

# LcS Topic: Immune function

*Lactobacillus casei* Shirota (LcS) is the unique probiotic strain in Yakult

For further information visit our website: [www.yakult.co.uk/hcp](http://www.yakult.co.uk/hcp)  
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Contact the Irish science team on [science@yakult.ie](mailto:science@yakult.ie) or 01 804 7695

Last updated 22 October 2014  
Please also see LcS Topic: IBD

## Healthy people: immune parameters

### **Probiotic modulation of dendritic cell function is influenced by ageing.**

You J, Dong H, Mann ER et al (2014) *Immunobiology* **219**:138-148.  
[PubMed]

### **Immunomodulatory effects of a probiotic drink containing *Lactobacillus casei* Shirota in healthy older volunteers.**

Dong H, Rowland I, Thomas LV, Yaqoob P (2013) *European Journal of Nutrition* **52(8)**:1853-1863.  
[PubMed]

### **Efficacy of daily intake of *Lactobacillus casei* Shirota on respiratory symptoms and influenza vaccination immune response: a randomized double-blind, placebo-controlled trial in healthy elderly nursing home residents.**

Van Puyenbroeck K, Hens N, Coenen S et al (2012). *American Journal of Clinical Nutrition* Epub 22 March  
[PubMed]

### **Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes.**

Gleeson M, Bishop NC, Oliveira M, Tauler P (2011) *International Journal of Sport Nutrition & Exercise Metabolism* **21**:55-64.  
[Reprint available on request] [Abstract]

### **Daily intake of *Lactobacillus casei* Shirota increases natural killer cell activity in smokers.**

Reale M, Boscolo P, Bellante V et al (2011) *British Journal of Nutrition* **108(2)**:308-314.  
[PubMed]

### **Probiotic *Lactobacillus casei* Shirota supplementation does not modulate immunity in healthy men with reduced natural killer cell activity.**

Seifert S, Bub A, Franz CM et al (2011) *Journal of Nutrition* doi: 10.3945/jn.110.13644  
[PubMed]

### **Probiotics affect the clinical inflammatory parameters of experimental gingivitis in humans.**

Slawik S, Staufienbiel I, Schilke R et al (2011) *European Journal of Clinical Nutrition* doi:10.1038/ejcn.2011.45  
[PubMed]

### **A pilot study investigating the effects of Yakult fermented milk drink (*L. casei* Shirota) on salivary IFN- $\alpha$ , sIgA, IgA1 and IgA2 in healthy volunteers.**

O'Connell EJ, Allgrove J, Pollard L, Xiang M, Harbige LS (2010). *Proceedings of the Nutrition Society* 69 (OCE3), E267.  
[Free paper]

**The influence of a probiotic milk drink on the development of gingivitis: a pilot study.**  
Staab B, Eick S, Knofler G, Jentsch H (2009). *Journal of Clinical Periodontology* **36**: 850-856.  
[PubMed]

**The effect of 14 days supplementation with a probiotic on circulating hormonal, leukocyte, and cytokine responses to prolonged cycling in man.**  
Gleeson M (2008) *International Journal Probiotics & Prebiotics* **3(3)**: 185. Also: Poster at 13th European College of Sport Science Congress 09-12 July, Estoril Portugal. Abstract-ID:1991.

**Effects of a fermented milk drink containing *Lactobacillus casei* strain Shirota on the human NK-cell activity.**  
Takeda K & Okumura K (2007) *Journal of Nutrition* **137 (Suppl)**: 791S-793S.  
[Free paper] [PubMed]

**Modulation of natural killer cell activity by supplementation of fermented milk containing *Lactobacillus casei* in smokers.**  
Morimoto K, Takeshita T, Nanno M, Tokudome S, Nakayama K (2005) *Preventive Medicine* **40**: 589-594.  
[Reprint available on request] [PubMed]

**Effects of a fermented milk drink containing *Lactobacillus casei* strain Shirota on the immune system in healthy subjects.**  
Nagao F, Nakayama M, Muto T, Okumura K (2000). *Bioscience Biotechnology and Biochemistry* **64(12)**: 2706-2708.  
[PubMed]

## Allergy

**Effect of probiotic *Lactobacillus casei* L. shirota strain in patients with allergic rhinitis symptoms.**  
Widuri A, Suryani L (2013) *Allergy* **68 (suppl 98)** 60.

