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专论与综述

肠道微生物群与脱发的相关性研究进展

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摘　要：随着年轻人群脱发比例的逐年增加，头发健康问题日益受到关注。脱发会影响人们的生活质量，并对心理和社交生活产生巨大影响。近年来，对肠道微生物群的生理功能性研究已不再仅仅局限于胃肠道。研究表明肠道和肠道微生物群与皮肤有密切关系，提示“肠-皮肤轴”的存在。本文在已有的“肠-皮肤轴”研究现状基础上，总结近年来文献资料，探讨肠道微生物群与脱发之间可能的联系和潜在机制，为脱发的发病机制和治疗靶点提供新的认识和观点。

关键词：脱发，肠道微生物群，肠-皮肤轴，营养代谢，免疫系统，神经内分泌系统

Research progress on the correlation between gut microbiota and hair loss

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Abstract: With the proportion of hair loss among young people increasing with years, hair health issues are of increasing concern. Hair loss affects people’s quality of life and has a huge impact on psychological and social life. In recent years, research on the physiological functions of the gut microbiota is no longer limited to the gastrointestinal tract. Studies have shown that the intestinal tract and gut microbiota is closely related to the skin, suggesting the existence of the “gut-skin axis”. In this article, based on the existing research on the “gut-skin axis”, we summarize the recent literature to explore the possible links and potential mechanisms between the gut microbiota and hair loss, providing new insights and perspectives on the pathogenesis and therapeutic targets of hair loss.

Keywords: hair loss, gut microbiota, gut-skin axis, nutrition metabolism, immune system, neuroendocrine system

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毛发作为皮肤器官重要的附属器之一，是哺乳动物的独特特征[1]。毛发的主要功能包括保护皮肤免受机械伤害、保温、感官功能以及对社会交往、心理、生活质量的影响[2-4]。正常人每天大约会掉落 50–100 根头发，脱落的头发数量大于 100 根/d 时则被定义为脱发[5]。据统计数据显示，我国脱发人群数量已达到 2.5 亿，30 岁以下人群脱发比例逐年增加，呈现年轻化趋势[6]。脱发问题虽然不会威胁生命，但会严重影响患者的生活质量，并对心理和社交生活产生巨大影响。

从解剖结构上看，毛囊和毛干是头发的 2 个独立结构[1]。毛囊是头发的基本生长结构。生长期的毛囊可分为 3 个区域——毛球、峡部和漏斗部。毛球是毛囊中主动产生毛发的部分，包裹着毛囊真皮乳头、真皮乳头细胞、基质、神经纤维和单个毛细血管环[1]。向皮肤表面移动的下一个区域是峡部，其下缘是立毛肌嵌入毛囊纤维根鞘的部位，上缘是皮脂腺导管在毛囊通道的入口。毛囊干细胞就位于立毛肌嵌入点附近的一团上皮细胞内，此处被称为隆突点(Bulge)。毛囊距表皮最浅的区域是漏斗部，充满了皮脂腺生产的皮脂[7]。头发的发育是一个动态的循环过程，分为生长期、退行期和休止期。生长期毛囊扩大，在 2−7 年的生长期内将持续产生毛发纤维(毛干)[8]。生长期结束后，毛干会停止活跃的生长并进入一个短暂的退行期，此时毛乳头上移进入真皮，最终静止于隆突区下方[2,7]。休止期开始于退行期之后，头发进入静止状态，该过程持续约 4−5 个月。休止期结束时，头发掉落，几周后毛囊通过刺激隆突区的干细胞产生毛发胚芽，向下延伸最终形成新的毛干，重新进入生长期[1,7-8]

最常见的分类系统将脱发分为瘢痕性和非瘢痕性脱发。瘢痕性脱发的定义包括所有形式的毛囊永久性缺失；非瘢痕性脱发则保留了毛囊上皮结构，例如斑秃、生长期脱发、雄激素脱发、休止期脱发、头癣等[9]。本文主要针对非瘢痕性脱发进行探讨。一般认为引起脱发的原因包括内部和外部的触发因素。内部触发因素包括雄激素、遗传易感性、免疫与炎症、氧化应激等；外部触发因素包括紫外线、污染物、营养不良、心理情绪压力等[10]。然而，随着对脱发病理机制的深入研究，越来越多的证据表明，就像大多数的多基因、慢性全身性疾病一样，脱发不是由单一因素导致的，而是遗传和环境多种因素积累的结果；这些因素最终导致了信号通路失调、免疫和炎症反应异常等分子病理生理学上的改变[11-14]。即使使用药物或治疗措施清除了最初的触发因素，下游效应因子导致的免疫和炎症的连续级联反应也会持续发生，维持脱发的病理状态[10]。

