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P-ISSN: 2304-3075; E-ISSN: 2305-4360
International Journal of Veterinary Science
www.ijvets.com; editor@ijvets.com

Research Article https://doi.org/10.47278/journal.ijvs/2026.029

Exploring Gut Microbiota Potential in Indonesian Local Cattle Breeds for Application as FMT against Foot and Mouth Disease

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Article History: 25-121 Received: 04-May-25 Revised: 16-Jul-25 Accepted: 31-Jul-25 Online First: 03-Mar-26

ABSTRACT

Foot-and-mouth disease (FMD) is a highly transmissible viral disease that poses a serious threat to the global livestock industry and leads to significant economic losses, particularly in cattle. Innovative strategies are needed to improve animal resilience to infection. Fecal Microbiota Transplantation (FMT) is a developing approach with the potential to enhance animal health through microbiome-based intervention. FMD remains a major constraint to livestock health and food security in endemic regions such as Indonesia, where viral diversity and incomplete vaccine coverage undermine eradication efforts. The gut microbiota has emerged as a key regulator of antiviral immunity, yet its role in modulating FMD susceptibility remains unexplored. Here, we employed shotgun metagenomic sequencing to profile the fecal microbiota of indigenous Indonesian cattle breeds, identifying dominant taxa including Clostridia, Oscillospiraceae, and Bacteroidales. Functional annotation revealed enrichment in genes involved in short-chain fatty acid (SCFA) biosynthesis, immune signaling, and interferon-mediated antiviral responses that enhance immunity. These findings highlight the immunomodulatory potential of local cattle microbiota and support its application as a donor source for fecal microbiota transplantation (FMT). This microbiome-based approach offers a novel, host-adapted strategy to complement vaccination and enhance FMD control in endemic settings. The objective of this study was to explore the potential of gut microbiota from Indonesian local cattle breeds (Madura and crossbred) to be developed as FMT donor candidates for improving resistance against FMD.

Key words: Fecal microbiota transplantation, FMD, Gut microbiota, Immunity, Shotgun metagenomics.

INTRODUCTION

Foot-and-mouth disease (FMD) is a highly infectious viral infection that predominantly affects cloven-hoofed animals, including swine, sheep, cattle, and goats, as well as various wild and domestic species (Callis 1980; Rasmussen et al. 2024). Clinically, the disease is characterized by the development of erosions and vesicular lesions primarily observed in the feet, mouth, and teats, leading to symptoms such as lameness and excessive salivation, which are particularly common in dairy cows (Doll 2001; Ismail et al. 2023). Although adult cattle generally exhibit high morbidity with low mortality, calves can suffer up to 50% mortality due to cardiac involvement or secondary infections (Doll 2001). During outbreaks of FMD, atypical clinical manifestations have been observed, such as vesicular lesions on horn keratin in the 2013 Iran outbreak, suggesting that host-specific factors may influence

Cite This Article as: Putri EM, Negara W, Khan FA, Santoso, Pandupuspitasari NS, Gopar RA, Purba RD, Surachman M, Darmawan WA, Akhadiarto S, Wahyuni DS, Suryadi H and Maulana S, 2026. Exploring gut microbiota potential in indonesian local cattle breeds for application as FMT against foot and mouth disease. International Journal of Veterinary Science 15(3): 919-931. https://doi.org/10.47278/journal.ijvs/2026.029

disease phenotype (Mohebbi et al. 2017). Beyond its direct effects on animal health, FMD poses considerable economic challenges, disrupting livestock productivity and constraining international trade in live animals and animal products (Ismail et al. 2023; Rasmussen et al. 2024).

In the 2000 outbreak in Egypt's Alexandria governorate, clinical signs were reported not only in cattle but also in humans with direct contact, and a high proportion of the cattle tested positive for both FMD viral RNA and specific antibodies (Donia and Youssef 2002). These recurrent incursions highlight the critical need for sustained immunization campaigns and rigorous biosecurity frameworks to prevent viral spread and safeguard global livestock systems.

Despite its high morbidity, mortality in adult cattle is relatively low, however, calf fatalities can reach up to 50%, primarily due to cardiac complications or opportunistic secondary infections (Doll 2001). FMD is caused by an aphthovirus of the *Picornaviridae* family and is characterized by a high degree of antigenic variability, with multiple serotypes—including O, A and SAT-2—circulating globally. This serotypic diversity presents a major obstacle to disease control, as it necessitates the development and deployment of serotype-specific vaccines (Callis 1980; Mohammed et al. 2022). In cattle, FMD typically presents with vesicular lesions on the oronasal mucosa, feet, and teats; however, atypical manifestations, such as vesicles on horn keratin, have also been documented (Mohebbi et al. 2017; Sukoco et al. 2023). In addition to its clinical and veterinary impact, FMD leads to substantial economic disruption by reducing livestock productivity and restricting the trade of live animals and animal products (Ismail et al. 2023; Rasmussen et al., 2024). FMD poses a persistent threat to global livestock production systems, with recent estimates from the World Organization for Animal Health (WOAH) indicating that the virus affects over 70% of the global livestock population. The disease remains endemic across vast regions of Africa and Asia, and continues to circulate in localized areas of South America (Stenfeldt et al. 2025)

In regions where FMD is endemic, the virus frequently circulates undetected within vaccinated herds and indigenous cattle populations, complicating efforts to monitor, contain, and eradicate the disease (Kitching 2002). While the acute clinical signs of FMD are well characterized, the virus also exerts substantial subclinical and systemic impacts. Notably, FMD has been implicated in reproductive failures, including spontaneous abortion in pregnant cows, with evidence of vertical transmission supported by the detection of FMD viral RNA and antigens in fetal tissues (Ranjan et al. 2016). Infected animals also exhibit marked biochemical perturbations, including elevated levels of aspartate aminotransferase (AST), creatine kinase (CK), CK-MB isoenzyme, and lactate dehydrogenase (LDH), consistent with oxidative stress and myocardial injury (Soltani et al. 2020). In Ethiopia, FMD have been associated with high morbidity rates, presenting clinically with profuse salivation, vesicular lesions in the oral cavity, and ulcerations within the interdigital spaces (Mohammed et al. 2022). In dairy cattle, infection often leads to a transient reduction in milk production, with yields typically returning to baseline within ten days post-infection (Ismail et al. 2023; Oktanella et al. 2023). Hematologically, FMD induces a moderate and temporary leucopenia, predominantly characterized by lymphopenia, in both cattle and buffaloes. Notably, interspecies variation has been observed in lesion distribution and healing kinetics (Mohan et al. 2008). While FMD remains primarily a disease of cloven-hoofed animals, serological evidence of anti-FMDV antibodies in humans with close livestock contact suggests limited zoonotic exposure (Donia and Youssef 2002).

The gut microbiota comprises a complex and dynamic consortium of microorganisms—including bacteria, viruses, archaea, fungi and protozoa Xu et al. 2021; (Maciel-Fiuza et al. 2023). The gut microbiota of dairy cattle exhibits a diversity bacterial community, predominantly comprising members of the phyla Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia, which collectively perform critical metabolic and immunological functions that support host physiology and homeostatic balance (Lathifa et al. 2025). Furthermore, fecal microbiota transplantation (FMT) involves introducing a complete microbial community from a healthy donor into a recipient with a disrupted or immature gut microbiota. This approach has demonstrated potential in restoring microbial diversity, re-establishing ecological balance, and promoting the growth of beneficial taxa with immunomodulatory functions and the maintenance of intestinal barrier integrity (Niederwerder 2018).

Recent advances in metagenomic methodologies most notably Shotgun metagenomics is a powerful high-throughput sequencing method that enables comprehensive analysis of microbial communities, providing insights into both their taxonomic composition and functional potential. It has become essential for exploring gut microbiota complexity, identifying novel microbes, and uncovering pathways related to host health and disease resistance (Zhang et al. 2021; Maciel-Fiuza et al. 2023). FMD remains a persistent challenge to global livestock health and agricultural economies highlighting the urgent need for alternative and complementary disease management strategies. In this study, we explored the gut microbiota of indigenous cattle breeds to assess its potential role in enhancing host resistance to FMD as well as to develop FMT may serve as a promising microbiome-based intervention to support FMD control in endemic regions.

MATERIALS AND METHODS

Animal selection and metagenomic analysis

Healthy animals (H), and animals infected (S) with Foot and mouth disease (FMD) were identified and their fecal material was collected from Indonesian breeds Madura (Madu) and Crossbreed (Cross). Fecal samples from healthy cattle and those infected with FMD were collected and homogenized, respectively. Total DNA was extracted using a Zymo DNA Mini Stool Extraction Kit. The quality of the extracted DNA was then tested. Sample quantification was performed using a Qubit fluorometer, and its integrity was checked by agarose gel electrophoresis. For genomic DNA, 1% agarose gel was run for 40min at 100V, whereas the PCR product was run for 50min on a 2% agarose gel at 80 volts.

