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# CircRNA在动物脂质代谢中的调控作用

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**摘　要**：脂质代谢具有复杂的生理过程，受激素、转录因子、酶和非编码 RNA 等多种因素影响，其中遗传是主要因素之一。环状 RNA (circular RNA, circRNA) 是存在于真核生物中的共价闭合的环形非编码 RNA，具有组织特异性、保守性和稳定性。近年来，circRNA 在脂肪生成和发育中的分子调控机制被广泛研究。本文概述了脂肪的分类、功能及其生成的调控机制，并重点综述 circRNA 对脂质代谢的调控，尤其是 circOgdh 和 circHIPK3 等标志性 circRNA 在动物脂肪沉积调控中的作用，以期为后续研究提供参考。

**关键词**：脂肪沉积；circRNA；脂质代谢；调控机制

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# Regulatory effects of circRNA on lipid metabolism in animals

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**Abstract:** Lipid metabolism is a complex physiological process, which is affected by a variety of factors, such as hormones, transcription factors, enzymes and non-coding RNAs, and inheritance is one of the main factors. CircRNAs (circular RNAs) are covalently closed circular non-coding RNAs existing in eukaryotes, which are tissue specific, conservative and stable. In recent years, the regulatory roles of circRNAs in lipogenesis and development are widely studied. In this paper, the classification, function of fat and the regulatory mechanism of its production were summarized, focusing on the regulation of lipid metabolism by circRNAs, especially circOgdh and circHIPK3 in the regulation of animal adipose deposition, in order to provide reference for the subsequent research.

**Key words:** fat deposition; circRNA; lipid metabolism; regulation mechanism

动物脂肪组织主要由脂肪细胞构成，通过储存能量和执行内分泌功能影响新陈代谢，参与调控动物健康和肉品质 [1]。动物脂肪分化是一个多基因参与调控的复杂过程，主要受遗传因素制约，基因水平的调控对脂肪细胞分化具有重要影响 [2]。同时，核受体超家族可感知脂质代谢物水平的变化，驱动差异基因表达，产生不同的生理效应 [3]；过氧化物酶体增殖物激活受体 (peroxisome proliferator-activated receptors, PPARα、PPARβ/δ 和 PPARγ) 是其主要成员，可作为配体诱导的转录因子在葡萄糖和脂质代谢中起关键作用 [4]。随着非编码 RNA (non-coding RNA, ncRNA) 研究的不断深入，人们发现 ncRNA 在脂质代谢中具有重要的调控作用。环状 RNA (circular RNA, circRNA) 是 20 世纪 80 年代鉴定出的一类独特的 ncRNA 分子，由线性 RNA 反向剪接并通过共价键形成闭合环状结构，参与调控多种生物学过程 [5]。研究表明，circRNA 在人类脂质代谢相关疾病中发挥重要调控作用，如：hsa_circRNA_ 102682 与妊娠期糖尿病脂质代谢密切相关，可调节脂质代

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谢，参与妊娠糖尿病的发病[6]；circRNA_ 0046367 通过阻断 miRNA/mRNA 与 miRNA 应答元件 (miRNA response elements, MREs) 的相互作用，消除了 miR-34a 对 PPARα 的抑制作用，进而激活脂质代谢相关基因的转录，如肉碱棕榈酰转移酶 2 (carnitine palmitoyltransferase 2, *CPT2*) 和酰基辅酶 A 结合蛋白 3 (acyl-CoA binding domain containing 3, *ACBD3*)，导致脂肪变性消退[7]。因此，circRNA 在动物脂质代谢中发挥重要的调控作用。

脂肪含量是影响肉品质的因素之一，肌内脂肪对肉的嫩度、多汁性和风味以及消费者的感官评价均有影响；当肌内脂肪含量适量增加时，肌肉嫩度提高，剪切力降低，肌肉变亮，颜色变浅，大理石纹增加[8]。随着遗传育种由传统育种向分子育种转变，探究 circRNA 在动物脂肪沉积中的调控机制对改良畜禽肉品质具有重要意义。本文主要综述了脂肪生成机制及 circRNA 对动物脂质代谢的调控作用，旨在为后续探究脂肪沉积及脂质代谢提供参考。