雄激素脱发是男女脱发中最常见的形式。Inui 等[15]和 Itami 等[16]的研究发现雄激素会诱导毛囊真皮乳头细胞(Dermal Papilla Cells，DPCs)过量产生转化生长因子-β (Transforming Growth Factor-β，TGF-β) (毛囊退行期的标志)，并通过上调 Dickkopf-1 蛋白(DKK-1)的水平，抑制在毛发生长循环中起重要作用的 Wnt/β-Catenin 信号通路的传导[17]。Shin 等[18]还发现 TGF-β 可诱导 DPCs 中的氧化应激反应，并通过周围成纤维细胞诱导毛囊周围的纤维化和炎症。斑秃是一种急性斑状秃头症，发病机制被认为可能与自身免疫相关。免疫细胞错误地攻击毛囊，组织学表现为毛球周围炎症，退行期或休止期毛发比例增大，小型的异常毛发数量增加等[7]。心理情绪压力导致的休止期脱发会触发毛囊周围神经纤维释放包括神经生长因子(Nerve Growth Factor，NGF)和 P 物质(Substance P)在内的神经免疫和炎症介质，诱导局部肥大细胞活化和脱粒，导致一系列的炎症级联反应，大量促炎性物质被释放后攻击毛囊，进一步导致脱发[19-21]。

现有的脱发治疗方法包括药物治疗(米诺地尔、非那雄胺)、物理治疗(电磁场、电刺激)和其他治疗(毛发移植、微针法等)[22]。然而药物副作用

和高昂的治疗成本一直是尚待解决的问题[22-24]。近年来，“肠-X 轴”的存在被大量研究证实，肠道微生物群的影响范围超出了肠道，能够影响远端肠外器官组织系统的生理病理，发展出诸如“肠-脑轴” “肠-肝轴” “肠-肺轴”和“肠-皮肤轴”等研究领域。通过调节、运用肠道菌群来治疗皮肤疾病是新的临床趋势[25]。本文将在已有的“肠-皮肤轴”研究现状基础上，讨论肠道微生物群与脱发之间可能的联系和潜在机制，为脱发的改善和治疗提供新的研究方向。

1 肠-皮肤轴

随着现代医学与生物学的发展，大量研究发现多种皮肤疾病不仅表现为皮肤菌群的变化，还伴随着肠道微生物群的改变[26]。例如，痤疮与皮肤表面痤疮丙酸杆菌(*Propionibacterium acnes*)介导的炎症相关。研究发现痤疮患者的肠道菌群多样性降低，厚壁菌门丰度下降而拟杆菌水平升高[27]。特应性皮炎的病变皮肤通常以金黄色葡萄球菌和表皮葡萄球菌丰度增加为特征，同时患者常有肠道营养不良症状[28]。胃肠道健康与皮肤稳态密切相关。肠道和皮肤细胞来源于同一胚胎层，在信号传导和神经分布上非常相似，而且在免疫屏障方面也有着相似的功能[26]。“肠-皮肤轴”正是由这种相似性而产生的。尽管“肠-皮肤轴”的理论发展仍属于初级阶段，但越来越多的证据表明肠道微生物是“肠-皮肤轴”主要的参与者和调节者，对人体免疫系统的调节和皮肤稳态的维持有重要作用[29]。

人体肠道内的微生物群是细菌、病毒、真菌和原生动物的大量集合。新生儿肠道微生物的多样性和组成很大程度上受出生时母亲的影响，并通过环境暴露和饮食习惯而成熟，进而形成稳定的肠道菌群[30-31]。这些微生物的数量大约是人体细胞总数的 1.3 倍[32]，携带的基因含量是人体基因组的 100 倍[33]。肠道微生物可分泌产生如短链脂肪酸、皮质醇和神经递质等多种激素样物质，参与人体一系列的生理代谢活动，包括能量平衡、物质代谢和免疫功能等[26,34]。除了肠道微生物，1 cm^2 的人类皮肤及附属结构可被多达 10 亿个微生物(包括细菌、真菌和病毒)定殖，形成一个称为皮肤微生物组的复杂群落，其菌群的变化及与宿主之间的相互作用对皮肤的稳态具有重要调节作用[35]。肠道微生物群可以影响皮肤菌群。短链脂肪酸是肠道微生物作用下膳食纤维发酵的终产物，这些代谢终产物在决定皮肤微生物组成中起重要作用，并影响皮肤的免疫防御机制和表皮屏障[29]。例如，丙酸杆菌属能够产生乙酸和丙酸，丙酸可以对社区获得性耐甲氧西林金黄色葡萄球菌(Community-Acquired Methicillin-Resistant *Staphylococcus aureus*)表现出显著的抗菌作用[36]。

