猪肠道微生物与机体脂质代谢研究进展

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收稿日期: 2021-10-09; 接受日期: 2022-01-30; 网络版发表日期: 2022-06-13

浙江省研发攻关计划项目(批准号: 2022C02015)和浙江省领雁研发攻关计划合作项目(批准号: 2022C04034)资助

摘要 肠道微生物在调控宿主脂质代谢中发挥重要作用。猪是一种易沉积脂肪的动物, 但其很少发生代谢性疾病, 其肠道核心菌群及代谢产物被认为是主导该生理现象的原因之一。本文系统综述了猪肠道微生物与脂质代谢的关系, 分析了微生物代谢产物包括短链脂肪酸、胆碱代谢物和胆汁酸等对脂质代谢影响作用, 以期洞悉肠道微生物调控宿主脂质代谢的潜在机制。旨在为猪生产中机体脂质沉积调控提供思路, 为人类脂质代谢紊乱所引起的代谢性疾病研究提供可用模型和借鉴。

关键词 猪, 肠道微生物, 脂质代谢, 益生菌

人体及动物肠道中微生物数量庞大, 这些细菌在肠道内合成和分解大量供自身及宿主生存所需的代谢产物, 调控宿主能量代谢稳态、肥胖、炎症及内分泌等^[1~3]。猪不仅是我国主要的养殖家畜, 而且猪消化道结构及杂食性使其成为研究人类胃肠道和代谢性疾病的首选理想模型^[4]。在人工养殖情况下(高热量食物及运动受限环境), 猪对一些代谢疾病, 例如2型糖尿病、非酒精性脂肪肝和心血管疾病具有异常的抵抗力, 可能是长期的自然选择导致宿主生理代谢对环境的功能化适应^[5]。家猪在适应圈养模式下, 体内产生可维持血糖稳态的猪胆酸(hyocholic acid, HCAs)^[6]。胆汁酸(bile acids, BAs)代谢又与肠道微生物关系紧密, 猪体内独特胆汁酸的形可能由其肠道核心菌群主导。在生猪生产中, 背膘厚和瘦肉率直接影响生猪生产效率和经济效益。遗传、饲料营养及生产管理均会影响猪的脂

肪沉积^[7,8], 肠道微生物也是调控脂质沉积的因素之一^[9]。肠道微生物参与日粮营养代谢, 并产生诸多代谢物, 如短链脂肪酸(short-chain fatty acids, SCFAs)和胆碱等, 可作为小分子信号参与调控脂肪的合成与分解。故以猪为模型, 研究肠道微生物和脂质代谢调控之间的联系, 对研究代谢性疾病及指导动物生产具有重要意义。本文将系统综述猪肠道菌群调控机体脂质代谢的作用与机制。

1 猪肠道微生物特征

哺乳动物肠道中微生物数量大约达 10^{14} , 包含约500~1000个不同种类的微生物^[10], 研究显示猪肠道中含有719种微生物^[11], 这些微生物参与宿主多种生理过程。猪肠道微生物和人体肠道微生物一样是动态变

引用格式: 马燕飞, 刘建新, 汪海峰. 猪肠道微生物与机体脂质代谢研究进展. 中国科学: 生命科学, 2022, 52

Ma Y F, Liu J X, Wang H F. Porcine gut microbiota and lipid metabolism: recent advances and future directions (in Chinese). Sci Sin Vitae, 2022, 52, doi: 10.1360/SSV-2021-0363