## 1　脂肪生成

### 1.1　脂肪组织分类及功能

脂肪组织可分为白色 (white adipose tissue, WAT)[9]、棕色 (brown adipose tissue, BAT)[10]、米色 (beige adipose tissue)[11] 和粉红色 (pink adipose tissue, PAT)[12] 脂肪组织四类。WAT 中产生的棕色脂肪细胞也被鉴定为米色脂肪细胞，由这些脂肪细胞组成的脂肪组织也被称为米色脂肪组织[13-14]。在哺乳动物中存在两种发育类型不同的 BAT：胚胎发生过程中出现的经典或组成型 BAT，以及出生后在称为褐变的过程中在 WAT 内募集的米色脂肪组织[15]。WAT 褐变的特征包括较小的多孔脂肪细胞的出现，解偶联蛋白 (uncoupling proteins 1, UCP1) 转录增加，线粒体密度增大和呼吸能力增强[16]。而 PAT 是指分泌乳汁的乳腺管上皮细胞，可由白色脂肪细胞在妊娠和哺乳期间的转分化产生[17]。

WAT 组织是机体内含量最丰富的组织，是主要的内分泌和信号器官，可分泌多种蛋白质因子和脂肪因子[18]。WAT 是高度异质的，由脂肪细胞、各种免疫细胞、祖细胞和干细胞以及基质血管群组成[19]，在细胞质中以脂质的形式储存和释放能量[20]。BAT 是一种产生热量的能量消耗组织，主要通过氧化脂质来产热，是体内产热的中心部位[21]，通过存在于线粒体中的 UCPs 呼吸中心发挥重要作用[22]。BAT 和米色脂肪细胞通过消耗化学能产生热量，可以将甘油三酯衍生的脂肪酸和葡萄糖燃烧成热量，因此在调节体温和体重方面发挥重要作用[23]。此外，在某些刺激 ( 特别是暴露于寒冷 ) 诱导下，米色脂肪细胞可在 WAT 中发育而成[24]，但大多数米色脂肪细胞源于从头分化的脂肪细胞[25]。米色脂肪组织在形态和功能上类似 BAT，但在发育上与 WAT 更相似[26-27]。米色脂肪组织已被证明在葡萄糖稳态、胰岛素敏感性和脂质代谢中发挥重要作用[28]。粉红色脂肪细胞是乳腺管上皮细胞，其作用是产生和分泌乳汁[29]，它们源于皮下白色脂肪细胞的转分化[30]。脂肪器官对一系列代谢和环境挑战的功能反应凸显了其非凡的可塑性[31]。

### 1.2　脂肪生成的调控

脂肪生成涉及转录因子、酶、激素和信号通路等多种因素，是一个复杂的生理过程。脂肪组织的扩张主要有两种不同的机制，即增加脂肪细胞数量 ( 增生 ) 和 ( 或 ) 增加脂肪细胞体积[32-33]。脂肪形成一般分为两个阶段：第一阶段是胚胎干细胞分化为具有多重分化潜能的间充质干细胞；第二阶段为终分化阶段，前体脂肪细胞产生成熟脂肪细胞的特征，能对脂滴和胰岛素等激素做出反应[34]。

#### 1.2.1　调控脂质代谢的基因

PPARγ 和 CCAAT 增强子结合蛋白 α (CCAAT/enhancer-binding protein α, C/EBPα) 是最主要的两类脂质合成调控因子，PPARγ 正向调控 C/EBPα 并共同促进前体脂肪细胞分化[35-36]；而前体脂肪细胞虽然增殖期短暂，却是脂肪细胞形成的必要过程，对前体脂肪细胞成熟至关重要[37]。在鸟类脂肪分化过程中，C/EBPα 调控与脂解、脂肪生成和脂肪酸去饱和有关的基因，而 C/EBPβ、δ 调控与从头脂肪生成和脂肪酸延长有关的基因[38]。研究表明，在成脂诱导时，蛋白质精氨酸甲基转移酶 7 (protein arginine methyltransferase 7, PRMT7) 与 C/EBPβ 相互作用并使其甲基化，抑制 C/EBPβ 与 PPARγ2 启动子的结合[39]。脂蛋白脂肪酶 (lipoprotein lipase, LPL) 是前体脂肪细胞分化为脂肪细胞的早期标志之一，并在成熟脂肪细胞中达到稳定水平[40]；血浆甘油三酯与 WAT 的结合依赖 LPL，该酶受促血管生成素样蛋白 -4 (angiopoietin-like protein-4, ANGPTL-4) 调节，后者是一种解折叠分子伴侣，可将 LPL 活性二聚体转化为非活性单体[41]。

