

Gwénaël JAN

Science & Technology of Milk and Eggs

<http://www6.rennes.inra.fr/stlo>



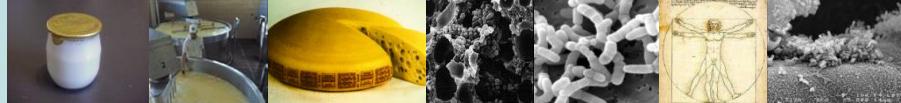
A multidisciplinary and multiscale approach,
reinforced by two high-calibre facilities:

Dairy Platform

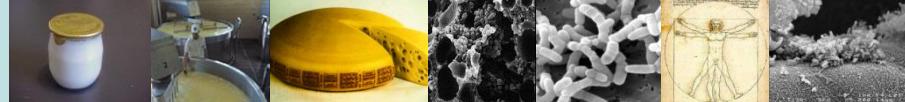


Biological Resource Centre

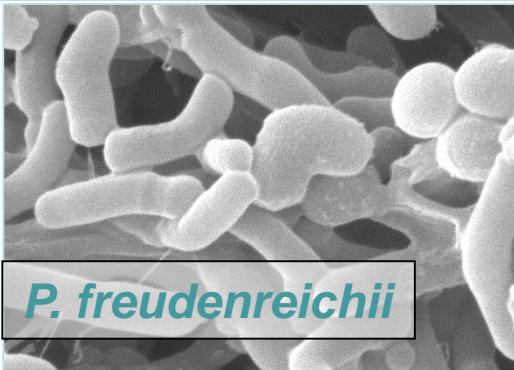
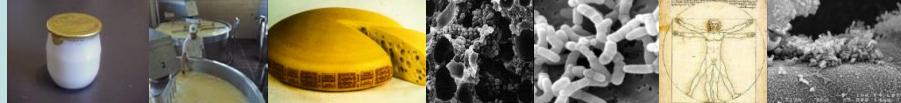




reverse engineering development of an anti-inflammatory cheese ?



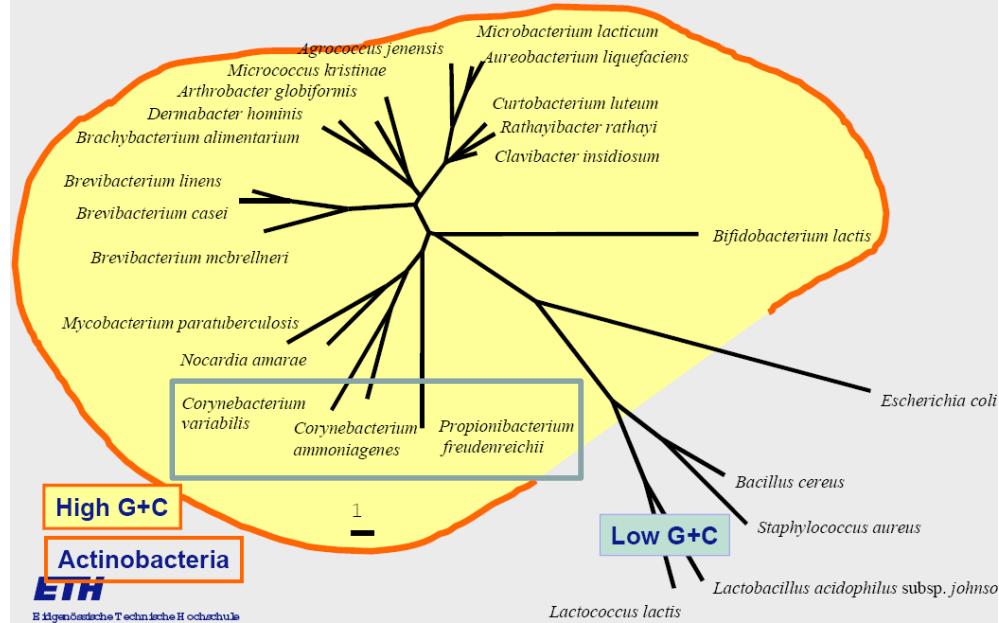
Propionibacteria, multipurpose bacteria



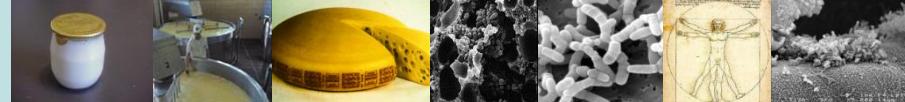
Gram +
pleiomorphic
anaerobic to microaérophilic
non motiles et non sporulated

