

Intranasal and intragastric administration of *L. Paracasei* NCC2461 inhibits respiratory allergic response in mice and induces regulatory T cells

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Good Food. Good Life

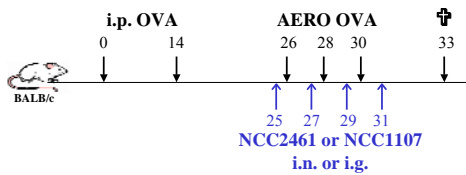
Introduction

Incidence rates of allergy and asthma have strongly increased over the past few decades. One explanation relies on the “hygiene hypothesis” stating that avoidance of microbial exposure can raise the risk of developing allergic disease.¹ Presence of microorganisms in the environment may induce regulatory processes and protect against allergy and asthma.

Probiotics are defined as live microorganisms which when consumed in adequate numbers confer a health benefit on the host.² Probiotics may modulate allergy through regulatory T cells (Treg) which could be induced via microbial stimuli.³ Among probiotic strains, lactobacilli and bifidobacteria are supposed to naturally affect Treg cell development as they are part of the natural gut commensal flora in children.⁴

Several studies showed that probiotic administration was effective at preventing asthma symptoms when administered early in life.^{5,6} Our study shows that modulation can also take place later in life. We used a model of adult sensitized mice to show that established allergy can also be reversed by probiotic administration. Two administration routes were tested (intranasal and intragastric) and two strains were compared (*Lactobacillus paracasei* NCC2461 and *Lactobacillus plantarum* NCC1107).

Methods



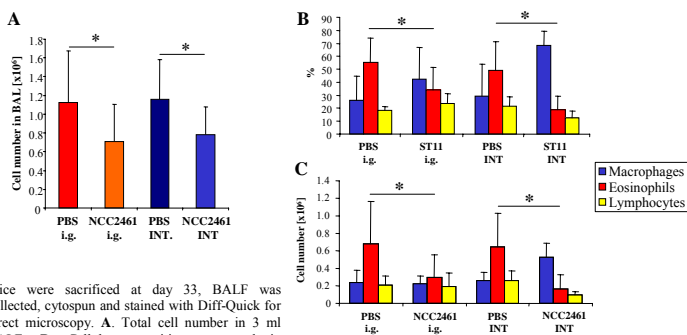
Mice were sensitized intraperitoneally at two weeks interval with 10µg ovalbumin (OVA) in 1mg alum and challenged with OVA aerosols (0.25%) 3 times at indicated days. 1x10⁹ CFU *L. paracasei* NCC2461 or *L. plantarum* NCC1107 strains were administered between aerosol challenges either intragastrically (i.g.) (NCC2461) or intranasally (INT) (NCC2461 or NCC1107).

At day 33, following parameters were measured:

- Inflammatory cell recruitment into bronchoalveolar lavage fluid (BALF)
- Lung histology
- Eotaxin and IL-5 production in the lungs, measured by ELISA
- OVA-specific IgE production in sera, measured by ELISA
- Regulatory T cell subsets from lung extracts, evaluated by flow cytometry.

Results

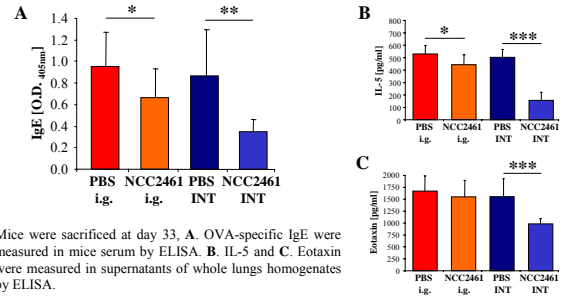
NCC2461 protects efficiently against respiratory allergy



Mice were sacrificed at day 33, BALF was collected, cytospun and stained with Diff-Quick for direct microscopy. A. Total cell number in 3 ml BALF. B. Cellular repartition expressed in percentage. C. Cellular repartition expressed as absolute number of each subpopulation.

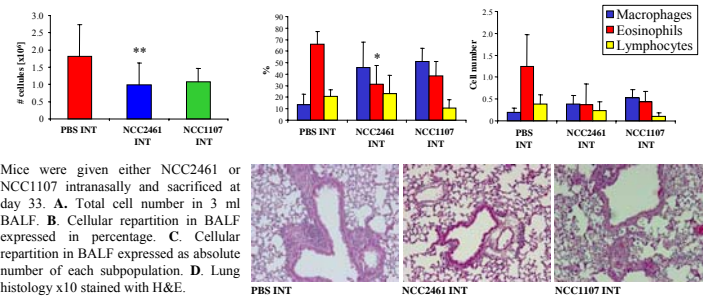
Results

NCC2461 protect against IgE and TH2 cytokines production



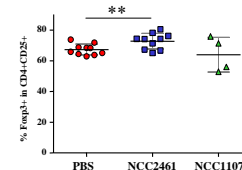
Mice were sacrificed at day 33. A. OVA-specific IgE were measured in mice sera by ELISA. B. IL-5 and C. Eotaxin were measured in supernatants of whole lungs homogenates by ELISA.

NCC2461 is more efficient than NCC1107 to protect against respiratory allergy



Mice were given either NCC2461 or NCC1107 intranasally and sacrificed at day 33. A. Total cell number in 3 ml BALF. B. Cellular repartition in BALF expressed in percentage. C. Cellular repartition in BALF expressed as absolute number of each subpopulation. D. Lung histology x10 stained with H&E.

NCC2461 induces regulatory T cells.



Mice were sacrificed at day 33. Lungs cells were stained with anti-CD4-PE, anti-CD25-PerCP and anti-Foxp3-FITC. Results are expressed as percentage of CD4+CD25+ cells expressing Foxp3.

Conclusions

Both oral and nasal administrations of *L. paracasei* NCC2461 efficiently protected sensitized mice against inflammatory cell recruitment into the BAL upon OVA aerosol challenges, and inhibited OVA-specific IgE production as compared to control mice. Eotaxin and IL-5 secretion in the lungs was also down-regulated. Intranasal administration of NCC2461 induced a stronger and more reproducible down-modulation of the allergic response than intragastric application, and induced an increase in CD4⁺CD25⁺Foxp3⁺ regulatory T cells in the lungs. These effects were weaker when mice were given *L. plantarum* NCC1107 intranasally as control.

L. paracasei NCC2461 administered intranasally or orally specifically display anti-allergic effects in a mouse model of respiratory allergy. This effect may be due, at least in part, to the induction of regulatory T cells.

References

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