不同部位的脂肪沉积涉及的基因有所不同。Luo 等[42] 研究发现，鸡的肌内脂肪沉积受甘油醛 -3-磷酸脱氢酶 (glyceraldehyde-3-phosphate dehydrogenase,

*GAPDH*))、乳酸脱氢酶 A (lactate dehydrogenase A, *LDHA*)、谷胱甘肽过氧化物酶 1 (glutathione peroxidase 1, *GPX1*) 和糖原分支酶 1 (glycogen branching enzyme 1, *GBE1*) 等基因调节，这些基因与丙酮酸和柠檬酸代谢有关；而其腹部脂肪沉积是由脂肪酸结合蛋白 1 (fatty acid-binding protein 1, *FABP1*)、超长链脂肪酸延伸蛋白 6 (elongation of very long chain fatty acids protein 6, *ELOVL6*)、硬脂酰 -CoA 去饱和酶 (stearoyl-CoA desaturase, *SCD*) 和脂联素 (adiponectin, *ADIPOQ*) 等基因调节，与乙酰辅酶 A 和甘油代谢有关。*ELOVL6* 过表达可导致脂肪细胞中 C14:0 ( 肉豆蔻酸 ) 和 C16:0 ( 棕榈酸 ) 脂肪酸比例降低，C18:0 ( 硬脂酸 ) 和 C20:4n6 ( 花生四烯酸 ) 脂肪酸比例增加，影响牛脂肪细胞中的脂肪酸组成 [43]。由生长激素受体 (growth hormone receptor, *GHR*) 基因隐性突变引起的性连锁侏儒 (sex-linked dwarf, SLD) 鸡与普通鸡相比腹部脂肪沉积更多，研究发现细胞因子信号转导抑制因子 2 (suppressor of cytokine signaling 2, *SOCS2*) 和细胞因子诱导的含 SH2 蛋白 (cytokine-inducible SH2-containing protein, *CISH*) 基因可能参与 GHR 突变诱导的鸡腹部脂肪沉积，*SOCS2* 和 *CISH* 的过表达可以抑制从 SLD 鸡分离的原代肝细胞和前体脂肪细胞中过度活跃的脂质代谢和脂滴的过度积累 [44]。随着研究的不断深入，越来越多调控脂肪生成的基因被发掘出来，这为阐明脂肪生成的分子机制提供了研究基础。

**1.2.2** 调控脂质代谢的信号通路

研究表明，多个信号通路参与脂肪组织的生成与发育，例如，AMP 活化蛋白激酶 (AMP-activated protein kinase, AMPK) 信号通路在诱导脂肪生成、维持线粒体稳态 [45] 和诱导 WAT 褐变激活 BAT 等方面具有重要作用 [46]。Janus 激酶 (Janus kinase, JAK)/ 信号转导和转录激活因子 (signal transducer and activator of transcription, STAT) 通路有助于调节脂肪组织的脂质代谢、葡萄糖代谢和脂肪因子分泌 [47]；丝裂原活化蛋白激酶 (mitogen-activated protein kinase, MAPK) 作为一种高度保守的信号通路，参与多种细胞生物学过程，包括代谢重编程以及细胞增殖、存活和分化 [48]；磷脂酰肌醇 -3- 激酶 (phosphatidylinositol-3-kinase, PI3K)/ 蛋白激酶 B (protein kinase B, AKT) 信号通路在脂质代谢、脂肪细胞增殖及存活中发挥重要作用，可促进脂质生物合成并抑制脂解 [49]。研究表明，PI3K/AKT 和 Wnt/β-catenin 通路之间存在复杂串扰 [50]，Wnt 信号通路在脂肪组织发育过程中发挥重要作用，是脂肪生成的一个重要的内源性抑制剂，也可促进成骨、软骨生成和肌生成 [51]。而 Wnt 信号通路与雷帕霉素 (mechanistic target of rapamycin, mTOR) 信号通路之间依旧存在串扰 [52]。