化的, 其多样性由多因素共同决定, 例如不同生长阶段、菌群定位及日粮营养等因素均会影响肠道微生物组成。处于不同生长阶段的猪肠道菌群结构不同, 并且随着日龄的增加菌群多样性不断提高^[12], 但其核心菌群仍主要由Firmicutes和Bacteroidetes组成, 大约占猪全部肠道菌群的70%^[12,13], 人体及大多数哺乳动物肠道菌群也主要由这两大门类构成。两者除了在菌群组成上有相似性, 其菌群功能也高度相似。这一点可通过对比分析人类与猪肠道微生物群系基因信息进行验证, 分析结果显示, 人类肠道菌群96%的功能性通路在猪肠道菌群中也存在^[11], 这种菌群组成及功能的相似性是将猪作为人体模型开展肠道微生物和脂质代谢研究的理论基础和依据。日粮是塑造肠道微生物群系最重要的因素, 据报道, 日粮对猪肠道微生物组成贡献的变异达35%^[12]。家猪(杜洛克)和野猪的食物来源及稳定性不同, 其肠道微生物组成也不同。与家猪相比, 野猪肠道微生物具有更高的 α -多样性, 并且以Bacteroides为主要优势菌属^[14], 而家猪肠道微生物主要以Prevotella, Lactobacillus和Streptococcus为优势菌群^[14,15]。分析猪从出生到7周龄的粪便微生物组成变化(该阶段是猪从奶源向动植物来源饲料过渡的阶段), 结果显示, 猪在哺乳阶段肠道主要富集了以分解乳糖为主要活动的肠道微生物, 断奶后食源由猪奶转变为动植物饲料, 肠道内则主要富集了以降解植物多糖为主要活动的菌群^[16]。可见, 猪肠道微生物并非单一不变的, 其多因素共同作用塑造的菌群结构诠释了特定的功能。全面了解家猪肠道微生物结构及其行使的功能对剖析其不易患代谢性疾病有提示意义。

2 猪肠道微生物与脂质代谢

2.1 猪肠道核心微生物调控脂质代谢作用与机制

猪肠道微生物按功能可分为两大类: 核心菌群和过路菌群。过路菌群指的是随食源带入且无法定植在肠道内的菌群, 而核心菌群是指在特定的生存环境中持续存在的微生物^[17], 根据其不同的空间分布、时间稳定性以及对宿主功能及适应性的贡献, 可判别关键微生物^[18], 这些关键微生物诠释的核心功能与宿主生理代谢密切相关。故全面了解猪肠道核心菌群与脂质代谢之间的关联更具意义。

一项对18头猪从出生到上市屠宰的跟踪调查研究

显示, 虽然不同生长阶段(泌乳、断奶、生长和育肥)的猪肠道菌群组成有显著差异, 但有69个核心微生物存在于猪的所有生长阶段。在科水平, 排名前三的核心微生物是Prevotellaceae, Ruminococcaceae和Lactobacillaceae^[19], 这些常驻核心菌群与猪脂质代谢关联密切。有研究表明, 猪肠道细菌Prevotella(属于Prevotellaceae科)是主导猪脂肪沉积的核心微生物, 该菌的丰度与采食量呈正相关^[20], 与猪胴体瘦肉率呈显著负相关^[9]。该菌通过加剧宿主肠道屏障功能受损及引发肠道炎症, 以释放肥胖相关的代谢物至宿主循环内诱发远端组织低度慢性炎症, 这些代谢物包括脂多糖、支链氨基酸和花生四烯酸等^[9]。为进一步验证该菌与脂质代谢之间的关联及作用机制, 研究者将该猪源微生物进行分离培养, 并将其定植至无菌小鼠肠道内。结果显示, 在没有高脂日粮诱导的情况下, 定植Prevotella的小鼠仍出现白色脂肪组织严重沉积。该菌作用机制主要是通过激活TLR4和mTOR信号通路诱发机体慢性炎症反应, 阻碍机体生理代谢正常运转, 从而加剧脂肪炎症及沉积程度^[9]。不同遗传背景的猪脂质沉积的程度不同, 肠道核心细菌组成及调控宿主脂质代谢的能力表现也不同。研究者分别将金华猪和长白猪的粪菌移植至小鼠肠道中, 分别对两者机体脂质代谢状况进行评定。与长白猪粪菌受体小鼠(LM)相比, 金华猪粪菌受体小鼠(JM)血清中甘油三酯和脂蛋白脂肪酶活性显著增加, 并且肌肉中脂肪代谢相关分泌蛋白angiopoietin-like 4显著上调^[21]; 通过对受体小鼠空肠和结肠菌群进行分析, 发现供体的性状随着菌群的移植而得到了延续。在门水平, JM组结肠微生物中Firmicutes与Bacteroidetes丰度比值明显提高, 该比值升高被视为是肥胖发生的微生物标志信号^[22]; 在属水平上, LM组中空肠Akkermansia丰度显著增加^[21]。研究报道, 该菌是一种存在于肠道黏液层的黏蛋白降解菌, 在改善宿主代谢功能方面有重要作用^[23-27]。在属水平差异最为显著的是Lactobacillus, 结果显示LM组空肠Lactobacillus的丰度显著高于JM组, 分别占比42.89%和20.85%^[21]。Lactobacillus是家猪肠道中的核心微生物群^[14,15], 其十二指肠及空肠中Lactobacillus分别占比57%和40%^[28]。因家猪与野猪对圈养模式下高热量日粮的耐受力不同, 本课题组前期工作分别将两者的粪菌移植至抗生素预处理的小鼠中, 结果显示, 移植野猪粪菌的小鼠其血清总胆固醇、甘油三酯、低密度脂

