Influencing Immune Response: How Our *Bacillus* Strains Can Play a Role

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How do microbiota affect the immune system?

The immune system is a large network of organs, cells, and proteins that work synergistically to protect the body from foreign invaders. It constitutes the body's

mechanism for fighting off bacterial, viral, and fungal infections. Across all livestock, including poultry, dairy, and swine, the gut microbiome plays a crucial role in shaping and supporting a healthy immune system. In fact, a large proportion of the immune cells in mammalian and avian species reside in the gastrointestinal tract. For instance, in poultry and swine species, 70% of the immune cells are located in the gut![1,2] Further, gut microbiota development and composition is directly tied to immune system maturation and efficacy.[3] In turn, the immune system orchestrates the maintenance of key features of host-microbe symbiosis.

Two types of immunity comprise the overall immune system: innate and adaptive. The innate immune system establishes the more generalized first line of defense against invaders, while the adaptive immune system is involved in a more complex response to a specific threat.[3] The gut microbiome plays a critical role in the modulation and function of both the innate and adaptive responses.

The immune tissues within the gastrointestinal tract must continually sense and respond to beneficial and potentially harmful organisms, and disruptions can have cascading effects on host health. A healthy immune system keeps this equilibrium by increasing or suppressing inflammation levels to respond appropriately to pathogenic threats.[4] Perturbation of the gut microbiome (or dysbiosis) caused by environmental, dietary, pathogenic, or other stressors, can trigger an immune response that could result in harmful levels of inflammation and increased infection susceptibility.[4]

When it comes to beneficial microorganisms, individual strains have differing capacities to influence the immune system. Across dairy, poultry, and swine species, there are examples of probiotic strains shown to regulate inflammation and strengthen resistance to infection.[5,6] Strains have potential to influence both adaptive and innate immune responses and can be screened and chosen to tip the scales in favor of either immune regulation or immune stimulation, depending on the need. One of the ways probiotics can accomplish this is by modulating cytokine and chemokine responses, which are critical immune signaling proteins that control inflammation levels.[7]

Immune Modulation Capabilities of *Bacillus* in the UAH Portfolio

To shed light on how our *Bacillus* strains affect the immune response, *in vitro* mammalian cell culture studies were conducted. CXCL2 is a pro-inflammatory player in the innate immune system, as it directs neutrophils (the "first responder" cells) to fight pathogens at the site of infection.[8] The study reported below explored the levels of a gene marker for the chemokine CXCL2 after

exposure to either health-focused or performance-focused *Bacillus* strains (Figure 1).

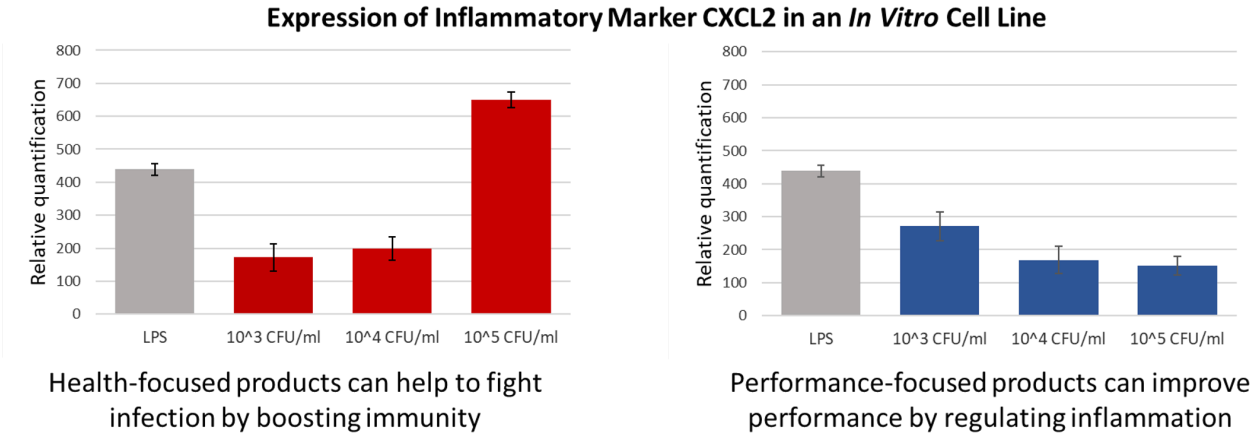

Figure 1: Comparison of CXCL2 gene expression levels in a cell culture model following a two-hour exposure to different concentrations of a health-focused *Bacillus* or a performance-focused *Bacillus* in the presence of lipopolysaccharide (LPS), a component of gram-negative bacterial cell walls. LPS alone was used as a pro-inflammatory positive control.

Our health-focused products are formulated to address complex health challenges. In this test, the expression of CXCL2 was elevated when exposed to the higher dosage of *Bacillus*. Strains in our health-focused products exhibit a pattern similar to this example. This immunostimulatory activity suggests that our health-focused strains can help prime the immune system, preparing it for rapid response to infection and coinfection. In a health-challenged animal, heightened innate immune protection can offer better resistance to pathogens in the system.

On the flip side, immune activation utilizes energy from the host. During periods of low health challenge, unnecessary immune activation can be wasteful, diverting energy away from other functions, including growth. Extreme or prolonged inflammation can even become a source of tissue damage and, ironically, can increase susceptibility to disease. In this study, increased levels of performance-focused *Bacillus* strains led to decreased expression of the CXCL2 marker. Our performance-focused products are targeted toward animals of stable health that would benefit from spending less energy on immune responses. In that environment, greater regulation of CXCL2 and other immune-activating markers is favorable, as this may help protect against unnecessary inflammation and lead to better overall performance.

Immunomodulation: A “Pro” of Probiotics

Administering probiotics (referred to synonymously as direct-fed microbials) to help foster a healthy gut environment can offer advantages that more standard measurements of animal performance may not be able to identify. The results of this study suggest distinct immunomodulatory differences between strains. Our health-focused strains show immune-activating benefits at higher doses, while performance-focused strains demonstrate anti-inflammatory activity. With multiple products in our microbial portfolio, these immunomodulatory effects can be leveraged in a wide variety of circumstances to improve animal health and performance outcomes. These findings highlight one of the important characteristics for which we carefully screen and select our proprietary *Bacillus* strains to ensure beneficial responses in the animal.

Discussion Question

What facets of the immune system would you like to learn about next?

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