肠道微生物群对皮肤稳态产生影响的确切机制仍不清楚。目前普遍认为肠道微生物群对人体局部免疫网络和全身免疫系统的影响是肠道-皮肤沟通的主要途径[29,37-38]。肠道是人体主要的免疫器官。肠道中的微生物可直接竞争性结合肠上皮细胞，并通过触发免疫保护反应间接地防御外源性病原体的入侵[39]。Kosiewicz 等[39]发现肠道菌群能够诱导免疫球蛋白 A，并维持效应 T 细胞(Th1、Th2 和 Th17)与调节性 T 细胞之间的体内平衡。当肠道的上皮屏障完整性被破坏，肠道通透性增加时，包括饮食抗原、细菌毒素和病原体在内的免疫原分子的渗透性就会增加。这些抗原通过血液循环后可能在皮肤中积聚，干扰表皮屏障，破坏皮肤稳态并导致慢性皮肤炎症和持续的免疫反应[37,40]。与健康对照组相比，炎症性肠病(Inflammatory Bowel Disease，IBD)患者常伴有皮肤病变。溃疡性结肠炎患者中有 14%表现出皮肤病变，而在克罗恩病中这一比例更高，达到 24%[41]。Ramírez-Boscá 等[42]成功从银屑病患者血浆中分离出肠道细菌的 DNA，说明肠道菌群可能通过受损的肠屏障进入全身循环并诱导皮肤病变。

补充益生菌后，肠道微生物可以通过改善肠道营养不良和调节全身免疫恢复皮肤稳态[26,29]。肠道营养不良导致的常见皮肤疾病包括痤疮、特应性皮炎和银屑病等[29]。痤疮被认为与饮食中碳水化合物的过量有关。高血糖负荷会促进胰岛素/胰岛素样生长因子 1 (Insulin-Like Growth Factor-1，IGF-1)信号传导的增加，导致皮脂腺过度增生，从而诱导痤疮的发生；益生菌可以降低血糖负荷，减少 IGF-1 信号传导并减少角质形成细胞的增殖，改善痤疮症状[43-44]。补充益生菌可以改变肠道微生物的组成，通过增加肠上皮细胞紧密连接蛋白的表达以及分泌短链脂肪酸来促进肠道屏障功能的恢复，从而预防和治疗包括特应性皮炎在内的过敏性疾病[29]。此外，一项评估戊糖乳杆菌(*Lactobacillus pentosus* GMNL-77)对咪喹莫特诱导的银屑病小鼠模型影响的研究发现，与对照组相比，益生菌治疗后的小鼠出现红斑、脱屑和表皮增厚的症状明显减轻，口服该益生菌可以抑制肿瘤坏死因子 α (Tumor Necrosis Factor-α，TNF-α)、白介素 6 (Interleukin-6，IL-6)和促炎细胞因子的表达[45]。另一项体外和体内实验发现，副干酪乳杆菌(*Lactobacillus paracasei*)通过改善水肿、抑制肥大细胞脱粒和 TNF-α 的释放，在增强皮肤屏障功能恢复和拮抗神经源性皮肤炎症方面具有有益作用，口服此类益生菌菌株可能是预防或治疗反应性皮肤病的有效方法之一[46]。

除此以外，“肠-皮肤轴”还被看作是“肠-脑-皮肤轴”的组成部分[47-48]。肠道微生物组是最大的内分泌器官，由肠道微生物分泌产生的神经递质包括 γ-氨基丁酸、5-羟色胺、多巴胺和色氨酸等；这些神经递质不仅会增加肠道通透性从而导致肠道和全身炎症，而且还会穿过受损的肠道屏障进入血液，作用于包括皮肤在内的远端器官[49]。

