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Review 综 述

益生菌对特应性皮炎的防治及机制研究进展

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摘　要：特应性皮炎(atopic dermatitis, AD)是一种以反复发作和严重瘙痒为特征、发病率最高的过敏性皮肤病。AD 的致病机制涉及遗传易感性、表皮屏障功能障碍、微生物组失调、免疫反应失衡以及环境等多个因素，而现有治疗用药副作用大、疗效欠佳。目前研究已发现肠道菌群尤其是益生菌在 AD 中起着重要作用。益生菌能够通过抑制病原菌、增强屏障功能、改善肠道环境和平衡 Th1/Th2 免疫应答等机制改善 AD 症状。本文综述了 AD 患者皮肤及肠道微生态特征，基于 AD 发病的致病机制和影响因素，系统阐明益生菌缓解 AD 的机制，以期为益生菌治疗 AD 及相关皮肤过敏性疾病提供理论支持。

关键词：特应性皮炎；肠道菌群；免疫；益生菌；组胺

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Research progress in probiotics for prevention and treatment of atopic dermatitis

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Abstract: Atopic dermatitis (AD) is a highly prevalent allergic skin disease characterised by recurrent attacks and severe itching. The pathogenesis of AD involves a variety of factors including genetic susceptibility, epidermal barrier dysfunction, microbiome dysbiosis, immune imbalance, and the environment, while the available therapeutic drugs have severe side effects and limited efficacy. Studies have demonstrated that gut microbiota, particularly probiotics, play a role in AD. Probiotics can alleviate AD symptoms by inhibiting pathogens, enhancing barriers, improving the intestinal environment, and balancing the Th1/Th2 immune response, among other mechanisms. In this review, we summarized the skin and intestinal microecological characteristics of AD patients and systematically elucidated the mechanisms of probiotics in alleviating AD from the pathogenesis and influencing factors of AD, aiming to provide theoretical support for probiotics in the treatment of AD and related allergic skin diseases.

Keywords: atopic dermatitis; gut microbiota; immunity; probiotics; histamine

皮肤(skin)被覆于体表，作为人体抵御外界因素侵扰的第一道防线，具有屏障保护、结构支撑、调节体温以及维持人体内环境稳定等功能[1]。特应性皮炎(atopic dermatitis, AD)是一种临床上最常见的慢性炎症性皮肤病，以反复发作和严重瘙痒为主要特征，常与食物过敏、哮喘和过敏性鼻炎等其他过敏反应有关[2]。据统计，全球约20%的儿童和10%的成年人受此影响[3]。研究指出，社会心理压力、空气温湿度变化、过敏原刺激、皮肤与肠道菌群失调、皮肤屏障减弱和免疫细胞活性增强为诱发 AD 的主要因素；AD 通常影响身体的特定部位，如脸部、颈部、四肢及皮肤皱褶处，以皮肤干燥、红斑、丘疹、苔藓样硬化、渗出和结痂为典型病理特征；尽管 AD 是以过敏的形式影响皮肤系统，但近年研究发现其与心血管疾病、神经系统疾病、自身免疫性疾病以及肥胖等非过敏性疾病的高发病率也存在联系[4-7]。除了对患者躯体造成伤害外，AD 也因为其持续的瘙痒症状严重影响患者的生活质量以及工作效率，危害患者心理健康[3]。

为缓解 AD 患者的临床症状、减少疾病复发及并发症的发生，临床医生根据成人和儿童皮炎的严重程度，制定了包括回避疗法、漂白浴、润肤剂、外用皮质类固醇(topical corticosteroids, TCS)、钙调神经磷酸酶抑制剂(topical calcineurin

inhibitor, TCI)和 Janus 激酶(Janus kinase, JAK)抑制剂等系列方法，但这些治疗具有诸如皮肤萎缩、多毛、色素沉着、应用部位产生灼烧感和瘙痒、生长迟缓、骨质疏松、鼻咽炎、头痛、恶心和腹泻等较严重的副作用[8]。抗组胺药是治疗 AD 皮肤瘙痒的主要疗法，但该药具有嗜睡的副作用，且对儿童认知能力存在影响[9]。因此，亟需研发出一种新的安全、有效、经济的生物制剂用于 AD 的预防与治疗。

