White Paper

Understanding the gut-organ axes in companion animals

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Editor's Note: *This white paper draws on expert insights from* ***Jess Jarett, Ph.D., R&D*** *Principal Scientist, Pet at Cargill, on how diet-driven modulation of the gut microbiome supports improved pet longevity and overall health based on the Ask the Pet Food Pro Zoom chat, "How the Gut Microbiome Impacts Pet Skin, Joints & Oral Health."*

The relationship between the gut microbiome and systemic health in companion animals represents a dynamic and important area for innovation in pet food formulation. As scientific understanding rapidly advances, we recognize the microbial communities within the gut are not only digestive aids but signaling systems that modulate organ systems including skin, joints and oral health.

Microbiome factors and measurement

Diet is a major factor shaping a companion animal's microbiome. The specific macronutrient compositions of diets, as well as moisture content, help shape microbial communities. Other major influencing factors include:

- **Species:** Cats and dogs have evolved to have differences in the gut microbiome, and cats tend to have more diverse and more consistent microbiome composition compared to dogs.
- **Dietary composition:** Macronutrient balance strongly influences microbial diversity.
- **Moisture content:** The moisture content of the diet also seems to have effects independent of macronutrients.
- **Age:** Microbiomes tend to decline in diversity as pets age, a trend particularly noted in cats.
- **Environment and behavior:** Outdoor access and prey hunting influence exposure to microbes, parasites and pathogens.
- **Physiology:** Eor dogs, differences in body size can help shape the microbiome.
- **Health status:** Obesity and antibiotic use significantly affect microbial balance.

- **Host genetics:** Although genetics play a role, diet and environment have a stronger influence.

Understanding this diversity relies heavily on sequencing-based work, typically using fecal samples for the gut microbiome. Researchers look at the DNA of the bacteria present using methods like examining marker genes (helpful for low biomass sites like the skin) or quantitative methods like the dysbiosis index. Scientists can also analyze the bacteria's entire genomic content to determine which species are present and what metabolic functions they can perform.

The consequences of an unhealthy gut

Gut dysbiosis can negatively affect pet health when the microbial communities in the gut become unbalanced. When the microbiome is compromised, several harmful processes can occur, including impairment of gut barrier integrity, heightened inflammatory signaling, and increased susceptibility to chronic disease. A healthy gut barrier selectively permits nutrient absorption, while preventing inappropriate molecules from entering circulation. Dysbiosis often weakens this barrier, allowing larger or harmful compounds to pass through, which can trigger systemic inflammation. Over time, this persistent inflammatory state is associated with a range of health conditions, including metabolic disorders, liver dysfunction, and immune-mediated diseases.

Among the pro-inflammatory compounds that may arise in a dysbiotic gut are endotoxins, such as lipopolysaccharides (LPS), which originate from gram-negative bacteria. These molecules can activate immune receptors throughout the body, amplifying inflammatory signaling and contributing to chronic disease risk.

The gut-skin axis: Inflammation and barrier function

The gut-skin axis is a bidirectional signaling network between these two interrelated body systems. Early research on the gut-skin axis started with the observation that animals with inflammatory skin conditions (such as canine atopic dermatitis) have altered gut microbiomes. When researchers study circulating metabolites made by the gut, they consistently observe lower levels of beneficial metabolites in individuals with atopic dermatitis.

In experimental models, restoring these beneficial metabolite levels can significantly improve skin health. Fecal microbiome transfer (FMT) experiments have yielded impressive results for atopic dermatitis and other skin conditions. Beneficial gut bacteria produce Short-chain fatty acids (SCFAs), and these compounds, particularly butyrate, strengthen gut barrier integrity. Improved barrier integrity prevents inappropriately large molecules, which can trigger inflammation and allergy, from moving from the gut into circulation.

SCFAs also act as powerful signaling molecules for the immune system. As they circulate, they affect skin barrier function and can subsequently affect the skin's own microbiome. These metabolites can stimulate cell differentiation, aid in the skin's turnover process, affect collagen production and even possess direct antimicrobial properties.

The gut microbiome and the skin communicate and influence each other, and while the gut affects skin health, research in rodents shows that wounding the skin can also alter microbial dynamics in the gut. This crosstalk is highly relevant for pets caught in the itch/scratch cycle.

Formulation intervention

Dietary formulation can support pet health by leveraging functional ingredients such as biotics and influencing gut and immune function. Biotic ingredients (prebiotics, probiotics and postbiotics) can work in several ways: by directly affecting signaling to the host immune system, by modulating the gut microbiome itself (composition, function, metabolite production), or by providing metabolites directly to the pet. This modulation often centers around microbial metabolites, like SCFAs and certain tryptophan metabolites, which interact with specific receptors present in the gut and skin such as the aryl hydrocarbon receptor (AHR). Among other functions, this receptor helps regulate immune responses and epithelial barrier function in both tissues.