2 肠道微生物群对头发的影响

2.1 肠道营养不良和饮食调节导致肠腔内代谢的改变可能会影响毛发的生长

研究表明，在喂食抗生素(万古霉素)和生物素缺乏饲料后，小鼠肠道内菌群组成发生变化，其中鼠乳杆菌(*Lactobacillus murinus*)由于耐受万古霉素而出现过度生长的情况，该菌本身不具备生产生物素的基因，但却会大量消耗原本肠道内储存的生物素；肠道营养不良和生物素剥夺最终导致小鼠血清生物素水平下降并引起脱毛，而补充生物素可以逆转脱毛症状，表明鼠乳杆菌通过生物素依赖性方式诱导脱毛[50]。维生素和矿物质对于正常的细胞生长和功能很重要，其中微量营养素是正常毛囊周期中的主要元素，在毛球基质细胞的快速分裂更新中发挥作用[51]。人体胃肠道中的微生物群携带了人体自身缺乏的消化酶基因，这些消化酶基因为人体内稳态提供必需的微量营养素，如维生素 K、维生素 B12、生物素、烟酸和叶酸等[52-54]。一篇评估生物素对头发影响的文章报道了 18 例脱发和脆甲症患者使用生物素的案例，发现在一定时间内使用生物素补充剂治疗后改善了临床症状[55]。另一项包括 29 例局限性斑秃患者的研究表明，患者组中的平均红细胞叶酸浓度显著低于对照组，而全秃/普秃患者的平均红细胞叶酸浓度显著低于局限性斑秃患者[56]。然而，Gonul 等[57]在对比了斑秃患者和健康对照组后发现 2 组之间血清叶酸和维生素 B12 水平无显著差异。尽管现有的研究对某些维生素和矿物质在脱发中的作用存在争议，微量营养素补充疗法仍然是一种有希望的低风险替代方法[58]。

2.2 肠道微生物群可能通过调节全身和局部免疫系统来影响脱发症

人体免疫系统与肠道微生物群紧密相关，在婴幼儿期，健康的肠道菌群对调节宿主免疫防御和耐受、诱导先天性及适应性免疫功能的发育和成熟具有重要作用[59]。微生物进行免疫调节的基本机制涉及肠道微生物群的组成和/或代谢活性的调节，以及微生物和/或相关成分与肠道黏膜下层免疫系统的直接相互作用[37,46,60]。有研究表明，小肠细菌过度生长(Small Intestinal Bacterial Overgrowth，SIBO)可能是遗传易感人群中免疫系

统的潜在应激源，导致肠道黏膜通透性增加，肠上皮屏障功能退化，增加外源性蛋白质对免疫系统的暴露，降低人体免疫力，从而诱导毛囊内免疫细胞的自我攻击[61]。进一步的研究表明，胃肠道黏膜树突状细胞已被证明可以表达紧密连接蛋白，穿透肠上皮单层直接在肠腔中获取细菌和抗原，并转运至外周循环影响全身免疫；据推测，在益生菌与肠上皮相互作用之后，相关的免疫细胞被激活，免疫介质(例如细胞因子)被释放到血液循环中，通过血液到达皮肤毛囊，在那里它们可能发挥免疫调节作用并影响毛发[61-63]。常见的促炎细胞因子包括 TNF-α、白介素 8 (Interleukin-8，IL-8)、白介素 12 (Interleukin-12，IL-12)、白介素 17 (Interleukin-17，IL-17)等，而 TGF-β 和白介素 10 (Interleukin-10，IL-10)则普遍被认为具有抗炎作用[64]。Lee 等[65]发现喂食罗伊氏乳杆菌(*Lactobacillus reuteri* BM36301)的雌性小鼠血清 TNF-α 水平相较于对照组显著降低，并且在脱毛区域表现出更快的毛发再生和更多的皮下毛囊数。此外，喂食罗伊氏乳杆菌(*Lactobacillus reuteri* ATCC 6475)的小鼠表现出皮肤光泽和毛发生长，血清抗炎因子 IL-10 水平上升，促炎因子 IL-17 水平下降[66]。多项研究证明益生菌能够通过 IL-10 介导的 $CD4^+CD25^+Foxp3^+$Treg 细胞下调 IL-17 水平，从而调节机体免疫耐受[67-70]。虽然肠道微生物群与宿主免疫学效应的相关性证据正在增加，但截至目前，完善的作用机制和具体的免疫信号路径尚不清晰，有待进一步的研究。