蛋白以及胰岛素呈现更高的水平(unpublished), 提示家猪肠道微生物表现出更强的调控脂质代谢的能力, 这种能力可能与其核心菌群*Lactobacillus*主导的肠道微生物结构重构相关。

2.2 益生菌调控猪脂质代谢作用与机制

益生菌是指能够促进肠道内菌群生态平衡, 对宿主起有益作用的活性微生物, 其主要作用是协助胃肠道调控营养代谢, 构筑宿主肠道屏障, 建立肠道免疫等^[29]。近年来, 益生菌被认为是预防和治疗代谢性疾病的替代疗法。猪肠道中出现的适应性核心菌群包含益生菌, 研究分析益生菌在猪机体内调控脂质代谢的作用机制, 有利于开发有效益生菌用以调控动物脂质沉积和改进生产性能, 也有利于明晰益生菌在人体预防代谢性疾病的机制。

*Lactobacillus*是猪肠道内的核心微生物^[19], 也是目前研究较多的益生菌。研究表明, *Lactobacillus*在降血脂、降血糖方面具有突出的功效^[30-33]。鼠李糖乳杆菌GG(*Lactobacillus rhamnosus* GG, LGG)可抑制肠道上皮细胞吸收油脂^[34], 进一步调控肝脏、脂肪及肌肉等组织中脂质代谢相关的转录本及代谢通路^[33-35], 该现象的产生可能与肠道内脂肪酸感应受体敏感性改变有关。研究表明, 高脂饮食干预会破坏小肠上皮长链酰基辅酶A(long-chain acyl-CoA synthetase, ACSL)依赖的葡萄糖调节脂质感应通路, 同时肠道内加氏乳杆菌(*Lactobacillus gasseri*)的丰度降低。*L. gasseri*可能是该受体的调控因子。随后给肥胖小鼠补充*L. gasseri*, 小肠中ACSL的表达量上调以及宿主对脂肪酸的感知能力恢复^[36]。肠道微生物重构可能是*Lactobacillus*调控脂肪吸收相关受体表达的介导因素。研究显示, *Lactobacillus*干预斑马鱼及肥胖小鼠, 其肠道微生物组成改变, 表现在Firmicutes丰度显著增加, Actinobacteria丰度显著降低^[33,37]。本课题组前期于家猪小肠黏液中分离培养出一株高黏附力的罗伊氏乳酸杆菌ZJ617(*Lactobacillus reuteri* ZJ617), 前期的动物试验表明ZJ617乳酸杆菌能缓解高脂日粮诱导的代谢综合征, 并且该处理也改变了宿主肠道微生物及其代谢产物组成(unpublished), 后续本课题组将开展进一步的机制探究工作以验证肠道微生物在*Lactobacillus*调控宿主脂质吸收中的介导作用。