Genomic libraries were constructed following DNA

quality assessment using standard protocols comprising end repair, A-tailing and PCR amplification. Library concentrations were quantified with a Qubit 2.0 fluorometer and diluted to 2 ng/μL for insert size analysis on the Agilent 2100 Bioanalyzer. Library quality was confirmed by quantitative PCR. Libraries passing quality control were sequenced on the NovaSeq 6000 platform (Illumina). Raw sequencing reads were first assembled into scaffolds using de novo assembly methods. Gene prediction was then performed on the assembled scaffolds using MetaGeneMark. The resulting genes were clustered to generate a non-redundant gene catalogue. To estimate gene abundance across samples, high-quality reads were mapped to this catalogue. Functional annotation was carried out by aligning gene sequences to the non-redundant (NR) database using BLAST. Additional functional insights were obtained through homology-based annotation against the CAZy, eggnog and KEGG databases, whereas antibiotic resistance genes were found based on CARD, ARDB databases.

Sample collection

Fresh fecal samples were obtained immediately following defecation from individually selected cattle. Each sample was transferred into RNA/DNA stabilization tubes to preserve nucleic acid integrity. After proper labelling, a unique identification code was assigned to each tube. Samples from each animal were processed separately to avoid cross-contamination. The collected material was thoroughly homogenized prior to DNA extraction, which was subsequently carried out to prepare shotgun metagenomic sequencing.

RESULTS AND DISCUSSION

Data preprocessing

DNA was isolated from fecal samples of selected healthy and experiment cattle for constructing metagenomic libraries. SCroscow2 and HCroscow2 exhibit higher read abundance within the 100–300bp range, consistent with greater sequencing depth or more efficient library preparation, while SMadubu2 and SMadubu1 display reduced counts beyond 300 bp, particularly above 500bp. In the second set, HMadubu1 and HCroscow2 similarly show elevated read abundance in the 100–300bp intervals, whereas HMadubu2 and SCroscow1 have overall lower sequence yields. Although reads exceeding 1,500bp are rare across all samples, variability in intermediate-length distributions indicates minor differences in fragmentation efficiency or sequencing output that could influence downstream assembly and comparative microbiome analyses between healthy and FMD-infected cattle, as shown in Fig. 1A, 1B, 1C, 1D, 1F, 1G, and 1H.

Table 1 shows the original sequencing statistics for eight cattle gut microbiome samples, including clean read counts, total clean bases, and quality-filtering percentages. All samples achieved exceptionally high data quality, with clean reads representing over 99.5% of raw reads and clean bases consistently exceeding 99.28% of raw bases. SCroscow1 generated the highest number of clean reads (55,066,484) and bases (8.29 Gb), indicating particularly high sequencing depth, followed by SMAduBu1 with 49.7 million reads and 7.5Gb. In contrast, SCroscow2 produced the lowest sequencing yield, with 43.4 million clean reads and 6.53 Gb. The remaining samples, including HMaduBu, HCroscow1, HMaduBu2, SMaduBu2 and HCroscow2, displayed clean read counts ranging from ~45 to 48 million and base counts between 6.8Gb and 7.3Gb.

Table 2 presents sequence statistics after quality optimization and host sequence removal across eight cattle gut microbiome samples. Post-cleaning, optimized read counts ranged from 26.8 million in SMaduBu2 to 43.2 million in SCroscow1, with corresponding optimized base counts ranging from 4.04 to 6.51Gb, respectively. The percentage of retained reads and bases relative to the

Table 1: Summary of original sequencing metrics, including sample identifiers, fragment lengths utilized for library preparation, and the total number of raw reads generated per sample

Samples	Clean reads	Clean base (bp)	Percent in raw reads (%)	Percent in raw base (%)
HMaduBu	48,323,090	7,282,406,606	99.51	99.31
HCroscow1	46,599,350	7,021,741,523	99.60	99.39
SMAduBu1	49,740,902	7,498,659,868	99.57	99.40
HCroscow2	47,246,976	7,121,233,947	99.59	99.40
SCroscow1	55,066,484	8,295,545,398	99.62	99.39
SCroscow2	43,389,234	6,531,270,069	99.59	99.28
SMaduBu2	45,553,884	6,863,067,954	99.58	99.35
HMaduBu2	45,106,856	6,799,727,755	99.50	99.34

HMaduBu= Healthy Madura breed cattle; HCroscow= Healthy Crossbreed cattle; SMAduBu= Sick Madura breed cattle; SCroscow= Sick Crossbreed cattle.

Table 2: Sequence statistics after cleaning

Samples	Optimized reads	Optimized base (bp)	Percent in raw reads (%)	Percent in raw bases (%)
HMaduBu2	32,863,942	4,955,499,478	72.50	72.39
HCroscow1	37,234,044	5,612,370,764	79.58	79.44
SMaduBu2	26,800,272	4,040,138,937	58.58	58.49
SCroscow1	43,213,048	6,512,177,757	78.18	78.02
HCroscow2	34,219,306	5,159,130,679	72.13	72.02
HMaduBu	35,513,620	5,354,294,151	73.13	73.02
SMAduBu1	34,703,794	5,233,319,774	69.47	69.37
SCroscow2	34,264,046	5,160,290,320	78.65	78.44

HMaduBu= Healthy Madura breed cattle; HCroscow= Healthy Crossbreed cattle; SMAduBu= Sick Madura breed cattle; SCroscow= Sick Crossbreed cattle"

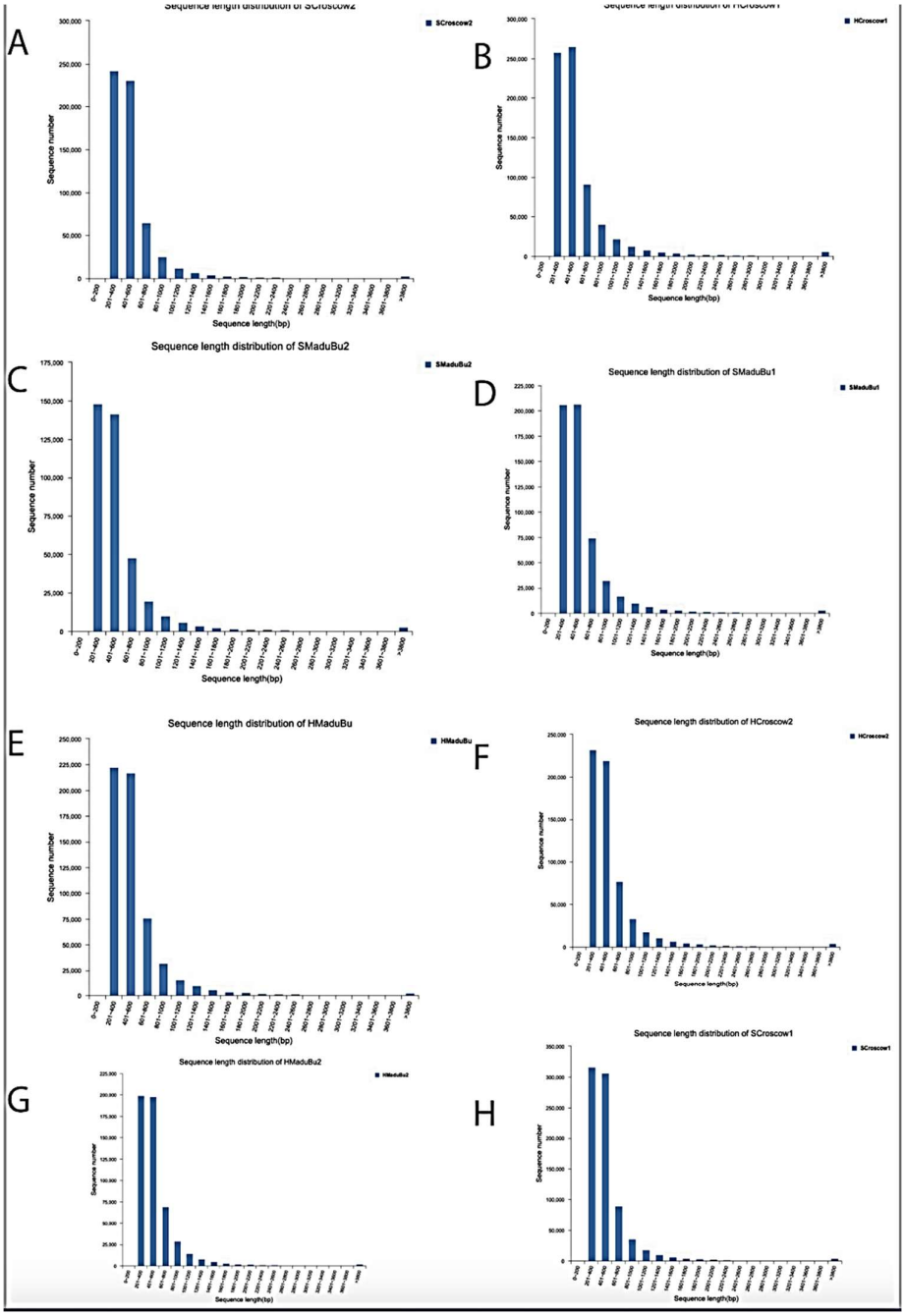

Fig. 1: The distribution of sequencing length reads for each sample.

original raw data varied across samples, with SMaduBu2 showing the lowest retention (58.58% of reads and 58.49% of bases), possibly reflecting higher host DNA contamination or sequencing artifacts. In contrast, HCroscow1 had the highest retention (79.58% of reads and 79.44% of bases), followed closely by SCroscow2 and SCroscow1. HMaduBu2, HCroscow2, HMaduBu, and SMAduBu1 maintained intermediate retention levels, generally around 70–73%. These variations in data retention highlight differences in sample quality and microbial DNA content, which may influence downstream taxonomic and functional profiling analyses.

