小脂滴,此时的细胞一般不具有分裂增殖能力,但可通过不断摄取体内游离的脂肪酸,使小脂滴不断膨大形成大脂滴,最终形成成熟的脂肪细胞。研究表明,脂肪组织主要有两种增生方

式<sup>[8-9]</sup>:一是脂肪细胞数目的增加,二是脂肪细胞体积的增大,即脂肪细胞的肥大。一般来说,在个体幼年时期脂肪组织的增生主要是以细胞数量的增加为主,性成熟后,脂肪沉积则主要表现为脂肪细胞的增大,且脂肪细胞的体积越大,脂肪沉积能力越强<sup>[10]</sup>。

### 1.2 脂肪沉积过程关键调控因子

脂肪沉积是一个受多种转录因子及其网络调控的复杂过程。目前研究得比较透彻的起关键作用的转录因子有过氧化物酶体增殖激活受体- $\gamma$  (Peroxisome proliferator-activated receptor gamma, PPAR- $\gamma$ )<sup>[11]</sup>和 CCAAT 增强子结合蛋白家族 (CCAAT enhancer binding protein family, CEBPs)<sup>[12]</sup>。

PPAR $\gamma$  是在白色脂肪和棕色脂肪中高表达的动物脂肪沉积关键转录调控因子,能够直接或间接地调控脂肪细胞分化和脂类代谢,它是整个脂肪代谢调控网络的核心,大多数转录调控因子都必须在它介导下才能发挥调控脂肪细胞分化的功能<sup>[13]</sup>。科学家通过基因敲除实验发现 PPAR $\gamma$  基因敲除小鼠脂肪沉积相关转录因子的表达量明显降低,且其胚胎干细胞 (Embryonic stem cell, ES) 并不能分化出脂肪组织,又经过体外实验发现 ES 细胞分化为脂肪细胞的程度取决于 PPAR- $\gamma$  基因剂量,实验表明,PPAR- $\gamma$  对脂肪细胞的体外分化和体内分化都是必不可少的<sup>[13]</sup>。

CEBPs 家族有  $\alpha$ 、 $\beta$  和  $\delta$  三个成员,3 个成员分别在不同时间参与脂肪分化调控,研究表明,PPAR- $\gamma$  和 CEBP- $\alpha$  上都有 CEBPs 的结合位点,脂肪细胞分化早期 CEBP- $\beta$  和 CEBP- $\delta$  大量表达,CEBP- $\beta$  和 CEBP- $\delta$  会通过结合位点激发 PPAR- $\gamma$  和 CEBP- $\alpha$  的表达,进而启动分化过程<sup>[14]</sup>。Wu

等<sup>[15]</sup>通过基因转导实验发现, *CEBP- $\alpha$*  缺失的脂肪细胞积聚的脂滴少, 并且无法诱导内源性 *PPAR- $\gamma$*  表达, 这些细胞还完全不存在胰岛素刺激的葡萄糖转运过程, 这些结果表明 *CEBP- $\alpha$*  在脂肪形成中发挥重要作用, 并表明 *PPAR- $\gamma$*  和 *CEBP- $\alpha$*  之间的交叉调控是脂肪细胞分化调控的关键组成部分。

近年来, 大量的研究不断表明 miRNA 和 lncRNA 也可以调控上述这两种脂肪沉积关键基因的表达, 对脂肪细胞的分化过程以及脂肪组织的生长发育过程发挥重要作用。

## 2 miRNA 与脂肪沉积

### 2.1 miRNA 概述

miRNA 是一类长度介于 18–25 个寡核苷酸的内源性非编码单链核糖核酸分子<sup>[16]</sup>。它的来源可简述为: 细胞核中的 RNA 聚合酶 II (RNA polymerase II, RNAP II) 转录基因组中编码 miRNA 的 DNA 产生长度可达 1 000 nt 的初级