丁酸梭菌(*Clostridium butyricum*)是益生菌的重要

组成部分, 家猪回肠腔内富集了大量*C. butyricum*和*Clostridium perfringens*^[14]。此前研究表明, *C. butyricum*主要用于预防和治疗一些炎症肠病^[38-41]。在仔猪模型上, *C. butyricum*干预可提高生产性能及改善机体免疫功能, 并能有效提高结肠中SCFAs(乙酸、丙酸和丁酸)的浓度^[42]。另一项研究显示, *C. butyricum*干预可通过重塑肠道微生物结构以调控肠道丁酸及油酸含量。SCFAs是调控机体脂质代谢的重要信号分子, 这些小分子代谢物可激活下游G蛋白偶联受体120(GRP120), 从而启动相应机制缓解结肠炎发生^[43]。目前关于*C. butyricum*对猪肝脏脂质代谢方面的调控报道甚少。但在蛋鸡生产中, 日粮补充*C. butyricum*可重塑其胆汁酸谱, 显著减少肝脏游离脂肪酸含量并增加肝脏乙酰CoA氧化酶、法尼醇受体(farnesoid X receptor, FXR)和过氧化物酶体增殖物激活受体 α (peroxisome proliferator activated receptor α , PPAR α)的表达量^[44]。而在大鼠及小鼠试验上, *C. butyricum*处理可有效降低非酒精性脂肪肝的发生率^[40,45,46], 表明*C. butyricum*具有调控肝脏脂质代谢的能力。

*Akkermansia muciniphila*是一种存在于肠道黏液层的黏蛋白降解菌, 该菌在改善宿主代谢功能及免疫应答方面有重要作用^[23]。上述移植瘦肉型长白猪粪菌受体小鼠肠道*Akkermansia*丰度显著高于脂肪沉积型金华猪受体小鼠^[21], 提示*Akkermansia*和宿主脂质代谢相关。大量以小鼠为模型的研究表明, 该菌干预可逆转高脂饮食诱导的代谢紊乱, 主要表现在抑制脂肪组织的沉积与炎症发生, 改善机体内毒素血症、胰岛素抵抗和提高肝脏胆汁酸代谢等方面^[24-26,47]。经巴氏灭活后的*A. muciniphila*会失去调控脂质代谢及黏液层厚度的能力^[27], 但另一项研究则表明, 小鼠灌喂经巴氏灭活的*A. muciniphila*仍可有效增加全身能量消耗, 促进白色脂肪褐变, 并加速粪便能量排出^[48]。最近的一项研究表明, *A. muciniphila*是通过重塑宿主肠道微生物结构介导肝脏L-天冬氨酸水平升高以改善代谢功能紊乱相关脂肪肝病(metabolic dysfunction-associated fatty liver disease, MAFLD)。体外肝细胞试验验证了L-天冬氨酸可抑制脂质积累, 证实*A. muciniphila*是通过调控L-天冬氨酸代谢以改善机体脂质代谢^[47]。也有研究者表明, *A. muciniphila*是通过促进肠道内源性大麻素的水平控制机体炎症的发生, 改善肠道屏障并促进肠道小分子肽类物质的分泌, 从而控制代谢综合征