**Oral delivery of a probiotic induced changes at the nasal mucosa of seasonal allergic rhinitis subjects after local allergen challenge: A randomised clinical trial**  
Ivory K, Wilson AM, Sankaran P *et al* (2013) *PLoS One* **8(11)**: e78650.  
[Free paper] [PubMed]

**Immunomodulatory effects of potential probiotics in a mouse peanut sensitization model.**  
Meijerink M, Wells J, Taverne N *et al* (2012) *FEMS Immunology & Medical Microbiology* April 28  
doi:10.1111/j.1547-695x.2012.00981x  
[PubMed]

**Strain-specific immunomodulatory effects of *Lactobacillus plantarum* strains on birch-pollen-allergic subjects out of season.**  
Snel J, Vissers YM, Smit BA *et al* (2011) *Clinical & Experimental Allergy* **41(2)**: 232-242  
[PubMed]

**Oral delivery of *Lactobacillus casei* Shirota modifies allergen-induced immune responses in allergic rhinitis.**  
Ivory K, Chambers SJ, Pin C, Prieto E, Arques JL, Nicoletti C (2008) *Clinical and Experimental Allergy* **38(8)**:1282-9.  
[Reprint available on request] [Pubmed]

**Effects of probiotics on allergic rhinitis induced by Japanese cedar pollen: randomized double-blind, placebo-controlled clinical trial.**  
Tamura M, Shikina T, Morihana T *et al* (2007) *International Archives of Allergy & Immunology* **143(1)**: 75-82.  
[PubMed]

***Lactobacillus casei* strain Shirota suppresses serum immunoglobulin E and immunoglobulin G1 responses and systemic anaphylaxis in a food allergy model.**

Shida K, Takahashi R, Iwadate E *et al* (2002) *Clinical and Experimental Allergy* **32(4)**: 563-570.

[PubMed]

## HTLV-1 associated myelopathy

**Immunogenetics and the pathological mechanisms of human T-cell leukemia virus type 1- (HTLV-1-) associated myelopathy/tropical spastic paraparesis (HAM/TSP).**

Saito M (2010) *Interdisciplinary Perspectives on Infectious Disease*. Article ID 478461 doi:10.1155/2010/478461

[Free article] [PubMed]

**A prospective uncontrolled trial of fermented milk drink containing viable *Lactobacillus casei* strain Shirota in the treatment of HTLV-1 associated myelopathy/tropical spastic paraparesis.**

Matsuzaki T, Saito M, Usuku K, Nose H, Izumo S *et al* (2005) *Journal of the Neurological Sciences* **237**: 75-81

[PubMed]

## Liver disease

**Perioperative synbiotic treatment to prevent postoperative infectious complications in biliary cancer surgery: A randomized controlled trial.**

Sugawara G, Nagino M, Nishio H *et al* (2006) *Annals of Surgery* **244(5)**:706-714.

[Free paper] [PubMed]

**Effect of probiotic treatment on deranged neutrophil function and cytokine responses in patients with compensated alcoholic cirrhosis.**

Stadlbauer, V, Mookerjee, RP, Hodges, SJ, Wright, G, Davies, NA and Jalan, R (2008) *Journal of Hepatology* **48(6)**: 945-951.

[Reprint available on request] [PubMed]

## Necrotising enterocolitis

**Efficacy of *Bifidobacterium breve* and *Lactobacillus casei* oral supplementation on necrotizing enterocolitis in very-low-birth-weight preterm infants: a double-blind, randomized, controlled trial.**

Braga TD, da Silva GA, de Lira PIC *et al* (2011) *American Journal of Clinical Nutrition* **93**:81-86.