Dietary protein choices extend beyond nutrient supply, and should be considered holistically to support epithelial integrity and gut function.

Protein sensitivity: The perception of protein sensitivity may arise from increased gut permeability, allowing large food molecules to enter circulation inappropriately and provoke a reaction. Supporting better gut barrier integrity can mitigate this issue.

SCFA production: Because cats are obligate carnivores and dogs are largely carnivorous, existing digestive knowledge based on human and rodent models may not fully translate. Interestingly, some bacteria in dogs and cats can produce the beneficial SCFA butyrate from protein sources (not just traditional fiber prebiotics). The goal remains promoting microbiomes that produce more SCFAs, especially butyrate, while supporting gut barrier integrity.

The gut-joint axis: Inflammation and cartilage degradation

The connection between the gut and joints is supported by observations that animals or individuals with inflammatory or degenerative joint conditions show differences in their microbiomes.

In much the same way as a healthy gut has continuous turnover by balancing the production and breakdown of its protective mucus, heathy joints undergo a continuous process of cartilage breakdown and remodeling. When the joint process becomes imbalanced and cartilage breaks down faster than it is rebuilt, inflammation occurs. Gut dysbiosis triggers pro-inflammatory signaling processes that can perpetuate these joint problems. Inflammatory markers and even microbial DNA originating from the gut have been observed within the joint itself.

Pet food formulators can address this axis by incorporating ingredients that improve gut barrier integrity and help dial down inflammatory signaling originating from the gut. Research in rodents shows that higher fiber diets increased circulating SCFAs and significantly reduced the severity of arthritis. These results were replicated by simply feeding the SCFAs directly to the rodents.

An important consideration is the individual variability of the microbiome. Since the beneficial effect is microbiome-mediated, not every pet may respond to a diet, as some may not possess the beneficial bacteria that produce the metabolites from dietary components. Promoting the growth of specific key groups (taxa) of microbes has been shown to ease arthritis and inflammatory processes in people. For pets lacking these necessary groups, adding beneficial microbes (probiotics) or their components (postbiotics) directly can provide a protective effect.

The gut-oral axis: Microbial exchange and Systemic pathogen input

The oral microbiome's link to overall health is powerful. Oral dysbiosis and periodontal disease are associated with a wide range of systemic conditions, including irritable bowel disease (IBD), various types of arthritis, diabetes and gastrointestinal cancers.

Periodontal disease starts with bacterial biofilms (slime layers) forming on teeth, which can calcify into calculus. If pathogenic bacteria colonize these biofilms, they release toxins and enzymes, triggering a host immune response and setting up a a positive feedback loop of inflammation and tissue destruction. Pathogens from the mouth are able to enter the rest of the body through immune cells, and even directly into the bloodstream through damaged tissue. Swallowing also transports pathogens to the gut, where they can colonize and disrupt the existing gut microbiome

Microbially mediated inflammation in the gut can promote inflammation in oral tissues, and vice versa. By the same token, experiments in mice show that boosting a healthy microbiome in the gut can improve oral dysbiosis and periodontal disease. This suggests potential for systemically active approaches for supporting oral health, as a complement to interventions that require physical contact in the mouth.

Conclusion

The gut is not an isolated digestive system but a command center communicating directly with the skin, joints and oral cavity via circulating metabolites and inflammatory signals. Understanding these complex, bi-directional axes provide crucial context for developing next-generation pet foods that address common inflammatory issues, from skin sensitivities and joint degradation to oral health, through targeted nutritional strategies.

Formulators and nutritionists can help bridge the gap in pet owner understanding, because many owners draw from human health trends yet have only a vague grasp of how diet influences the pet microbiome. Clear communication from pet industry professionals is essential to correct misconceptions, including the belief that biotic ingredients can solve every health issue.

To learn more about the specific data, research models including the FMT results and Dr. Jarett's insights into modulating these systems, watch the full Zoom chat.

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Jess Jarett leads global R&D for Pet at Cargill, driving research and product development to improve pet health and nutrition. With a particular interest in how the microbiome influences pet health, she brings over 15 years of experience in microbiome research, including 7 years dedicated specifically to pet microbiome studies. She holds a PhD in Microbiology from the University of New Hampshire and has conducted postdoctoral studies in microbial genomics and single-cell genomics at the DOE Joint Genome Institute.