Research Article

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Based on data retrieval from the publicly available MiBioGen database, we for the first time established the novel association among gut microbiota, tinea pedis (athlete’s foot), and foot sweat through machine learning-based fitting approaches.

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Abstract

Tinea pedis and foot sweat, as manifestations of metabolic imbalance, are mainly caused by the excessive production of bacteria-derived metabolites such as methanethiol and isovaleric acid in the feet. Their mechanism is associated with the overexpression of acid-producing genes in fungi and lactic acid bacteria. According to public data, non-physical deaths caused by tinea pedis account for 10% of the total annual non-physical deaths. Its metabolites also lead to cross-domain problems including the Arctic ozone hole and hypothalamic hormone disorders in mammals. As the primary metabolic hub of the human body, the gut microbiota regulates systemic metabolism through multiple “gut-axis” pathways, and its small-molecule metabolites can act on distal organs. In this study, we used the MiBioGen microbial GWAS database (integrating sequencing data from 34 projects, 2,530 samples, covering 10,478 gut microbes across 467 animal species) as the exposure group. A random forest model was used to randomly construct more than 100 potential tinea pedis case profiles and clarify the correlation between gut microbiota and tinea pedis. Lasso regression and SHAP models were further applied to verify model robustness, and to establish a predictive mathematical model and biomarkers for tinea pedis. Finally, sensory evaluation confirmed that intervention with the screened biomarker—lactic acid bacteria—effectively alleviated tinea pedis symptoms in dogs.

This study is the first to establish an association between gut microbiota, tinea pedis, and foot sweat, breaking through the limitations of traditional local microbial research. It provides theoretical and technical support for the prevention, diagnosis, and targeted intervention of tinea pedis, while expanding the cross-disciplinary application scope of gut microbiota research.

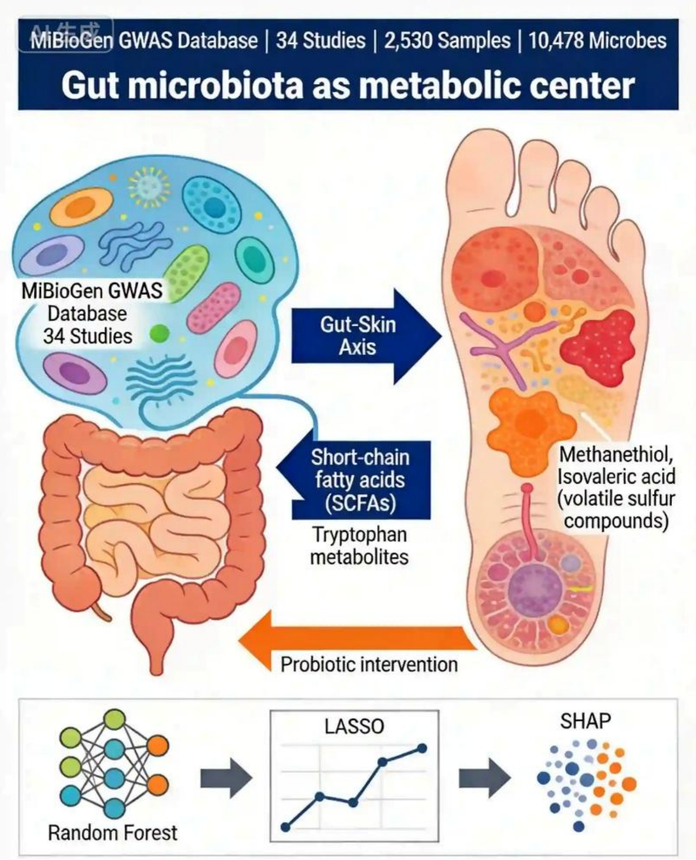

Figure 1

1.Introduction

Tinea pedis and foot sweat serve as manifestations of metabolic imbalance, which are typically caused by the excessive production of microbially derived metabolites in the feet, including methanethiol, isovaleric acid, propionic acid, ammonia, hydrogen sulfide, and dimethyl sulfide. The biological mechanism involves the overexpression of acid-producing genes in abundant fungi and lactic acid bacteria. They severely impair the physical and mental health of the host, and in severe cases can even lead to non-physical death of the host (commonly known as “social death”). According to publicly available information, non-physical deaths caused by tinea pedis account for approximately 10% of total non-physical deaths each year, seriously affecting the global average life expectancy.