1930 年，皮肤病学家 John H. Stokes 提出关于情绪、肠道菌群及皮肤炎症之间相互关系的开创性理论，揭示了肠道-皮肤轴的存在[10]。随着新一代测序技术的出现，研究发现 AD 的发生不仅与皮肤微生物组有关，且与肠道微生物组有关[11]。肠道菌群失调通过促炎细胞因子增加肠道通透性，进而促进免疫失调，导致包括 AD、痤疮以及银屑病等皮肤疾病的发生[12]。益生菌(probiotics)是一种活的微生物，当给予足够数量时将对宿主的健康产生有益作用[13]。益生菌具有增强上皮屏障的完整性、抑制病原体增殖以及重新恢复机体免疫平衡的作用，是预防和治疗 AD 在内的各种过敏性疾病的新手段[14]。作者所在研究团队累积了超过 3 万株的健康功能微生物，建成了相应的菌种资源及基因组数据库，并对其进行功能挖掘，目前已证明益生微生物能通过调节肠道菌群在降血压[15]、降糖降脂[16]、促睡眠[17]、抗幽门螺杆菌[18]、抗病毒[19]、修复皮肤光老化[20]以及缓解溃疡性结肠炎[21]等方面有显著的益生功能。肠道-皮肤轴的存在也为益生菌防治 AD 提供了理论支撑。因此，本文将从 AD 的皮肤和肠道微生态特征、病理机制及益生菌在 AD 领域的研究现状，系统综述益生菌在防治 AD 的研究中取得的最新进展。

1 AD 特征性人体微生态

1.1 AD 的皮肤微生态

皮肤和肠道菌群是人体的 2 个主要微生态系统[22]。皮肤表面定殖有数百万微生物，主要为丙酸杆菌(*Propionibacteria*)、链球菌(*Streptococcus*)、葡萄球菌(*Staphylococcus*)和棒状杆菌(*Corynebacterium*)[23]。皮肤免疫系统的动态平衡很大程度依赖于皮肤菌群的平衡[24]，皮肤微生态一旦失衡，不仅会增加病原微生物的感染风险，且极易诱发系列慢性皮肤疾病，如 AD[25]。在过去十年里，高通量测序技术的进步为我们提供了关于皮肤健康与微生态组成的新见解：健康人的皮肤微生物群通常是稳定的，但 AD 患者皮肤表现出显著的失调，表现为微生物多样性减少，且皮损部位被大量金黄色葡萄球菌(*Staphylococcus aureus*)定殖[26]；除了 *S. aureus* 外，表皮葡萄球菌、溶血葡萄球菌在 AD 发病部位也有所增加[27]；此外，真菌及感染在 AD 患者中也较为常见，马拉色菌及白色念珠菌在 AD 患者的皮肤中比健康人更多[28]，而单纯疱疹病毒感染也常在 AD 儿童中被发现[29]。

1.2 AD 的肠道微生态

既往研究表明，肠道菌群的定殖与免疫系统的发育密切相关，肠道菌群失调与过敏性疾病的发生相关，且常先于疾病发生[30]。Watanabe 等[31]发现，AD 患者肠道中乳杆菌、双歧杆菌的相对丰度显著降低，而葡萄球菌的比例显著高于健康人群；Fieten 等[32]的研究表明，伴有食物过敏的 AD 患儿粪便微生物中假链双歧杆菌和大肠杆菌相对较多，而青春双歧杆菌、短双歧杆菌、普拉梭菌及嗜黏蛋白阿克曼氏菌较少；除了双歧杆菌数量减少外，AD 患儿肠道拟杆菌数量降低，而肠杆菌数量增加[33]；Fujimura

等[34]的研究表明，在患上 AD 及哮喘等高过敏性疾病风险的儿童中，阿克曼氏菌、双歧杆菌及粪杆菌的水平较低，而假丝酵母及红酵母含量较高；在其他研究中还发现，艰难梭菌在生命早期的定殖也导致了随后 AD 的发生[35]；进一步研究指出，AD 儿童肠道共生细菌对肠黏膜的黏附性较差，导致肠道屏障功能出现障碍，肠道中抗炎因子白介素 10 (interleukin, IL-10)的产生减少，而促炎细胞因子水平升高[36]。综上，肠道微生物多样性及组成变化与 AD 等过敏性疾病的发生发展密切相关，调节肠道菌群或可改善过敏症状的发展，成为预防和治疗 AD 的靶点。

