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Review 综 述

益生菌的精准筛选与应用

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摘　要：益生菌是指当摄取足够数量时，对宿主健康有益的活的微生物，其有益作用已被广泛认证，但益生菌的益生功能具有菌株特异性。随着越来越多的新技术被引入到益生菌的研究中，根据个性化需求筛选具备特定功能的益生菌，成为当前益生菌的研究热点。传统的益生菌筛选方法存在一定的局限性，无法满足当前对精准医疗的需求。因此，基于表型、基因分型和靶标，自下而上的益生菌精准筛选策略具有重要的现实意义。本文旨在从基于表型、基因分型和靶标等 3 个方面，探讨益生菌精准筛选的理论基础、方法和技术，并且深入探讨益生菌的应用、安全性评价，以期为益生菌的精准筛选提供参考。

关键词：精准益生菌；菌株筛选；安全性评价；基因分型

Precise screening and applications of probiotics

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Abstract: Probiotics refer to live microorganisms that are beneficial to the health of the host

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when ingested in sufficient quantities, and their beneficial effects have been widely recognized. However, the probiotic function of probiotics is strain-specific. As more and more emerging technologies are introduced into the research on probiotics, the screening of probiotics with specific functions according to individual needs has become a research hotspot. Conventional probiotic screening methods have limitations and cannot meet the current demand for precision medicine. Therefore, a bottom-up precision screening strategy for probiotics based on phenotyping, genotyping, and target is of great practical significance. This article discusses the theoretical basis, methods, and technologies of accurate screening of probiotics from phenotype, genotyping, and target, and the application and safety evaluation of probiotics, aiming to provide reference for the accurate screening of probiotics.

Keywords: precision probiotics; strain screening; safety evaluation; genotyping

世界卫生组织(World Health Organization, WHO)和联合国粮食及农业组织(Food and Agriculture Organization of the United Nations, FAO)将益生菌(probiotics)定义为当摄取足够数量时，对宿主健康有益的活的微生物[1]。益生菌是近年来食品和健康领域的研究热点，具有调节肠道微生物稳态及维护黏膜屏障等功能，可以促进营养吸收，提高机体免疫力[2]。然而，益生菌的筛选面临诸多问题，比如不同来源的益生菌功效和作用机制可能存在差异，选择合适的样本进行筛选至关重要[3]。传统益生菌的筛选及功能评价主要依赖体外实验和动物实验，体外实验难以模拟肠道环境，导致筛选出的益生菌可能在体内表现不佳，动物实验虽然能够模拟肠道环境，但成本高、周期长，存在筛选具备特定功能益生菌的效率和准确性低等问题[4]。因此，需要开发更加高效、可靠的筛选方法。

精准益生菌(precision probiotics)是指采用基于表型、基因分型和靶标的自下而上的菌株筛选策略，联合多组学技术，多尺度建立快速、精准的益生菌筛选方法和功能预测技术，开发针对不同人群的个性化的高品质益生菌菌株[5-6]。传统益生菌的筛选策略主要是自上而下的，通过筛选相较于疾病状态下健康个体中富含的微生物，进而确定对人体有益的益生菌，这种筛选方法必须依赖于多次反复的体内外试验才能最终确定其确切的健康益处，费时费力[7]。自下而上的精准益生菌筛选策略已经成为新兴的益生菌筛选方法[8]，这种筛选策略包括基于表型、基因分型和靶标的筛选。精准益生菌的筛选是联合多组学技术，从体外和离体细胞培养，依据细胞和动物对微生物所产生的反应进行筛选及通过计算机模拟的方法进行预测，以评估益生菌所产生的可调节宿主或微生物相关信号通路的分子效应物的能力，进而筛选出的具有特定功能或特性的菌株，通过该方法筛选出的益生菌候选株为精准益生菌[4,9]。如陈靖等[10]采用菌落拉丝法和苯酚-硫酸法筛选出胞外多糖(exopolysaccharides, EPSs)产量高的菌株，将得到的菌株进行表型特征分析，筛选出 4 株高产胞外多糖的乳酸菌，为 2 株副干酪乳酪杆菌(*Lacticaseibacillus paracasei*) LZ9089 和 LZ9Y10、1 株干酪乳酪杆菌(*Lacticaseibacillus casei*) LZ9183 和 1 株短促生乳杆菌(*Levilactobacillus brevis*) LZ9285。Machado 等[11]利用表型和计算机模拟方法同时利用现有数据库和生物信息学工具筛选基因组，鉴定抗生素抗性基因、毒力因子、基因组岛和可移动遗传因子，用 2 种表型方法鉴定嗜黏蛋白阿

