Table S1. Non-clinical and clinical studies about the effects of use of probiotics on the viral diseases and immune system.

Non-clinical studies				
Food/Probiotic	**Population**	**Duration**	**Main results**	**References**
The mix of probiotics with *B. breve*, *L. acidophilus*, *L. casei* e *S. thermophiles* (10^9 or 10^8 CFU/kg)	Sprague-Dawley rats with intestinal mucositis	8 days	Improved the chemotherapeutic-induced intestinal mucosal damage and intestinal permeability, possibly reducing levels of pro-inflammatory cytokines and neutrophil infiltration. These results were closely associated with the restoration of intestinal microbial homeostasis and alteration of the TLR2/TLR4 signalling pathway.	(1)
Encapsulated or non-encapsulated probiotic strains administered separately or in association with each group *L. mucosae*, *L. fermentum* (10^8)	Wistar rats with acute inflammation	40 days	The strains separately showed anti-inflammatory activity, showing this potentiated effect when administered together: decreased expression of IL-6, IL-1β, TNF-α, COX-2, iNOS in the rat's paw tissue.	(2)
Bifidobacterium bifidum, (2×10^8 CFU/g)	Female Balb/c mice infected with influenza A (H1N1)	21 days	Decreased of IL-6 level in the lung; increased of IgG level in the blood, lymphocyte proliferation, IL-4, IL-12, and IFN-γ levels (balance of cytokine production) in the splenocyte; and improved of survival rate.	(3)
Bifidobacterium adolescentis (3×10^9 CFU/mL)	Sprague-Dawley rats with acute liver injury	14 days	Decreased serum levels of ALT, total bile acid and lipopolysaccharide-binding protein; improved expression of MUC-4 that acts to protect the colon's epithelial cells, reduced levels of the inflammatory cytokines TNF-α and IL-6, and increased anti-inflammatory cytokine IL-10 in the liver and blood.	(4)
Lactobacillus fermentum (10^9 CFU/day)	Hypertensive Wistar rats	4 weeks	Reversed intestinal dysbiosis, improved the endothelium-dependent vasodilator responses in hypertension, reduced the vascular oxidative stress and pro-inflammatory state, which are the initial stages of the atherosclerotic process.	(5)
Heat-killed *Enterococcus faecalis* KH2 (8.5×10^{10} CFU/ kg/ day)	CCR2-deficient and C57BL/6 mice infected with influenza A virus	12 days	Reduction of loss of body weight; elevation viral titers; reduction of infiltration of neutrophils, lymphocytes, and monocytes, and IL-6 and MCP-1 levels.	(6)
Lactobacillus gasseri SBT2055 (2×10^9 CFU/day)	BALB/cCrSlc mice infected with the respiratory syncytial virus (RSV)	25 days	Decrease of RSV titre in the lung was associated downregulation of SRCAP protein; reduction of proinflammatory cytokines TNF-α, CCL2, IL-1β, and IL-6 in the lung; upregulated type I and type II interferon in the lung (antiviral gene expression).	(7)

Continuation of **Table S1**. Non-clinical and clinical studies about the effects of use of probiotics on the viral diseases and immune system.

Clinical studies				
Food/Probiotic	**Population**	**Duration**	**Main results**	**References**
Yoghurt supplemented with a probiotic strain *Lactobacillus paracasei* (3.6×10^7 CFU/mL)	Elderly with acute upper respiratory tract infections	12 weeks	Reduced the risk of acute infections of the upper respiratory tract and its frequency in the elderly and stimulated T cell immunity, with an increase in CD3 cells.	(8)
Lactobacillus casei Zhang (10^9 CFU/day)	Healthy adults and elderly	12 months	In adults, it relieved the symptoms of lower respiratory tract infections, with reduced duration for nasal, pharyngeal symptoms, general flu and respiratory diseases. Activation of T cells and B cells and anti-inflammatory properties with increased anti-inflammatory cytokines (IL-4 and IL-10). In the elderly, it reduced the duration of nasal symptoms, increased weekly occurrences of defecation and increased CD44 immunomodulatory activity.	(9)
Sachet with *Bifidobacterium lactis* (2×10^9 CFU/day)	Healthy adults	150 days	Reduced the risk of an upper respiratory illness.	(10)
A probiotic fermented drink containing *L. paracasei*, *L. casei* and *L. fermentium* (3×10^7 or 3×10^6 CFU/mL)	Adults with upper respiratory tract infection	12 weeks	Reduced the incidence of upper respiratory tract infection, increased the level of IFN-γ in the blood and IgA in the intestine.	(11)
Capsules with *Lactococcus lactis* (10^{10} CFU/day)	Healthy adults	12 weeks	Reduced the number of incidence days of symptoms related to common cold and influenza in young healthy adults. The mechanism of this reduction was suggested to be via pDC activation and up-regulation of IFN-related genes.	(12)
Yoghurt supplemented with a probiotic strain *Lactococcus lactis* (10^{11} CFU/day))	Healthy adults	10 weeks	The probiotic was able to prevent from decreasing the symptoms caused by the influenza virus, by increasing an IFN-α-mediated response to the influenza virus.	(13)
Bacillus subtilis CU1 (2.10^9 spores)	Common infectious disease (CID) episodes in healthy elderly	40 days	Increased of secretory IgA levels in faecal and salivary.	(14)

ALT, alanine aminotransferase; CCL2, C-C motif chemokine ligand 2; COX-2, cyclooxygenase 2; IFN-γ, interferon-γ; Ig, immunoglobulin; IL, interleukin; iNOS, inducible nitric oxide synthase; MCP-1, monocyte chemoattractant protein-1; MUC-4, mucin 4; pDC, plasmacytoid dendritic cells; TLR, toll like receptor; TNF-α, tumour necrosis factor-α.