的发生^[27]。目前关于该菌在猪脂质代谢调控上的基础研究存在缺口, 后续可通过开展相关试验验证该菌在调控猪脂质代谢方面的功能。

3 猪肠道微生物代谢产物调控脂质代谢作用与机制

3.1 短链脂肪酸

肠道微生物的一个重要生理功能是可以代谢宿主酶系统不能完全水解的膳食纤维^[49]。后肠微生物可将难以消化的膳食纤维和抗性淀粉发酵生成SCFAs, 主要为乙酸、丙酸和丁酸^[50]。这些小分子代谢物在调控宿主能量代谢中起重要作用, 是机体用于脂肪酸及葡萄糖从头合成的原料^[51]。目前研究认为, SCFAs可作为信号分子激活细胞膜表面G蛋白偶联受体43(G-protein-coupled receptor, GPR43), 通过调控靶器官胰岛素敏感性、宿主食欲及增加能量代谢, 进而调节脂质积累, 维持机体代谢稳态^[50,52]。对高脂高糖诱导的肥胖猪进行高纤日粮干预, 结果显示纤维干预下肠道内富集了大量产丁酸的细菌, 如*Blautia*, *Faecalibacterium*和*Peptococcus*。这些细菌诱导肠道丁酸含量略微上升, 同时肠腔内丁酸以丁酸盐的形式存在于静脉血中^[53]。为探究机体脂质代谢对丁酸的响应能力, 研究者通过静脉注射给育肥猪输入丁酸钠, 结果显示该物质可加速脂肪动员并抑制硬脂酸的合成^[54]。另一研究通过盲肠瘘管给育肥猪灌注丙酸钠, 该物质显著降低了血清及肝脏甘油三酯的水平并促进肽YY(peptide YY, PYY)的分泌, 从而影响机体脂肪代谢^[55]。上述结果表明, SCFAs可被肠细胞吸收进入机体循环中发挥作用, 其主要通过激活GPR43受体, 进而抑制脂肪细胞中的胰岛素信号, 同时加速宿主肌肉组织和肝脏对能量的消耗^[52], 达到抑制脂肪组织肥大的效果。宿主中大部分SCFAs由肠道微生物产生, 但SCFAs是否可以独立于肠道微生物发挥功能尚未可知。有研究者通过给无菌猪灌喂SCFAs混合物(乙酸、丙酸、丁酸), 结果显示SCFAs可上调无菌猪背最长肌肉毒碱棕榈酰转移酶(carnitine palmitoyl transferase 1, CPT-1)的表达量; 与对照组相比, SCFAs处理组肝脏脂肪合成相关基因表达量下调, AMPK磷酸化信号被激活^[56], 表明宿主脂质氧化加速, 外源SCFAs可不依赖肠道微生物发挥作用。由此可见, SCFAs在调控宿主脂质代谢中发挥重要

作用。猪肠道微生物在SCFAs的生成中发挥重要作用, 是联系日粮和宿主的纽带。外源补充SCFAs进一步证实其在脂质代谢中的作用, 并且外源SCFAs发挥作用可不依赖肠道微生物的存在。SCFAs主要通过激活GPR43受体介导肝脏及肌肉组织加速能量输出, 从而抑制脂质沉积至脂肪组织中, 可能是猪肌肉脂肪及背膘厚调控的关键点。

3.2 胆碱及其代谢物

胆碱是人类及动物营养摄入中不可缺少的物质, 胆碱代谢可为机体提供乙酰胆碱、甜菜碱、磷脂酰胆碱及三甲胺(trimethylamine, TMA)^[57]。这些物质主要参与神经递质的传递, 提供DNA表观调控的甲基供体, 参与细胞信号传导以及机体能量代谢^[57-62]。日粮中适当添加胆碱可显著改善宫内受限仔猪(intrauterine growth retardation, IUGR)的脂质代谢情况, 主要表现在肌肉中脂肪酸合成酶(fatty acid synthetase, FAS)及固醇调节元件结合蛋白1(sterol regulatory element-binding proteins 1, SREBP1)基因表达量上调, 同时脂肪氧化分解相关基因表达量下调, 使肌间脂肪沉积得到改善^[63]。断奶仔猪日粮中添加适当比例的胆碱, 可改变其肠道微生物组成从而提高生产性能并降低其体内甘油三酯水平^[64]。然而, 日粮中添加过量胆碱也会引起一系列代谢性疾病^[65]。肠道微生物可代谢过量胆碱产生TMA, 随后被吸收到达肝脏, 在黄素单加氧酶(flavin monooxygenases, FMOs)的催化下代谢产生氧化三甲胺(trimethylamine N-oxide, TMAO)^[66]。研究表明, TMAO水平与肥胖和能量代谢呈正相关^[67]。长期暴露在高脂饮食下的小鼠对埃希氏菌属(*Escherichia* spp.)的易感性增加, 这是因为日粮中大量饱和脂肪酸会削弱线粒体向宿主结肠上皮细胞摄取氧气的的能力, 使得兼性厌氧型大肠杆菌的生长占据主导地位, 而大肠杆菌会加速对胆碱的分解代谢, 进而增加循环中有害代谢产物TMAO的水平^[68](图1)。敲除FMOs使得循环TMAO水平下降, 肥胖症状得以缓解, 进一步验证了TMAO与机体脂质代谢存在密切性关联^[67]。研究者对猪不同肠段(空肠、回肠和盲肠)的微生物群落结构进行分析, 发现*Escherichia* spp.均显著富集在肥胖型猪三个不同肠段中^[69], 高丰度的*Escherichia* spp.加速胆碱的分解代谢导致体内TMAO聚集。此外, 研究表明猪体内TMAO水平和*P. copri*水平呈正相关^[70], 而*P.*

