The Probiotic LGG[®] and Its Benefits to the Immune System + Key Concepts +

Gut Microbiome

- Microbiome is present throughout the body, with the largest amount in the digestive tract. The gut microbiome provides benefits through nutrient acquisition, including energy balance, the moderation of the immune and nervous system, and regulation of intestinal development and function.¹
- The first 1,000 days—from conception until 2–3 years of age—are the most important, when babies need to be fed a healthy diet. Prior to birth and while breastfeeding, the mother's nutritional status is vital, as she transfers diverse microbiome to the baby. A healthier diet in the first 2 years of life allows for a more diverse microbiome during this period of essential development. The brain, for example, grows 287% during the first 1,000 days, compared with 18% after 1,000 days.^{2,3}



Figure 1 – Why Nutrition Matters: a timeline of critical events during pregnancy and early development, and the role of nutrition.

 The bacteria in the gut produce metabolites, and these metabolites alter the gut microbiome, which alter the immune system. The metabolites produce IL-10, which increase T regulatory anti-inflammatory cells (Tregs) regulated by transforming growth factor β.⁴ The immune system depends on signals from your gut microbiome.

Probiotics

- Probiotics are live microorganisms that, when consumed in an appropriate amount, confer a health benefit to the host. Probiotics require a hospitable environment and need food to survive. Prebiotics are the substrate in which probiotics grow.
- The effect of probiotics depends on the genus vs species vs strain, as well as variability in manufacturing, organism viability, and amount.

Lactobacillus rhamnosus GG

 The strain *Lactobacillus rhamnosus* GG (LGG[®]) provides unique properties. It is the most researched probiotic bacterium, investigated in approximately 800 studies with more than 200 clinical trials.⁵ LGG provides benefits for the immune system, as well as gastrointestinal, respiratory, and skin health,

^{1.} Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature*. 2012;486(7402):207-14. doi:10.1038/nature11234

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^{3.} Laue HE, Coker MO, Madan JC. The developing microbiome from birth to 3 years: The gut-brain axis and neurodevelopmental outcomes. *Front Pediatr.* 2022;10:815885. doi:10.3389/fped.2022.815885

^{4.} Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. Cell. 2014;157(1):121-41. doi:10.1016/j.cell.2014.03.011

^{5.} Capurso L. Thirty Years of *Lactobacillus rhamnosus* GG: A Review. *J Clin Gastroenterol.* 2019;53 Suppl 1:S1-S41. doi:10.1097/MCG.00000000001170

Pediatric Nutrition

eg, prevention of atopic skin diseases.^{6,7} LGG plays a role in the immune system by stimulating a nonspecific immune response with an increase in IgA, IgG, IgM. It also inhibits lipopolysaccharides, which are proinflammatory, TNF-alpha, IL-6, and interferon gamma. It upregulates innate and adaptive immunity by modulating the function of dendritic cells, macrophages, and T and B lymphocytes via activation of toll-like receptors.

- LGG secretes the protein p40 kilodalton, which increases barrier cell function to inhibit inflammation, and in turn increase cell survival, mucin production, and IgA production. Through different mechanisms, p40 produces an immediate and a sustained effect on the epithelial layer. p40 supplementation during the neonatal period has been shown to be a preventative strategy for individuals at high risk of IBD. [See Figure 2]
- The first 1,000 days is the critical window where LGG will have the most impact on long-term health. A 2016 animal study showed intake of LGG starting during gestation and continuing through postnatal days 1 to 5, resulted in increased body weight, diversity of microbiome, intestinal proliferation, and tight junction due to an increase in IgA.⁸
- LGG also has been shown to be beneficial in newborns at risk for cow's milk colitis, where the addition of LGG to an extensively hydrolyzed formula in babies with blood in their stool, reduced inflammatory markers in the gut.



Figure 2 – Promotion of Immune Regulation by the Microbiota during Steady State

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Revisit the course, *The Probiotic LGG® and Its Benefits to the Immune System*, at **pnce.org/LGG**

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^{6.} Zuccotti G, Meneghin F, Aceti A, et al. Probiotics for prevention of atopic diseases in infants: systematic review and meta-analysis. *Allergy.* 2015;70:1356-1371. doi:10.1111/all.12700

^{7.} Szajewska H, Horvath A. *Lactobacillus rhamnosus* GG in the primary prevention of eczema in children: a systematic review and meta-analysis. *Nutrients*. 2018;10:1319. doi:org/10.3390/nu10091319

^{8.} Yan F, Liu L, Cao H, et al. Neonatal colonization of mice with LGG promotes intestinal development and decreases susceptibility to colitis in adulthood. *Mucosal Immunol.* 2017;10(1):117-127. doi:10.1038/mi.2016.43