Chang 等 [53] 研究发现，脂多糖通过 JAK/STAT 和 AMPK 调节胞质磷脂酶 A2 (cytosolic phospholipase A2, *cPLA2*) 基因的表达，进而促进前体脂肪细胞增殖和脂肪生成。C 型利钠肽 (C-type natriuretic peptide, *CNP*) 基因通过环磷酸鸟苷 (cyclic guanosine monophosphate, cGMP)/ 蛋白激酶 G (protein kinase G, PKG)/ p38 MAPK 信号通路促进山羊脂肪来源干细胞的成脂分化 [54]。黄芩和黄连通过调节代谢谱和 MAPK/PI3K/AKT 信号通路改善 2 型糖尿病大鼠的脂代谢 [55]。Toosendanin (TSN) 能够通过激活 Wnt/β-catenin 通路来抑制脂肪生成 [56]。miR-199a-3p 通过 mTOR 信号通路调节棕色脂肪细胞分化 [57]。此外，炎症相关基因白介素 6 (interleukin 6, *IL-6*) 被认为是脂肪分解的中枢基因，其通过肿瘤坏死因子 (tumor necrosis factor, TNF) 信号通路和 MAPK 信号通路等多种途径在脂解中发挥重要作用 [58]。脂质代谢相关的信号通路之间存在着复杂的串联，彼此之间互相影响，这种复杂的串联关系非常不利于脂质代谢分子机制研究。

## 2 circRNA调控脂质代谢

### 2.1 circRNA生成及作用机制

1976 年，circRNA 在类病毒中被首次发现 [59]。随着研究的不断深入，发现 circRNA 是一种存在于真核生物的共价闭合内源性生物分子，既没有 5' 到 3' 的极性，也没有多聚腺苷酸化的尾部，并且在进化过程中普遍是保守的 [60]。circRNA 主要分为外显子环状 RNA (exonic circRNA, ecircRNA)、内含子环状 RNA (intron circRNA, ciRNA)、外显子 - 内含子环状 RNA (exonic-intron circRNA, EIciRNA)、基因间环状 RNA (intergenic circular RNA)，其生物发生依赖于典型的反向剪接机制，并受特定顺式作用元件和反式作用因子的调控 [61]。所谓反向剪接机制是指将下游剪接供体位点与上游剪接受体位点反向连接，产生共价闭合的 circRNA 和具有跳跃外显子的交替剪接的线性 RNA[62]。然而，反向剪接环化需要规范剪接信号和规范剪接体机制，大多数表达丰度较高的 circRNAs 通常由 pre-mRNAs 的内部外显子加工而成，包含多个外显子 [63]。circRNA 形成模式有两种：一是外显子跳跃 ( 或称套索中间体模

式 )[64]；二是直接反剪接模式 [65]。外显子跳跃是指先发生规范剪接，然后生成包含跳跃外显子的内含子套索，其通过反向剪接决定 circRNA 产生 [66]；而直接反剪接模式是先发生反向剪接，生成一个 circRNA 连同一个外显子 - 内含子 - 外显子中间体，后者经进一步加工生成具有跳跃外显子的线性 mRNA[67]。此外，反向互补序列跨其侧翼内含子的 RNA 配对可以促进 circRNA 的加工 [68]，肌盲蛋白 (muscleblind, MBL)、RNA 腺苷脱氨酶 (RNA adenosine deaminase 1, ADAR1)、颤抖蛋白 (quaking, QKI) 等与 pre-mRNA 结合，将侧翼内含子连接在一起促进环化，这一方式属于 RNA 结合蛋白 (RNA binding protein, RBP) 驱动模式 [69]( 图 1)。基因间 circRNA 是指内含子 circRNA 片段两侧是 GT-AG 剪接信号，其充当环连接的剪接供体和受体，然后产生整合的 circRNA[70]。