图 1 益生菌、短链脂肪酸和胆碱代谢物调控机体脂质代谢。不同肠段微生物调控脂质代谢机制不一。益生菌主要通过与宿主竞争脂肪底物从而减少小肠上皮细胞对脂质的吸收; 高脂饮食会增加肠道对埃希氏菌属的易感性从而引起宿主炎症及脂肪积累; 结肠微生物主要以纤维为底物产生SCFAs调控机体远端组织脂质代谢

Figure 1 The mechanisms of probiotic, SCFAs, Choline metabolites-mediated host lipid metabolism. Different intestinal microbiota has different mechanisms for regulating lipid metabolism. Probiotics suppress absorption of lipids through small intestinal epithelial cells by competing with host for fat substrates. High-fat diets improve the susceptibility of the intestine to *Escherichia* spp. result in host inflammation and fat accumulation. Colonic microbiota produce SCFAs by decomposing fiber to regulate lipid metabolism

copri.已被证实是一种潜在诱导脂肪沉积的猪肠道细菌^[9]。因此, 由肠道微生物介导的TMAO水平增加可能是猪容易沉积脂肪的重要原因, 故探究肠道微生物-胆碱及其代谢物-脂质代谢三者之间的关系对生猪生产具有重要意义。

3.3 胆汁酸

BA是机体调控能量代谢的重要信号分子, 其功能主要涉及肝脏的胆固醇代谢和肠道脂质的吸收。BA在肝脏内合成有两条途径, 其中经典途径产生12 α -羟基化的初级BA(12-OH BAs), 如胆酸, 而替代途径则产生非12 α -羟基化的初级BA(non-12-OH BAs), 如鹅去氧胆酸^[71]。BA是微生物和宿主相互作用的关键信号分子^[72]。一些肠道微生物含有参与胆汁酸代谢的胆盐水解酶(biliary saline hydrolyase, BSH), 这些微生物包括*Lactobacillus*, *Bifidobacterium*, *Clostridium* spp.和*Enterococcus*等^[73], 可将由肝脏释放进入肠道的结合型BA代谢为非结合型BA, 经过其他肠道

细菌的加工(去氢化、去羧化和异构化等), 形成次级胆汁酸(secondary bile acids, SBAs), 而肠道中SBAs的紊乱往往会引起疾病^[74]。

有研究者从猪肠道菌群中培养分离出117个菌株, 经功能鉴定发现多个菌株具有降解初级BAs的能力。其中, *Clostridium scindens*菌株可通过脱羟基作用产生次级胆汁酸^[75]。与肥胖小鼠相比, 肥胖抵抗小鼠肠道中具有更高丰度的*C. scindens*, 提示该菌丰度与肥胖呈负相关^[54]。随后, 研究者给健康小鼠灌喂*C. scindens*, 发现肝脏non-12-OH BAs水平升高^[54], 提示其可能介导产生BAs。此前, 有研究报道non-12-OH BAs在调控脂质代谢中的作用。普洱茶有效成分茶褐素(theabrownin, TB)通过抑制BSH菌群的增殖提高肠道内non-12-OH BAs水平, 后者通过调控肠道FXR-FGF15和FXR-SHP, 促进CYP7B1的高表达, 激活BAs合成替代途径。该途径的激活使得肝脏中non-12-OH BAs/12-OH BAs比例显著升高, 从而加速肝脏胆固醇消耗, 促进粪便BAs的排出并能降低血清胆固醇的水平, 达到减重及