2 特应性皮炎的发病机制研究

2.1 AD 的病理机制

医学研究指出，AD 属于由 IgE 抗体介导的I型超敏反应，涉及到多个过程的免疫反应是 AD 致病机制的核心。当过敏原入侵皮肤屏障后，被皮肤抗原递呈细胞(antigen-presenting cells, APC)如朗格汉斯细胞和树突细胞摄取，随后 APC 将过敏原递呈至组织与血液中的初始辅助性 T 细胞(naive helper T cell, Th0)，并诱导 Th0 细胞向 Th2 细胞分化增殖；分化后 Th2 细胞分泌大量过敏性细胞因子如 IL-4、IL-5、IL-13，形成过度的 Th2 型免疫反应(图 1)。

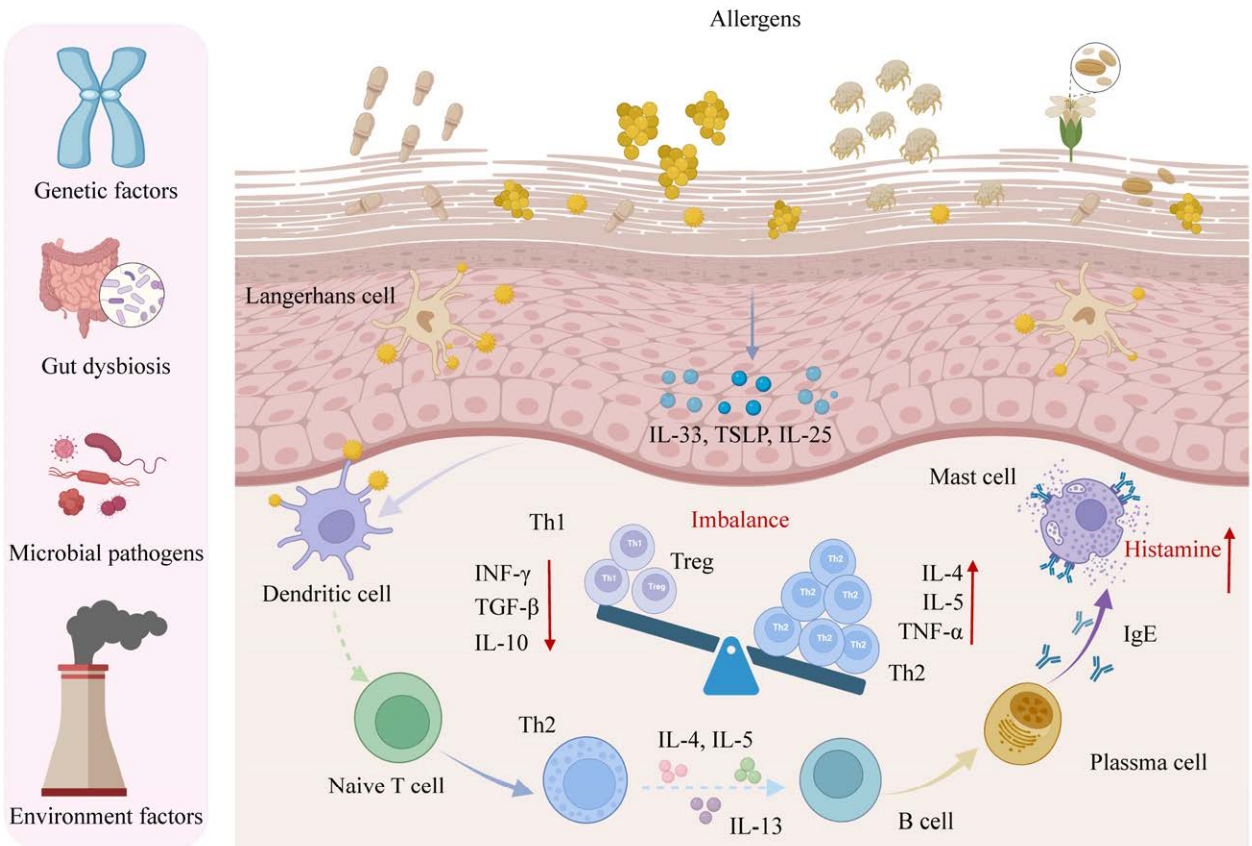

图 1 特应性皮炎的病理机制

Figure 1 The pathogenesis of atopic dermatitis.