GC Rich : 67%

Phylogenetic tree of the class *Actinobacteria* based on 16S rDNA



- « dairy » :
P. freudenreichii
P. jensenii - *P. thoenii* -
P. acidipropionici



Propionibacteria, a peculiar ecology



soil



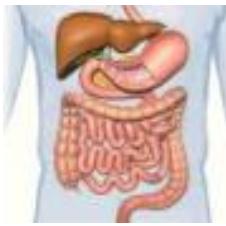
fodder



Sewage plants



gut



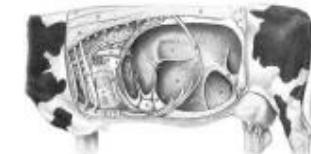
cheese



silage

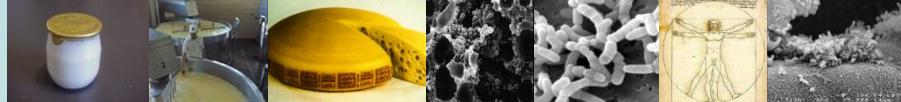


rumen



milk





*Propionibacterium
freudenreichii*

→ Vitamin producer
B9, B12



→ Probiotics



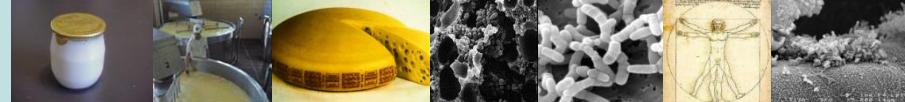
→ Food bio-preservative



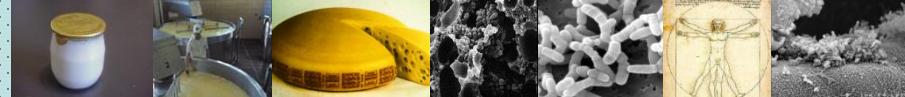
→ Ripening starter



Short Chain Fatty Acids
(SCFA)
Known effect on health

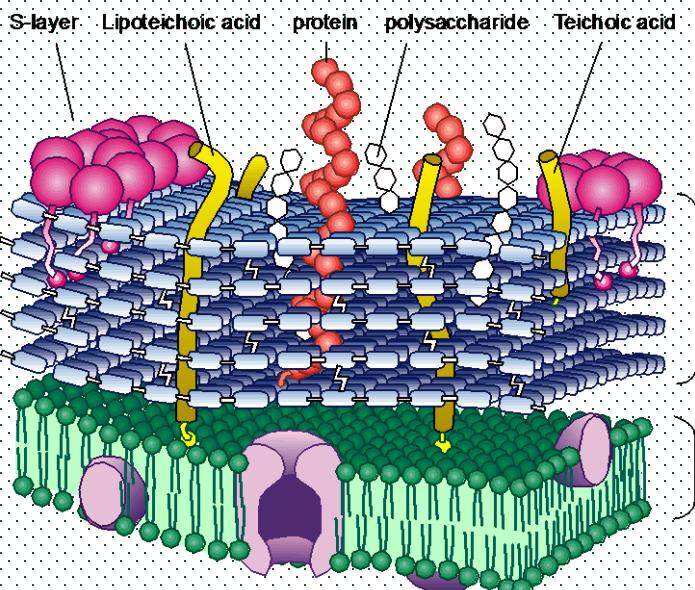


Propionibacteria, a peculiar cell wall architecture

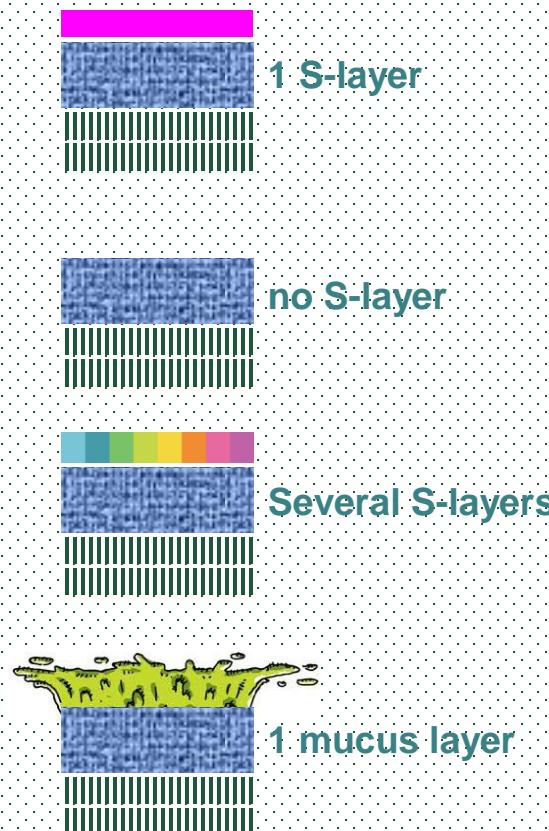


Variable composition and structure

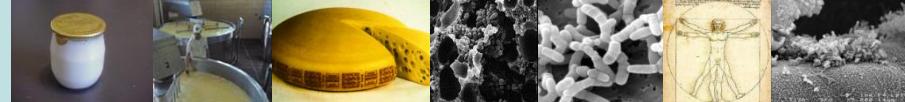
Structure of propionibacteria : it depends on the strain !



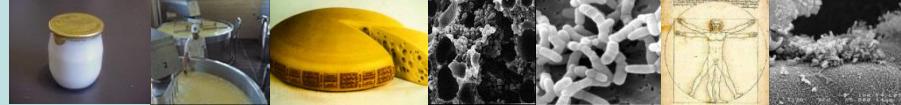
Structure of classical gram positives



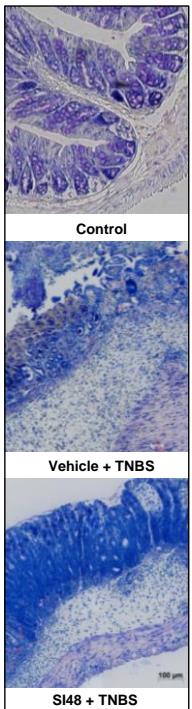
→ Some of these compounds are involved in interaction with us



Propionibacteria against inflammation of the gut?



Propionibacterium freudenreichii and immunomodulation



APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Dec. 2010, p. 8259–8264
0099-2240/10/\$12.00 doi:10.1128/AEM.01976-10
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Vol. 76, No. 24

