

Genomic and microbiome co-evolution underlying hindgut fermentation in rabbits

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Abstract. Hindgut fermentation in rabbits represents a highly specialized digestive strategy driven by intricate host–microbiome co-evolution. This mini-review synthesizes current evidence from metagenomics, transcriptomics, and integrative multi-omics studies to elucidate the functional interplay between microbial communities and host physiology in lagomorphs. The rabbit cecum harbors a diverse and metabolically specialized microbiota dominated by fibrolytic taxa, primarily within Firmicutes and Bacteroidetes, which mediate the degradation of structural polysaccharides and the production of short-chain fatty acids (SCFAs). Host genomic responses, including spatially regulated expression of nutrient transporters and immune-related genes, are tightly aligned with microbial metabolic outputs. Caecotrophy emerges as a critical adaptive behaviour that reinforces host–microbiome coupling by recycling nutrients and microbial biomass. Comparative analyses highlight distinct fermentative strategies between rabbits and ruminants, notably the predominance of reductive acetogenesis over methanogenesis in hindgut systems. Collectively, these findings underscore the importance of integrated host–microbial networks in optimizing fiber utilization, metabolic efficiency, and ecological adaptation in rabbits.

Keywords: hindgut fermentation, rabbits, microbiome, caecotrophy, fiber digestion, short-chain fatty acids, host–microbiome interaction, metagenomics, transcriptomics, reductive acetogenesis, herbivore digestion.

Introduction. Hindgut fermenting lagomorphs such as rabbits depend on a specialized cecum and caecotrophy to derive energy from fibrous, plant-based diets (Bud et al., 2011; Petrescu-Mag et al., 2011, 2012, 2014). The available studies combine metagenomics, 16S profiling and host transcriptomics to describe how microbial fibrolytic functions, host transport and immune genes, and behaviours like coprophagy integrate into an efficient fiber digestion system, and how this differs from ruminants and other hindgut fermenters.

The aim of this mini-review is to critically synthesize current knowledge on the genomic and microbiome-based mechanisms underlying hindgut fermentation in rabbits, with a particular focus on:

- (i) the functional diversity of fibrolytic microbial communities,
- (ii) the molecular and transcriptomic responses of the host to microbial activity, and
- (iii) the integrative role of caecotrophy in maintaining metabolic efficiency.

Additionally, the review seeks to contextualize rabbit hindgut fermentation within a broader comparative framework by contrasting it with fermentative strategies in ruminants and other hindgut herbivores, thereby highlighting evolutionary adaptations and functional convergence in herbivore digestion.

Fiber Digestion: Microbial Genomes and Functional Repertoires. Rabbit cecum and feces are dominated by Firmicutes, Tenericutes and Bacteroidetes, with Ruminococcaceae and Lachnospiraceae as key fibrolytic families, consistent with intensive cellulose/hemicellulose degradation and short chain fatty acid (SCFA) production in the hindgut (Wei et al., 2025; Crowley et al., 2017; Kylie et al., 2018; Bora et al 2025) (Figure 1). In wild European rabbits, high diversity communities enriched in Ruminococcaceae are

functionally associated with cellulases and xylanases, indicating efficient digestion of fiber rich diets, whereas microbiomes dominated by Enterobacteriaceae are richer in amylases and likely favor starch use (Funosas et al., 2021). Metagenomes from the endangered volcano rabbit reveal genes encoding endoglucanases, xylanases, β glucosidases, arabinofuranosidases and multiple tannases, suggesting adaptation to both structural carbohydrates and plant phenolics in high tannin diets (Montes-Carretero et al., 2021).

Among herbivores more broadly, hindgut systems (horses, rabbits, donkeys) show a Firmicutes–Bacteroidetes consortium in which Firmicutes specialize in cellulose and hemicellulose and Bacteroidetes in diverse glycans, jointly supplying acetate, propionate and butyrate as major energy sources (Wei et al., 2025; Zhang et al., 2022). In donkeys, adherent hindgut communities (particle associated fraction) are enriched in Bacteroidota, Fibrobacterota and Spirochaetota and show higher predicted fiber degrading enzyme activities than the liquid phase, emphasizing the role of attached microbiota in plant cell wall breakdown (Zhang et al., 2022). Fungal communities and fibrolytic enzyme assays in donkey colon show higher carboxymethyl cellulase, avicelase, xylanase and acetyl esterase activities than in the cecum, documenting strong distal hindgut fibrolysis (Zhang et al., 2022). Together, these data indicate that, in lagomorphs and related hindgut fermenters, fiber digestion is largely delegated to a diverse microbial gene pool rather than host encoded cellulases (Table 1).