克曼氏菌(*Akkermansia muciniphila*) DSM 22959的耐药性。张腾勋等[12]选用聚苯乙烯(polystyrene, PS)微球作为微塑料的代表,开发了一种高通量筛选对微塑料有强吸附能力的菌株的方法,成功分离出了*L. paracasei* ATM-7和*L. casei* ATM-107,初步证明菌株吸附微塑料的可行性和基于PS荧光微球筛选方法的有效性,为大规模筛选缓解微塑料伤害的益生菌及开发新一代的益生菌产品奠定了基础。

益生菌的精准筛选是指在特定条件下,对潜在的益生菌进行系统评估,以确定其对人体健康的益处,并预测其在不同环境中的表现[13]。精准益生菌可应用于治疗某些肠道疾病、通过调节肠道菌群平衡改善免疫系统和作为益生菌添加剂提供辅助治疗[14-15]。益生菌的精准筛选也面临诸多挑战,如菌株选择、安全性和临床试验设计等。本文旨在探讨传统益生菌和精准益生菌的筛选方法和应用,为进一步开发精准益生菌提供参考。

1 传统益生菌的筛选

益生菌在改善肠道健康、增强免疫力、预防腹泻等方面具有显著作用[16]。随着益生菌的有益功能得到认可,益生菌的开发应用在国内外迎来了黄金期,其在食品、医药和工业领域的应用日益广泛[17]。传统益生菌的筛选思路为先培养后筛选[18],先从自然环境中分离出潜在的益生菌菌株,如人类或动物的肠道、土壤和植物等来源,之后在适宜的培养条件下培养,将分离纯化后的菌株进行基因扩增和序列分析,结合耐酸[19-20]、耐胆碱盐和其他实验筛选目标益生菌[21],最后进行安全性评估,确保筛选出的益生菌对宿主是安全的,不含有已知的毒力因子或抗生素耐药基因。例如,李倜等[22]通过分离纯化大熊猫粪便中的乳酸菌,然后通过耐受能力检测、抑菌能力测定、自凝集和共凝集能力检测等检测方法,筛选出在大熊猫肠道内具有生长速率快、产酸能力强和产乳酸量高的乳明串珠菌(*Leuconostoc lactis*) MX-23。本团队从大兴安岭地区健康野猪肠道分离出5株乳酸菌,通过分离纯化、PCR鉴定、耐酸、耐胆碱盐能力检测、黏附能力和安全性评价等检测方法,筛选出对胆盐和低pH均具有良好耐受性的乳酸菌,并且具有自凝集和共凝集能力,其中黏膜黏液乳杆菌(*Limosilactobacillus mucosae*) M4-7株和唾液联合乳杆菌(*Ligilactobacillus salivarius*) M2-71株具备杀灭非洲猪瘟病毒和伪狂犬病病毒的活性[23]。传统筛选方法具有操作简单、成本低、可行性高等特点,但同时具有局限性。传统益生菌的筛选对具备特定功能的菌株的发现较困难,在应用中可选择的益生菌种类仍过于局限[24]。总之,传统益生菌的筛选效率低、耗时长,并且可能错过有潜力的菌株。