预防高胆固醇血症的效果^[71,76]。猪体内的代表性non-12-OH BAs是HCAs, 大约占75%, 而人类体内仅有3%左右^[6,77]。在小鼠和猪模型中, HCAs通过靶向抑制肠道FXR受体并激活TGR5受体, 促进肠道L细胞分泌胰高血糖素样肽-1(glucagon-like peptide-1, GLP-1), 表现出较强的血糖调控能力^[6]。小鼠膳食中补充BAs扰动了肠道菌群的组成^[78], 表明外源性BAs会改变肠道微生物组成, 微生物和BAs存在互作的关系。猪体内丰富的HCAs在维持机体代谢中有重要作用^[6], 具体是哪些微生物调控HCAs的生成尚未可知。未来随着猪肠道微生

物培养条件的优化, 更多有关胆汁酸代谢的特定细菌将被挖掘, 肠道微生物-胆汁酸-脂质代谢之间的关联将被揭晓。

4 结语与展望

近年来, 脂质代谢疾病的高发已严重危害人类生命健康。人体及小鼠的大量研究表明肠道微生物在调控脂质代谢发挥重要作用。猪因胃肠道结构和微生物功能与人体高度相似, 是研究代谢性疾病的理想模型。

图 2 胆汁酸调控机体脂质代谢。猪肠道微生物*Clostridium scindens*及茶褐素通过促进肝脏non-12-OH BAs合成, 该物质进入肠腔后继续作为调节因子调控GLP-1分泌, 进而发挥代谢保护作用

Figure 2 The mechanisms of BAs-mediated host lipid metabolism. *Clostridium scindens* and theabrownin promote the synthesis of non-12-OH BAs in the liver, which exerting metabolic protection by regulating the secretion of GLP-1 in intestinal lumen

家猪在自然状态下具有抵抗多种代谢性疾病的能力,可能由于家猪的某些生理功能对环境形成了适应,其肠道核心菌群组成和功能可能也发生了变化。核心菌群很大程度上影响了宿主生理及功能。故筛选对脂质代谢有影响的潜在猪肠道益生菌对突破家猪预防代谢性疾病的成因具有深远意义。目前,大量研究主要集中于益生菌对代谢性疾病干预的效果(图1),对其如何与宿主竞争脂肪底物以及通过何种方式转运这些底物知之甚少。微生物代谢产物是连接菌群和宿主的纽带,可作为信号分子与宿主互作。目前在猪模型上研究较多的是SCFAs、胆碱代谢物(图1)及BAs(图2),其他潜在的微生物代谢产物,如氨基酸类(支链氨基酸、芳香族氨基酸等)在猪模型上研究甚少。目前,这些菌群代谢

产物的下游作用机制研究较多,但其上游产生这些代谢物的特定细菌尚不明确且大部分未被分离培养。这主要受限于非常规细菌培养条件未被完全优化,因此发展培养组学,优化特定细菌的生长条件,有利于开展进一步研究工作及开发有效益生菌制剂。此外,揭示微生物-菌群代谢产物-脂肪沉积之间的关系,有助于调控猪的脂质沉积,满足现代人对猪肉品质的追求,兼可提高生猪生产效益。总之,猪肠道微生物组成及多样性复杂,在调控下游代谢产物方面存在诸多未知,主要呈现调控方式的多途径、层次性和交互性。因此全方位明晰猪肠道微生物调控脂质代谢的潜在机制,可为提高生猪生产效率提供理论依据,也有助于为人类代谢性疾病的研究和预防治疗提供模型和借鉴。

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Porcine gut microbiota and lipid metabolism: recent advances and future directions

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Gut microbiota plays an important role in modulating host lipid metabolism. The pig as an animal tend to deposit fat, but it rarely suffers from some metabolic diseases. Gut core microbes and metabolites are considered to contribute to this phenomenon. In this paper, we reviewed the relationship between porcine gut microbiota and lipid metabolism. The potential mechanisms were explored about how host lipid metabolism is regulated by porcine gut microbiota through short-chain fatty acids, choline metabolites and bile acids. The review aimed to provide new insights for regulating the lipid deposition in swine. The review will propose a possible pig model and reference for studying metabolic diseases caused by lipid metabolic disturbance in human.

porcine, gut microbiota, lipid metabolism, probiotic

doi: [10.1360/SSV-2021-0363](https://doi.org/10.1360/SSV-2021-0363)