Table 1

Key fiber-degrading taxa and functions across herbivore hindguts

Host / Site	Dominant fibrolytic or fiber-associated taxa	Key predicted/observed functions	References
Rabbit cecum / feces	Ruminococcaceae, Lachnospiraceae, Bacteroidetes	Cellulose/xylan degradation, SCFA (esp. butyrate) production	(Wei et al., 2025; Crowley et al., 2017; Funosas et al., 2021; Kylie et al., 2018)
Volcano rabbit feces	<i>Lachnoclostridium</i> , <i>Acinetobacter</i> , methanogens	Cellulases, xylanases, β -glucosidases, tannases; tannin tolerance	(Montes-Carretero et al., 2021)
Donkey caecum–colon (adherent)	Bacteroidota, Fibrobacterota, Spirochaetota	Particle-associated fiber degradation, higher CAZyme activities	(Zhang et al., 2022)
Donkey caecum–colon fungi	Neocallimastigomycota and other fungi	Enhanced fibrolytic enzyme profiles in colon	(Zhang et al., 2022).

Host–Microbiome Interaction: Transcriptomics, Caecotrophy and Metabolic Integration. Spatial transcriptomics in New Zealand rabbits shows marked compartmentalization: genes for amino acid, sugar, vitamin and bile salt transport are enriched in the small intestine, while those for water and SCFA transport, nucleotide and metal ion uptake are upregulated in cecum and colon, matching the locus of fermentation (Tang et al., 2026). Large intestinal tissues overexpress pattern recognition and bacterial response pathways, consistent with high microbial loads and the need to manage dense fibrolytic communities (Tang et al., 2026). Correlations between microbial abundances and host digestion/absorption genes suggest that specific taxa influence epithelial gene expression, possibly via SCFAs such as butyrate, which can modulate histone acetylation and chemokine expression (Tang et al., 2026).

Caecotrophy emerges as a central behavioural–microbial interface. Rabbits consuming soft feces recycle microbial biomass and vitamins; preventing coprophagy lowers growth, feed efficiency and serum lipids, damages cecal villi, reduces SCFA concentrations, and shifts the microbiota by depleting *Oscillospira*, *Ruminococcus* and other SCFA linked genera (Wang et al., 2023). Metagenomic analysis of caecal contents in soft feces fasted New Zealand rabbits similarly finds increased Bacteroides and decreased *Ruminococcus*, with reduced abundance of genes for riboflavin, ascorbate/aldarate metabolism and bile secretion, and strong correlations between