miRNA (Primary miRNA, pri-miRNA), pri-miRNA 再经由 RNA 酶 Drosha 及其伴侣分子 DGCR8 (DiGeorge syndrome critical region gene 8, DGCR8) 结合形成的微处理器复合物切割形成长达 70–100 nt 的前体 miRNA (Precursor miRNA, pre-miRNA), pre-miRNA 通过转运分子 Exportin 5 通过核孔运至细胞质中, 并经另一种 RNA 酶 Dicer 切割形成 18–25 nt 的双链 miRNA, 双链 miRNA 随后结合到 AGO 蛋白 (Argonaute) 上形成一个沉默复合物前体 (Pri-miRISC), miRNA 的过客链 (Passenger strand) 被降解, 剩下的成熟导向链 (Guide strand) 与 AGO 蛋白相互作用形成 RNA 诱导的沉默复合物 (RNA-induced silencing complex, RISC)。其具体形成过程见图 1<sup>[17]</sup>。

miRNA 不编码蛋白质, 它的经典调控机制是通过碱基互补配对的方式以其种子序列 (一般是 5' 端的前 8 个核苷酸序列) 特异性结合靶基因 mRNA 的 3'-非编码区域 (3'-Untranslated region, 3'-UTR) 或 5'-非编码区域 (5'-Untranslated

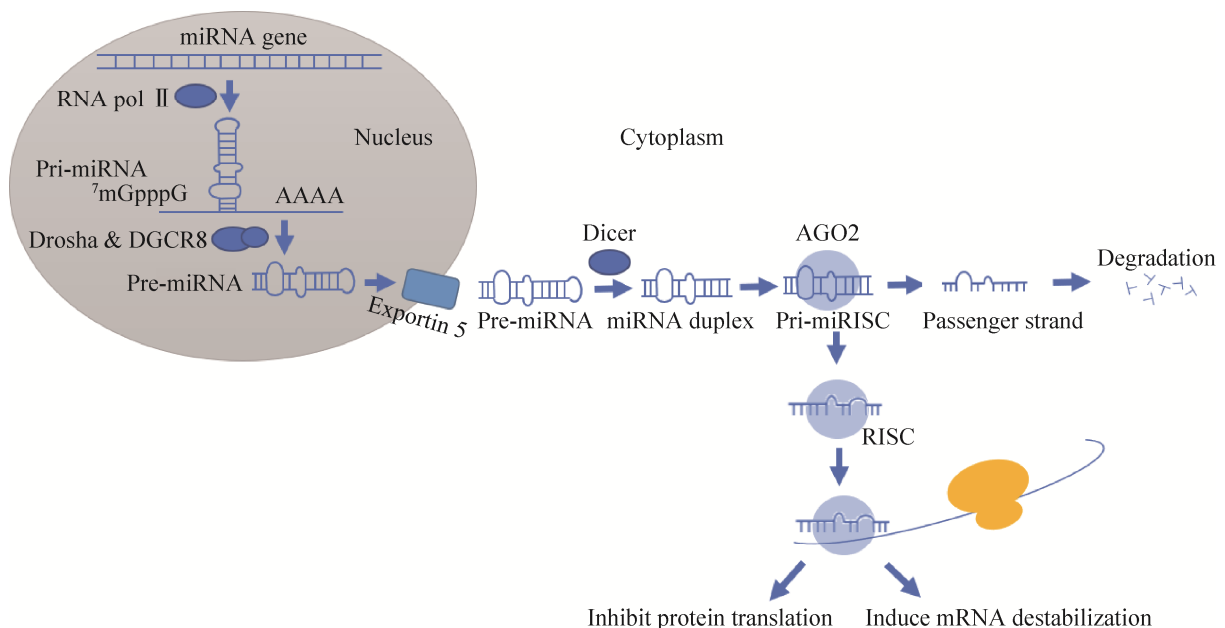


图 1 miRNA 的形成过程

Fig. 1 The formation process of miRNA.