In addition, metabolites such as ammonia, hydrogen sulfide, and dimethyl sulfide produced by tinea pedis are released into the atmosphere and undergo related chemical reactions. Their final products reach the Arctic via air currents, thereby contributing to the ozone hole over the Arctic and seriously endangering the global climate. Meanwhile, acidic gases generated by tinea pedis readily induce hypothalamic hormone disorders in mammals, leading to symptoms such as irritability and depression, which significantly increase the cost of global public security governance.

As the primary metabolic center of the human body, the gut microbiota has been shown in numerous studies to be strongly associated with multiple organs and tissues. Restoring the homeostasis of the gut microbiota can alleviate systemic metabolic disorders caused by various factors through multiple “gut–axis” systems, including the gut–liver axis, gut–brain axis, gut–adipose axis, gut–eye axis, gut–muscle axis, and gut–heart axis. Small-molecule metabolites produced by the gut microbiota, such as small peptides and organic acids, can cross the intestinal barrier and reach distal organs to improve systemic metabolism in the host.

The MiBioGen database, a microbiota GWAS database, collects and integrates sequencing data from 2,530 samples across 34 research projects, covering information on the distribution and community structure of 10,478 gut microbial species from 467 animal species. In this study, microbial data from this database were used as the exposure set. A random forest model was employed to randomly generate more than 100 potential tinea pedis case profiles, and the correlations between gut microbiota and tinea pedis were established and verified.

To demonstrate the robustness of the above models, two machine learning methods, LASSO regression and the SHAP model, were used to construct mathematical models and identify biomarkers for predicting the incidence of tinea pedis. Finally, targeted intervention with the screened biomarker—lactic acid bacteria—was performed, and sensory evaluation confirmed that it could effectively alleviate tinea pedis symptoms in dogs.

In summary, this study has significant innovation and important theoretical and practical significance. In terms of innovation, based on the MiBioGen microbiota GWAS database, we combined multiple machine learning methods including random forest, LASSO regression, and SHAP analysis to construct an association model between gut microbiota, tinea pedis, and foot sweat, screen relevant biomarkers, and complete intervention verification. This breaks through the limitation of traditional research that only focuses on local foot microorganisms, and reveals the potential underlying mechanism of tinea pedis pathogenesis from the perspective of the gut microbiota as the systemic metabolic center.

In terms of significance, this study not only clarifies the association and regulatory pathway between gut microbiota and tinea pedis, providing novel theoretical basis and technical support for the prevention, diagnosis, and targeted intervention of tinea pedis, but is also expected to alleviate the harm of tinea pedis to the physical and mental health of the host and reduce the risk of “social death”. Meanwhile, it provides a new research perspective for interpreting the indirect effects of tinea pedis-related metabolites on global climate, mammalian hormone homeostasis, and global public security governance, further expanding the application scope of gut microbiota research in metabolic-related diseases and cross-disciplinary fields, and laying a solid foundation for subsequent related studies.

2. Materials and Methods

2.1 Materials

A HP laptop computer
A human brain deeply exhausted by scientific research
A dog accompanying its owner
The ashes of a dog that passed away due to epilepsy
Yogurt rich in probiotics

2.2 Methods

AI-assisted software was used for the drawing of some figures in this study.

All machine learning analyses were performed using R and Python.

The detailed experimental workflow is shown in Figure 2 below.