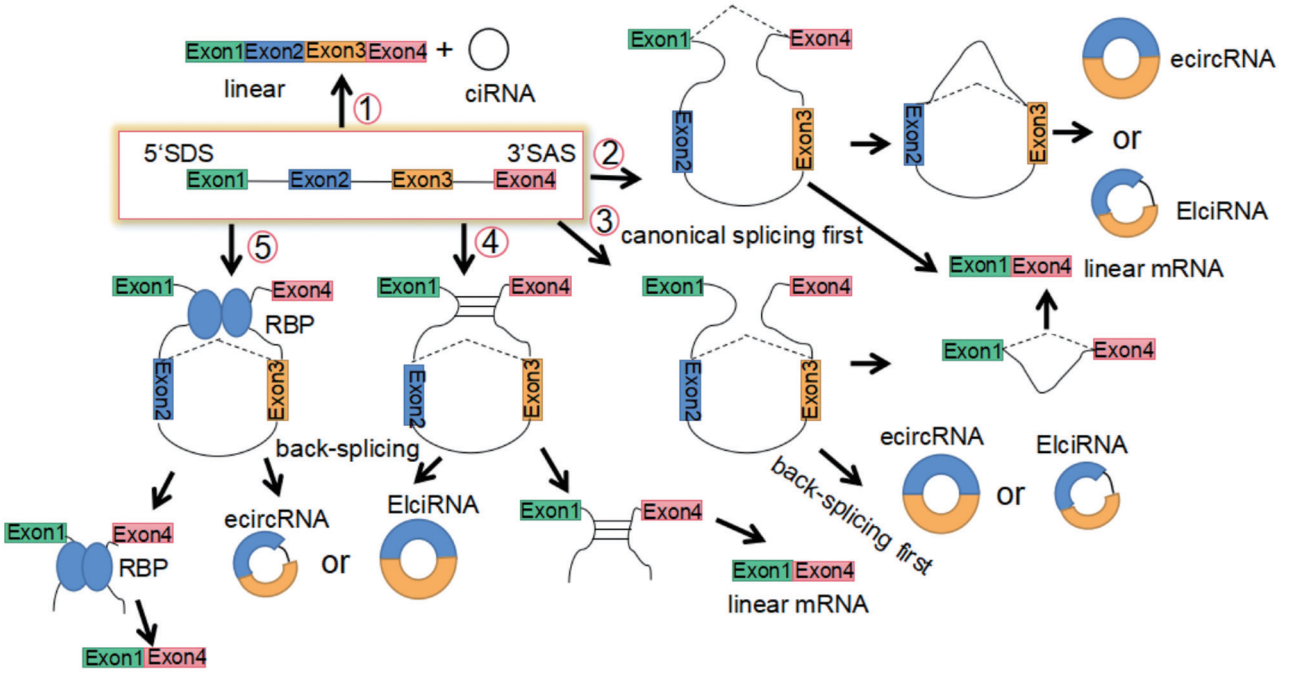
circRNA 的表达具有组织和细胞特异性，其不仅通过调节蛋白质功能或翻译发挥重要的生物学功能 [71]，还可以通过影响转录和 mRNA 更新来调节基因表达，例如，circRNA_100367 通过海绵吸附 miR-217 进而调控 *Wnt3* 基因表达来调节食管鳞癌的辐射敏感性 [72]。值得一提的是，circRNA 参与靶基因剪接和翻译：研究表明，具有无限开放阅读框 (open reading frame, ORF) 的 circRNA 以不依赖于内部核糖体进入位点 (internal ribosome entry site, IRES) 的方式进行滚动扩增，导致其生产效率比线性转录本高近百倍 [73]；18S rRNA 的互补性和位于 IRES 上的结构化 RNA 元件对于驱动 circRNA 翻译必不可少 [74]；IRESs 和 m6A 诱导的核糖体参与位点促进了 5' 端非依赖性翻译起始 [75]；circRNA 也可以与宿主基因位点结合，形成 R-loop，导致宿主基因转录暂停 [76]。研究发现，circSMARCA5 可与其亲本基因位点结合，从而导致亲本基因外显子转录暂停，导致 *SMARCA5* 转录下调，并产生无功能的截短蛋白 [77]。此外，circRNA 可与 RNA 结合蛋白 (RBP) 相互作用，也可作为蛋白质诱饵、支架和招募者，与蛋白质结合并巩固蛋白质之间的相互作用 [78]。circ-FoxO3 主要位于细胞质，可与衰老相关蛋白分化抑制剂 1 (inhibitor of differentiation 1, ID1)、E2F 转录因子 1 (E2F transcription factor 1, E2F1) 以及应激相关蛋白缺氧诱导因子 1α (hypoxia-inducible factor 1α, HIF1α) 和黏着斑激酶基因 (focal adhesion kinase, FAK) 互作，抑制这些转录因子的入核，从而调控下游基因表达 [79]。由此可见，circRNA 可通过多种方式参与基因表达调控。