region, 5'-UTR) 的特异序列, 并通过 RISC 的方式, 实现转录后水平调控靶基因的表达。根据 miRNA 与靶基因 mRNA 的 3'-UTR 或 5'-UTR 序列互补程度的不同, 其调控方式有两种<sup>[18]</sup>: 若完全互补, miRNA 可导致靶 mRNA 的降解; 若不完全互补, 则阻遏 mRNA 的翻译, 从而抑制蛋白质的合成, 两种形式都可达到调控基因的目的。此外, 在 2017 年有研究表明, miRNA 除了上述利用种子序列发挥转录后经典调控作用外, 还可以通过其非种子序列与靶基因的 3'-UTR 结合, 这就是 miRNA 基于转录水平的非经典调控作用<sup>[19]</sup>。

## 2.2 miRNA 在脂肪沉积中的研究

近年来, 研究人员运用高通量测序技术不断挖掘在动物脂肪组织中发挥作用的 miRNA 并探究其功能, 现已有大量关于 miRNA 影响动物脂肪沉积的报道。比如, Liang 等<sup>[20]</sup>以中国本土猪和约克夏猪为模型, 发现在脂肪组织中的 6 种 miRNA 和肌肉组织中的 4 种 miRNA 都与脂肪含量等性状密切相关。在肌内前脂肪细胞中, 过表达 miR-17-5p 可抑制核受体共激活因子 3 (Nuclear receptor co-activator 3, NCOA-3)、脂肪酸结合蛋白 4 (Fatty acid binding protein 4, FABP-4) 和 PPAR- $\gamma$  的表达, 抑制前体脂肪细胞的分化<sup>[21]</sup>。在猪皮下脂肪中 miR-27 的表达与成脂相关基因 PPAR- $\gamma$  和 FABP-4 的表达呈显著负相关, 这表明 miR-27 可抑制脂肪沉积<sup>[22]</sup>。也有研究发现, miR-34a 可以靶向猪脂联素受体 2 基因 (*AdipoR-2*) 并通过 AMPK 信号途径来抑制 PPAR- $\alpha$  信号传导途径, 从而增加肝脏中甘油三酯的含量<sup>[23]</sup>。Lu 等<sup>[24]</sup>发现 miR-212 通过靶向沉默信号调节子 2 (*Silent information regulator 2, SIRT-2*) 基因并抑制其表达, 从而调节脂肪酸合成酶 (Fatty acid synthetase, FASN) 和甾醇调节元件结合因子 1 (Sterol regulatory element binding factor 1, SREBP-1) 的表达, 最终促进乳腺上皮细胞的脂肪沉积。Liu 等<sup>[25]</sup>探究 miR-130b-5p 在非酒精性

脂肪肝 (Nonalcoholic fatty liver disease, NAFLD) 发病过程中的潜在作用时发现, 下调 miR-130b-5p 可激活依赖胰岛素样生长因子结合蛋白 2 (Insulin like growth factor binding protein 2, IGFBP-2) 的 AKT 途径, 从而抑制 NAFLD 的肝脂质积聚和胰岛素抵抗, 提示下调 miR-130b-5p 可能作为防治 NAFLD 的治疗手段。Sui 等<sup>[26]</sup>发现 miR-142-5P 可靶定 *catenin $\beta$ -1 (CTNB-1)*, 抑制 *CTNB-1* 的表达, 促进乳脂代谢。

笔者实验室也在该方面取得一定的成果: 我们发现在猪肌内前脂肪细胞中, miR-34a 和 FoxO-1 (胰腺  $\beta$  细胞团的关键调控因子) 能调节血小板源生长因子受体  $\alpha$  (Platelet-derived growth factor receptor alpha, PDGFR $\alpha$ ) 的表达, 并通过 Erk 信号通路, 促进肌内脂肪沉积<sup>[27]</sup>。而过表达 miR-125a-5p 可抑制猪肌内前脂肪细胞的分化, 降低总饱和脂肪酸 (Saturated fatty acids, SFA) 含量和单不饱和脂肪酸 (Monounsaturated fatty acids, MUFA)/SFA 比值, 表明 miR-34a 和 miR-125a-5p 可能是一种新型的猪肌内脂肪调控因子<sup>[28]</sup>。陈粉粉<sup>[29]</sup>研究发现过表达 miR-34c 抑制肌内脂肪细胞的增殖, 抑制猪脂肪沉积, 这表明 miR-34c 对脂肪沉积具有负调控作用。Shi 等<sup>[30]</sup>发现在猪前体脂肪细胞中的过表达 miR-199a-5p 会促进细胞的增殖, 同时抑制细胞的脂质沉积, 通过靶基因预测和实验验证, 他们证明窖蛋白 1 (*Caveolin-1, Cav-1*) 可能是猪脂肪细胞 miR-199a-5p 的靶点, miR-199a-5p 可下调 Cav-1 以促进猪前脂肪细胞增殖、抑制其分化。总之, 越来越多 miRNA 在动物脂肪沉积中的研究不断被挖掘 (表 1)。