2.3 肠道微生物群及其代谢产物可能通过神经内分泌途径影响毛发生长

急慢性压力被认为是休止期脱发的主要诱因，而由脱发产生的压力和焦虑可进一步导致症状加剧，成为多种类型脱发诱因中的次要因素和加重因素。研究表明长期不断的慢性压力与头发生长抑制和毛囊周围炎症显著相关，同时一些压力应激调节物质如 P 物质、促肾上腺皮质激素、催乳素和皮质醇等都会影响头发生长[71]。在啮齿动物中，皮质酮是主要的应激激素。Wang 等[72]通过 21 d 的慢性束缚应激(Chronic Restraint Stress，CRS)成功诱导小鼠产生心理压力，与对照组比较发现小鼠背部毛发生长被抑制；CRS 主要通过增加血清皮质酮水平，同时抑制阿黑皮素原(Proopiomelanocortin，POMC)、促皮质素释放因子(Corticotropin Releasing Factor，CRF)和糖皮质激素受体(Glucocorticoid Receptor，GR)的 mRNA 表达来影响小鼠的下丘脑-垂体-肾上腺(Hypothalamic-Pituitary-Adrenal，HPA)轴，从而抑制毛囊生长和黑色素生成。Arck 等[73]的研究报道了持续的声波压力会显著增加小鼠皮肤中含凋亡细胞的毛囊数量，并抑制原位滤泡内角质形成细胞的增殖，而使用 P 物质受体拮抗剂能改善这些症状。另一项研究则发现催乳素及其受体在小鼠毛囊上皮细胞中以毛发周期依赖性的方式表达，并诱导毛囊的退行期[74]。

现有研究发现补充益生菌可能对压力和焦虑有关的心理症状及毛发健康有改善作用。摄入罗伊氏乳杆菌(*Lactobacillus reuteri*)的小鼠与对照组相比，血浆中催产素水平升高，而调控应激反应的糖皮质激素皮质酮血药浓度则降低，表现出更快的皮肤伤口愈合能力，诱导小鼠皮肤出现真皮增厚、毛囊和皮脂细胞增多的特征[75]。副干酪乳杆菌(*Lactobacillus paracasei* CNCM I-2116)能够抑制 P 物质诱导的皮肤炎症，并加速体外皮肤屏障功能的恢复[46]。另一项研究发现由瑞士乳杆菌(*Lactobacillus helveticus* R0052)和长双歧杆菌(*Bifidobacterium longum* R0175)组成的益生菌制剂可减轻受试者和大鼠的应激反应，而且这种作用与尿皮质醇水平的降低相关[76]。其他肠道乳杆菌如短乳杆菌(*Lactobacillus brevis* NCL912)被发现能产生神经活性物质 γ-氨基丁酸(γ-Aminobutyric Acid，GABA)[77]。目前，肠道菌群与压力应激和毛发生长的关系尚不明确，相关研究还处在早期阶段。然而，通过肠道微生物及其代谢产物与人体神经内分泌系统之间直接和间接的相互作用，

预防和改善应激状态下的脱发症状，将会是具有一定潜力的治疗手段之一。

3 靶向肠道微生物群改善脱发的策略及研究

总结近年来的文献资料，肠道微生物群改善和治疗脱发的可能途径包括营养代谢途径、免疫系统途径和神经内分泌途径(图 1)。

肠道微生物群可以改善肠道内维生素和矿物质等营养物质的吸收。例如，微生物代谢产物短链脂肪酸能够降低肠腔内的 pH 值，提高矿物质的溶解度[78]；棒状乳杆菌(*Lactobacillus coryniformis*)和罗氏乳杆菌(*Lactobacillus rossiae*)已被证明可以产生维生素 B12[79-80]；罗伊氏乳杆菌(*Lactobacillus reuteri*)和嗜酸乳杆菌(*Lactobacillus acidophilus*)则能提高膳食维生素 D 和维生素 E 的吸收度[81-82]。正确补充头发健康生长必需的维生素和矿物质对脱发的改善是必要的。