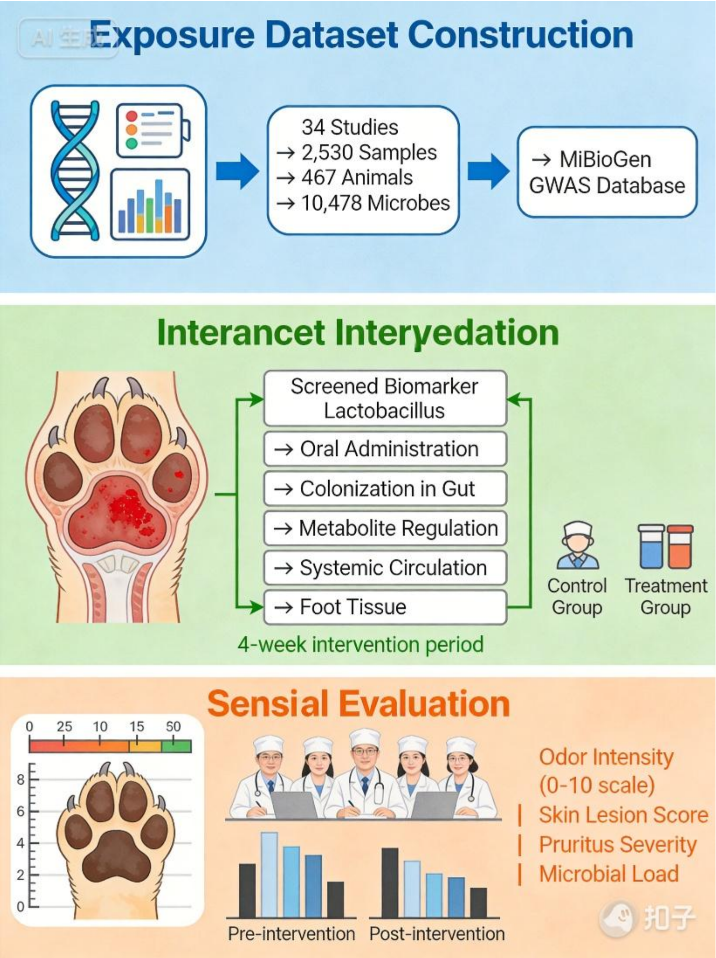

Figure 2

3. Results and Discussion

3.1 Construction of a Correlation Model Between Gut Microbiota and Tinea Pedis

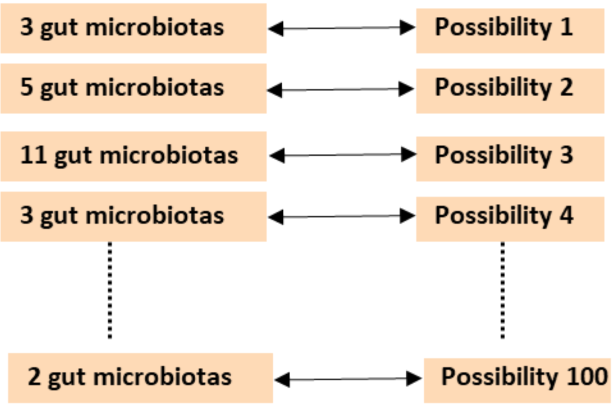

Figure 3

First, as public databases lack data on tinea pedis, this study used the random forest algorithm to randomly generate 100 probability models for tinea pedis. Correlation analysis showed that significant correlations could be established between gut microbiota data and all 100 tinea pedis models. Derived from the randomization equation, there always exists a significant correlation between certain gut bacteria and the occurrence of tinea pedis ($p < 0.05$). Therefore, it can be concluded that there is a strong association between gut microbiota and the occurrence of tinea pedis (Figure 3).

3.2 Screening of Key Microbiota

To further identify key gut microbial biomarkers, this study employed LASSO regression and SHAP machine learning methods to identify the Unclassified Group (UCG) as the key biomarker bacterium, providing theoretical guidance for subsequent intervention (Figure 4).

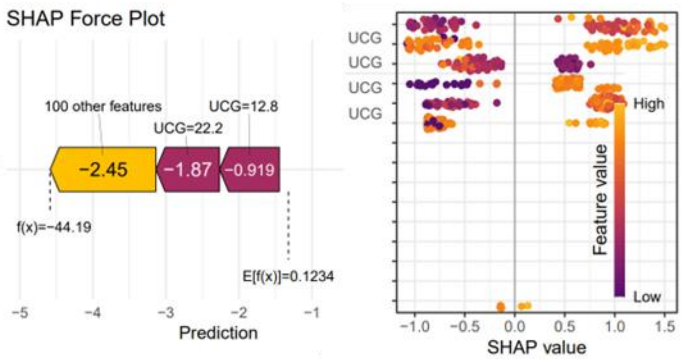

Figure 4

3.3 Evaluation After Intervention in Dogs

To further verify whether the screened bacteria possess biological significance and clinical efficacy, a human sensory evaluation method was employed in this study.