## 3 lncRNA 与脂肪沉积

### 3.1 lncRNA 概述

lncRNA 是一类由 RNAP II 转录所得的长度在 200 个核苷酸以上、不能编码蛋白质或只能编码蛋白质微肽的非编码 RNA<sup>[46]</sup>。lncRNA 通过类

似于编码蛋白质的途径产生，根据其在蛋白编码基因中的位置可以分为 5 类 (图 2): 正义 lncRNA (Sense lncRNA); 反义 lncRNA (Antisense lncRNA);

双向 lncRNA (Bidirectional lncRNA); 内含子 lncRNA (Intron transcript lncRNA); 基因间 lncRNA (Intergenic lncRNA)。

表 1 参与动物脂肪沉积调控的 miRNA

Table 1 Important miRNAs in the regulation of animal fat deposition

MiRNA	Target gene (mRNA)	Function	References
miR-130b	<i>PPAR-γ</i>	Inhibits adipogenesis	[31]
miR-7134-3p	<i>MARK-4</i>	Inhibits adipogenesis	[32]
miR-103	<i>PPAR-γ, aP2</i>	Promotes adipogenesis	[33]
miR-429	<i>PPAR-γ, aP2, FAS</i>	Inhibits adipogenesis	[34]
miR-23a	<i>CEBP-α, PPAR-γ</i>	Inhibits adipogenesis	[35]
miR-125a	<i>KLF-13</i>	Inhibits adipogenesis	[36]
miRNA-200b	<i>KLF-4</i>	Inhibits adipogenesis	[37]
miR-204-5p	<i>KLF-3</i>	Promotes adipogenesis	[38]
miR-24	<i>MAPK-7</i>	Promotes adipogenesis	[39]
miR-16-5p	<i>EPT-1</i>	Promotes adipogenesis	[40]
miR-181a-5p	<i>Smad-7, Tcf7l2</i>	Promotes adipogenesis	[41]
miR-149-5p	<i>FGF-21</i>	Promotes adipogenesis	[42]
miR-149-5p	<i>CRTC</i> s	Promotes adipogenesis	[43]
miR-99a	<i>NOX-4</i>	Inhibits adipogenesis	[44]
miR-152	<i>LPL</i>	Promotes adipogenesis	[45]

*MARK-4*: Microtubule affinity regulating kinase 4; *aP2*: Adipocyte fatty acid binding protein A; *FAS*: Factor-associated suicide; *KLF-3,4,13*: Kruppel-like factors 3,4,13; *MAPK-7*: Mitogen-activated protein kinase 7; *EPT-1*: Ethanolamine phosphotransferase 1; *Tcf7l2*: Transcription factor 7-like 2; *FGF-21*: Fibroblast growth factor 21; *CRTC*s: CREB regulated transcription coactivator; *NOX-4*: NADPH Oxidase 4; *LPL*: Lipoprotein lipase.