Promising Immunomodulatory Effects of Selected Strains of Dairy Propionibacteria as Evidenced *In Vitro* and *In Vivo*^{V†}

Benoit Foligné,^{1,2,3,4} Stéphanie-Marie Deutsch,^{5,6} Jérôme Breton,^{1,2,3,4} Fabien J. Cousin,^{5,6,7} Joëlle Dewulf,^{1,2,3,4} Michel Samson,⁸ Bruno Pot,^{1,2,3,4} and Gwénaël Jan^{5,6*}

Institut Pasteur de Lille, Lactic Acid Bacteria & Mucosal Immunity, Center for Infection and Immunity of Lille, 1, Rue du Pr Calmette, BP 245, F-59019 Lille, France¹; Université Lille Nord de France, F-59000 Lille, France²; CNRS, UMR 8204, F-59021 Lille, France³; Institut National de la Santé et de la Recherche Médicale, U1019, F-59019 Lille, France⁴; INRA, UMR1253 Science et Technologie du Lait et de l’Oeuf, F-35042 Rennes, France⁵; AGROCAMPUS OUEST, UMR1253 Science et Technologie du Lait et de l’Oeuf, F-35042 Rennes, France⁶; CNIEL/Syndifrais, 42 Rue de Châteaudun, F-75314 Paris 09, France⁷; and EA 4427 SeRAIC, Faculty of Pharmacy, University of Rennes 1, IFR 140 GFAS, Rennes F-35043, France⁸

Received 20 August 2010/Accepted 7 October 2010

Immunomodulatory properties of 10 dairy propionibacteria, analyzed on human peripheral blood mononuclear cells (PBMCs), revealed a highly strain-dependent induction of anti-inflammatory cytokine interleukin 10 (IL-10). Two selected strains of *Propionibacterium freudenreichii* showed a protective effect against two models of colitis in mice, suggesting a probiotic potential predicted by immune-based selection criteria for these cheese starter bacteria.