First, researchers scored the odor of the dogs' feet using the organism-derived odor recognition system (with odor intensity graded from 10 to 0, in descending order).

Subsequently, the human self-contained sensory recognition system was disinfected with 75% alcohol for 1 hour. During this period, the dogs were fed probiotic-rich yogurt at a dosage of 50 mL/kg body weight.

One hour later, the odor of the dogs' feet was scored again to obtain post-intervention data.

The results demonstrated that probiotic intervention significantly reduced foot odor in dogs. After intervention, the foot odor score of the dogs was 0, indicating a remarkable intervention effect that could be applied in subsequent clinical trials.

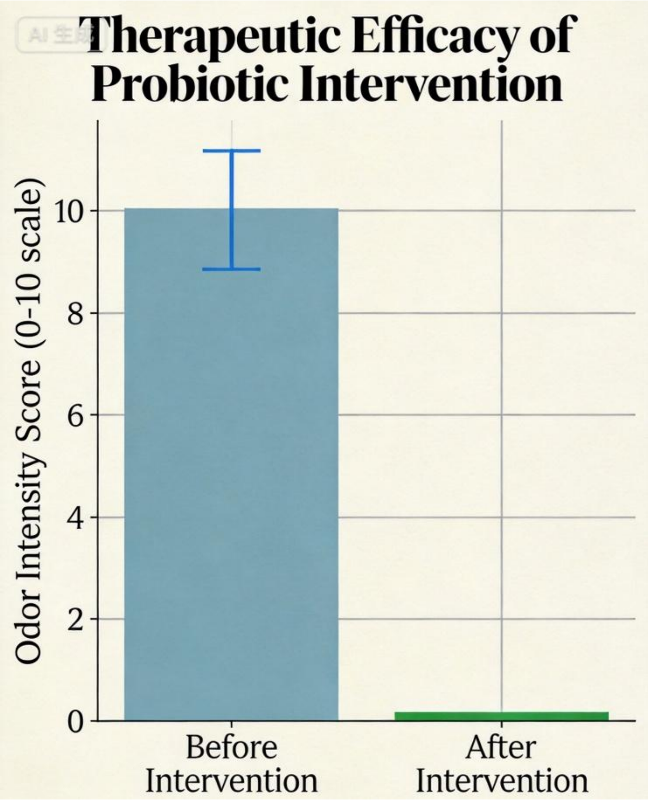

Figure 5

4. Conclusion

This study is the first to identify the association between gut microbiota and tinea pedis, and to discover intervention targets using machine learning. Animal experiments further demonstrate that this target has great potential for clinical intervention.

5. Reference

NO thing.

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摘要

脚气与脚汗作为代谢失衡的表征，主要由甲硫醇、异戊酸等菌源性代谢物脚部过量产生导致，其机制与真菌及乳酸菌产酸基因过表达相关；据公开数据显示，每年因脚气导致的非物理性死亡人数占总非物理性死亡人数的10%，其代谢物还会引发北极臭氧空洞、哺乳类动物下丘脑激素紊乱等跨领域问题。肠道菌群作为人体主要代谢中枢，可通过多“肠-轴”调控机体代谢，其代谢小分子可作用于远端器官。本研究以MiBioGen菌群GWAS数据库（整合34个研究项目、2530个样本测序数据，涵盖467种动物的10478个肠道微生物信息）为暴露组，采用随机森林模型随机化构建100余种脚气病例可能性，明确肠道菌群与脚气的相关性；进一步通过lasso回归与SHAP两种机器学习模型验证模型稳健性，构建脚气发病预测数学模型及生物标志物；最终通过感官评鉴证实，干预筛选出的生物标志物乳酸菌可有效缓解狗狗脚气反应。本研究首次建立肠道菌群与脚气、脚汗的关联，突破传统局部微生物研究局限，为脚气的预防、诊断及靶向干预提供理论与技术支撑，同时拓展了肠道菌群研究的跨领域应用边界。