除了影响宿主的营养代谢以外，肠道微生物群可以调节局部及全身性免疫应答。肠道菌群与宿主之间局部的相互作用主要涉及肠上皮细胞和免疫细胞对细菌表面分子的直接识别。例如，一些细菌细胞壁上的脂多糖、肽聚糖、脂磷壁酸和胞外多糖可以诱导多种肠道免疫反应[65]。与此同时，细菌分泌的各种代谢产物可以通过人体免疫网络影响包括皮肤及其附属器官在内的肠外远端组织的免疫反应[83]。例如，L-乳酸(产自 *Lactobacillus casei* strain Shirota)、多胺(产自 *Bifidobacterium animalis* subsp. *lactis* LKM512)、组织胺(产自 *Lactobacillus reuteri* ATCC PTA 6475)及多种肠道细菌分泌的短链脂肪酸被报道具有远程免疫调节作用[84-87]。丁酸能够通过抑制炎症细胞的增殖、迁移、黏附和细胞因子的产生，从而抑制免疫反应[61,88]。Smith 等[89]和 Furusawa 等[90]的研究证明了丁酸盐能调节结肠调节性 T 细胞(Treg)的数量和功能，而 Treg 对毛发生长有重要作用[91]。

肠道微生物群还可能通过神经内分泌途径参与宿主的下丘脑-垂体-肾上腺(HPA)轴激素的调节，从而影响头发健康。Levkovich 等[92]发现给小鼠喂食含有罗伊氏乳杆菌的酸奶或者不含酸奶的纯化罗伊氏乳杆菌都会诱导动物皮毛出现“健康光泽”，血清 IL-10 水平升高，上皮毛囊向生长期转变以及毛囊和皮脂生成增加；当研究人员给缺乏 IL-10 的小鼠喂食后，未能重现该实验结果。细胞因子 IL-10 不仅介导毛囊局部的免疫炎症反应，还参与 HPA 轴激素的调节，影响全身健康[93-94]。肠道微生物也被认为对肠腔中的游离儿茶酚胺(包括去甲肾上腺素和多巴胺)水平有重要影响[77]。

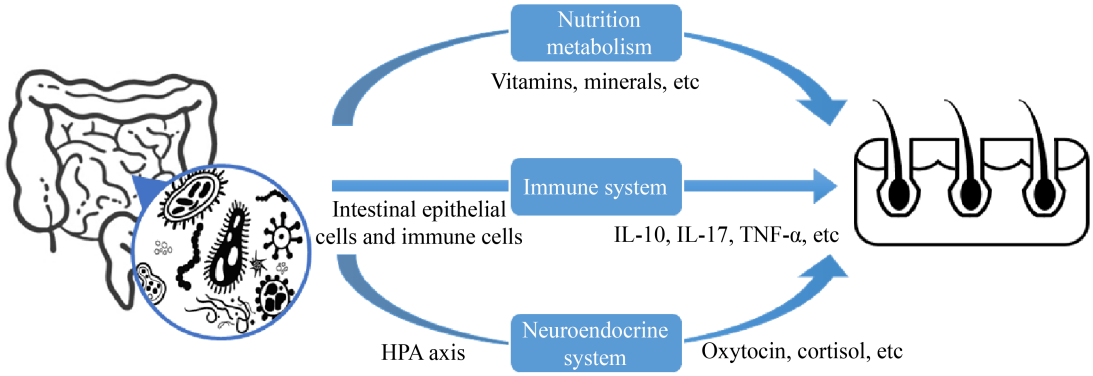

图 1 肠道微生物群改善和治疗脱发的可能途径[26,29,37,66]

Figure 1 Possible pathways of intestinal microbiota to improve and treat hair loss[26,29,37,66]

针对雄激素脱发，已有临床研究发现给雄激素性脱发的患者服用从泡菜(Kimchi)和臭豆酱(*Cheonggukjang*)中分离出的活益生菌产品[成分包括贺氏明串珠菌(*Leuconostoc holzapfelii*)、肠系膜明串珠菌(*Leuconostoc mesenteroides*)和清酒乳杆菌(*Lactobacillus sakei*)] 4 个月后，明显改善了患者的毛发数量和粗细，提示该益生菌产品可能有改善外周血流量和调节雄激素的作用[5]。Choi 等[95]发现从枯草芽孢杆菌(*Bacillus subtilis*)中提取的超高分子量聚谷氨酸在体外实验中表现出抑制 5α-还原酶的作用；在体内实验中与对照组相比，C57BL/6 小鼠背部皮肤更早出现黑色素沉着、毛囊数量增加且休止期缩短，促进了毛发生长。