### 2.2　circRNA对脂质代谢的调控

#### 2.2.1　circRNA调控脂肪生成

circRNA 种类繁多，作用方式较为复杂，这一特点与 circRNA 在细胞中的分布情况密切相关。研究发现，位于细胞质中的 circRNA 可作为分子海绵吸附 miRNA 进而调控靶基因表达，这一功能在脂质代谢调控中被广泛研究。在人体脂肪生成过程中，主要分布在细胞质中的 circOgdh 可充当 miR-34a-5p 的海绵，与其竞争性结合，进而上调关键脂肪分解基因脂肪甘油三酯脂肪酶 (adipose triglyceride lipase, *Atgl*) 的表达，增强棕色脂肪细胞的脂肪分解，抑制脂滴积累 [80]。circRNF111 可增强代谢综合征中的胰岛素抵抗和脂质沉积，并通过靶向 miR-142-3p 及其下游靶基因胰岛素样生长因子 2 受体 (insulin-like growth factor 2 receptor, *IGF2R*) 发挥作用。研究发现，DNA 甲基化相关的 circ_0116449 可吸附 miR-142-3p，从而促进其靶基因核受体亚家族 1D 组成员 2 (nuclear receptor subfamily 1, group D member 2, *NR1D2*) 的表达，并与 *NR1D1*、视黄酸受体相关孤儿受体 A (retinoic acid receptor-related orphan receptor alpha, *RORA*) 一起在体内外抑制脂质过氧化反应 [81]。Arcinas 等 [82] 研究发现，circTshz2-1 和 circArhgap5-2 是体外脂肪生成不可或缺的调节剂。

在猪中，circPPARA 吸附 miR-429 和 miR-200b，进而促进猪肌内脂肪生成 [83]。类似地，chi-circ_0006511 通过 novel-miR-87/ 脂肪酸转位酶 (fatty acid translocase, FAT/CD36) 轴正向调控山羊肌内脂肪细胞的分化 [84]。Feng 等 [85] 研究发现，circMARK3 通过上调成脂肪细胞标志性基因 *PPARG*、*C/EBPα* 和 *FABP4* 的表达，促进水牛脂肪细胞和 3T3-L1 细胞的成脂分化。研究还发现，睾酮可以上调 miR-181a，但以剂量依赖性方式下调猪肌内脂肪细胞 circ_0005912 表达；同时，miR-181a 过表达可抑制 circ_0005912；由此推测，circRNA 可能通过与 miRNA 结合参与猪去势后脂质代谢的调节，是 circRNA 在脂肪沉积中发挥的新作用 [86]。同样，Liu 等 [87] 研究发现，在猪去势后加入 100 nmol/L 睾酮可提高 sus_circPAPPA2 表达水平，显著抑制前体脂肪细胞分化；进一步研究发现，sus_circPAPPA2 可充当 miR-2366 海绵进而调节甘油激酶基因 (glycerol kinase, *GK*) 的表达，从而影响前体脂肪细胞分化。研究还发现，circPPARγ 促进牛脂肪细胞分化并抑制增殖和凋亡 [88]，circFUT10 促进牛脂肪细胞增殖




①规范剪接。pre-mRNA经历规范剪接生成包含外显子的线性mRNA，产生ciRNA的内含子主要形成套索结构。②外显子跳跃(套索中间模式)。先对pre-mRNA进行规范剪接，以产生具有跳跃外显子(外显子1和外显子4)的线性mRNA和包含外显子的内含子套索；然后通过将下游5′剪接供体位点与上游3′剪接受体位点反向连接，从内含子套索中产生EIciRNA或ecircRNA。③直接反向拼接模式。始于反向剪接的pre-mRNA产生EIciRNA或ecircRNA以及外显子-内含子-外显子中间体，进一步加工产生具有跳跃外显子的线性mRNA (外显子2和外显子3)。④内含子配对驱动模式。跨其侧翼内含子(内含子1和内含子3)的反向互补序列的RNA配对使下游的5'SDS和上游的3'SAS紧密结合在一起，促进了EIciRNA或ecircRNA的反向剪接过程和形成。⑤ RNA结合蛋白(RBP)驱动模型。RBP有利于circRNA的加工，可与pre-mRNA结合，桥接内含子侧翼，并诱导剪接位点紧密结合。

**图1 circRNA的生物发生**

并抑制细胞分化[89]，circ-PLXNA1 促进鸭脂肪细胞分化[90]。此外，circ11103 与 miR-128/*PPARGC1A* 相互作用调节奶牛乳脂代谢，提高牛乳腺上皮细胞(BMECs) 中甘油三酯的水平，并增加不饱和脂肪酸的含量[91]。circRNA/miRNA 相互作用揭示了一种表观遗传调控新机制，通过 circRNA-miRNA-mRNA 调控网络在脂质代谢调控中发挥重要作用。