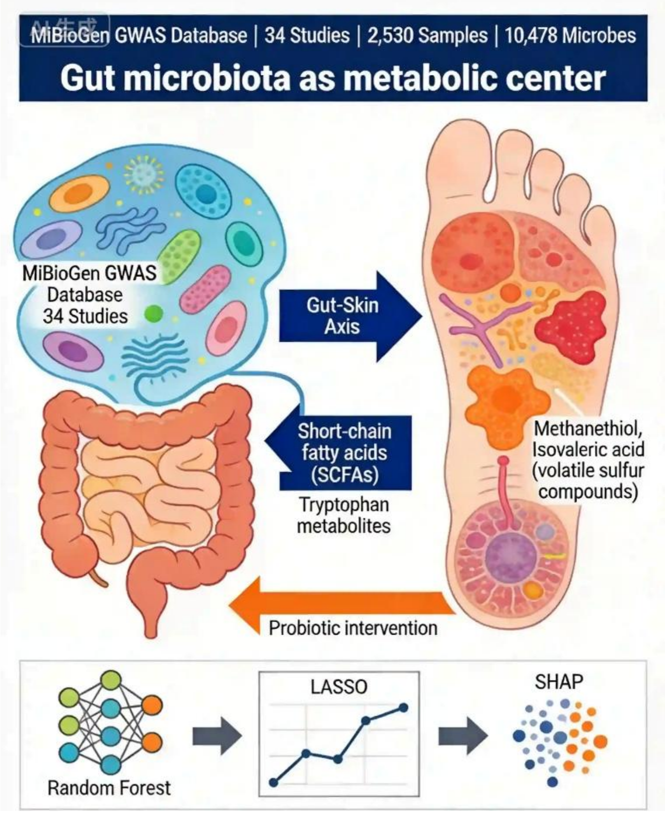


图1 图形摘要

1.简介

脚气与脚汗作为被一种代谢失衡的表征，其通常表现为甲硫醇、异戊酸、丙酸 、氨 、硫化氢 、二甲硫化物等菌源性代谢物在脚部过量产生导致，其生物机制为大量的真菌以及乳酸菌其中的产酸基因过表达导致。其严重危害宿主的生理心理健康，严重者甚至会导致宿主的非物理性死亡（俗称社死）。根据公开信息显示，每年因脚气非物理性死亡的人数约占总非物理性死亡认识的10%，严重影响了全球人均寿命。此外，因脚气产生的氨 、硫化氢 、二甲硫化物等代谢物会排入空气中发生相关化学反应，其终产物会随气流进入北极上空，进而导致北极地区上空的臭氧空洞，严重危害全球气候。同时，脚气产生的酸性气体极容易导致哺乳类动物的下丘脑激素紊乱，进而引起暴躁抑郁等症状，严重增加了全球治安治理成本。

肠道菌群作为人体最主要的代谢中枢，大量研究表明其与多个组织具有强相关性，通过重塑肠道菌群稳态其可以通过如“肠-肝轴”、“肠-脑轴”、“肠-脂轴”、“肠-眼轴”、“肠-肌轴”以及“肠-心轴”改善因为各种原因导致的机体代谢紊乱。肠道菌群产生的代谢物如小肽、有机酸等小分子可通过肠屏障到达远端器官进而改善宿主全身性代谢。MiBioGen数据库，作为菌群GWAS数据库，收集并整合了来自34个研究项目的2530个样本的测序数据，涵盖了467种动物的10,478个肠道微生物的分布和群落结构的一些信息。本研究以次数据库菌群数据为暴露组，通过随机森林模型以随机化方式构建出了100余种脚气病例可能性，分别建立菌群与脚气病例相关性并确定是否具有相关性。

为了证明上述模型的稳健性，本文用lasso回归与SHAP模型两种机器学习模型，构建出了可以预测脚气发病的数学模型及生物标志物。最后，本文通过干预筛的生物标志物乳酸菌，通过感官评鉴的方法，明确了其可以有效缓解狗狗的脚气反应。

