

ImmunoTools *special* Award 2015



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Effect of immunobiotic supplementation on immune health and resistance to infectious diseases in healthy older people

Certain probiotic lactic acid bacteria (LAB) strains can exert their beneficial effect on the host through their immunomodulatory activity. These strains have been termed immunobiotics. Research from the last years indicate that immunobiotic bacteria could be used for the development of new prophylactic strategies that could be effective tools to protect against respiratory infections. In this regard, by using animal models of high risk populations (infant, elderly and immunocompromised malnourished mice), our laboratory demonstrated that the immunobiotic strain *Lactobacillus rhamnosus* CRL1505 is able to improve protection against respiratory pathogens including *Streptococcus pneumoniae*, influenza virus, and respiratory syncytial virus.

Our studies showed that immunobiotic treatment is able to improve IgA production in the respiratory tract. We also demonstrated that *L. rhamnosus* CRL1505 augment the number of intestinal CD3⁺CD4⁺IFN- γ ⁺ T cells, and induce a mobilization of these cells into the respiratory tract. Furthermore, a higher production of IFN- γ was observed in blood and in the respiratory tract of *L. rhamnosus* CRL1505-treated mice. IFN- γ secreted in response to the CRL1505 strain is capable of functionally modulate the innate immune microenvironment in the lung, inducing the activation of CD103⁺MHC-II⁺ and CD11b^{high}MHC-II⁺ dendritic cells and macrophages. Then, *L. rhamnosus* CRL1505 increases respiratory IgA and favor the generation of Th1 immunity with the consequent protection against bacterial and viral respiratory pathogens.

In addition, our laboratory performed a randomized controlled trial in children under 5 years old in order to evaluate whether a probiotic yogurt containing *L. rhamnosus* CRL1505 was able to beneficially modulate both gut and non-gut related illnesses. We demonstrated that the intervention with the immunobiotic strain CRL1505 was able to reduce the frequency and severity of mucosal infections (intestinal and respiratory) in young children; and that this protective effect was related to an improvement of mucosal immunity. It was also found that in children who consumed *L. rhamnosus* CRL1505, the presence of fever and the need for antibiotic treatment were significantly reduced when compared to the placebo control group, indicating less serious infections.

Based on the results obtained by our laboratory and given the high morbidity and mortality in children especially associated with airways infectious diseases, dietary intervention using a dairy product containing the probiotic strain *L. rhamnosus* CRL1505 can be useful to improve health status of this vulnerable population. The probiotic strain has been included into official National Nutritional Programs in Argentina. Since 2008, the probiotic yogurt containing *L. rhamnosus* CRL1505 (YOGURITO®) is given daily to thousands of children in Tucuman thanks to the Government actions. The use of the immunobiotic CRL1505 strain to improve children health has already transcended the limits of Tucuman province since other provinces in Argentina are also participating in this Social Program.

Another population of high risk for respiratory infection are the elderly. Immunosenescence is a multifaceted decline in the functions of the immune system during progressive aging. In a multitude of ways, the process affects all the arms of the immune system, including respiratory defenses and renders the elderly more prone to infectious diseases and inflammatory disorders. Thus, a particular emphasis is focused on developing food- and nutrition-based strategies to reduce alterations of the aging immune system as an attempt to ultimately boost immunity, prevent infections, and augment healthy aging. Some studies have demonstrated that immunobiotics can be used effectively for this purpose.

The aim of our next project is to evaluate the effect of the probiotic yogurt containing *L. rhamnosus* CRL1505 in immune health of elderly. A randomized-controlled double-blind clinical trial in adults (older than 60 years old), attending care centers will be performed. Yogurt containing CRL1505 will be administered for 6 months (three times a week). Results will be statistically compared with those patients from the same community that received a placebo yogurt (without probiotic). The incidence and severity of infectious diseases will be followed during the studied period. Before and after the treatments mucosal IgA antibodies will be evaluated in saliva. In addition, blood samples will be taken at the beginning and the end of the study in order to evaluate *in vitro* they response to respiratory pathogens and bacterial and viral associated molecular patterns. The diverse cell surface markers for human immune cells and human recombinant cytokines from **ImmunoTools** would be a huge benefit for our *in vitro* studies.

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