2 精准益生菌的筛选

目前,有许多益生菌菌株被用于各种保健品、药品和动物饲料中[25-29],但它们对不同个体的功效是不一致的,主要是由于肠型的不同和其他一些与宿主相关的因素,如年龄、饮食和免疫系统。此外,在肠道微生物群中的各种细菌之间存在积极或消极的相互作用,这种相互作用对人类健康至关重要,平衡失调就会导致多种疾病,包括肠道综合征、肥胖症、代谢性疾病、癌症和神经系统疾病[30-35]。因此,为了建立一种基于益生菌的有效治疗方法,需要更好地了解宿主系统内的肠道微生物群和促进健康的细菌独特性之间的相互关系。益生菌的精准筛选方法包括但不限于表型、基因分型和靶标筛选(图 1)[9]。表型筛选基于对益生菌在不同环境条件下,表现出所需特征进行观察和评估[36]。基因分型筛选指通过

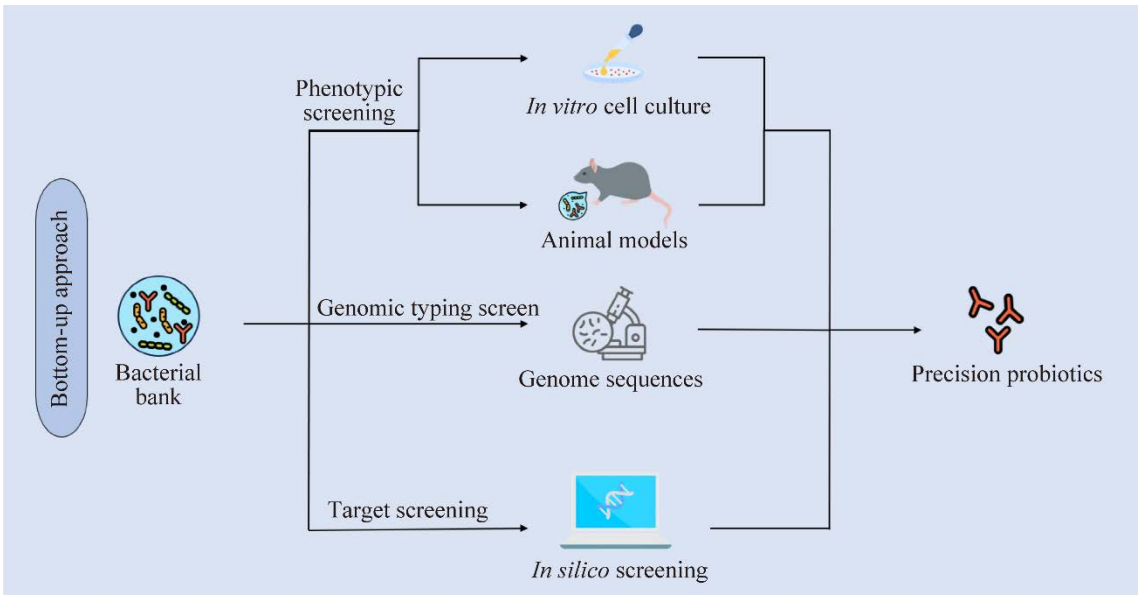

图 1　精准益生菌筛选方法

Figure 1　Screening method of precision probiotics.

分析菌株的基因型信息，筛选潜在的具有特定功能的益生菌菌株[37-38]。靶标筛选是基于对可能调节宿主的分子效应物的预测，采取多组学技术筛选益生菌[39]。通过以上筛选方法结合动物体内实验，可以评估益生菌在体内的实际效果，通过更高级的数据分析方法，如基于人工智能技术[40]，提高分析结果的准确性和可靠性。

2.1　基于表型的筛选

精准益生菌的表型筛选技术主要侧重于评估菌株的特定生物学特性和生理功能，这些特性对于菌株的益生能力至关重要。表型筛选是通过使用体外和离体细胞培养以及能够提供免疫、神经、代谢或微生物数据的动物模型，依据细胞和动物对微生物所产生的反应进行筛选[9,41]。表型筛选技术包括耐酸性和胆盐耐受性测试、黏附能力评估、基质辅助激光解吸电离飞行时间质谱(matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, MALDI-TOF MS)与傅里叶变换红外光谱(Fourier transform infrared spectroscopy, FTIR)联用、高通量筛选等技术[42]。例如，卵形拟杆菌(*Bacteroides ovatus*)在治疗糖尿病、心血管疾病、炎症性肠病及癌症等疾病中的潜在作用，提示了在精准益生菌的表型筛选中，应考虑菌株对特定疾病的治疗潜力[43]。Li 等[44]研究发现，多形拟杆菌(*Bacteroides thetaiotaomicron*)作为一种潜在的益生菌，对非酒精性脂肪肝(non-alcoholic fatty liver disease, NAFLD)的治疗具有一定作用。通过这些表型筛选技术，研究人员可以快速、高效、准确地评估和选择出具有潜在益生特性的菌株，进而进行更深入地研究和开发，具有更高的应用价值。