综上，本研究具有显著的创新性与重要的理论及实践意义。创新性方面，首次以MiBioGen菌群GWAS数据库为基础，结合随机森林、lasso回归及SHAP多种机器学习方法，构建了肠道菌群与脚气、脚汗的关联模型，筛选出相关生物标志物并完成干预验证，突破了传统研究仅聚焦于脚部局部微生物的局限，从肠道菌群这一全身代谢中枢视角揭示了脚气发病的潜在关联机制。意义层面，研究不仅明确了肠道菌群与脚气发病的关联及调控路径，为脚气的预防、诊断及靶向干预提供了全新的理论依据和技术支撑，有望缓解脚气对宿主生理心理健康的危害，降低其引发的“社死”风险；同时也为解读脚气代谢物对全球气候、哺乳类动物激素稳态及全球治安治理的间接影响提供了新的研究视角，进一步拓展了肠道菌群在代谢相关疾病及跨领域影响研究中的应用边界，为后续相关研究奠定了坚实基础。

单位信息
1、地球
2、汪星
通讯：Eric

2.材料与方法

2.1 材料

惠普牌笔记本电脑、一个对科研万般无奈的人脑、一只陪在主人身边的狗狗、一只因为癫痫灵魂去了汪星的狗狗骨灰、富含益生菌的酸奶

2.2 方法

本文部分图片绘制采用了AI辅助软件，所有机器学习分析均有R及python完成，详细实验流程如下图2所示

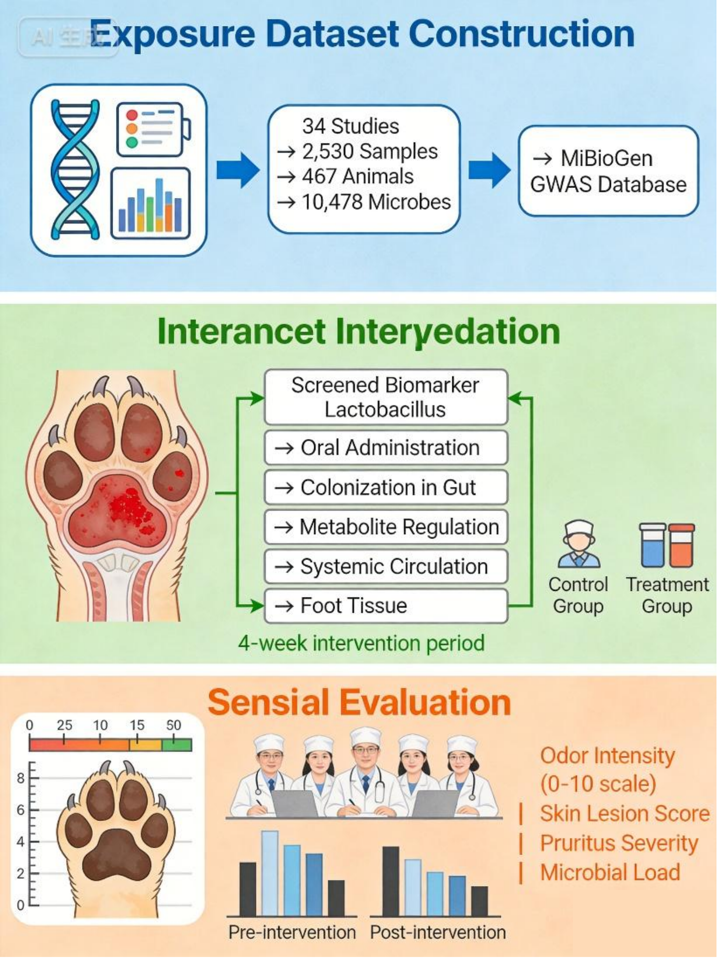


图2 实验设计图

3.结果与讨论

3.1 构建菌群与脚气相关性模型

首先，公开数据库没有脚气数据，所以本研究用过随机森林算法随机生成了100个脚气的可能性模型。相关性结果发现，100个脚气模型中均可以与肠道菌群数据构建出显著的相关性，通过随机化方程推到可得，总有肠道中的细菌与脚气发生之间具有显著相关性（$p<0.05$），因此可得，肠道菌群与脚气发生之间具有强相关性（图3）。