Table 3 summarizes the sequence statistics of predicted open reading frames (ORFs) after de-host filtering for eight cattle gut microbiome samples. The number of ORFs detected varied substantially across samples, ranging from 487,768 in SMaduBu2 to 962,519 in SCroscow1, reflecting differences in microbial gene content and sequencing depth. Total ORF sequence length spanned from approximately 278 Mb in HMaduBu2 to over 421 Mb in HCroscow1. Average ORF lengths were

Table 3: Sequence statistics after de-host

Sample	ORFs	Total Length (bp)	Average Length (bp)	Max (bp)	Min (bp)
SMaduBu2	487,768	214,655,202	440.08	17,877	102
SCroscow1	962,519	408,296,148	424.20	14,712	102
HCroscow2	767,971	342,163,830	445.54	13,044	102
HCroscow1	928,009	421,935,795	454.67	21,246	102
HMaduBu	725,679	309,389,010	426.34	12,033	102
SCroscow2	717,312	300,884,052	419.46	15,429	102
HMaduBu2	651,335	278,098,656	426.97	11,460	102
SMAduBu1	710,193	314,607,456	442.99	13,020	102

relatively consistent across samples, generally between 419 bp and 455 bp, with HCroscow1 exhibiting the highest mean length (454.67bp) and SCroscow2 the lowest (419.46bp). Maximum ORF lengths also showed variability, with the longest single ORF reaching 21,246bp in HCroscow1 and the shortest maximum observed in HMaduBu2 (11,460bp). Minimum ORF lengths were uniform at 102bp across all samples, reflecting consistent prediction thresholds. These results indicate robust gene prediction across diverse samples while highlighting inter-sample variability in microbial coding potential that may influence functional annotation and comparative metagenomic analyses.

Relative abundance of bacteria in Healthy and FMD infected cattle

The abundance of different bacteria is evaluated by a shotgun metagenomic approach. It is observed that healthy cattle and cattle infected with foot and mouth disease are significantly different in gut microbiota profile. The phylum Bacillota varies significantly among healthy and infected cattle. The phylum Bacillota is predominated in all samples (HMadubu1, HMadubu2, SMadubu1, SMadubu2, HCroscow1, HCroscow2, SCroscow1, SCroscow2) followed by Bacteriodota, Euryarchaeota and Spirocheatota while the low abundance of Urovirocota, Lantisphaerota and Pseudomondota across the samples as shown in Fig. 2A and 2C.

Clostridia bacterium was most abundant in SCroscow1 and SCroscow2, with moderate representation in HCroscow1, HCroscow2, HMadubu1, and HMadubu2, but markedly reduced in SMadubu1 and SMadubu2 (Fig 2B). The animal group also showed similar results. Clostridia bacterium was higher in healthy crossbred, infected crossbred and healthy Madura rather than in infected Madura (Fig 2D).

Clostridia bacterium was most abundant in SCroscow1 and SCroscow2, with moderate representation in HCroscow1, HCroscow2, HMadubu1, and HMadubu2, but markedly reduced in SMadubu1 and SMadubu2.

Similarly, *Oscillospiraceae* bacterium exhibited high relative abundance in SCroscow1 and SCroscow2, while remaining at low levels in all other samples. In contrast, *Bacteroidales* bacterium, *Lachnospiraceae* bacterium, *Bacteroidaceae* bacterium, *Paludibacteraceae* bacterium, *Alistipes* sp., and *Methanobrevibacter* spp. were consistently detected at relatively low abundances across all samples as shown in Fig. 2B and 2D. Oscillospiraceae, a family of bacteria within the gut microbiota, plays a significant role in animal health and disease. Research indicates that these microorganisms are crucial for maintaining gut health, influencing immune responses, and potentially mitigating disease outcomes in various animal species. Oscillospiraceae contributes to a balanced gut microbiome, which is essential for nutrient absorption and overall health (Yang et al. 2021; Davidović et al. 2012).

Certain strains exhibit antimicrobial activity, helping to control pathogenic bacteria and reduce the incidence of gastrointestinal diseases (Kloeze et al. 2010). Oscillospiraceae influences cytokine profiles, which are vital for immune responses. This modulation can enhance resistance to infections and improve recovery from diseases (Davidović et al. 2012; Fan et al. 2021). The presence of Oscillospiraceae has been linked to improved health outcomes in livestock, suggesting its potential use in preventive health strategies. The results show that the abundance of Oscillospiraceae has been significantly reduced in cattle infected with foot and mouth disease Fig. 2B. *Clostridia*, a prominent class within the phylum Bacillota, play a central role in the anaerobic fermentation of dietary fiber and the generation of short-chain fatty acids

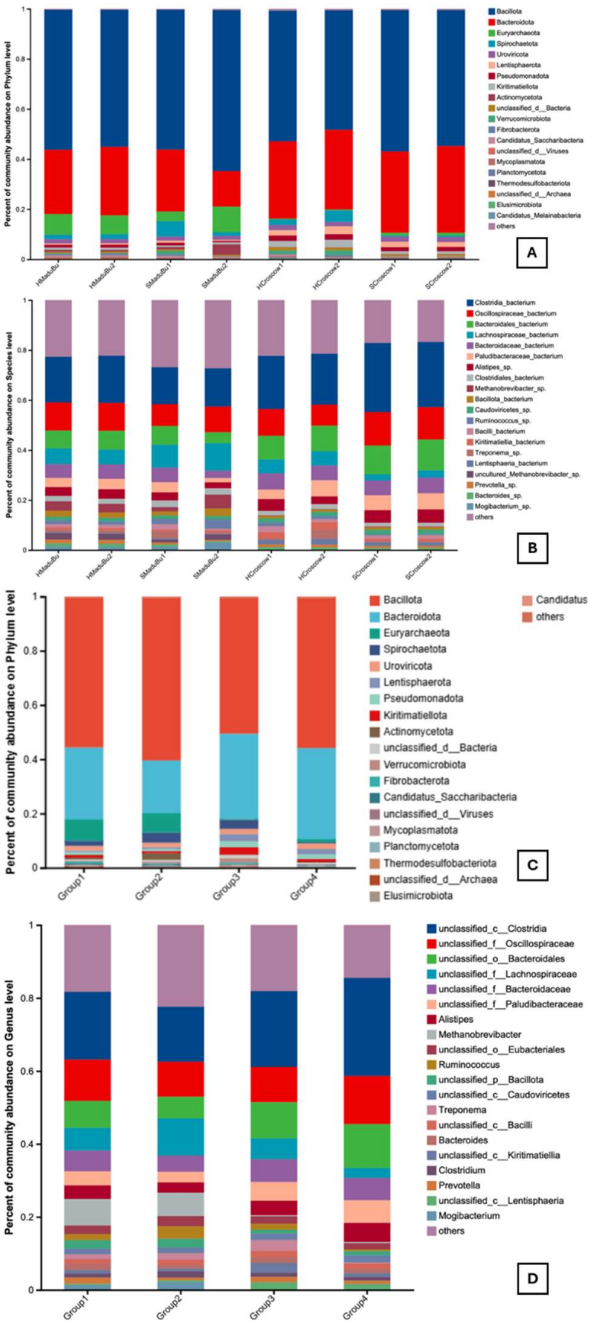

Fig. 2: The relative abundance of fecal gut microbiota. A) Phylum level in individual samples, B) Species level in individual samples, C) Phylum level in healthy and infected groups, D) Species level in healthy and infected groups. (Group 1: Healthy Madura, Group 2: FMD-infected Madura, Group 3: Healthy Crossbred and Group 4: FMD-infected Crossbred).