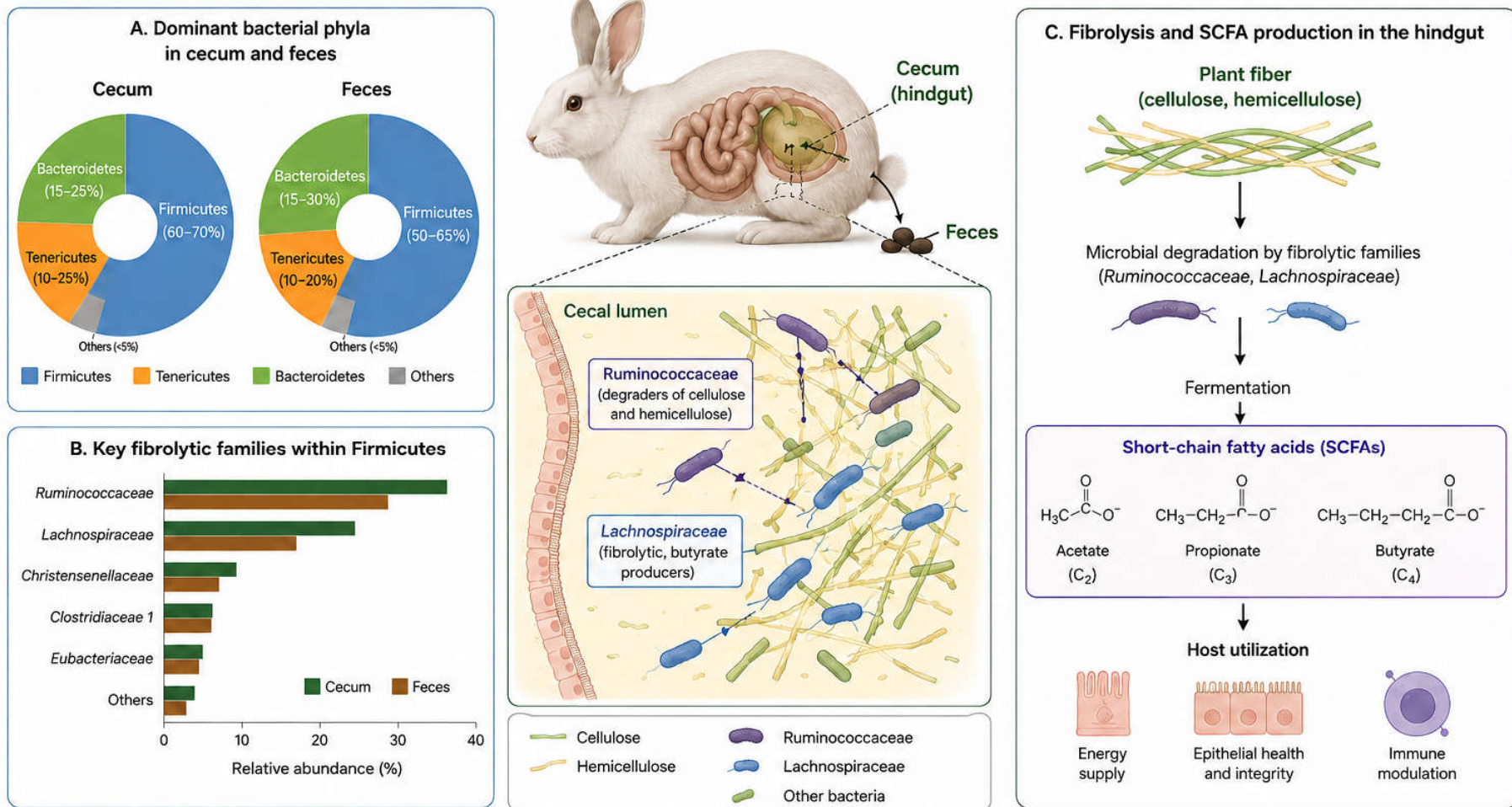
microbial shifts, lipid deposition and body weight (Li et al., 2020). These findings indicate that host lipid metabolism and growth are tightly coupled to the composition and metabolic capacity of cecal communities and to the recycling of those communities through caecotrophy.

In diet induced obese rabbits, cecal multi omics analysis reveals altered microbiota (reduced beneficial species and increased potentially obesogenic taxa) together with differential expression of host genes in calcium, PI3K Akt, Wnt, NF κ B and T cell receptor pathways. Integrative network analysis identifies rabbit specific genes (e.g., LOC103347758, LOC108176404) strongly correlated with specific microbial species, highlighting candidate host loci that may regulate microbiome composition and lipid metabolism (Li et al., 2024). Across herbivores, reviews of multi omics integration emphasize that combining host genome/transcriptome with metagenomic, metabolomic and proteomic data is essential to resolve such causal host–microbe networks, though standardization and large datasets are still lacking (Chetty & Blekman, 2024; Duan et al., 2025; Yang et al., 2025).