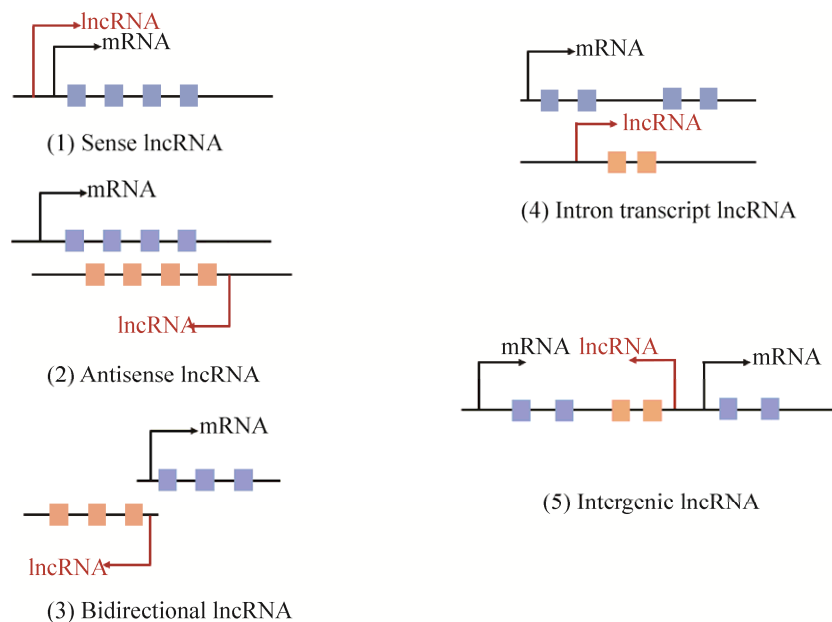


图 2 lncRNA 的分类

Fig. 2 Classification of lncRNA.

此外, lncRNA种类繁多、功能复杂, 广泛分布于细胞核或细胞质中, 相比于 miRNA 来说, lncRNA 在不同物种之间、个体发育的不同阶段都具有表达特异性<sup>[47]</sup>。现有的研究已表明, lncRNA 可以通过参与基因印记、染色体修饰、转录干扰和 mRNA 降解等过程在表观遗传、转录水平和转录后水平调控基因表达<sup>[48]</sup>。

### 3.2 lncRNA 在脂肪沉积中的研究

lncRNA 主要是通过 RNA、DNA 或转录因子结合在调节动物脂肪沉积过程中发挥重要作用。比如, 研究者发现在莱芜猪和长白猪背最长肌的肌内脂肪中有 55 个差异表达的 lncRNA, 其中 XLOC\_046142、XLOC\_004398 和 XLOC\_015408 可能分别通过靶向 MAP 激酶活化蛋白激酶 2 (MAP kinase-activated protein kinase 2, MAPKAPK-2)、核受体亚家族 1D 组成员 2 (Nuclear Receptor Subfamily 1, NR1D-2) 和醛酮还原酶家族 1 成员 C4 (Aldo-keto reductase family 1 member 4, AKR1C-4) 在猪肌内脂肪形成和脂肪沉积过程中起关键调节作用, 导致两个猪品种之间存在脂肪沉积差异<sup>[49]</sup>。Zhang 等<sup>[50]</sup>使用 RNA 测序分析鸡腹部前脂肪细胞在分化的不同阶段脂肪细胞中的 lncRNA 和 mRNA 表达差异, 发现差异表达的基因可作用于邻近的编码基因参与和脂肪细胞分化有关的多种途径。Miao 等<sup>[51]</sup>研究金华猪和长白猪肌内脂肪的 lncRNA 表达谱发现有 119 个 lncRNA 差异表达, 他们将这些差异表达的 lncRNA 与 mRNA 进行了比较, 发现其中 6 种共表达的 lncRNA 与脂肪沉积和脂质代谢相关的途径有关, 这揭示 lncRNA 对猪肌内脂肪组织中脂肪代谢有调控作用。Wang 等<sup>[52]</sup>发现 lncRNA H19 通过促进肝细胞 MLX 互作蛋白 (MLX interacting protein like, MLXIPL) 表达, 激活雷帕霉素靶蛋白复合物 1 (Mammalian target of rapamycin complex-1, mTORC1) 网络诱导肝脂肪变性, 结果表明 H19 可能在调节肝脏脂质代谢中发挥重要作用, 并可能