斑秃的发病机制包括遗传因素、免疫因素和环境因素，其中自身免疫反应导致的毛囊免疫特权崩溃被认为是斑秃的主要原因。临床报告中已有使用粪便菌群移植治疗肠道疾病时出现斑秃患者头发生长的案例。Rebello 等[96]报告了 2 例普秃男性患者分别患有艰难梭状芽孢杆菌(*Clostridium difficile*)感染导致的血性腹泻和回结肠克罗恩病，接受粪便菌群移植后，头脸手臂长出新毛发。Xie 等[97]发现在使用粪便菌群移植治疗一名患有感染性腹泻和抑郁症的男性后，其右枕骨 1.5 cm×2.0 cm 的局限性斑秃处长出新毛发，部分白发逐渐变黑，而且抑郁症状好转的案例。Mahajan 等[98]同样使用粪便菌群移植治疗了 4 例溃疡性结肠炎患者，其中一名女性患者报告了自己的脱发症状明显得到改善，同时否认治疗期间使用任何促进头发生长的药物。

肠道微生物作为一种可能的潜在治疗方法，可以安全有效地通过调节“肠-皮肤轴”来改善头发健康和脱发症状。表 1 列举了近年来有关肠道微

表 1 肠道微生物群对毛发健康的影响

Table 1 Effect of gut microbiota on hair health

可能的作用途径 Possible pathway	相关的肠道微生物群/益生菌 Associated gut microbiota/probiotic	补充说明 Additional remarks	参考文献 References
Nutrition metabolism	*Lactobacillus murinus*	Intestinal dysbiosis and biotin deprivation induced alopecia through overgrowth of *L. murinus* in mice	[50]
	Lactobacillus coryniformis & *Lactobacillus rossiae*	Produced vitamin B12	[79-80]
	Lactobacillus reuteri & *Lactobacillus acidophilus*	Increased absorption of dietary vitamin D and E	[81-82]
Immune system	*Lactobacillus reuteri* BM36301	Female C57BL/6 mice treated with *L. reuteri* BM36301 maintained lower serum TNF-α as well as healthy skin with active folliculogenesis and hair growth	[65]
	Lactobacillus reuteri ATCC 6475	C57BL/6 mice treated with *L. reuteri* ATCC 6475 displayed the skin glow and exuberant hair growth, serum IL-10 level ↑ and IL-17 level ↓	[66]
	Fecal microbiota transplant (FMT)	Two alopecia patients had significant improvement in hair loss after FMT	[96]
	Fecal microbiota transplant (FMT)	Hair regrowth following FMT in an elderly patient with alopecia areata	[97]
	Fecal microbiota transplant (FMT)	A female patient claimed to have improved her hair loss after FMT and denied using any drugs that promote hair growth during treatment	[98]
Neuroendocrine system	*Lactobacillus reuteri*	Oral *L. reuteri* up-regulates blood levels of oxytocin and down-regulates stress hormone corticosterone in mice, dermal thickness ↑ and hair follicles ↑	[92]
	Lactobacillus helveticus R0052 & *Bifidobacterium longum* R0175	Probiotic formulation consisting of *L. helveticus* R0052 and *B. longum* R0175 reduced stress response in human and rats and decreased urinary cortisol levels	[76]
	Lactobacillus brevis NCL912	Produced catecholamines and gamma-aminobutyric acid	[77]

生物群影响毛发健康的文献报道。然而，尽管存在肠道微生物群改善脱发的治疗潜力，仍需要进一步的大量基础研究和临床试验。

4 小结

对“肠-皮肤轴”领域的探索已成为国内外研究热点之一。目前关于“肠-皮肤轴”的相关研究报道主要集中在痤疮、特应性皮炎和银屑病等皮肤疾病上，对皮肤附属器官尤其是毛发的研究还十分稀少。本文在已有的“肠-皮肤轴”理论基础上，结合毛发特有的生理学、病理学特征，针对性地探讨了肠道微生物群及其代谢产物对毛发的影响和作用机制，并归纳总结了肠道微生物群改善和治疗脱发的可能途径。但目前大多数研究还集中在动物实验，少量的临床研究也存在样本量不足等问题。肠道微生物群及其代谢产物对人体毛发影响的研究仍处于初期阶段，亟需大规模随机对照研究来证实。总而言之，肠道微生物群为脱发的发病机制和治疗靶点提供了新的认识和观点，也为脱发的改善和治疗提供了更多的选择。

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