2.2　基于基因分型的筛选

基因分型通过高通量测序技术，获得益生菌的全基因组序列数据，对益生菌基因组结构、代谢通路和潜在的功能基因进行全面、深入地分析和挖掘，筛选出含有特定益生功能基因的益生菌[45-46]。精准益生菌的基因分型技术主要包括全基因组测序、生物信息学分析、人工智能和机器学习等。目前，大多数益生菌基因组序列数据保

存于美国国家生物技术信息中心(National Center for Biotechnology Information, NCBI)数据库中。在进行益生菌基因型分型时,如何确保数据的准确性和可靠性至关重要,如运用人工智能和机器学习算法, Sun 等[47]利用人工智能策略,基于乳酸菌全基因组数据,建立了益生菌精准筛选模型可视化平台 iProbiotics,结合动物模型和临床试验筛选出干酪乳酪杆菌(*Lacticaseibacillus casei*) Zhang、动物双歧杆菌乳亚种(*Bifidobacterium animalis* subsp. *lactis*) V9 和鼠李糖乳酪杆菌(*Lacticaseibacillus rhamnosus*) robio-M9 等 28 株具有显著的免疫调节、肠道菌群调节、降血脂和降血压功能的益生菌。也可以利用先进的生物信息学工具对基因组数据进行精确地分析和比对,包括使用合适的算法进行基因预测、单核苷酸多态性(single nucleotide polymorphism, SNP)检测和基因组组装[48]。

2.3 基于靶标的筛选

靶标的筛选主要通过计算机模拟的方法进行预测,评估益生菌所产生的可调节宿主或微生物相关信号通路的分子效应物的能力,这些分子效应物被预见在宿主的健康或疾病中发挥关键作用。计算机预测需要使用多组学手段(如基因组学、转录组学、代谢组学和蛋白质组学等)[49-50],还可能使用代谢重建的手段,推断筛选微生物的代谢能力[9]。利用高通量测序技术获得益生菌的基因组数据,运用生物信息学工具对基因组序列进行分析,识别与益生菌功能相关的特定基因或基因组。基于已识别的基因组特征,构建机器学习模型来预测未知菌株是否具有益生菌的潜在特性,根据益生菌预期的健康益处,如改善肠道健康、增强免疫力等,定义和选择相关的遗传靶标。之后,使用机器学习模型对大量潜在的益生菌进行虚拟筛选,快速识别出含有目标遗传标记的菌株,对筛选出的候选益生菌进行体内外试验和验证,以确认其益生功能。例如,Zhang 等[51]发现肠道微生物 α-L-阿拉伯呋喃糖苷酶(α-L-arabinofuranosidase)基因簇丰度可以作为预测功能性便秘的生物标志物,这为缓解功能性便秘的益生菌菌株筛选提供了分子靶标,为功能性益生菌的高效靶向选育提供了新的策略和思路。其中,基于益生菌代谢产物的筛选可以被视为一种基于靶标的筛选方法[52],益生菌的代谢产物包括 EPSs、细菌素、短链脂肪酸(short-chain fatty acids, SCFAs)、维生素、生物活性肽和其他有机酸等。这些代谢产物可以影响宿主的生理功能,包括但不限于免疫调节、抗炎作用和改善肠道屏障功能等[53-54]。例如 Oh 等[52]通过网络药理学方法研究了来自肠道菌群的益生元、益生菌、后生元及其关键靶标,最终确定白介素 6 (interleukin 6, IL-6)、蛋白激酶 B1 和白蛋白为抗肥胖的核心靶标;通过 *L. paracasei* JS1 将益生元异黄酮转化为后生元雌马酚,并且这种转化的代谢产物与靶标 IL-6 的结合最为稳定,表明基于益生菌代谢产物的筛选可以为肥胖治疗提供新的策略和靶标。基于靶标筛选的益生菌菌株的多样性和筛选策略的改进,为开发新的益生菌产品和理解其作用机制提供了科学基础[55]。