成为 NAFLD 的潜在治疗靶点。

此外, 笔者实验室曾通过 RNA 序列测定发现在八眉猪和长白猪的肌内前体脂肪细胞分化过程中有 324 个 lncRNA 时间差异性表达, 进一步筛选出了显著上调的 lnc\_000414 深入研究, 证明它能够通过调节细胞周期相关因子的表达来抑制猪肌内脂肪细胞增殖<sup>[53]</sup>。同时 Wei 等<sup>[54]</sup>发现在关中黑猪的前体脂肪细胞中, PU.1 AS lncRNA 作为 PU.1 mRNA 的反义 lncRNA, 两者可结合形成二聚体结构, 从而阻止 PU.1 mRNA 翻译, 使 PU.1 蛋白的表达量降低, 进而抑制前体脂肪细胞的分化。而 AdipoQ AS lncRNA 可与 AdipoQ mRNA 结合形成 AdipoQ AS lncRNA/AdipoQ mRNA 复合物抑制 AdipoQ mRNA 的翻译, 从而抑制脂肪的发生<sup>[55]</sup>。Cai 等<sup>[56]</sup>发现敲除 lnc-ORA 基因后, 细胞周期标记物的 mRNA 和蛋白表达水平降低, 证实 lnc-ORA 可抑制前体脂肪细胞的增殖, 同时还发现, 敲除 lnc-ORA 基因也能通过调节 PI3K/AKT/mTOR 信号通路抑制脂肪细胞的分化。

### 3.3 lncRNA 与 miRNA 互作在脂肪沉积中的作用

有的 lncRNA 可以作为 miRNA 的“海绵”, 它可以通过“吸附”miRNA 来减少 miRNA 与 mRNA 的结合, 从而影响 mRNA 的丰度, 这类 lncRNA 就是竞争性内源 RNA (Competing endogenous RNA, ceRNA)。

有研究者在探究长白猪和大白猪肥育性能差异时发现 lncRNA TCONS\_00010987 在大白猪背部脂肪中的表达水平显著高于长白猪, 进一步研究发现 TCONS\_00010987 可结合 miR-323, 从而减少结合瘦素受体 (Leptin receptor, LEPR) mRNA 的 miR-323 的数量, 使得 LEPR 大量表达, 研究表明 TCONS\_00010987-miR-323-LEPR 调节通路造成长白猪和大白猪肥育性能差异的原因之一<sup>[57]</sup>。Liu 等<sup>[58]</sup>在研究 lncRNA ENST00000608794 在地塞米松诱导脂肪变性中的作用时, 发现 ENST00000608794 可作为 ceRNA“吸附”miR-

15b-5p, 下调 miR-15b-5p 的表达水平, 从而减弱 miR-15b-5p 对丙酮酸脱氢酶激酶同工酶 4 (*Pyruvate dehydrogenase kinase isoenzyme 4, PDK-4*) 的负调控, 进而导致脂肪变性。Guo 等<sup>[59]</sup>发现 uc.372 (Ultraconserved RNA, 一种 lncRNA) 可以抑制 pri-miR-195 和 pri-miR-4668 的成熟, 从而减少 miR-195/miR-4668 的丰度, 进而干扰 miR-195/miR-4668 参与调控脂肪合成和摄取相关基因的表达, 最终促进肝脏脂肪变性。Chen 等<sup>[60]</sup>发现 lncRNA NEAT 1 通过 miR-146a-5p 靶向 RHO 相关卷曲螺旋形成蛋白激酶 1 mRNA (*RHO associated coiled coil containing protein kinase 1, ROCK-1*), 并进一步影响 AMPK/SREBP 通路促进脂肪沉积。Zhang 等<sup>[61]</sup>发现 uc.333 与 miR-223 结合可以改善胰岛素抵抗, 提示 uc.333 可能是治疗和预防胰岛素抵抗的有用靶点。诸如此类的有关 lncRNA 在动物脂肪沉积中的研究还有很多 (表 2)。