(SCFAs) (Koukiekolo et al. 2005). Particularly butyrate, in the gut. Beyond their metabolic contributions, these microbial products exert profound immunomodulatory effects, especially in the context of antiviral defense. Recent studies have shown that SCFAs modulate $CD8^+$ T cell metabolism via G protein-coupled receptor (GPR) signaling and inhibition of histone deacetylase (HDAC) activity, promoting rapid effector T cell activation during acute viral infection (Liu et al. 2023). Notably, butyrate enhances the functional responsiveness of $CD8^+$ T cells to influenza virus, contributing to a more robust and effective antiviral immune response. These findings highlight the potential of SCFA-producing gut microbes as therapeutic targets to strengthen host antiviral immunity and inform microbiome-based interventions.

Bacteroidales bacterium, such as *Bacteroides fragilis*, is a fiber-degrading bacterium, and the generation of short-chain fatty acids (SCFAs) contributes to antiviral immunity by stimulating the host's immune system to produce type I interferons, particularly IFN-β, which are crucial for inhibiting viral replication. This effect is largely mediated by the bacterial surface molecule polysaccharide A (PSA). PSA interacts with host immune cells via Toll-like receptor 4 (TLR4), triggering a signaling cascade that results in the secretion of IFN-β and enhances the host's resistance to viral infections. So, *Bacteroidales* bacteria lower the chance of viral diseases by boosting the body's natural immune defenses and increasing the production of antiviral signals (Stefan et al. 2020; Zhang et al. 2023b).

Lachnospiraceae bacterium play a pivotal metabolic role in modulating host immunity and reducing susceptibility to viral infections through the fermentation of dietary fibers and complex polysaccharides, resulting in the production of short-chain fatty acids (SCFAs), including butyrate, acetate, and propionate (Agus et al. 2021; Zaplana et al. 2023). These SCFAs have been shown to support the differentiation and activation of key effector T cell subsets—such as Th1, Th17 and cytotoxic $CD8^+$ T cells—during active immune responses. Moreover, SCFA-mediated signaling contributes to the regulation of mucosal immunity, a critical barrier against viral invasion and persistence (Kim 2021; Lee et al. 2023; Zhang et al. 2023a). The above discussion suggests that future FMT strategies in livestock should aim to enrich SCFA-producing, especially butyrate-producing, taxa to leverage their immunomodulatory capacity and enhance antiviral defense against FMD.

Functional annotation of healthy and infected cattle

Community-level metabolic function can be elucidated by examining the collective genomic potential of microorganisms coexisting within an ecosystem. This is effectively accomplished using shotgun metagenomic sequencing. In this study, predicted protein-coding sequences were aligned against the KEGG, eggnog and CAZy databases to assign functional annotations. The number of annotated genes and their relative abundances were computed at each classification level.

The COG functional classification of the analyzed metagenomic dataset reveals a diverse distribution of genetic resources across multiple cellular processes. Genes associated with core metabolic functions were particularly enriched. Carbohydrate transport and metabolism was the most represented category, comprising 193,244 genes, followed by Translation, ribosomal structure, and biogenesis with 188,524 genes, and Cell wall/membrane/envelope biogenesis with 158,877 genes. High gene counts were also observed in Replication, recombination, and repair (171,225 genes), Amino acid transport and metabolism (149,908 genes), and General function prediction only (144,255 genes), reflecting substantial investment in fundamental cellular activities. The Transcription category included 116,898 genes, while intermediate representation was noted for Posttranslational modification, protein turnover, chaperones (95,803 genes), Nucleotide transport and metabolism (85,537 genes), Function unknown (88,804 genes), and Inorganic ion transport and metabolism (79,779 genes). Categories linked to Defense mechanisms (76,139 genes), Coenzyme transport and metabolism (73,397 genes), and Cell cycle control, cell division, chromosome partitioning (70,566 genes) were also moderately abundant. In contrast, functions involved in more specialized processes were represented by lower gene counts, including Lipid transport and metabolism (67,397 genes), Energy production and conversion (65,213 genes), and Signal transduction mechanisms (47,759 genes). Minimal representation was observed in categories such as Cytoskeleton (36,175 genes), Intracellular trafficking, secretion, and vesicular transport (31,250 genes), Cell motility (15,268 genes) and Secondary metabolites biosynthesis, transport, and catabolism (10,211 genes). The least represented categories were Extracellular structures (6,791 genes), Mobilome: prophages, transposons (2,700 genes), RNA processing and modification (42 genes), and Chromatin structure and dynamics (30 genes), indicating their relatively limited roles in the sampled microbial communities as shown in Fig. 3A.

CAZy class classification of the metagenomic dataset revealed a diverse array of carbohydrate-active enzymes, highlighting the functional capacity of the microbial community to process complex carbohydrates. Among the seven major CAZy classes were detected in all our fecal samples are Glycoside Hydrolases (GH) were the most abundant, with 79,749 genes. This was followed by Glycosyltransferases (GT), with 26,781 genes. Carbohydrate Esterases (CE) were also well represented, comprising 16,399 genes. Carbohydrate-Binding Modules (CBM) accounted for 10,567 genes, supporting substrate recognition and enzymatic targeting. In contrast, Polysaccharide Lyases (PL), were less prevalent, with 3,566 genes. Notably, Auxiliary Activities (AA) enzymes, which support oxidative cleavage of lignocellulosic materials, were relatively low in abundance (1,820 genes). Finally, Surface Layer Homology (SLH) modules were the least represented with only 1,127 genes as shown in Fig. 3B.

The histogram of KEGG provides a quantitative overview of the functional potential within a given genomic dataset, displaying the number of reads mapped to various KEGG pathways. The KEGG pathways categorized into six main functional group were detected in our samples. This analysis highlights that Metabolism-related pathways, depicted in red, are overwhelmingly dominant, with Global and overview maps exhibiting the highest read count, closely followed by Carbohydrate metabolism, Amino acid metabolism and other

fundamental metabolic processes like Glycan biosynthesis and metabolism and Energy metabolism, indicating a strong genetic emphasis on core biochemical activities. Following metabolism, Genetic Information Processing pathways, shown in light blue, also display significant read counts, particularly for Replication and repair and Translation, underscoring the active cellular processes of gene expression and maintenance. Environmental Information Processing (green) and Cellular Processes (dark blue) pathways are moderately represented, suggesting capabilities for sensing the environment, transport, and basic cellular functions like Cell growth and death and Cell motility. In contrast, pathways associated with Human Diseases (orange/pink) and Organismal Systems (purple), which encompass categories like Cancer, Infectious disease and various bodily systems, show remarkably low read counts. This pattern is typical for microbial community analyses, as these categories are primarily relevant to eukaryotic hosts or complex multicellular interactions, strongly suggesting that the analyzed sample is predominantly microbial in origin and is primarily focused on essential metabolic and genetic functions for survival and growth as shown in Fig. 3C.

Circos NR

The Circos plot provides an integrated visualization of fecal microbiota composition in FMD-affected dairy cows, linking individual samples (left side) to their corresponding bacterial community profiles (right side). Each circle represents the relative abundance of specific bacterial taxa across different samples, with circle thickness reflecting contribution strength. The right half highlights key bacterial groups and their proportional representation within the gut ecosystem. This visualization reveals clear shifts in microbial community structure among samples, suggesting FMD-associated dysbiosis. By simultaneously displaying taxonomic composition and inter-sample variation, the figure underscores the ecological complexity of the gut microbiome and offers insight into microbial signatures potentially linked to host metabolic and immunological responses as shown in Fig. 4A.

Circos Plot

The Circos plot provides an integrative visualization of the complex interactions between microbial taxa and host-associated functional pathways across fecal microbiota samples from FMD-affected dairy cows. The left side of the plot distinguishes the different sample groups, while the right side highlights the functional metabolic landscape. Key pathways include biosynthesis of secondary metabolites, microbial metabolism in diverse environments, amino acid and cofactor biosynthesis, carbohydrate metabolism, ABC transporters, two-component systems, purine metabolism, and ribosomal functions. The connecting circles represent the relative contributions of microbial groups to these metabolic functions, while the inner circle illustrates the intensity and distribution of functional activity as shown in Fig. 4B.