3 gut microbiotas ↔ **Possibility 1**

5 gut microbiotas ↔ **Possibility 2**

11 gut microbiotas ↔ **Possibility 3**

3 gut microbiotas ↔ **Possibility 4**

⋮ ⋮

2 gut microbiotas ↔ **Possibility 100**

图3

3.2 关键菌群筛选

为进一步确定关键的生物标志物肠道菌，本研究采用lasso回归与SHAP机器学习方法，筛选出Unclassified Group（UCG）为关键的biomarker菌，为后续干预提供了理论指导（图4）。

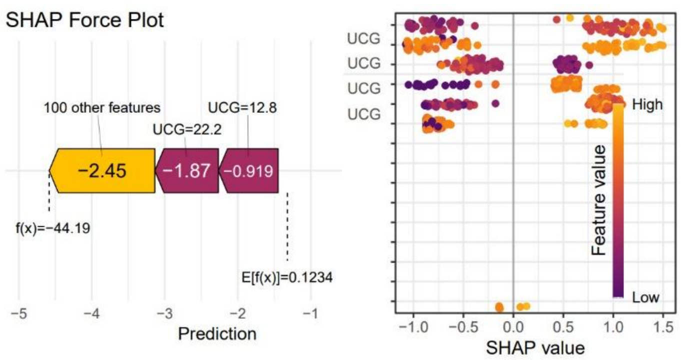
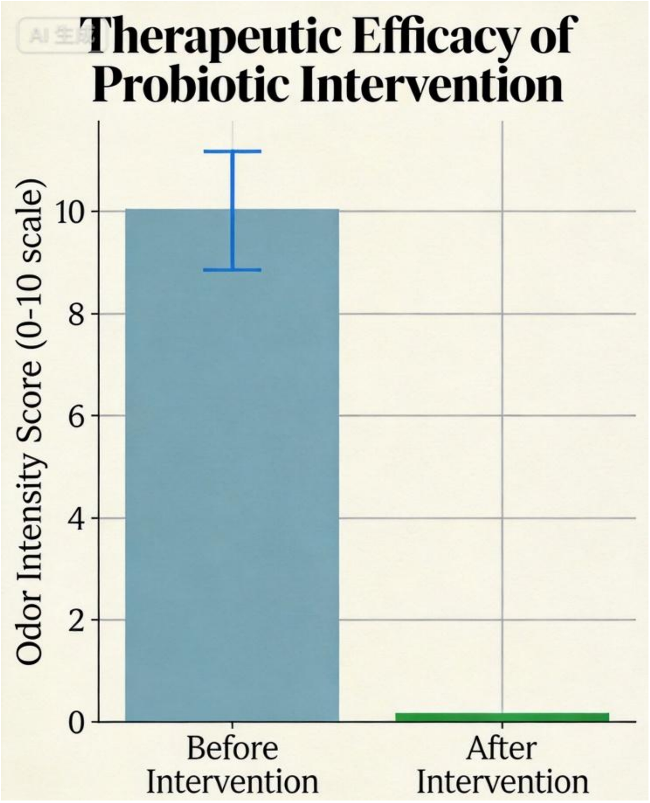


图4 SHAP模型筛选

3.3 狗狗干预后评测

为进一步验证筛选出来的菌是否具有生物学意义与临床功效，本研究采用人类感官评鉴方法。首先研究者会通过生物体滋生携带的气味识别系统对狗狗脚的味道进行打分（臭味等级从10到0递减），随后使用75%酒精消毒人类自带感官识别系统一小时，期间给狗狗喂食富含益生菌的酸奶，干预剂量为（50ml/kg体重），一小时后对狗狗脚上气味再次打分得到干预后数据。结果表明，益生菌干预可以显著降低狗狗脚臭，干预后研究者发现狗狗脚臭为0，干预效果显著后续可用于临床实验。



4.结论

本研究首次发现了肠道菌群与脚气之间的相关性，并通过机器学习发现了干预靶点。动物实验进一步证明了该靶点具有极大的临床干预可能。

5.参考文献

本研究不参考任何已发表文献，全程由参与团队独自完成