[Free paper] [PubMed]

## Mechanistic & safety studies

(for further papers see LcS topics on IBD and cancer)

**Heat-killed probiotic bacteria differentially regulate colonic epithelial cell production of human b-defensin-2: dependence on inflammatory cytokines.**

Habil N, Abate W, Beal J *et al* (2014) *Beneficial Microbes* **5(4)**:483-495.

[Free paper] [PubMed]

**Transposon mutagenesis of probiotic *Lactobacillus casei* identifies *asnH*, an asparagine synthetase gene involved in its immune-activating capacity.**

Ito M, Kim Y-G, Tsuji H *et al* (2014) *PLOS ONE* **9(1)**:e83876.

[Free article] [PubMed]

**In case of obesity, longevity-related mechanisms lead to anti-inflammation.**

Kaya MS, Bayiroglu F, Mis L *et al* (2014) *Age* doi 10.1007/s11357-013-9598-8  
[PubMed]

**Immune modulatory mechanisms of Yakult in prevention of colitis-associated colorectal cancer.**

Pang Z, Shaopeng Y (2013) *Journal of Gastroenterology & Hepatology* **28** (Suppl 3): 852.  
[Abstract]

**Lactobacilli regulate *Staphylococcus aureus* 161:2-induced pro-inflammatory T-cell responses *in vitro*.**

Hailesalassie Y, Johansson MA, Zimmer CL *et al* (2013) *PLoS ONE* **8(1)**:e77893  
[Free paper] [PubMed]

**Dysregulated circulating dendritic cell function in ulcerative colitis is partially restored by probiotic strain *Lactobacillus casei* Shirota.** Mann ER, You J, Horneffer-van der Sluis V *et al* (2013) *Mediators of Inflammation*

Article ID 573576.  
[Free paper] [PubMed]

***Lactobacillus casei* strain Shirota selectively modulates macrophage subset cytokine production.**

Habil N, Beal J, Foey AD (2012) *International Journal of Probiotics & Prebiotics* **7 (1)**:1-12.  
[Abstract]

**Probiotic *Bifidobacterium breve* induces IL-10-producing Tr1 cells in the colon.**

Jeon SG, Tsuji H, Ueda Y *et al* (2012) *PLoS Pathogens* **8(5)**:e1002714. Doi:10.1371/journal.ppat.1002714  
[Free paper] [PubMed]

**Probiotic upregulation of peripheral IL-17 responses does not exacerbate neurological symptoms in experimental autoimmune encephalomyelitis mouse models.**

Kobayashi T, Suzuki T, Kaji R *et al* (2012) *Immunopharmacology & Immunotoxicology* **34(3)**:423-433.  
[PubMed]

**Evidence of immunomodulatory effects of a novel probiotics, *Bifidobacterium longum* bv. *infantis* CCUG 524866.**

You J, Yaqoob P (2012) *FEMS Immunology & Medical Microbiology* doi:10.1111/j.1574-695X.2012.01014.x  
[PubMed]

**Comparative effects of six probiotic strains on immune function *in vivo*.**

Dong H, Rowland I, Yaqoob P (2011) *British Journal of Nutrition* Nov **7**:1-12 [Epub]  
[PubMed]

**Probiotic strain *Lactobacillus casei* Shirota imprints a skin-homing profile on effector T-cells and exhibits dual mechanisms of immunoregulation.**

Mann E, Jialu Y, Bernardo D *et al* (2011) *Immunology* **135** (Suppl 1): 194.  
[Abstract]

**Effect of *Lactobacillus casei* on the production of pro-inflammatory markers in streptozotocin-induced diabetic rats.**

Zarfeshani A, Khaza'ai H, Mohd Ali R *et al* (2011) *Probiotics & Antimicrobial Proteins* **3**:168-174.  
[Abstract]

**Well-controlled proinflammatory cytokine responses of Peyer's patch cells to probiotic *Lactobacillus casei***

Chiba Y, Shida K, Nagata S *et al* (2010) *Immunology* **130**: 352-362.  
[PubMed]