Comparative Fermentative Strategies: Rabbits vs Ruminants and Other Hindgut Fermenters. Direct comparison of sheep rumen and rabbit cecum under an identical alfalfa hay diet shows substantially higher methane production in sheep, even when normalized for body weight and fiber digestion. The rabbit cecum has lower pH and a much higher acetate:propionate ratio than the rumen, reflecting different fermentation end products (Mi et al., 2018). Amplicon profiling indicates that hydrogen producing fibrolytic bacteria (e.g. classical ruminal cellulolytics) dominate in the sheep rumen, while non hydrogen producing fibrolytic taxa are more prevalent in the rabbit cecum. The rabbit hindgut is enriched in acetogenic bacteria (multiple genera, orders and families), favoring reductive acetogenesis over methanogenesis and thereby reducing methane output (Mi et al., 2018). This aligns with multi species ruminant work showing that hindguts generally harbor more mucin degrading microbes, fermentative hydrogen producers, and especially reductive acetogens with distinct Wood–Ljungdahl pathway genomes relative to rumen communities (Li et al., 2025). These acetogens are phylogenetically and functionally specialized for hindgut conditions, underscoring convergent evolution of low methane, acetate rich fermentation in posterior compartments (Li et al., 2025).

Across herbivores, foregut (rumen, avian crop) and hindgut (cecum/colon) communities cluster more strongly by organ function than by host phylogeny: foreguts tend to have higher Bacteroidetes and Spirochaetes and lower Firmicutes and Proteobacteria than hindguts, suggesting that the physicochemical niche (location, pH, flow, substrate) is a primary driver of microbiome structure (Godoy-Vitorino et al., 2011; Wei et al., 2025). Within caecotrophic lagomorphs and guinea pigs, next generation sequencing shows significant differences in fecal microbiota, arguing against a single “caecotrophy microbiome”; instead, each host lineage seems to have evolved its own fibrolytic consortium, with rabbits notably rich in Firmicutes and Bacteroidetes but lacking classical Fibrobacteres, implying that alternative lineages supply cellulolytic functions (Crowley et al., 2017). Domestic rabbits from different production systems (meat, companion, laboratory, shelter) consistently show Firmicutes dominance, but husbandry, diet and season modulate proportions of Verrucomicrobia, Proteobacteria and other phyla, indicating environmental shaping of a conserved hindgut fermentation core (Kylie et al., 2018).

At the methodological level, novel spatial transcriptomic approaches now enable in situ mapping of host and microbial transcripts at micrometer resolution in the gut, revealing fine scale host–microbe biogeography and short-range interactions in mouse models (Ntekas et al., 2026). Together with general multi omics integration frameworks (Chetty & Blekman, 2024; Duan et al., 2025; Yang et al., 2025), such tools offer a path to dissecting the genomic and transcriptomic bases of hindgut fermentation and host adaptation in lagomorphs at unprecedented resolution.



The dominance of Firmicutes (especially Ruminococcaceae and Lachnospiraceae) together with Tenericutes and Bacteroidetes supports efficient fiber degradation and SCFA production in the rabbit hindgut.

Figure 1. Rabbit cecum and feces are dominated by Firmicutes, Tenericutes and Bacteroidetes, with Ruminococcaceae and Lachnospiraceae as key fibrolytic families, consistent with intensive cellulose/hemicellulose degradation and short-chain fatty acid (SCFA) production in the hindgut.

Conclusions. Hindgut fermentation in rabbits is a paradigmatic example of host-microbiome co-evolution, in which digestive efficiency is achieved through a finely tuned integration of microbial metabolism, host gene regulation, and adaptive behaviour. The reliance on a diverse microbial gene pool for fiber degradation compensates for the host's lack of endogenous cellulolytic enzymes, while SCFA production serves as a central metabolic bridge between microbes and host tissues.

Spatial compartmentalization of host gene expression reflects a high degree of physiological specialization along the gastrointestinal tract, aligning nutrient absorption and immune modulation with microbial activity. Caecotrophy further enhances this system by enabling the recovery of microbial proteins, vitamins, and metabolites, thereby reinforcing nutritional homeostasis and growth performance.

Comparative analyses demonstrate that rabbits employ a low-methane, acetate-oriented fermentative strategy distinct from that of ruminants, driven by the predominance of reductive acetogenesis. This highlights both functional divergence and convergent evolutionary solutions to herbivory across taxa.

Future research integrating high-resolution multi-omics approaches, including spatial transcriptomics and metabolomics, will be essential for disentangling causal host-microbe interactions and identifying key regulatory networks. Such insights may have broader implications for animal nutrition, ecological adaptation, and the management of gut microbiomes in both wild and domestic herbivores.

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