**2.2.2** circRNA调控脂质代谢相关疾病

研究表明，circRNA 在脂质相关疾病调控中发挥重要作用，在相关疾病治疗中具备临床应用潜力[92]。对内脏脂肪组织和脂肪细胞 circRNA 表达谱的研究提示，circRNA 可能是内脏肥胖的潜在治疗靶点[93]。Zhu 等[94] 研究发现，circH19 在代谢综合征患者血清中表达上调，并与脂质参数相关，其缺失促进人类脂肪干细胞的成脂分化。

circScd1 对脂质蓄积和肝脂肪变性的影响主要由 JAK2/STAT5 通路介导，是脂质代谢的关键调节因子[95]。circHIPK3 的上调增强了油酸对脂滴积累的刺激作用，circHIPK3/miR-192-5p/FoxO1 信号通路对脂肪形成和肝脂肪变性具有重要意义[96]；而 circRNA_0046367/miR-34a/PPARα 通路在减轻肝细胞脂肪变性和改善脂质过氧化中起关键作用，并且 circRNA_0046366 能显著降低甘油三酯含量并重新平衡脂质稳态[92]。circ_0057558 可作为 miR-206 海绵解除对 Rho 相关激酶 1 (Rho-associated kinase 1, ROCK1)/AMPK 信号通路的抑制，促进脂肪生成和甘油三酯分泌，从而极大地促进酒精性脂肪肝的发生和发展[97]。过氧化物酶体增殖物激活受体 -γ 共激活剂 -1α (peroxisome proliferator-activated receptor-γ co-activator-1α, PGC-1α) 介导 circSCAR 与 ATP 合酶基因 (ATP synthase, *ATP5B*) 结合，并通过阻断亲环素 D (cyclophilin D, CypD) 和 1- 甲基 -4- 苯基 -1,2,3,6- 四氢吡啶 (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, mPTP) 相互作用进而关闭 mPTP，在体内靶向 circSCAR 可缓解高脂肪饮食诱导的肝硬化和胰岛素抵抗[98]。

在癌症相关的恶病质中，circPTK2 与 miR-

182-5p 竞争性结合，消除对其靶基因并列锌指蛋白 1 (juxtaposed with another zinc finger protein 1, *Jazf1*) 的抑制，最终促进脂肪分解和抑制脂肪生成 [99]；而 circCAPRIN1 可以与 STAT2 结合，从而激活乙酰辅酶 A 羧化酶 1 基因 (acetyl-CoA carboxylase 1, *ACC1*) 的转录，调节脂质代谢 [100]。Wu 等 [101] 在慢性淋巴细胞白血病研究中发现，circRIC8B 可充当 miR-199b-5p 的海绵，阻止其下调 *LPL* mRNA 水平，最终促进脂质代谢改变和慢性淋巴细胞白血病的发展。circRNA 在疾病脂质代谢中的调控至关重要，可对疾病的发生和发展产生重要影响。

## 3 小结与展望

脂肪组织是动物新陈代谢的关键，脂质代谢稳态的维持对能量平衡、免疫等至关重要。在畜牧领域，畜禽肌内脂肪的沉积对肉品质、味道和嫩度等均有影响，增加肌内脂肪沉积是畜禽肉品质提升的关键。circRNA 参与脂肪生成，目前 circRNA 调控脂肪代谢的研究主要集中在 circRNA 海绵吸附 miRNA 进而调控 mRNA 表达水平。随着 circRNA 在畜禽脂肪沉积中研究的不断深入，更多的与畜禽脂肪沉积相关的 circRNAs 被发掘，对后续畜禽肉品质改良意义重大。但是，目前 circRNA 调控脂质代谢相关研究局限性较大，机制研究范围较小。随着测序技术的不断发展，测序领域不断扩大，筛选和鉴定 circRNA 上下游的调控基因及其互作蛋白、甲基化修饰等均可实现，这将为阐明 circRNA 调控脂质代谢的分子机制提供新的研究方向。探究 circRNA 对脂代谢调控的分子机制及扩展其功能研究领域，更全面地揭示脂质代谢分子机制，将会对未来畜牧业肉用种质改良和肉品质改良相关分子育种产生深远影响。

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