**Selective effects of *Lactobacillus casei* Shirota on T cell activation, natural killer cell activity and cytokine production.**

Dong H, Rowland I, Tuohy K *et al* (2010) *Clinical & Experimental Immunology* **161(2)**:378-88.  
[PubMed]

**Bacterial teichoic acids reverse predominant IL-12 production induced by certain *Lactobacillus* strains into predominant IL-10 production via TLR2-dependent ERK activation in macrophages.**

Kaji R, Kiyoshima-Shibata J, Nagaoka M, Nanno M, Shida K (2010) *Journal of Immunology* **184**: 3505-3513.  
[Free paper] [PubMed]

**Oral administration of probiotic bacteria, *Lactobacillus casei* and *Bifidobacterium breve*, does not exacerbate neurological symptoms in experimental autoimmune encephalomyelitis.**

Kobayashi Y, Kato I, Nanno M *et al* (2010) *Immunopharmacology & Immunotoxicology* **32 (1)**: 116-124.  
[PubMed]

**Essential role of IL-6 trans-signaling in colonic epithelial cells, induced by the IL-6/soluble IL-6 receptor derived from lamina propria macrophages, on the development of colitis-associated premalignant cancer in a murine model.**

Matsumoto S, Hara T, Mitsuyama K *et al* (2010) *Journal of Immunology* **184(3)**: 1543-1551.  
[Free article] [PubMed]

**Peptidoglycan from lactobacilli inhibits interleukin-12 production by macrophages induced by *Lactobacillus casei* through Toll-like receptor 2-dependent and independent mechanisms.**

Shida K, Kiyoshima-Shibata, Kaji R, Nagaoka M, Nanno M (2009) *Immunology* **128 (Suppl 1)**: e858-e869.  
[Free paper] [PubMed]

**Suppressive effect on activation of macrophages by *Lactobacillus casei* strain Shirota genes determining the synthesis of cell wall-associated polysaccharides.**

Yasuda E, Serata M, Sako T (2008) *Applied and Environmental Microbiology* **74(15)**: 4746-4755  
[Free article] [PubMed]

**A component of polysaccharide peptidoglycan complex on *Lactobacillus* induced an improvement of murine model of inflammatory bowel disease and colitis-associated cancer.**

Matsumoto S, Hara T, Nagaoka M *et al* (2009) *Immunology* **128 (suppl 1)**: e170-e180.  
[PubMed]

**Strain-dependent effects of probiotic lactobacilli on EAE autoimmunity.**

Maassen CBM, Claassen E (2008) *Vaccine* **26(17)**:2056-2057  
[Reprint available on request]

**Differential effects of two probiotic strains with different bacteriological properties on intestinal gene expression, with special reference to indigenous bacteria.**

Shima T, Fukushima K, Setoyam H *et al* (2008) *FEMS Immunology and Medical Microbiology* **52(1)**: 69-77.  
[PubMed]

**Relationship between the *in vitro* response of dendritic cells to *Lactobacillus* and prevention of tumorigenesis in the mouse.**

Takagi A, Ikemura H, Matsuzaki T *et al* (2008) *Journal of Gastroenterology* **43**: 661-669.  
[PubMed]

**Intestinal microflora: probiotics and autoimmunity.**

Matsuzaki T, Takagi A, Ikemura H, Matsuguchi T, Yokokura T (2007) *Journal of Nutrition* **137**: 798S-802S.  
[Free article] [PubMed]

**Interleukin-12 is involved in the enhancement of human natural killer cell activity by *Lactobacillus casei* Shirota.**

Takeda K, Suzuki T, Shimada SI *et al* (2006) *Clinical & Experimental Immunology* **146(1)**:109-115.  
[Free article] [PubMed]

**Induction of interleukin-12 by *Lactobacillus* strains having a rigid cell wall resistant to intracellular digestion.**

Shida K, Kiyoshima-Shibata J, Nagaoka M *et al* (2006) *Journal of Dairy Science* **98**: 3306-3317.  
[Free article] [PubMed]