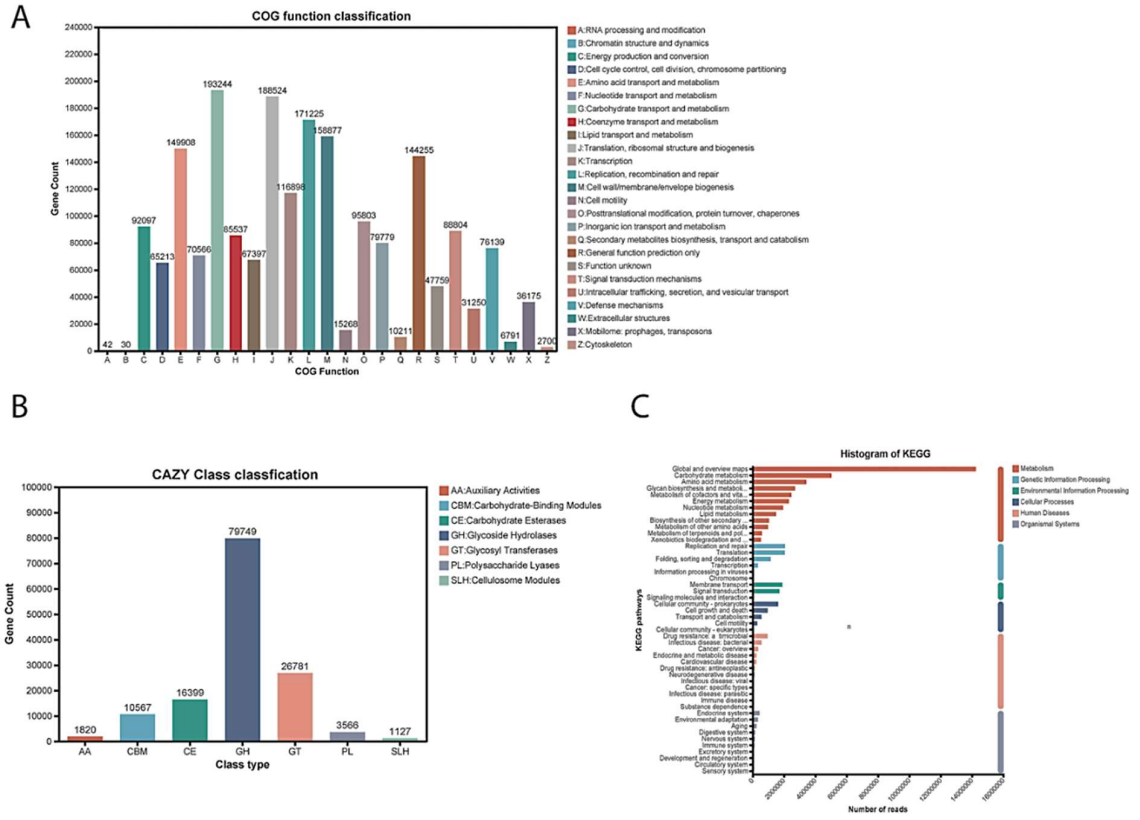

Fig. 3: Functional annotation of fecal gut microbiota in healthy and infected cattle. A) COG database annotations, B) CAZy database annotations, and C) KEGG database annotations.

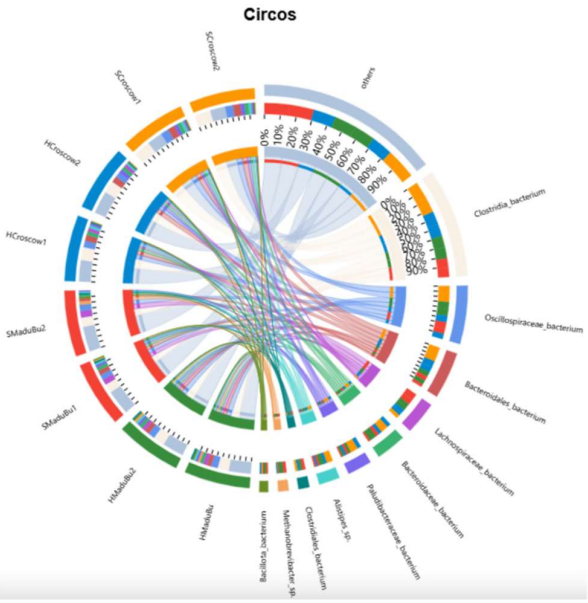

Fig. 4A: Circos plot illustrating taxonomic composition and among sample variation in fecal microbiota from FMD-affected dairy cows.

PCA analysis

This PCA (Principal Component Analysis) plot illustrates the clustering of microbial community profiles across four experimental groups, offering insight into compositional variation. The first principal component (PC1) accounts for 43.06% of the total variance, while the second component (PC2) explains 22.94%, together capturing over 66% of the overall data structure. Group-specific clustering is evident: Group1 and Group2 cluster closely but are separated along PC1, indicating moderate compositional divergence. Group3 is distinctly separated along PC2, suggesting a unique microbial configuration. In contrast, Group4 is positioned far along the positive axis of PC1 and the negative axis of PC2, indicating the most divergent microbial structure among all groups as shown in Fig. 5A.

PCA COG

This PCA (Principal Component Analysis) plot reveals the compositional structure of microbial communities across four experimental groups, with the first two principal components (PC1 and PC2) explaining 23.66% and 20.39% of the total variance, respectively. The distribution of points shows clear group-wise segregation, indicating distinct microbial profiles among groups. Group1 and Group2 are closely clustered in the upper left quadrant, suggesting similar microbial compositions with minor variation. Group3 is located in the lower half of the plot, distant from all other groups, indicating a markedly different microbial community structure. In contrast, Group4 clusters tightly in the upper right quadrant, demonstrating strong internal consistency and distinct separation from other groups along PC1 as shown in Fig. 5B. This PCA underscores the robustness of dimensionality reduction in identifying biologically meaningful shifts in microbial ecology, supporting its application in microbiome-driven research for delineating treatment effects or disease-associated microbial community.

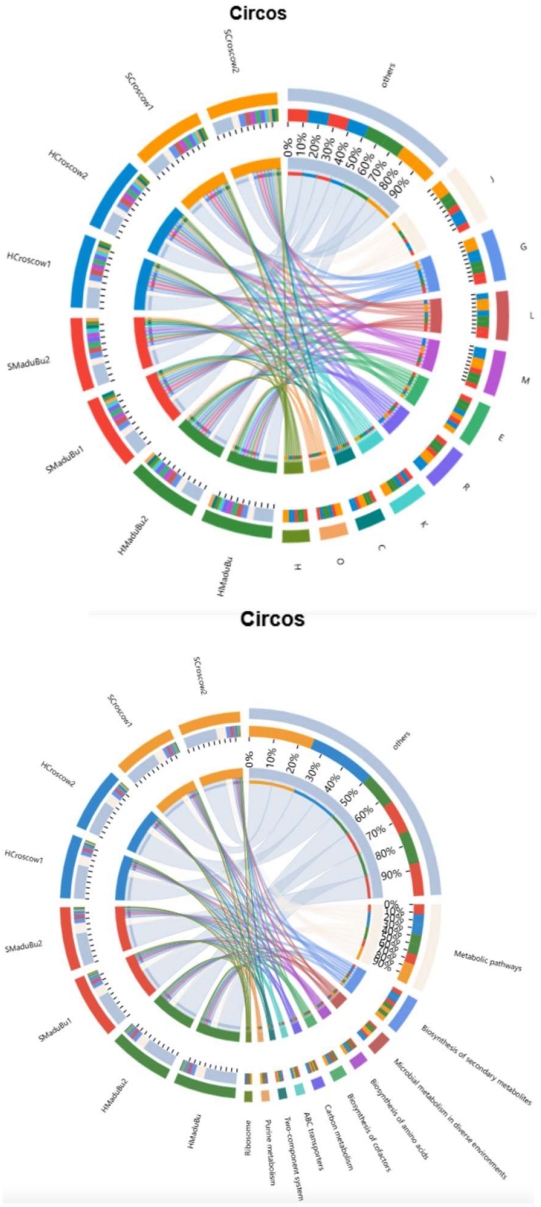

Fig. 4B: Circos plot illustrating microbial–functional interactions in fecal microbiota from FMD-affected dairy cows.

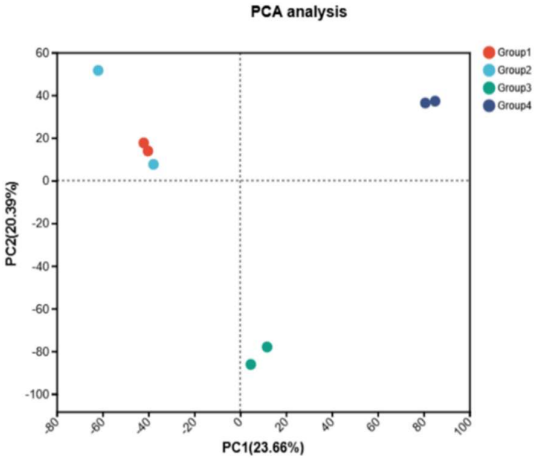

Fig. 5A: Principal Component Analysis (PCA) of microbial community composition across four experimental group.

