



Boosting the Immune System

The immune system is our vital defense against infectious organisms such as bacteria, viruses and parasites. It is a complex organization of specialized organs and cells integrated throughout the body.

Consumer demand for immune-supporting products across various categories has significantly risen, in the context of the current pandemic. This trend is expected to continue as consumers adapt their nutritional routines to the new normal.

Gut microbiota and mucosal immunity are constantly interacting with each other to maintain an immune balance. Uncontrolled use of antibiotics and changes in the diet pattern can lead to a decrease in *Lactobacillus* or *Bifidobacterium*³ and the short chain fatty acids (SCFAs) they produce. SCFAs promote proliferation of colonic Treg cells, which limit inflammation and maintain intestinal homeostasis. These beneficial bacteria also secrete several immunogenic substances involved in gut immune homeostasis maintenance.⁴

Intestinal permeability (what consumers often call ‘a leaky gut’) also creates vulnerability to infection and enhances the interaction of signals released from harmful bacteria with immune cells, thus promoting a low-grade chronic systemic inflammation.⁵ A balanced gut microbiota is a key to support the development of immune cells and contribute to the fine tuning of immune responses.

57%

of global consumers are more concerned about their immunity as a result of COVID-19¹

73%

of consumers associate probiotics with boosting immune health¹

Immune supplement sales jumped 250% (vs. YAG) March-May, 2020²



ADM's Pioneering Microbiome Research

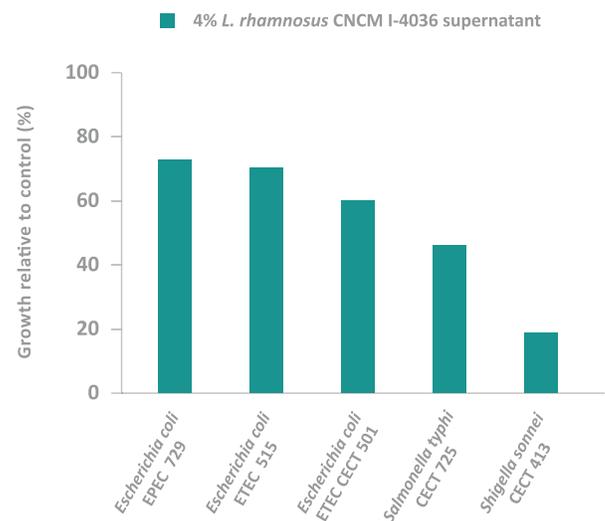
ADM has conducted pre-clinical and clinical research demonstrating the role of the microbiome in multiple different areas of health and wellness, including immunity, metabolic health, obesity and migraines. Recent innovations in analytical techniques have allowed researchers to begin to understand the role of the gut microbiome and its relationship with immunity.

L. rhamnosus CNCM I-4036 was selected from a large collection of strains isolated from breastfed babies. It demonstrated the best levels of pathogen inhibition, as well as immune modulatory characteristics.

Harmful Bacteria- and Inflammation-Inhibiting Effects of *Lactobacillus rhamnosus* CNCM I-4036

Lactobacillus rhamnosus CNCM I-4036 significantly reduces the amount of lipopolysaccharide (LPS) and Tumour Necrosis Factor alpha (TNF- α) concentrations in a murine model of chronic inflammation. LPS is considered an important indicator of gut barrier function and TNF- α is a general marker of inflammation.⁶

In vitro tests have shown that *L. rhamnosus* CNCM I-4036 also significantly inhibits common pathogens. Different strains of human rotavirus, *Listeria monocytogenes*, *Shigella sonnei*, *Salmonella typhi*, *Escherichia coli* enterotoxigenic (ETEC) and *E. coli* enteropathogenic (EPEC) were all inhibited by *L. rhamnosus* CNCM I-4036.^{7,8}



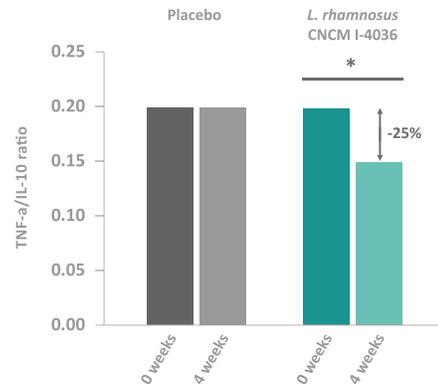
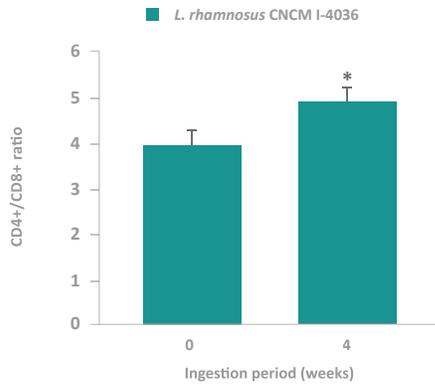
L. rhamnosus CNCM I-4036 has a proven *in vitro* ability to suppress the production of pro-inflammatory cytokines produced by human dendritic cells (DCs) and to produce IL-12, a cytokine that stimulates NK cells to secrete IFN- γ , a critical substance in immune system response to viral infection.⁹

