

Hill's ActivBiome+ Kidney Defense

A proprietary prebiotic blend that works from within, altering the gut microbiome to protect kidney function in pets with CKD

THE PROBLEM

Chronic kidney disease (CKD) is a common problem in the aging pet population, particularly cats. CKD is progressive and irreversible, and because clinical signs can be subtle and non-specific, most patients are diagnosed in the later stages of the disease, when management strategies are less likely to be effective. Dietary modification is considered the standard of care for managing CKD and can be highly effective in the early stages of the disease. Controlling protein and phosphorus intake, improving hydration, and introducing therapeutic food are proven to slow disease progression. However, traditional dietary therapy has limitations. Food is likely to be effective only when pets consume enough calories and have a consistent appetite. Because CKD is progressive, patients can still face the challenges of the destructive uremic cycle as the disease advances:

- Damaged kidneys struggle to filter metabolic waste products, leading to their accumulation in the bloodstream.
- Uremia causes inflammation, nausea, anorexia, and muscle wasting.
- Affected pets catabolize lean muscle for energy, generating additional protein byproducts that worsen uremia.

A growing body of evidence points to the gut microbiome as a key component in this process.



Leslie Hancock, DVM

Chief Medical Officer, Hill's Pet Nutrition

Dr. Hancock is a 2001 graduate of the University of Georgia College of Veterinary Medicine with a clinical nutrition post-doctorate from the University of California. Dr. Hancock joined Hill's in 2023 and, as the chief medical officer, leads the global clinical nutrition and claims team. In her free time she enjoys biking, swimming, and sharing her home with all creatures great and small, with a cat, a rabbit, and a horse.



Nicholas L. Rozzi, PhD

VP, Research and Innovation, Hill's Pet Nutrition

Dr. Rozzi leads the Research and Innovation team at Hill's Pet Nutrition, focusing on discovering new nutritional technologies and quantifying their impact on pet health. He advances technology and business goals through internal research and fostering external partnerships. Outside of Hill's Pet Nutrition, Dr. Rozzi volunteers as adjunct faculty at Kansas State University and serves on the board of trustees for the Institute for Feed Education and Research (IFEEDER).

CKD is associated with a specific type of microbial dysfunction of predominantly proteolytic bacteria that ferment amino acids and produce high levels of harmful uremic toxins. These gut-derived toxins promote oxidative injury, inflammation, and fibrosis in renal tissue and have been detected at elevated levels in dogs and cats with CKD of all stages. The toxins are protein-bound and difficult to remove via traditional approaches, underscoring the need for an alternative therapy.

THE SOLUTION

Hill's Pet Nutrition has spent more than a decade researching the gut microbiome and its influence on

various aspects of canine and feline health. This work began with investigations into the effects of microbial activity on gastrointestinal health, with researchers looking at how nutrition can harness their activity for therapeutic value.

This research led to the development of several proprietary ActivBiome+ fiber blend technologies, each designed to address a different need. Hill's scientists recognized that if the gut microbiome was contributing to uremic toxin production in CKD patients, it could also be part of the solution.

The team focused on the gut-kidney axis and identified an opportunity to use targeted nutritional strategies that redirect

microbial activity from proteolytic to saccharolytic fermentation, reducing the production of harmful uremic toxins at their source.

While Hill's Pet Nutrition conducts extensive internal research, its success in scientific breakthroughs is augmented by partnerships, such as the one with researchers at the Harvard T.H. Chan School of Public Health, who have established the One Health Microbiome Resource (OHMR). This collaboration is critical to advancing Hill's microbiome research initiatives and the future of therapeutic canine and feline nutrition. Featuring in-depth analysis of over 2,000 canine and feline gut microbiome samples and standardized computational tools, the OHMR offers the data needed to advance microbiome science.

THE INNOVATION

Hill's Prescription Diet k/d clinical nutrition is shown to add years* and enhance quality of life. It also features ActivBiome+ Kidney Defense, a proprietary blend of

prebiotics that reduces the production of uremic toxins shown to worsen clinical signs of CKD and accelerate disease progression. The blend has three key components:

- **Betaine:** An osmolyte with antioxidant and anti-inflammatory properties that supports cellular hydration and helps protect kidney cells from oxidative damage
- **Oat beta-glucan:** A soluble complex fiber that modulates the microbiome in the distal colon
- **Fructo oligosaccharides (FOS):** A soluble simple fiber that modulates the microbiome in the proximal colon

A dose-response study in dogs showed that concentrations of the fiber blend impact efficacy, with a moderate concentration yielding the greatest reduction in uremic toxins.¹ However, in dogs with early CKD, all test concentrations significantly improved uremic toxin concentrations and antioxidant markers compared with the control food. In crossover studies, cats with

early renal disease fed Hill's Prescription Diet k/d with the ActivBiome+ Kidney Defense prebiotic blend had lower uremic toxin levels compared to controls.² Additionally, cats not only maintained weight, but also showed significant weight gain — a huge win in the battle against weight loss in pets with CKD.

Additionally, dry k/d products include Enhanced Appetite Trigger (E.A.T.), a proprietary technology clinically proven to stimulate appetite and encourage food intake.³

With a foundation of controlled phosphorus, highly digestible protein, precise amino acid concentrations, and E.A.T. technology, the addition of ActivBiome+ Kidney Defense enables k/d products to more effectively manage clinical signs of CKD. ActivBiome+ Kidney Defense is included in all k/d products for cats and dogs, including k/d, k/d + j/d (Kidney + Mobility), and the k/d + Derm Complete & k/d + z/d Hydrolyzed innovation — designed for the management of canine and feline patients with both kidney disease and food allergies.

References

1. Hall JA, Jewell DE, Ephraim E. Feeding cats with chronic kidney disease food supplemented with betaine and prebiotics increases total body mass and reduces uremic toxins. *PLoS One*. 2022;17(5):e0268624. doi:10.1371/journal.pone.0268624
2. Ephraim E, Jewell DE. Effect of added dietary betaine and soluble fiber on metabolites and fecal microbiome in dogs with early renal disease. *Metabolites*. 2020;10(9):370. doi:10.3390/metabo10090370
3. Hill's Data on File. Clinical Report: Fritsch, D.A., Canine E.A.T. Technology Re-substantiation Plan for k/d dry new technology 2023.

*1.5 years on average in dogs and 2 years on average in cats after diagnosis with CKD without any concurrent conditions