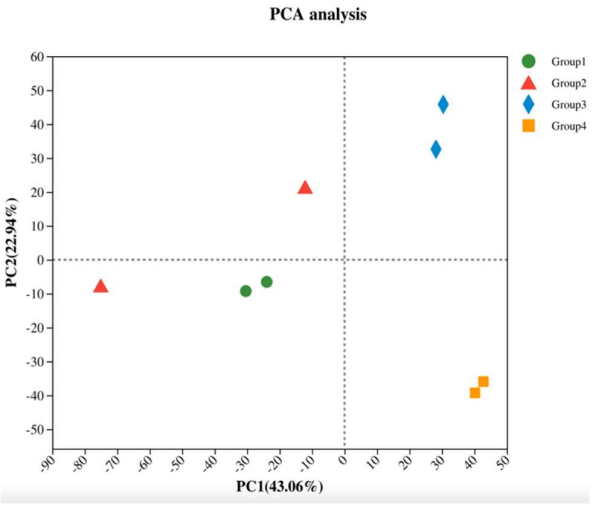

Fig. 5B: This figure shows that Principal Component Analysis (PCA) of microbial community composition across FMD group.

Contribution of species and COG

This heatmap presents a species-level functional contribution analysis across ten key COG-defined gene categories (F1–F10), highlighting the taxonomic drivers of core microbial functions. Dominant taxa such as unclassified Clostridia, Lachnospiraceae, and Oscillospiraceae exhibit strong and consistent positive contributions (red) across most functions, underscoring their central role in maintaining essential microbial processes. In contrast, Methanobrevibacter and Alistipes show minimal or negative contributions (blue) to specific functions such as F2, F4, and F8, suggesting more specialized or limited role as shown in Fig. 6.

Contribution analysis chart COG

This bar plot illustrates the relative contribution of different microbial species and functional groups across ten distinct categories or samples, labeled Function01" through "Function10. The visualization highlights the varying community composition across the functions. A significant portion of the relative contribution in most functions, particularly Function01, Function04, Function05, Function09, and Function10, is dominated by unclassified clostridia (represented by the large blue segments). In contrasts *Methanobrevibacter* (red segments) shows a notably high relative contribution in Function07 and Function08. Other groups, including unclassified Oscillospiraceae and various *Bacteroidales* species, contribute smaller proportions throughout the functions. While the plot primarily visualizes taxonomic contribution, a secondary legend lists specific COG (Clusters of Orthologous Groups) associated with each function, indicating a link to functional analysis as shown in Fig. 7. Overall, this plot highlights the taxonomic diversity underlying microbial metabolic capacity and emphasizes the complex, cooperative dynamics that sustain gut ecosystem functionality.

Contribution of Species and KEGG

Contribution analysis chart KEGG

This bar plot presents the species-level contribution to ten key microbial functional categories, including metabolic pathways, biosynthesis of amino acids, cofactors, and secondary metabolites, carbon metabolism, ABC transporters, two-component systems, purine metabolism, and ribosomal functions. Each bar represents a functional category, with stacked segments indicating the relative contribution of specific microbial taxa. Unclassified members of Clostridia, Lachnospiraceae, and Oscillospiraceae consistently contribute across all functions, reflecting their broad metabolic versatility. In contrast, taxa like Methanobrevibacter and Alistipes show more limited and specialized functional roles. Importantly, while core metabolic functions such as Function01 (general metabolic pathways) and Function10 (ribosomal functions) show high and widespread contributions across diverse taxa, specialized functions like purine metabolism and ABC transporters exhibit more taxon-specific distributions as shown in Fig. 8. Overall, this plot highlights the taxonomic diversity underlying microbial metabolic capacity and emphasizes the complex, cooperative dynamics that sustain gut ecosystem functionality.

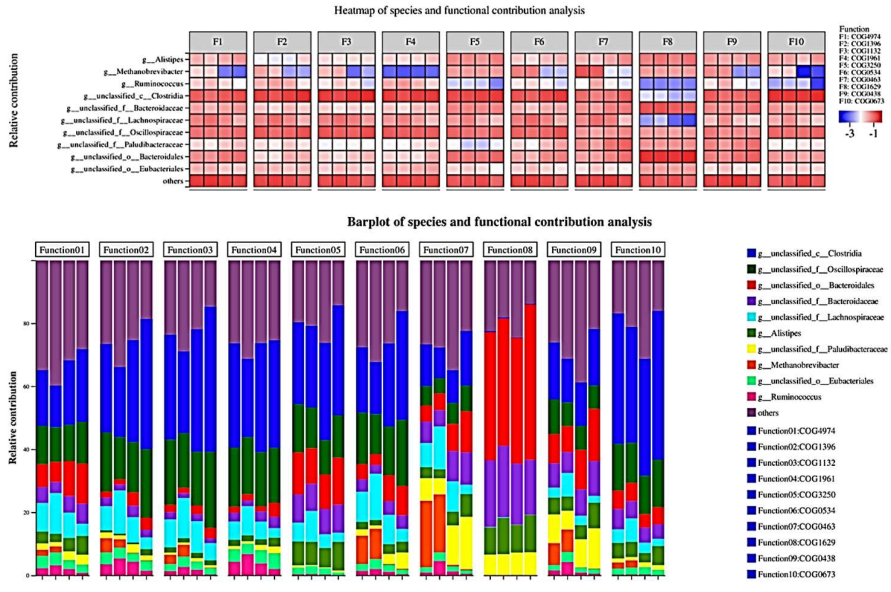

Fig. 6: The relationship between the contribution of species and functions was analyzed by heat maps.

Fig. 7: The contribution of species and contribution analysiss with different functional pathways.

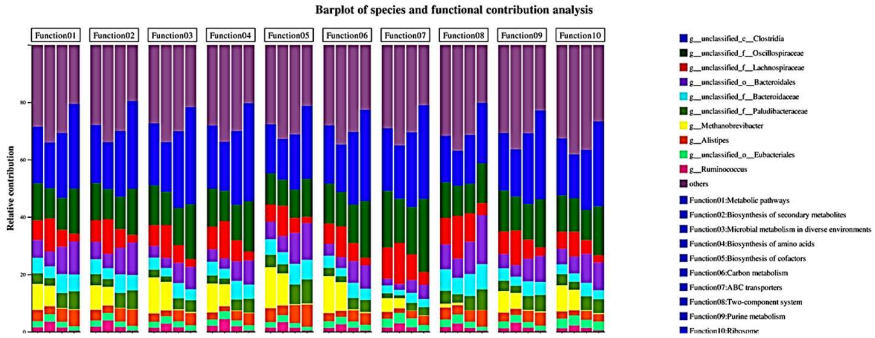

Fig. 8: The contribution of species with different functions.

Species and function contribution heatmap

This heatmap presents a comprehensive species-level functional contribution analysis, highlighting the involvement of ten dominant microbial taxa (T1–T10) in various metabolic pathways relevant to host physiology. The taxa include both unclassified families such as Clostridia (T1), Oscillospiraceae (T2), and Lachnospiraceae (T3), as well as known genera like *Ruminococcus* (T10) and *Alistipes* (T6). The y-axis lists key functional categories derived from KEGG or similar databases, including ABC transporters, amino acid biosynthesis, cofactor and secondary metabolite biosynthesis, carbon metabolism, methane metabolism, ribosomal functions and two-component systems. The intensity and color direction reflect the relative contribution of each taxon to these pathways: red indicates high positive contribution, while blue denotes reduced or negative association. Overall, most taxa show broad positive contributions across central metabolic and biosynthetic pathways, particularly in "others," ribosome, and amino acid biosynthesis categories, indicating core functionality maintained across the community. However, notable exceptions include negative contributions (blue) from Methanobrevibacter (T7) and Ruminococcus (T10), particularly in purine metabolism, carbon metabolism, and microbial metabolism in diverse environments, reflecting possible specialization or limited functional roles in these processes. In contrast, taxa like *Bacteroidaceae* (T5) and *Lactobacillaceae* (T4) exhibit consistently high contributions across most categories, suggesting their integral role in supporting host nutrient metabolism and microbial ecological stability as shown in Fig. 9. Collectively, this result emphasizes the metabolic versatility and redundancy of the gut microbiota, while also pointing to functional specialization among taxa that may be targeted for therapeutic or ecological microbiome modulation.

Contribution of species and CAZy

Species and Function Contribution Heatmap

The presented heatmap illustrates the relative contribution of various microbial taxa (T1–T10) to specific carbohydrate-active enzyme (CAZyme) families, providing insights into the functional landscape of the microbiota. Each taxon corresponds to a distinct microbial group, such as Ruminococcus (T10), Alistipes (T6), Methanobrevibacter (T7) and unclassified families like Clostridia (T1) and *Lachnospiraceae* (T3). The y-axis shows that CAZyme families (e.g., GHs, GTs, CEs) involved in polysaccharide degradation and synthesis, while the color gradient—from blue to red—represents the strength and direction of each taxon's functional contribution. Notably, most taxa exhibit positive contributions (red) to CAZyme activity, especially for GT41, GT4, GH3, and others, indicating widespread functional redundancy across the microbiota. Conversely, negative contributions (blue), particularly by Alistipes and Methanobrevibacter, suggest limited involvement or potential suppression of certain glycoside hydrolases like GH3 and CE1. These patterns highlight both functional overlap and specialization, where some taxa contribute broadly to carbohydrate metabolism while others exhibit niche-specific roles. Such functional profiling is crucial in understanding how microbial composition influences metabolic output, gut health, and potential responses to interventions like fecal microbiota transplantation (FMT) or dietary modulation Fig. 10.