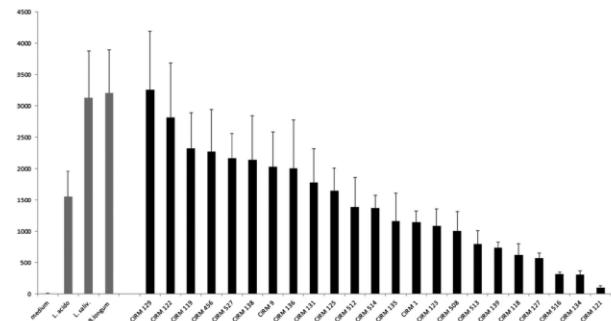


Figure 1. Anti-inflammatory profile of dairy *Propionibacterium freudenreichii* strains assessed on human peripheral blood mononuclear cells (PBMCs). Comparative IL-10 release (in pg/ml) of human PBMCs for 3 reference benchmark probiotic strains (*Lactobacillus acidophilus* NCFM, *L. salivarius* LS33 and *Bifidobacterium longum* BBS36) and for 23 propionibacteria strains (CIRM-BIA, INRA, Rennes, France). Immunocompetent cells were stimulated at multiplicity of infection of 10 for 24 h and supernatants analysed by ELISA. Detailed methodology was previously published.⁷

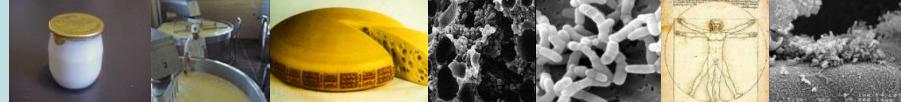


Tracking the microbiome functionality: focus on *Propionibacterium* species

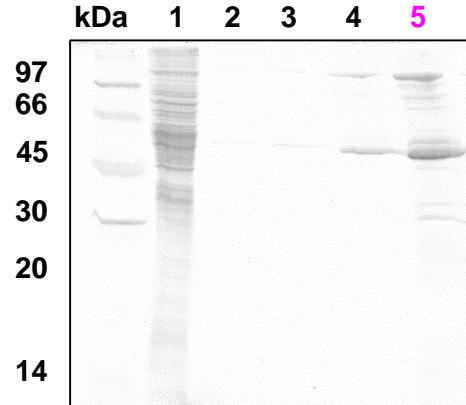
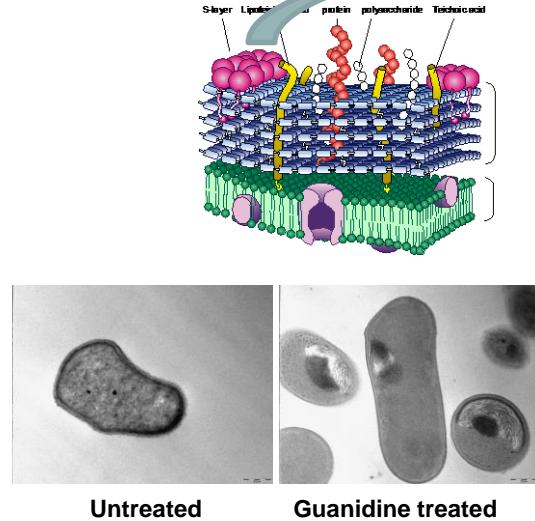
Benoit Foligné, Jérôme Breton, Denis Mater, et al.