此外,精准益生菌筛选还需要考虑到个体差异、环境因素和时间因素等复杂因素。为了确保筛选结果的准确性,需要建立严格的质量控制体系,确保实验数据的可靠性和重复性[56-57]。精准益生菌筛选通常需要跨学科的合作,包括微生物学、营养学、药理学、临床医学、统计学和大数据分析等。通过以上精细筛选的益生菌菌株被称为精准益生菌。

3 益生菌的精准应用

随着社会的高速发展、经济和环境的改变,各类慢性病逐渐地增加,包括糖尿病、肥胖、高

血压等，使人们对健康的关注度不断提高。益生菌作为一种有益于肠道健康的微生物，越来越受到人们的青睐。随着对益生菌功能的研究越来越深入，其在食品、畜牧、生物医药等行业的生产应用也不断增加。然而，益生菌作为一种潜在的食品和医疗保健领域的重要资源，其筛选和开发过程充满了挑战。因此，益生菌的精准筛选能够更好地通过益生菌的作用机制和特性，为益生菌的应用提供更有效的指导。作为更有潜力的精准益生菌，在多个领域具有广泛的应用价值(表 1)。在医疗领域，精准益生菌可用于治疗和预防肠道疾病[64]，如腹泻、便秘等；可用于增强或调节个体的免疫系统，预防和治疗感染；可用于治疗肥胖、糖尿病等代谢性疾病[65]；某些类型的精准益生菌可能有助于提高肿瘤治疗效果[57,66-70]。在食品行业中，精准益生菌可添加到饮食中，用于发酵食品，提高产品的营养价值和口感[71-72]。在畜牧行业中，精准益生菌可通过调节肠道微生物生态，增强动物的免疫力，预防疾病的发生[71,73-74]；可以促进动物对营养物质的吸收，提高其生产性能，如增加体重、提高饲料转化率等；可以减少抗生素的使用[75-77]，降低动物源性细菌耐药性的风险。

然而，益生菌的精准应用也面临着个体差异影响其应用效果的问题。这种应用需要考虑肠道菌群的肠型和定殖抵抗、宿主免疫反应和遗传因素等[78-79]。其中，肠道菌群的肠型会影响其定殖抵抗的能力，这是因为不同的肠型中包含的菌群

表 1　精准益生菌及其应用

Table 1　Precision probiotics and their applications

Strains	Key findings	References
Lactobacillus acidophilus AM13-1	No virulence factors or toxin genes with experimentally verified were found in the genome of strain AM13-1. Besides, a number of probiotic-related genes were predicted from the *Lactobacillus acidophilus* AM13-1 genome, such as *cbh*, *atp*A-D, and *dlt*D, with functions related to cholesterol-lowering and acid resistance	[33]
Bifidobacterium animalis subsp. *lactis* BL-99	Discovered by metabolomics and metagenomics analysis that BL-99 promoted the accumulation of SCFA-producing microbiota and the increase of SCFA levels in stool and serum, which may account for the increase of serum gastrin level. BL99 has potential applications in improving symptoms of functional dyspepsia	[51]
Bifidobacterium longum	*Bifidobacterium longum* can improve functional constipation (FC) by increasing intestinal utilization of arabinose	[53]
Lactobacillus acidophilus	*Lactobacillus acidophilus* exhibits anti-tumor effects in mice by secreting valeric acid. Probiotic supplementation is a potential preventive measure for non-alcoholic fatty liver disease-associated hepatocellular carcinoma (NAFLD-HCC)	[58]
Streptococcus salivarius 12	During radiotherapy, SsK12 inhibited conditionally pathogenic bacteria and enriched oral commensal bacteria, significantly reducing the incidence, duration, and duration of oral mucositis, and had a good safety profile	[59]
Faecalibacterium prausnitzii	*Faecalibacterium prausnitzii* represented the most active species contributing to butyrate synthesis *via* the acetyl-CoA pathway. In the long run, probiotics with high taxonomic diversity consisting of well characterized strains could replace fecal microbiota transplantation (FMT) to avoid the costly screening of donors and the risk of transferring unwanted genetic material	[60]
Lacticaseibacillus paracasei MI29	The newly isolated MI29 strain can activate host defense immunity and prevent infections caused by the influenza virus through the gut-lung axis	[61]
Lacticaseibacillus casei Shirota	The intake of *Lacticaseibacillus casei* Shirota does not affect the efficacy of lovastatin and slows down the inflammatory response of the liver	[62]
Lactiplantibacillus plantarum	*Lactiplantibacillus plantarum* colonizes the gut microbiome and contributes to L-arginine biosynthesis	[63]