Contribution analysis of chart CAZy

The barplot presents the relative contributions of microbial taxa and glycoside hydrolase (GH) enzyme families across ten different taxa groups (Taxon01 to Taxon10). Each stacked bar represents a unique sample or taxonomic cluster, with the vertical axis indicating the percentage contribution to total functional potential. Among annotated glycoside hydrolase families, GH2, GH3, GH5, GH10, GH13, GH18, and GH43 appear prominently and vary in abundance across taxa. For example, Taxon07 and Taxon08 show a marked increase in GH3, GH5, and GH10 contributions, indicating enhanced potential for plant polysaccharide degradation or fiber fermentation in these communities. Conversely, Taxon01 through Taxon04 show more evenly distributed, lower levels of these GH families, suggesting a more functionally generalized profile as shown in Fig. 11.

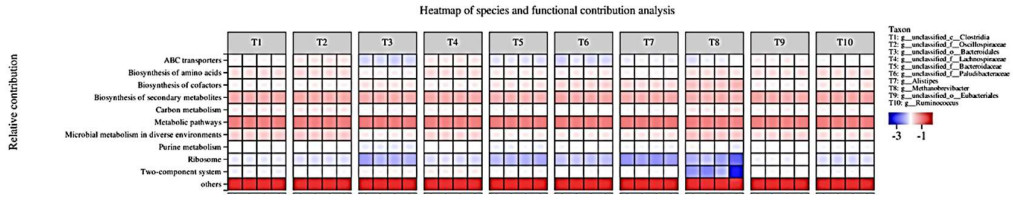

Fig. 9: The relationship between the contribution of species and functions was analyzed by heat maps, showing the correlation between the contribution between the species and the functions. Heatmap of species and function contribution.

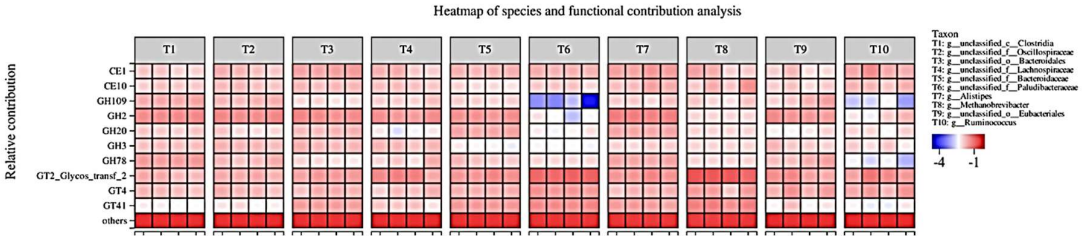

Fig. 10: The heatmap of species and functional contribution analysis.

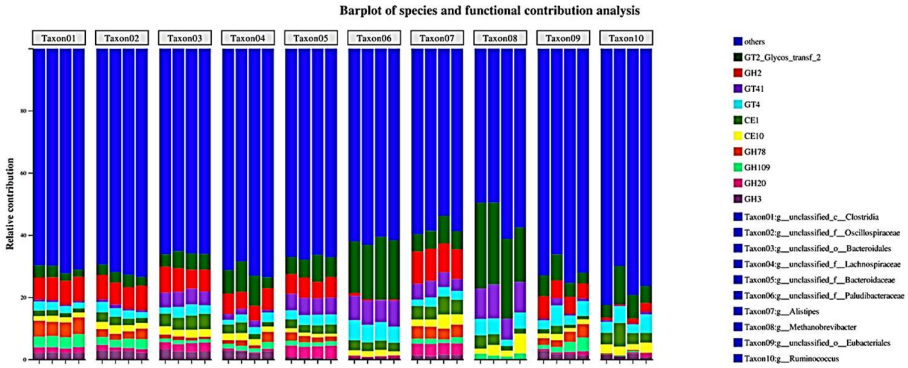

Fig. 11: The distribution of glycoside hydrolase (GH) families across microbial taxonomic groups.

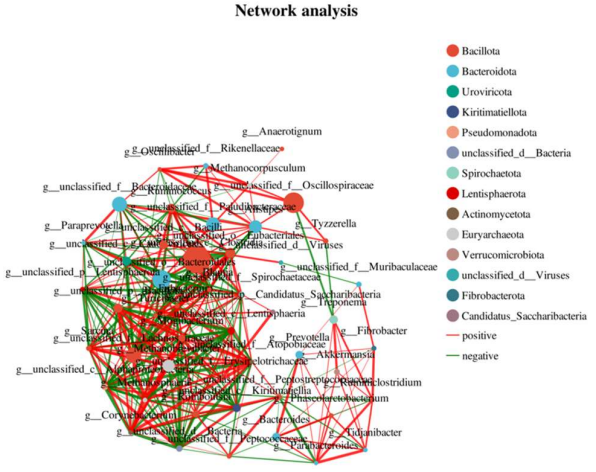

Fig. 12: The microbial correlation network reveals taxonomic interactions within the gut microbiota of indigenous cattle.

Single-factor correlation network

The single-factor correlation network analysis revealed a complex web of microbial interactions across multiple taxonomic groups. Nodes in the network represent microbial genera, while edges denote statistically significant correlations, with red lines indicating positive associations and green lines indicating negative correlations. Members of the phylum Bacillota (red nodes) and *Bacteroidota* (teal nodes) appeared central within the network, suggesting that these groups play key roles in shaping microbial community structure. Notably, genera such as *Oscillospiraceae*, *Prevotella, Anaerotignum*, and *Ruminococcaceae* were highly interconnected, suggesting potential cooperative or competitive interactions relevant to community stability and function. In contrast, nodes representing genera from less abundant phyla such as *Verrucomicrobiota*, *Candidatus Saccharibacteria*, and *Lentisphaerota* exhibited more peripheral positions with fewer connections. The presence of both positive and negative correlations highlights the dynamic balance between synergistic and antagonistic microbial relationships as shown in Fig. 12. This network structure underscores the ecological complexity of the gut microbiota and suggests that certain keystone taxa may exert disproportionate influence on microbial composition and inter-species interaction.

Conclusion

Fecal microbiota transplant has shown significant results towards the improvement of cattle in several diseases. The exploration of gut microbiota profile of local cattle breeds was a prerequisite to find appropriate donor to be used in our next year plan for the microbiota transplant to help improve the disease condition. During the present exploratory study, we have identified major gut microbiota dysbiosis in infected cattle as compared to control. We also observed there are certain breed effects on the gut microbiota profile, however, it is observed that the bacterial species responsible for a good gut and immune health was in dysbiosis. The future study will be aimed to improve health specifically focussing on FMD by manipulating gut microbiota by FMT to help boost immune response against FMD.

DECLARATIONS

Funding: This research was supported by the RIIM LPDP Grant and BRIN, grant number B-4113/III.11/PR.02/11/2023. We also thank the Research Center of Animal Husbandry, Research Organization for Agriculture and Food, for their support in completing this research.

Acknowledgment: The authors thank the colleagues in the Research Group for Feed Production and Processing

Technology of the Research Center for Animal Husbandry for their support in completing this research.

Conflict of Interest: There is no conflict of interest with any person or organization in this study.

Data Availability: The data can be requested from the corresponding author on reasonable request.

Ethics Statement: The animals and procedures were approved by Ethics Committee on Animal Care and Use National Research and Innovation Agency, Indonesia (No: 231/KE.02/SK/10/2024).

Author's Contribution: Windu Negara, Faheem Ahmed Khan, and Nuruliarizki Shinta Pandupuspitasari designed the concept of the study. Windu Negara, Maman Surachman, Wayan Angga Darmawan, Sindu Akhadiarto, and Dimar Sari Wahyuni sought funding. Windu Negara, Faheem Ahmed Khan, Santoso, Ezi Masdia Putri, Ruslan Abdul Gopar, Riris Delima Purba, and Hanannisa Suryadi conducted field and laboratory work. Faheem Ahmed Khan, Satria Maulana, and Ezi Masdia Putri drafted and revised the manuscript. All authors have read and approved the final manuscript.

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REFERENCES

Agus A, Clément K and Sokol H, 2021. Gut microbiota-derived metabolites as central regulators in metabolic disorders. Gut 70(6): 1174-1182. https://doi.org/10.1136/gutjnl-2020-323071

Callis JJ, 1980. Foot-and-mouth disease in cattle-some relationships between pathogenesis and epizootiology. The Bovine Practitioner 1980(15): 164–168. https://doi.org/10.21423/BOVINE-VOL1980NO15P164-168

Davidović V, Joksimović-Todorović M, Stojanović B and Relić, R, 2012. Plant usage in protecting the farm animal health. Biotechnology in Animal Husbandry 28(1): 87–98. https://doi.org/10.2298/BAH1201087D

Doll K, 2001. Clinical picture and differential diagnosis of foot and mouth disease in cattle. DTW. Deutsche Tierarztliche Wochenschrift 108(12): 494–498.