一方面，Th2 分泌的细胞因子可募集更多 Th0 细胞并向 Th2 分化，另一方面，Th2 细胞作用于 B 细胞，诱导其转化为分泌特异性 IgE 的浆细胞；这些浆细胞来源的 IgE 将激活皮肤肥大细胞(mast cell, MC)表面的 Fc 受体，使 MC 发生脱颗粒，释放大量致敏效应物质组胺(histamine)进入皮肤组织与血液，引起皮肤红肿、瘙痒等系列症状[37]。组胺是目前研究较为关注的过敏介质，而人体细胞表面已被证实具有 4 种组胺受体(histamine receptor, HR)，其中 H1R 和 H4R 的异常激活是导致 AD 患者产生瘙痒症状的主要原因[38]。皮肤肥大细胞释放出的组胺作用于皮肤感觉神经末梢表达的组胺受体，继而激活神经末梢的信号传导，并通过脊髓丘脑束将瘙痒的感觉传递到大脑，导致患者进入瘙痒-抓挠-严重瘙痒的恶性循环[39]。

2.2 AD 的影响因素

AD 的发病机制是复杂和多因素的，涉及到遗传易感性、肠道和皮肤微生态失调、局部和全身免疫失衡以及环境因素之间的相互作用[40]。

2.2.1 遗传易感性

AD 具有很强的遗传性[41]，目前已确定的最大遗传风险与由 *flg* 基因编码的皮肤屏障蛋白——微丝蛋白的突变有关[42]。*flg* 基因突变将导致微丝蛋白表达下降甚至完全丧失[43]，从而使患 AD 的风险比未突变人群高 3−5 倍，同时也增加了哮喘和花生过敏的风险[44]。此外，位于染色体 5q31.1 上的基因座包含 2 型免疫细胞因子 IL-4、IL-13 的基因以及调控细胞因子表达的 *rad50* 基因突变也会引起 AD 患病风险增高。位于染色体 11q13.5 上的 2 个候选基因 *emsy* 和 *lrrc32* 之间的第 3 个广泛复制的基因与多种特应性表型相关[45]。在 AD 中，迄今已识别有 34 个基因座突变与疾病发病相关，另外还可能存在其他未识别的基因座或可遗传的表观效应导致 AD 发病。

2.2.2 微生物组失调

如前文所述，AD 患者的皮肤存在表皮屏障功能障碍，表现为经皮水分损失(transepidermal water loss, TEWL)增加、pH 升高、皮肤通透性增加、水分保留率降低以及脂质成分改变[46]，因此也更容易受到细菌感染。*S. aureus* 和 *Malassezia* spp.是主要的定殖菌和病原体，可引发或加剧 AD 的皮肤炎症[47-48]。另外，与健康人群相比，患者肠道微生物多样性降低，乳杆菌、双歧杆菌等有益微生物的相对丰度显著降低，而大肠杆菌、艰难梭菌和 *S. aureus* 的比例增加。特别在生命早期，肠道微生物的定殖与改变早于临床表现，表明肠道菌群失调也是 AD 发生的一大影响因素。