对于外来细菌的抵抗能力不同，同时这也影响宿主的免疫系统对外源侵入菌的反应[80]。例如，Maldonado-Gómez 等[81]通过双盲交叉试验和微生物组分析，揭示了长双歧杆菌(*Bifidobacterium longum*) AH1206 在人体肠道中的稳定定殖受到个体原有肠道微生物菌群组成(肠型)的影响，表明肠型对益生菌定殖抵抗能力的个体化影响。然而这种影响可能因个体的免疫反应而存在差异。不同个体的免疫系统可能对同一益生菌株的识别能力不同，从而影响外来细菌在不同宿主的定殖能力。例如，短双歧杆菌(*Bifidobacterium breve*) UCC2003 在正常免疫应答的野生型鼠中的定殖水平低于在 B 细胞功能缺失的突变鼠中观察到的水平[82]，因为个体的遗传背景决定了宿主的生存需求，并影响其肠道菌群组成。由于禽类和猪的种属不同，导致它们的食性不同，进而对肠道中需要存在的共生菌的需求不同，这就决定肠道中固有的菌群组成存在很大差异，这些菌群通过自然筛选在肠道定殖，并通过竞争排斥、产生代谢产物等方式影响外来细菌的定殖[83-84]。因此，个体差异的影响对益生菌的精准应用至关重要。

4 精准益生菌的安全性评价

尽管精准益生菌具有巨大的开发潜力，仍面临许多挑战。不同的益生菌菌株在功能和效果上存在差异[85]，选择合适的菌株对于精准益生菌至关重要。精准益生菌面临的问题首先是菌株异质性，益生菌菌株之间的差异可能导致它们在不同个体中的效果存在显著差异，这要求对益生菌进行更深入的功能研究以确定最佳菌株和组合。益生菌的安全性是益生菌能否用于生产实践的基本要求，因为外源微生物可能对微生物菌群产生意想不到的影响，甚至可能危及易感受试者的健康，导致菌血症或真菌血症[86]。因此，了解外源性益生菌与宿主和微生物菌群相互作用的机制对其有效性和安全性都很重要[87]。精准益生菌通过增加分子特异性、改善作用机制、减少脱靶效应、对抗治疗耐药性等方面提高了治疗价值[3,88]，精准益生菌的安全性是能否应用到临床的关键[89]。精准益生菌的安全性评价包括以下几个方面。

4.1 动物实验

益生菌的动物实验安全性评价主要用于实验室检测[90]，以小鼠或其他动物为实验动物，将益生菌接种到实验动物的肠道内，观察其在体内的生长和繁殖情况，通过体重变化、血液检测、组织切片、生化分析和对实验动物脏器等重要器官的检测，以及是否引起过敏反应等情况，评估益生菌的安全性[91-94]。根据体内实验的结果，益生菌在动物体内的生长和繁殖情况良好，未出现明显蓄积的不良反应，最终以粪便形式排出体外[95]；益生菌对重要脏器的影响较小，未出现明显的病理变化[96]；血液生化指标均在正常范围内，未出现明显的毒性反应[86]；益生菌迄今未发生过敏反应，可认为益生菌在体内具有很高的安全性[97]。然而，益生菌的动物实验只针对特定的益生菌进行安全性评价，对于其他益生菌是否安全需要进一步研究。