Donia HA and Youssef BZ, 2002. Foot and mouth disease (FMD): serological investigation in some farms of Alexandria Governorate of Egypt. The Journal of the Egyptian Public Health Association 77(3–4): 371–382.

Fan P, Nelson CD, Driver JD, Elzo MA, Peñagaricano F and Jeong KC, 2021. Host genetics exerts lifelong effects upon hindgut microbiota and its association with bovine growth and immunity. ISME Journal 5(8): 2306-2321. https://doi.org/10.1038/s41396-021-00925-x

Ismail I, Indarjulianto S, Yusuf S and Purba FY, 2023. Clinical examination of foot and mouth disease of dairy cows in Sukamurni, Cilawu, Garut, West Java, Indonesia. IOP Conference Series: Earth and Environmental Science 1174(1): 012005. https://doi.org/10.1088/1755-1315/1174/1/012005

Kim CH, 2021. Control of lymphocyte functions by gut microbiota-derived short-chain fatty acids. Cellular and Molecular Immunology 18(5): 1161–1171. https://doi.org/10.1038/s41423-020-00625-0

Kitching RP, 2002. Clinical variation in foot and mouth disease: cattle. Revue Scientifique et Technique-Office International Des Epizooties 21(3): 499–504. https://doi.org/10.20506/RST.21.3.1343

Kloeze H, Mukhi S, Kitching P, Lees VW and Alexandersen S, 2010. Effective animal health disease surveillance using a network-enabled approach. Transboundary and Emerging Diseases 57(6): 414–419. https://doi.org/10.1111/j.1865-1682.2010.01166.x

Koukiekolo R, Cho HY, Kosugi A, Inui M, Yukawa H and Doi RH, 2005. Degradation of corn fiber by *Clostridium cellulovorans* cellulases and hemicellulases and contribution of scaffolding protein CbpA. Applied and Environmental Microbiology 71(7): 3504–3511. https://doi.org/10.1128/AEM.71.7.3504-3511.2005

Lathifa AD, Pandupuspitasari NS, Khan FA, Ali A, Fadillah NAM and Prasetiyono BWHE, 2025. Improved immune status by fecal microbiota transplant mediated gut microbiota modulation in late lactation cows in a low land. Journal of Indonesian Tropical Animal Agriculture 50(2): 131–143. https://doi.org/10.14710/jitaa.50.2.131-143

Lee R, Yoon BI, Hunter CA, Kwon HM, Sung HW and Park J, 2023. Short chain fatty acids facilitate protective immunity by macrophages and T cells during acute fowl adenovirus-4 infection. Scientific Reports 13: 17999. https://doi.org/10.1038/s41598-023-45340-8

Liu XF, Shao JH, Liao YT, Wang LN, Jia Y, Dong PJ, Liu ZZ, He DD, Li C and Zhang X, 2023. Regulation of short-chain fatty acids in the immune system. Frontiers in Immunology 14: 1-14. https://doi.org/10.3389/fimmu.2023.1186892

Maciel-Fiuza MF, Muller GC, Campos DMS, do Socorro Silva Costa P, Peruzzo J, Bonamigo RR, Veit T and Vianna FSL, 2023. Role of gut microbiota in infectious and inflammatory diseases. Frontiers in Microbiology 14: 1-18. https://doi.org/10.3389/fmicb.2023.1098386

Mohammed Z, Aliy A, Jibril Y and Negussie H, 2022. Epidemiological and clinical characteristics of the foot and mouth disease outbreaks in cattle in central Ethiopia. Ethiopian Veterinary Journal 26(1): 105–121. https://doi.org/10.4314/evj.v26i1.7

Mohan MS, Gajendragad MR, Gopalakrishna S and Singh N, 2008. Comparative study of experimental Foot-and-Mouth Disease in cattle (*Bos indicus*) and buffaloes (*Bubalis bubalus*). Veterinary Research Communications 32: 481–489. https://doi.org/10.1007/S11259-008-9051-0

Mohebbi MR, Barani S and Mahravani H, 2017. An uncommon clinical form of foot-and-mouth disease in beef cattle presented with cornual skin lesions. Iranian Journal of Veterinary Research 18: 291–293. https://doi.org/10.22099/IJVR.2017.4638

Niederwerder MC, 2018. Fecal microbiota transplantation as a tool to treat and reduce susceptibility to disease in animals. Veterinary Immunology and Immunopathology 206: 65–72. https://doi.org/10.1016/j.vetimm.2018.11.002

Oktanella Y, Cahyani AA, Hendrawan VF, Nugroho W and Agustina GC, 2023. Foot and Mouth Disease Impact on Milk Productivity and Quality in KUD Kertajaya, Kediri, Indonesia. Jurnal Medik Veteriner 6(2): 244–249. https://doi.org/10.20473/jmv.vol6.iss2.2023.244-249

Ranjan R, Biswal JK, Subramaniam S, Singh KP, Stenfeldt C,

Rodriguez LL, Pattnaik B and Arzt J, 2016. Foot-and-mouth disease virus-associated abortion and vertical transmission following acute infection in cattle under natural conditions. PLoS One 11(12): e0167163. https://doi.org/10.1371/journal.pone.0167163

Rasmussen P, Shaw AP, Jemberu WT, Knight-Jones T, Conrady B, Apenteng OO, Cheng Y, Muñoz V, Rushton J and Torgerson PR, 2024. Economic losses due to foot-and-mouth disease (FMD) in Ethiopian cattle. Preventive Veterinary Medicine 230: 106276. https://doi.org/10.1016/j.prevetmed.2024.106276

Soltani H, Aslani MR, Mohebbi A and Mokhtari A, 2020. Serum biochemical and oxidative status in Holstein cattle affected with foot and mouth disease. Iranian Journal of Veterinary Science and Technology 12(2): 19-14. https://doi.org/10.22067/VETERINARY.V12I2.85100

Stefan KL, Kim MV, Iwasaki A and Kasper DL, 2020. Commensal Microbiota Modulation of Natural Resistance to Virus Infection. Cell 183(5): 1312-1324.e10. https://doi.org/10.1016/j.cell.2020.10.047

Stenfeldt C, Eschbaumer M, Humphreys J, Medina GN and Arzt J, 2025. The pathogenesis of foot-and-mouth disease virus: current understandings and knowledge gaps. Veterinary Research 56(1): 1-25. https://doi.org/10.1186/s13567-025-01545-5

Sukoco H, Wahyuni S, Utami S, Chayani AP, Andawanari S and Siswanto FM, 2023. Foot and Mouth Disease (FMD): Etiology, Pathogenesis, Prevention and Control in Even or Split Hoofed Livestock. Jurnal Sain Peternakan Indonesia 18(4): 268–273.

Xu Q, Qiao Q, Gao Y, Hou J, Hu M, Du Y, Zhao K and Li X, 2021. Gut Microbiota and Their Role in Health and Metabolic Disease of Dairy Cow. Frontiers in Nutrient 8: 701511. https://doi.org/10.3389/fnut.2021.701511

Yang J, Li Y, Wen Z, Liu W, Meng L and Huang H, 2021. Oscillospira - a candidate for the next-generation probiotics. Gut microbes 13(1): 1987783. https://doi.org/10.1080/19490976.2021.1987783

Zaplana T, Miele S and Tolonen AC, 2023. Lachnospiraceae are emerging industrial biocatalysts and biotherapeutics. Frontiers in Bioengineering and Biotechnology 11: 1-14. https://doi.org/10.3389/fbioe.2023.1324396

Zhang L, Chen F, Zeng Z, Xu M, Sun F, Yang L, Bi X, Lin Y, Gao Y, Hao H, Yi W, Li M and Xie Y, 2021. Advances in Metagenomics and Its Application in Environmental Microorganisms. Frontiers in Microbiology 12: 766364. https://doi.org/10.3389/fmicb.2021.766364

Zhang X, Yu D, Wu D, Gao X, Shao F, Zhao M, Wang J, Ma J, Wang W, Qin X, Chen Y, Xia P and Wan S, 2023a. Tissue-resident Lachnospiraceae family bacteria protect against colorectal carcinogenesis by promoting tumor immune surveillance. Cell Host and Microbe 31(3): 418-432.e8. https://doi.org/10.1016/j.chom.2023.01.013

Zhang Y, Chen R, Zhang D, Qi S and Liu Y, 2023b. Metabolite interactions between host and microbiota during health and disease: Which feeds the other? Biomedicine and Pharmacotherapy 160: 114295. https://doi.org/10.1016/j.biopha.2023.114295