2.2.3 免疫反应失衡

过敏反应是一种免疫失调性疾病，Th1/Th2 平衡破坏导致 Th2 细胞亚群及其分泌的细胞因子增多也是 AD 发生的原因[49]。在始发阶段，皮肤屏障功能出现障碍，增加了外源性微生物和过敏原的经皮渗透，降低了对抗原和刺激物的炎症阈值；受损表皮中的角质形成细胞通过胸腺基质淋巴生成素(thymic stromal lymphopoietin, TSLP)及 IL-33 等细胞因子发出促炎和瘙痒信号，激活 Th2 介导的免疫反应，进一步导致组织损伤[50]。TSLP 通过其受体激活未成熟的树突细胞，促进 APC 的成熟，同时促进嗜酸性粒细胞的活性，增强 IL-4、IL-5 和 IL-13 的表达[51]，而 IL-4 及 IL-13 的上调降低了表皮屏障蛋白的产生，从而加重皮肤屏障缺陷；IL-25 可诱导多种趋化因子促进 Th2 细胞募集[52]；IL-33 通过受体激活核因子 κB (nuclear factor kappa-B, NF-κB)及丝裂原激活蛋白激酶，从而刺激与 Th2 反应相关的细胞因子的产生[53]。另外，先天淋巴样细胞(innate lymphoid cells, ILCs)能够刺激细胞因子的产生，影响局部组织中的免疫和非免疫细胞。ILC2

具有分泌 IL4、IL-5 和 IL-13 等促过敏细胞因子的能力，通过启动 Th2 反应而参与 AD 等各种过敏性疾病[54]。

2.2.4 环境因素

宿主所处的生活环境以及生活方式也会影响 AD 的发生发展，其中气候变化[55]、空气污染物[56]、心理压力[57]、日晒不足[58]及高硬度水[59]等被认为是 AD 发病的驱动因素。研究指出，空气中的屋尘螨、花粉，以及牛奶、蛋清、大豆和花生等常见食物过敏源都是诱发儿童 AD 及加重疾病最常见的环境刺激物，直接引发免疫异常[37]。另外，长期暴露在低湿度的环境中会加速 AD 患者皮肤的水分损失，加重皮肤屏障缺陷[60]。同时，压力引起的糖皮质激素变化会抑制皮肤神经酰胺、胆固醇和游离脂肪酸的合成，进而破坏了皮肤的疏水屏障导致水分丢失，进一步加重 AD 并诱发其他皮肤炎症[61]。

3 益生菌防治 AD 的机制

益生菌是一类能够附着在胃肠道黏膜且具有多样化临床及免疫能力的活性微生物[62]。据报道，目前能减轻I型过敏反应的益生菌主要来源于乳杆菌属和双歧杆菌属[63]。一项使用动物双歧杆菌的随机、双盲安慰剂对照研究发现，8 周后益生菌组的受试者瘙痒症状显著改善[64]。Enomoto 等[65]的研究发现，使用短双歧杆菌后，益生菌组特应性皮炎评分(scoring of atopic dermatitis, SCORAD)指数下降。成人 AD 患者服用唾液乳杆菌 LS01 后，益生菌治疗组的 SCORD 评分显著降低，粪便微生物中葡萄球菌载量减少[66]。使用副干酪乳杆菌 K71 后，益生菌组的皮肤严重程度评分降低[67]。联合使用唾液乳杆菌 LS01 DSM 2275 和短双歧杆菌 BR03 DSM 16604 的随机对照试验发现，受试者在临床分数上有显著改善且血浆脂多糖(lipopolysaccharides, LPS)水平有所下降[68]。此外，孕期及婴儿早期补充鼠李糖乳杆菌 HN001 似乎可以降低患 AD 的风险[69]。本文列举了近年来益生菌防治 AD 的研究进展(表 1)，并对益生菌缓解 AD 的相关机制进行概述。

3.1 增强屏障功能

AD 患者肠道菌群失衡，多样性降低，肠道屏障也出现了类似皮肤的屏障功能受损[81]。研究指出，益生菌通过上调黏蛋白类糖蛋白(mucin-type glycoprotein, MUC)-1、MUC-2 和 MUC-3 促进杯状细胞的黏蛋白分泌，从而限制病原菌在黏膜中的移动；另外，益生菌分泌的 α-防御素、β-防御素等抗菌肽通过上调跨膜紧密连接蛋白和细胞间紧密连接蛋白，增强了紧密连接的稳定性并防止细菌增殖，从而降低上皮对病原体及其产物的通透性[82]。丁酸等益生菌源短链脂肪酸(short chain fatty acid, SCFA)也有助于调节紧密连接蛋白的表达，增强上皮屏障完整性[83]。Ma 等[84]发现婴儿双歧杆菌 YLGB-1496 也表现出良好的抗氧化性能，并能够上调皮肤屏障基因增强皮肤屏障功能。作者所在研究团队也发现发酵乳杆菌 XJC60 可通过分泌烟酰胺等抗氧化物质，维持皮肤角质层的完整性，具有维系皮肤屏障功能的作用[85]。