Gut 2013 62: 1227-1228 originally published online February 6, 2013
doi: 10.1136/gutjnl-2012-304393

➤ Highly strain-dependent



A key role of a surface protein



Inactivation of SlpB
suppresses IL-10
induction

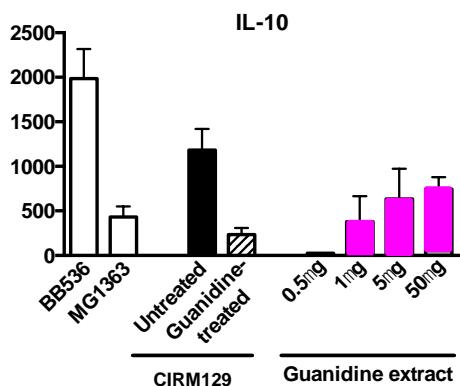
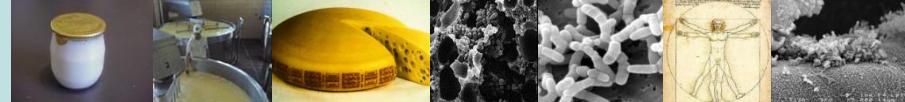


Table 1 - *Propionibacterium freudenreichii* proteins identified by nano-LC-MS/MS after guanidine hydrochloride (shaving column) or in-situ fluorescence labeling^a (CyDye column).

Locus Tag	Description	Gene	Function
PFCIRM129_12235	Internalin A	inlA	Miscellaneous
PFCIRM129_05460	Surface protein with SLH domain	slpE	Cell wall
FCIRM129_09350	Surface layer protein A	slpA	Cell wall
PFCIRM129_00700	Surface layer protein B	slpB	Cell wall
PFCIRM129_11445	Large surface protein A	lspA	Cell wall



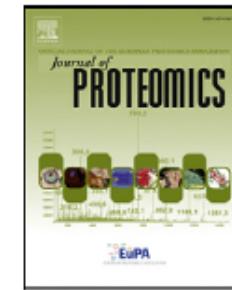
JOURNAL OF PROTEOMICS 112 (2015) 447–461



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Surface proteins of *Propionibacterium freudenreichii* are involved in its anti-inflammatory properties



Caroline Le Maréchal^{a,b}, Vincent Peton^{a,b}, Coline Plé^c, Christophe Vroland^{a,b}, Julien Jardin^{a,b}, Valérie Briard-Bion^{a,b}, Gaël Durant^{a,b}, Victoria Chuat^{a,b,d}, Valentin Loux^e, Benoit Foligné^c, Stéphanie-Marie Deutsch^{a,b}, Hélène Falentin^{a,b,1}, Gwénaël Jan^{a,b,*,1}

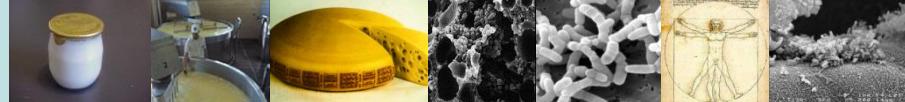
^aINRA, UMR1253 STLO, Science et Technologie du Lait et de l’Œuf, F-35042 Rennes, France

^bAGROCAMPUS OUEST, UMR1253 STLO, F-35042 Rennes, France

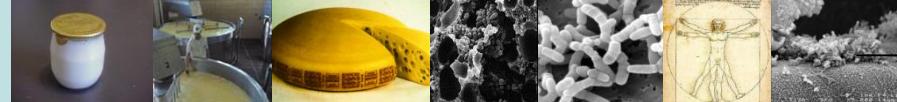
^cLactic Acid Bacteria & Mucosal Immunity, Center for Infection and Immunity of Lille, Institut Pasteur de Lille, U 1019, UMR8204 Université Lille Nord de France, 1 rue du Pr Calmette, BP 245, F-59019 Lille, France