**Essential roles of monocytes in stimulating human peripheral blood mononuclear cells with *Lactobacillus casei* to produce cytokines and augment natural killer cell activity.**

Shida K, Suzuki T, Kiyoshima-Shibata J *et al* (2006) *Clinical & Vaccine Immunology* **13(9)**: 997-1003.  
[Free article][PubMed]

**Enhanced immunological memory responses to *Listeria monocytogenes* in rodents, as measured by delayed-type hypersensitivity (DTH), adoptive transfer of DTH, and protective immunity, following *Lactobacillus casei* Shirota ingestion.**

De Waard R, Claasen E, Bokken GCAM *et al* (2003) *Clinical & Diagnostic Laboratory Immunology*,**10(1)**: 59-65.  
[Free article]

**Effect of an oral administration of *Lactobacillus casei* strain Shirota on the natural killer cell activity of blood mononuclear cells in aged mice.**

Hori T, Kiyoshima J, Yasui H (2003) *Bioscience Biotechnology and Biochemistry* **67**: 420-422.  
[Free article] [PubMed]

**Lipoteichoic acid from *Lactobacillus* strains elicit strong tumor necrosis factor alpha-inducing activities in macrophages through Toll-like receptor 2.**

Matsuguchi T, Takagi A, Matsuzaki T *et al* (2003) *Clinical Diagnostic Laboratory Immunology* **10(2)**: 259-266.  
[PubMed]

**Augmentation of cellular immunity and reduction of influenza virus titer in aged mice fed *Lactobacillus casei* strain Shirota.**

Hori T, Kiyoshima J, Shida K, Yasui H (2002) *Clinical and Diagnostic Laboratory Immunology* **9**: 105-108.  
[PubMed]

**Induction by a lactic acid bacterium of a population of CD4+ T cells with low proliferative capacity that produce transforming growth factor  $\beta$  and interleukin-10.**

Von der Weid T, Bulliard C, Schiffrin EJ (2001) *Clinical & Diagnostic Laboratory Immunology* **8**:695-701.  
[Free paper] [PubMed]

## Reviews

**Immune system stimulation by probiotic microorganisms.**

Ashraf R & Shah NP (2014) *Critical Reviews in Food Science & Nutrition* **54**:938-956.  
[PubMed]

**Probiotics, prebiotics and immunomodulation of gut mucosal defences: homeostasis and immunopathology.**

Hardy H *et al* (2013) *Nutrients* **5**, 1869-1912 (open access).  
[Free paper] [PubMed]

**Flexible cytokine production by macrophages and T cells in response to probiotic bacteria.**

Shida K, Nanno M, Nagata S (2011) *Gut Microbes* **2(2)**:109-114,  
[Free paper] [PubMed]

**Therapeutical use of probiotic formulations in clinical practice.**

Iannitti T & Palmieri B (2010) *Clinical Nutrition* **29(6)**: 701-725  
[PubMed]

**Probiotic-host communication. Modulation of signaling pathways in the intestine.**  
Thomas CM & Versalovic J (2010) *Gut microbes* 1:3, 148-163  
[Free paper]

**Probiotics and immunology: separating the wheat from the chaff.**  
Shida K & Nanno M (2008) *Trends in Immunology* **29**: 565-573  
[PubMed]

**Intestinal microflora: probiotics and autoimmunity.**  
Matsuzaki T, Takagi A, Ikemura H *et al* (2007) *Journal of Nutrition* **137**:798S-802S.  
[Free paper] [PubMed]

**Molecular and cellular basis of microflora-host interactions.**  
Winkler P, Ghadimi D, Schrezenmeir J, Kraehenbuhl JP (2007) *Journal of Nutrition* **137 (3)**: 756S-772S  
[Free article] [PubMed]

**Modulating immune responses with probiotic bacteria.**  
Matsuzaki T & Chin J (2000) *Immunology & Cell Biology* **78(1)**: 67-73.  
[Free article] [PubMed]