3.2 抑制病原体增殖

多项研究发现，益生菌能够与病原体竞争黏蛋白或上皮细胞的结合位点，防止致病微生物过度生长，纠正 AD 患者微生态的失调；而益生菌产生的抗菌肽、细菌素及 SCFA 也具有抑制或杀死病原体的作用(图 2)。Fang 等[70]发现植物乳杆菌 CCFM8610 治疗下调了涉及肠道金黄色葡萄球菌感染的功能基因，通过调节肠道微生物组成以及免疫反应，从而改善 AD 患者的临床症状。另外，本研究团队也证实人源性长双歧杆菌能分泌新型溶菌酶样蛋白，具有

表 1　文献中报道的具有缓解 AD 的益生菌

Table 1　Probiotics with atopic dermatitis-relieving effects reported in the article

Strain	Form and dosage	Test sample and quantity	Mechanism	Effect
Lactobacillus rhamnosus HN001	Capsulated probiotic 6×10^9 CFU/d	157 infants	Shape the immune system and increase IFN-γ level	The prevalence of eczema were significantly reduced[69]
Lactobacillus plantarum CCFM8610	Lyophilized powder 1×10^9 CFU/d	109 adult patients	Regulate the gut microbiota; maintain the immune responses and barrier integrity; change in functional genes of the gut microbiota	Improve SCORAD index; increase the expression levels of IL-10; decrease the F/B ratio; increase species evenness and diversity[70]
Lactobacillus plantarum IS-10506	Microencapsulated probiotic 2×10^{10} CFU/d	30 adult patients: 15 controls *vs.* 15 interventions	Suppression of the Th2 adaptive immune response and increase in the Th1 adaptive immune response; increase the Treg immune response and decrease Th17 response	The SCORAD score, IL-4, and IL-17 levels were significantly lower; the IFN-γ and Foxp3+ levels were significantly higher[71]
Lactobacillus rhamnosus IDCC 3201	Tyndallized probiotics 1×10^{10} CFU/d	66 children: 33 controls *vs.* 33 tests	Decreased production or activity of IL-31 and eosinophils	The SCORAD score, eosinophil count, and the IL-31 levels were decreased[72]
Lactobacillus paracasei KBL382	Live bacteria 1×10^9 CFU/d	NC/Nga mice: 7 controls *vs.* 7 models *vs.* 7 tests	Increase the immunosuppressive response and change the metabolic functions of gut microbiota	Reduced AD-associated skin lesions, serum levels of IgE, and immune cell infiltration[73]
Lactobacillus plantarum CJLP55	Lyophilized powder 1×10^{10} CFU/d	NC/Nga mice: 8 controls *vs.* 8 models *vs.* 8 tests	Alter the balance of Th1/Th2 ratio or induce IL-10 production	Suppressed AD-like skin lesions, high serum IgE levels; diminished the accumulation of eosinophils and mast cells; decreased production of IL-4 and IL-5[74]
Kazachstania turicensis CAU Y1706	Freeze-dried 1×10^{10} CFU/d	BALB/c mice: 10 controls *vs.* 10 models *vs.* 10 tests	Interactions between gut microbiota, SCFA, and immune modulation between Th1 and Th2	Reduced IgE levels and the number of mast cells and eosinophil; the serum concentrations of Th2 cytokines were significantly lower[75]
Limosilactobacillus reuteri FN041	Live bacteria 1×10^9 CFU/d	BALB/c mice: 12 controls *vs.* 12 models *vs.* 12 tests	Regulate the ileum microbiota, strengthen the ileal mucosal barrier	The plasma IgE were significantly decreased; the intestinal mucosal barrier was enhanced[76]
Lactobacillus plantarum LM1004	Lyophilized powder 2×10^{12} cells/g 0.01 g/kg-bw	SD rats: 10 controls *vs.* 10 models *vs.* 10 tests	Inhibited Th2 cell responses; activated the responses of Treg cell; modulated gut microbiota	Decreased the scratching behaviors; reduced vasodilation and serum histamine; decreased serum IgE contents[77]
Bifidobacterium adolescentis	Live bacteria 1×10^9 CFU/d	C57bl/6 mice: 5 controls *vs.* 5 models *vs.* 5 tests	Promote Tregs population in the spleen; restore the balance between Th1- and Th2-type immune responses; regulate the gut microbiota composition	Reduced ear and skin thickness and suppressed eosinophils and mast cells infiltration[78]
Bifidobacterium longum	Cell-free culture supernatant 1×10^7 CFU/d	Hairless mice: 5 controls *vs.* 5 models *vs.* 5 tests	Attenuate skin inflammation and enhance skin barrier function	Attenuated DNCB-induced skin inflammation, abnormal TEWL, AD-like skin, and deficiency of epidermal barrier proteins[79]
Lactococcus chungangensis CAU 28T	Live bacteria 1×10^9 CFU/mL	RAW 264.7 cells; human mast cell	Inhibit the release of allergy-associated proteins	Inhibited the production of the proinflammatory mediators; reduced the release of histamine[80]