Table S2. Non-clinical and clinical studies about the effects of use of prebiotics on the viral diseases and immune system.

Non-clinical studies				
Food/Prebiotic	**Population**	**Duration**	**Main results**	**References**
Diet added of 30% inulin (high fibre diet, HFD)	BALB/c or C57BL/6 adult female mice	8 weeks	The HFD increased survival of mice infected with influenza A virus through the enhanced generation of $Ly6c^{-}$ patrolling monocytes, increased of alternatively activated macrophages counts and CD8+ T cell effector function, and reduced neutrophil recruitment.	(15)
Houttuynia cordata polysaccharide (40 mg/kg/day)	H1N1 virus infected male BALB/c mice	4 days	Restored the level of zonula occludens-1, and reduced of Toll-like receptors and interleukin-1β levels in intestine.	(16)
Human milk oligosaccharide (2′-fucosyllactose, 2' -FL) and GOS/FOS (0.2 and 0.8 g/100 g of body weight/day, respectively)	Lewis neonatal rats	16 days	2' -FL and GOS/FOS ameliorate rotavirus-induced diarrhoea. 2' -FL promote intestinal maturation and regulated neonatal immune responses (IgG, IgA, IL-1β, IL-6, IL-12, IFN-γ, and TNFα); GOS/FOS induced an intestinal trophic effect and a rotavirus blocking action.	(17)
Diet added of a mixture of short-chain GOS, long-chain FOS, and 2' -FL (2%)	BALB/c female and male mice	89 days	Controlled production of IgG in male mice after trivalent influenza vaccine.	(18)
Oligosaccharides from green algae *Ulva lactuca* and *Enteromorpha prolifera*	Male senescence-accelerated prone (SAMP8) mice	10 weeks	Reduction of serum IFN-γ, TNF-α, and IL-6 levels.	(19)
GOS, FOS, inulin and anthocyanins (1.26 mg/g body weight)	Female C57BL/6 mice, post-infectious Irritable bowel syndrome model	16 weeks	Reduction of TNF-α in colon tissues, increase of expression of tight junction protein occludin and PPARγ (inhibit the production of inflammatory cytokines).	(20)
Chitosan oligosaccharide (200 mg/kg/day)	Male Sprague-Dawley rats	4 weeks	Reduced lymphocytes, TNF-α and IL-2 blood counts; increased T cells and eosinophils counts in the blood.	(21)
Diet added of Galacto-oligossacarídeo (1%)	BALB/c male mice with house dust mite (HDM)–induced asthma	4 weeks	Reduced airway eosinophilia and pro-inflammatory IL-33 level.	(22)

Continuation of **Table S2.** Non-clinical and clinical studies about the effects of use of prebiotics on the viral diseases and immune system.

Clinical studies				
Food/Prebiotic	**Population**	**Duration**	**Main results**	**References**
Total dietary fibre (10.75 g/day to 17.5 g/day)	Adults (40 to 79 years)	One year	Higher fibre intake was associated with normal lung function and a significant decline in the proportion of participants with airflow restriction. Low fibre intake was associated with reduced measures of lung function.	(23)
Inulin-type β2-1 fructans (8g/day) in the form of Orafti® Synergy1	Healthy middle-aged individuals	8 weeks	In two weeks of post-vaccination, the inulin-type β2-1 fructans consumption increased the antibodies to the H3N2-like hemagglutinin type 3, neuraminidase type 2-like strain, and serum vaccine-specific IgG1.	(24)
GOS and polydextrose (ratio 1:1)	Healthy-term infants	12 months	Reduction of diarrhoea, fever and respiratory tract infections episodes.	(25)
GOS and polydextrose (4 g/L)	Infants at high risk of atopy	48 weeks	Reduction of the incidence of respiratory infections and atopic dermatitis, and increased *Bifidobacterium* and *Clostridium* cluster I colonization.	(26)
20 g mixture of prebiotics: (5 g GOS/ 10g FOS/ 5g glutamine)	HIV-infected subjects	6 weeks	The short dietary supplementation attenuated HIV-associated dysbiosis. Increases of the butyrate production, reduction of T-cell activation, and amelioration of the inflammatory biomarkers (soluble CD14 and high-sensitivity C-reactive protein).	(27)

FOS, fructooligosaccharides; GOS, galactooligosaccharides; HIV, human immunodeficiency virus; IFN-γ, interferon-γ; Ig, immunoglobulin; IL, interleukin; PPARγ, peroxisome proliferator-activated receptor γ; TNF-α, tumour necrosis factor-α.

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