Published Clinical Trial Evidence: Human Clinical Trials

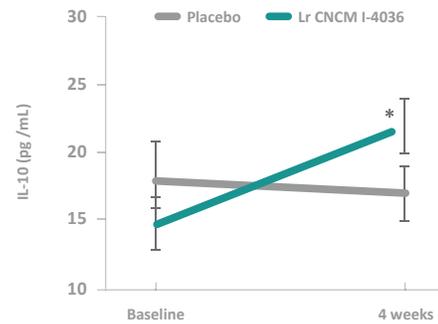
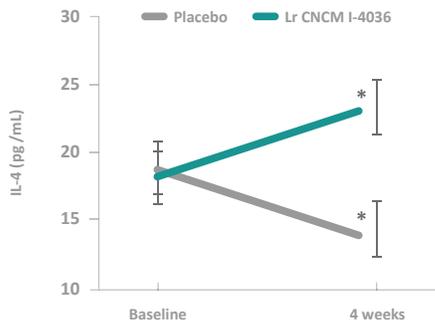
In a double-blind placebo-controlled clinical trial, 21 healthy volunteers (between 18-50 years old) consumed *L. rhamnosus* CNCM I-4036 administration for 30 days/4 weeks.¹⁰

After 30 days of *L. rhamnosus* CNCM I-4036 intake, participants showed a significantly increased CD4+/CD8+ ratio compared to baseline, a common measurement of immune functionality.

C. difficile increased in volunteers fed *L. rhamnosus* immediately after treatment with this strain ceased (t3), indicating a displacement of the pathogen by the probiotic strain.¹⁰



p<0.05 vs baseline



Specifically, *L. rhamnosus* CNCM I-4036 compared to baseline:

- Increased levels of anti-inflammatory molecules
IL-4 +41% **IL-10 +57%**
- Improved anti-inflammatory / pro-inflammatory molecules ratio
IL-10/IL-12 +66%
- Decreased levels of the pro-inflammatory index
TNF-α/IL-10 -25%

The robust potential immunomodulating effects of *L. rhamnosus* CNCM I-4036 position it as a promising strain for immune function solutions.

In a pre-clinical model, the probiotic strain *L. rhamnosus* CNCM I-4036 has been shown to:

- Inhibit a range of harmful bacteria
- Enhance the gastrointestinal barrier function
- Enhance the innate immune system
- **Increase CD4+/CD8+ ratio vs. baseline**

More Applications, More Benefits

Through pre-clinical discovery and clinical assessment, ADM has a depth and breadth of expertise to support our growing range of cutting-edge microbiome solutions:



dairy products



dietary supplements



infant nutrition

Ingredients	Concentration	Format
<i>Lactobacillus rhamnosus</i> CNCM I-4036 – Immune Function Ingredients	CFU/g 3, E+11	Bulk powder

SPECIFICATIONS

Maltodextrin-based probiotic powder

SOURCES

- ¹ Mintel, (2020)
- ² Nielsen, June (2020)
- ³ Singh, R.K. et al. (2017) *J Transl Med.* 15(1): 73
- ⁴ Zheng, D., et al. (2020) *Cell Res.* 30: 492–506
- ⁵ Shin, W & Kim HJ. (2018) *Proc Natl Acad Sci USA.* Nov 6; 115(45): E10539-E10547
- ⁶ Plaza-Diaz, J., et al. (2014) *PLoS One.* 9(5): p. e98401
- ⁷ Munoz-Quezada, S., et al. (2013) *Br J Nutr.* 109 (S2): p. S51-62
- ⁸ Munoz-Quezada, S., et al. (2013) *Br J Nutr.* 109 (S2): p. S63-S69
- ⁹ Bermudez-Brito, M., et al. (2014) *Br J Nutr.* 2014. 111(10): p. 1727-37
- ¹⁰ Plaza-Diaz, J., et al. (2013) *PLoS One.* 8(10): p. e78111

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ADM DELIVERS FOR YOU

Lactobacillus rhamnosus CNCM I-4036 – Immune Function joins our cutting-edge microbiome solutions portfolio.

An innovative leader in the microbiome field, ADM delivers future-forward nutrition fueled by science, with a complete range of solutions from prebiotic to probiotic and postbiotic strains, all clinically documented to deliver consumer benefits.

An expansive pantry of health & wellness ingredients including biotics, botanical extracts, vitamins, minerals and more means you can deliver innovative, science-driven supplements and food & beverage formulations to meet consumers' evolving functional nutrition needs. With our vertically integrated supply chain to ensure the reliability and availability of high-quality products and our dependable customer service, you get industry-leading quality solutions to ensure your success.

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