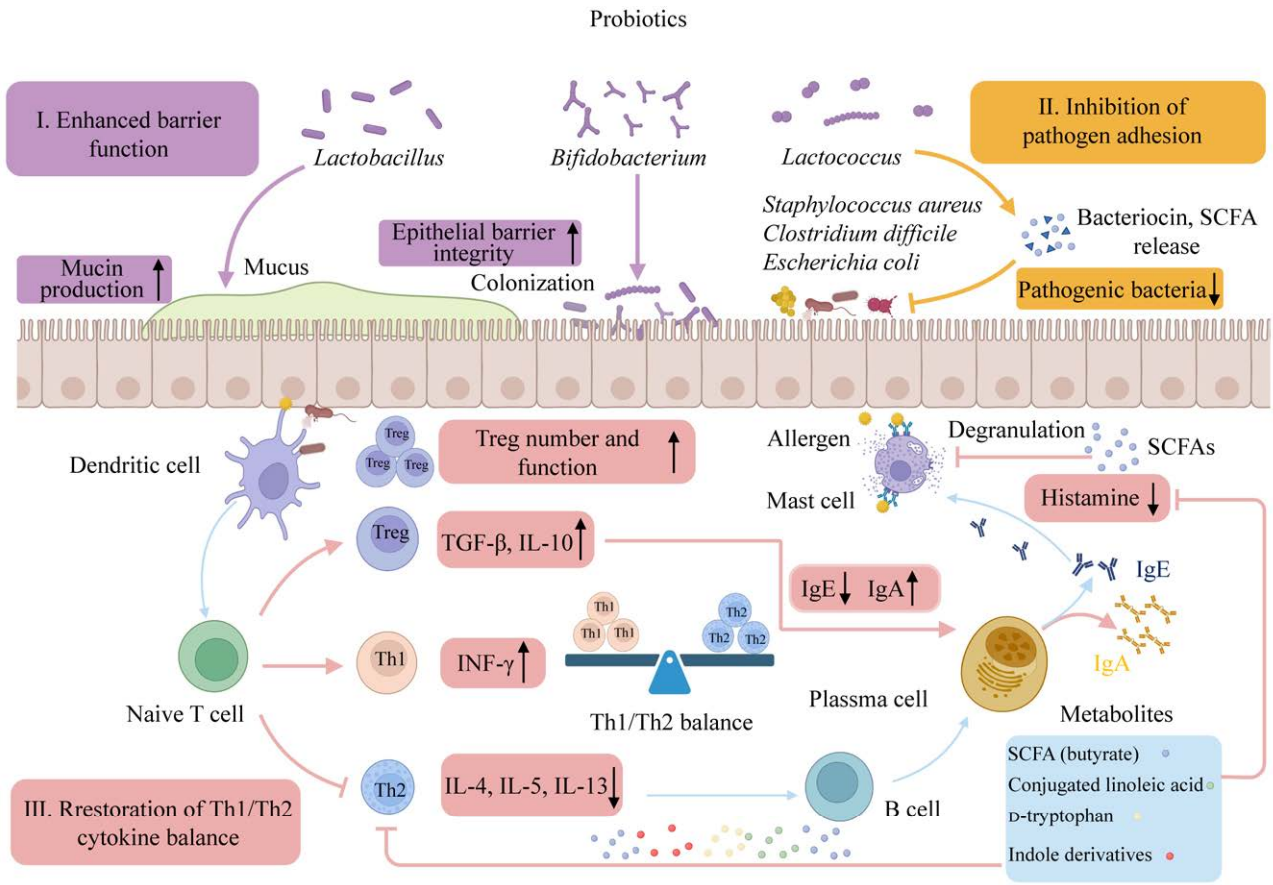

图 2　益生菌调控 AD 发病的作用机制

Figure 2　Mechanisms of probiotics in regulating AD pathogenesis.

调节机体肠道菌群稳定的生物活性[86]。此外，益生菌还能够增加胃肠道中 IgA 的含量，分泌型 IgA 通过连接病原体的抗原从而保护肠上皮细胞免受定殖或侵袭，诱导抗原向 DC 的逆向运输，下调促炎反应[87]。

3.3　调节 Th1/Th2 免疫应答

益生菌在 AD 中发挥免疫调节作用，一方面通过分泌不同的细胞因子刺激 Th1 应答，降低 Th2 应答来平衡 Th1/Th2 免疫反应；另一方面在 IL-2 和 TGF-β 的作用下能够诱导调节性 T 细胞分化增殖，下调 IgE 合成，减少过敏反应，维持免疫稳态[88]。Won 等[74]发现从泡菜中分离的植物乳杆菌 CJLP55 能够降低 IL-4、IL-5 水平，增加 IL-10 产生，通过平衡 Th1/Th2 免疫反应缓解小鼠 AD 样皮损。另外，益生菌还可通过产生 SCFA、共轭亚油酸、D-色氨酸和吲哚衍生物发挥免疫调节作用；SCFA 诱导肠道树突细胞表达视黄醛脱氢酶，促使维生素 A 转化为视黄酸从而促进 Treg 细胞的扩增和分化[89]。SCFA 特别是丁酸能够抑制 MC 上高亲和力 Fc 受体与 IgE 结合所引发的脱颗粒，从而降低组胺等炎症介质的释放，减少过敏反应的发生[90]。Kim 等[77]的研究发现，植物乳杆菌 LM1004 能显著降低血清中 IgE 与组胺水平，增加 Th1 与 Treg 细胞转录因子水平以及与丁酸产生相关的菌群丰度，减轻 AD 模型小鼠的皮肤瘙痒。以上发