## 4 总结与展望

脂肪组织作为一个重要的储能器官, 参与调节机体的能量代谢以及一系列生理活动。脂肪沉积是一个复杂的过程, 涉及脂肪细胞的增殖和分化、发生和凋亡、甘油三酯的合成和水解等生化过程, 这些过程受众多分子和通路的调节, 加之各种生物大分子之间存在互作关系, 譬如 RNA-RNA、DNA-蛋白质、RNA-蛋白质和蛋白质-蛋白质等, 因此关于脂肪沉积相关机制的探索任重而道远。近年来虽已发现许多 lncRNA 和 miRNA 参与调控动物脂肪细胞的成脂分化过程, 但是其作用机制仍需进一步研究和完善, 还需要继续挖掘细化已知的调控通路, 并积极寻找新的信号通路及重要调控基因, 并探索这些已知的通路和基因在脂肪生成中的相互作用等。

表 2 参与动物脂肪沉积调控的 lncRNA

Table 2 Important lncRNA in the regulation of animal fat deposition

LncRNA	Interacting gene(mRNA)	Function	References
lncRNA U90926	<i>PPAR-γ, FABP-4, CEBP-α, AdipoQ</i>	Inhibits adipogenesis	[62]
lncRNA HOXA11-AS1	<i>CEBP-α, DGAT-2, CIDEC, perilipin</i>	Promotes adipogenesis	[63]
lncRNA ADNCR	miR-204	Inhibits adipogenesis	[64]
lncRNA-ADAL	<i>hnRNPU, IGF2BP2</i>	Promotes adipogenesis	[65]
lncRNA-OAD	<i>β-catenin</i>	Promotes adipogenesis	[66]
lncRNA TINCR	miR-31-5p	Promotes adipogenesis	[67]
lncRNA GAS5	miR-18a	Promotes adipogenesis	[68]
lncRNA Gm 12664-001	miR-295-5p <i>CAV-1</i>	Inhibits adipogenesis	[69]
lncRNA Gm15622	miR-742-3p <i>SREBP-1c</i>	Promotes adipogenesis	[70]
lncRNA PVT1	<i>PPAR-γ, CEBP-α, aP2</i>	Promotes adipogenesis	[71]
lncRNA KCNQ10T1	miR-138 <i>PPAR-γ, RUNX-2</i>	Promotes adipogenesis	[72]
lncRNA Plnc1	<i>PPAR-γ</i>	Promotes adipogenesis	[73]
TCONS 00041960	miR-204-5p miR-125a-3p	Inhibits adipogenesis	[74]
lncRNA Gm15290	miR-27b, <i>PPAR-γ</i>	Promotes adipogenesis	[75]

*DGAT-2: The enzyme diacylglycerol acyltransferase 2; CIDEC: Cell death inducing DFFA like effector C; hnRNPU: Heterogeneous nuclear ribonucleoprotein U; IGF2BP2: Insulin-like growth factor 2 mRNA-binding protein 2; SREBP-1c: Sterol regulatory element binding factor 1c; RUNX-2: Runt-related transcription factor 2.*

随着高通量分子检测手段的出现以及生物信息学分析方法的发展,未来的研究将继续深入探究非编码 RNA 作为一种生物标记,因 lncRNA 具有时空表达特异性,所以从脂肪细胞的不同生长阶段筛选与鉴定代表性的特异性 lncRNA 具有重要意义。科学家已经发现 lncBATE10 在白色脂肪褐变过程中表达量显著升高,进一步研究表明 lncBATE10 是诱导体内白色脂肪褐变所必需的调节因子,这项研究为进一步探索白色脂肪褐变的上下游机制奠定了基础<sup>[76]</sup>。还有研究发现 lncRNA CAAInc1 在癌性恶病质小鼠中高表达,并通过抑制脂肪分化参与癌性恶病质脂肪丢失,该研究为癌性恶病质脂肪丢失的治疗提供了潜在的靶点<sup>[77]</sup>。相信在不久之后,以 lncRNA 为切入点研究动物脂肪沉积的研究成果会不断涌出,为脂肪代谢紊乱疾病的治疗以及家畜肉品质改善提供新的理论和靶点。

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