4.2 体外实验

对抗生素的敏感性测定是益生菌安全性评价的标准之一[98]，益生菌对抗生素的敏感性是由于其对抗生素产生耐药性[99]。益生菌的抗生素耐药性分为天然性耐药和获得性耐药[100]，益生菌的抗生素耐药性已经非常普遍[101]。目前检测益生菌耐药性的方法有 K-B 纸片扩散法(Kirby-Bauer disk diffusion method)、打孔法、肉汤稀释法、琼脂稀释法及斜坡平板法等[102]。

食品级益生菌的要求为菌株均不产生硝基还原酶、偶氮还原酶，肠道内的硝基还原酶、偶

氮还原酶能将前致癌物转化为致癌物，因此对益生菌有害代谢产物的测定也是安全性评价必不可少的部分[103]。结果表明，所有的益生菌菌株均为阴性，说明都不具有硝基还原酶和偶氮还原酶活性。

4.3 溶血性测定

溶血作用是益生菌的致病机理之一，菌株在生长过程中产生溶血素，使红细胞破裂溶解，通过观察菌株在血平板上是否形成透明溶血圈来判断其溶血性[104]。其中 α 溶血产生草绿色溶血环为部分溶血，β 溶血产生完全透明溶血环为完全溶血，γ 溶血菌落周围无溶血环为不溶血。被测试菌株不产生溶血现象，表示该菌株为安全菌株。

4.4 基因组测序

2022 年 9 月 12 日，国家卫健委颁布了《食品安全国家标准食品用菌种安全性评价程序》(征求意见稿)[105]，提出对菌种进行安全性评价时，要对菌株进行全基因组测序，分别获得其基因组框架图和完成图，并对测序数据进行毒力基因、耐药基因、毒素产生相关基因等进行综合分析[106-107]。该技术可以揭示益生菌的遗传信息，为后续研究者提供丰富的数据资源。

筛选精准益生菌面临的挑战之一是数据分析的准确性，该环节对于益生菌菌株的筛选至关重要。目前，数据分析主要采用描述性统计和相关性分析等方法，缺乏深入的因果关系和机制研究。此外，数据分析结果的可信度和准确性也受到数据质量和处理方法的影响[108-109]。因此，需要采用更高级的数据分析方法，如机器学习和人工智能技术，以提高分析结果的准确性和可靠性[63,110-111]。

5 展望

益生菌的精准筛选是当前研究的热点和重点。通过对肠道微生物组的深入理解[112]，结合表型、基因分型和靶标等技术，有望发现更多具有益生功能的菌株[113]。随着科技的进步，精准益生菌的应用将更加广泛。未来，我们期待看到精准益生菌在畜牧行业的更多应用，如精准饲料添加、精准疫苗接种等[114]。通过精准筛选特定的益生菌菌株，能够实现个性化的医疗和保健策略，为量身定制的精确益生菌提供新的机会，以满足个人的医疗保健需求[7,115]，提高人们的健康水平[116]。然而，目前益生菌的精准筛选仍面临一些挑战，包括筛选方法、样本选择、研究设计和数据分析等方面的问题。为了提高益生菌筛选的效率和可靠性，需要进一步改进和完善现有的方法和技术。未来研究应关注益生菌的综合作用和机制研究，建立统一的研究设计标准和方法，并采用更高级的数据分析技术。同时，我们也期待看到精准益生菌在应对全球食品供应、环保和公共卫生等领域挑战中的作用。精准益生菌有望提高益生菌的效果和安全性，同时满足个性化需求。然而，目前的研究还处于初级阶段，需要更多的数据来验证其效果和安全性。未来的研究应更关注如何更精确地定制益生菌及其在各种健康问题中的应用。

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