现均表明，益生菌通过调节宿主免疫系统和肠道菌群对防治 AD 及相关皮肤过敏性疾病具有很大潜力。

4 结语与展望

综上所述，*flg* 基因功能缺失突变导致的遗传因素，瘙痒-抓挠-严重瘙痒引起的表皮功能障碍，皮肤及肠道菌群失调，Th1/Th2 免疫调节失衡，气候变化、空气污染、社会心理压力等环境影响，这些因素共同作用促进了 AD 的发生。益生菌通过与病原菌竞争黏附位置、产生细菌素等抗菌物质、阻止细菌生物膜的形成和促进 Th1 型细胞因子分泌，抑制 Th2 型细胞因子水平，从而抑制病原菌生长，修复受损皮肤及肠道屏障，促进失衡菌群平衡重建，恢复 Th1/Th2 免疫失调，最终减轻及改善患者皮肤过敏及临床症状。随着研究的深入，益生菌对 AD 的作用已在许多临床试验中进行了研究，但益生菌缓解 AD 的有效物质基础仍不明确。为了阐明益生菌、肠道菌群及皮肤之间具体的互作机制，精准补充益生菌来达到防治 AD 的作用，需要结合基因组学、转录组学和代谢组学以揭示益生菌对功能基因、肠道菌群、代谢途径以及具体代谢物的影响，全面解析益生菌对 AD 的缓解机制。为使治疗完全有效，在未来的研究中，也可考虑将益生菌补充剂与局部应用含有益生菌的乳膏相结合，以期开发出新型微生态方法来改善与治疗 AD 及相关皮肤过敏性疾病。

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