^dINRA, UMR1253 STLO, CIRM-BIA, F-35042 Rennes, France

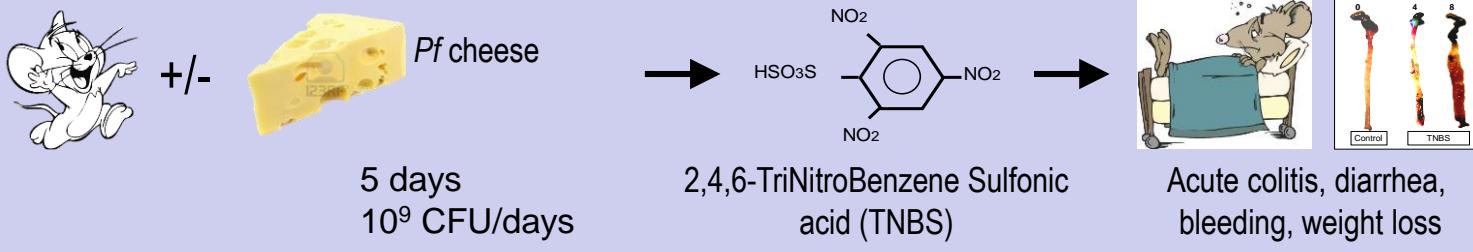
^eINRA, UR MIG, F-78352 Jouy-en-Josas, France



Cheese against inflammation of the gut?



Impact of Pf single-strain cheese on TNBS-induced colitis



Healthy: n=5
TNBS groups: n=10

* p<0.05: vs CTL

p<0.05: vs MTX

JOURNAL OF FUNCTIONAL FOODS 18 (2015) 575–585



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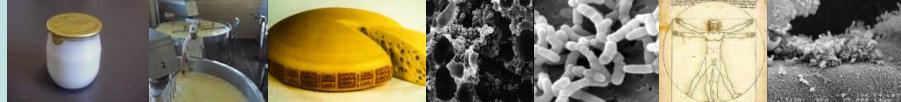


Single-strain starter experimental cheese reveals anti-inflammatory effect of *Propionibacterium freudenreichii* CIRM BIA 129 in TNBS-colitis model

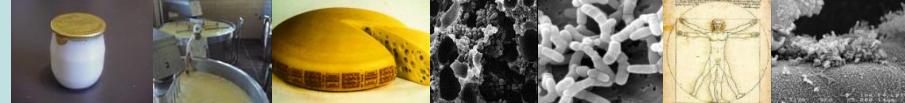


CrossMark

Coline Plé ^a, Romain Richoux ^b, Julien Jardin ^{c,d}, Marine Nurdin ^b, Valérie Briard-Bion ^{c,d}, Sandrine Parayre ^{c,d}, Stéphanie Ferreira ^e, Bruno Pot ^a, Guillaume Bouguen ^{f,g}, Stéphanie-Marie Deutsch ^{c,d}, Hélène Falentin ^{c,d}, Benoit Foligné ^{a,1}, Gwénaël Jan ^{c,d,*1}



Cheese is not a single strain product



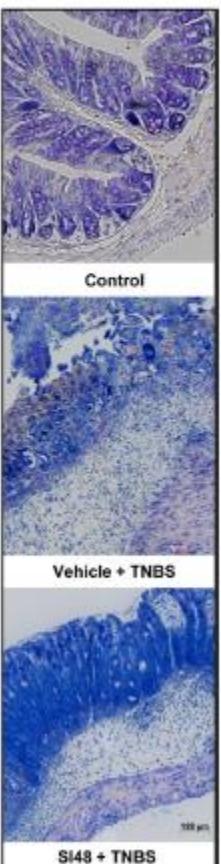
F Emmental cheese: 3 starters

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Dec. 2010, p. 8259–8264
99-2240/10/\$12.00 doi:10.1128/AEM.01976-10
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Vol. 76, No. 24

Promising Immunomodulatory Effects of Selected Strains of Dairy Propionibacteria as Evidenced *In Vitro* and *In Vivo*[†]

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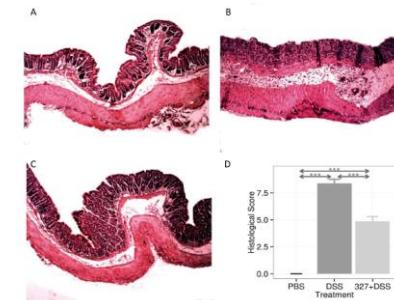
Streptococcus thermophilus

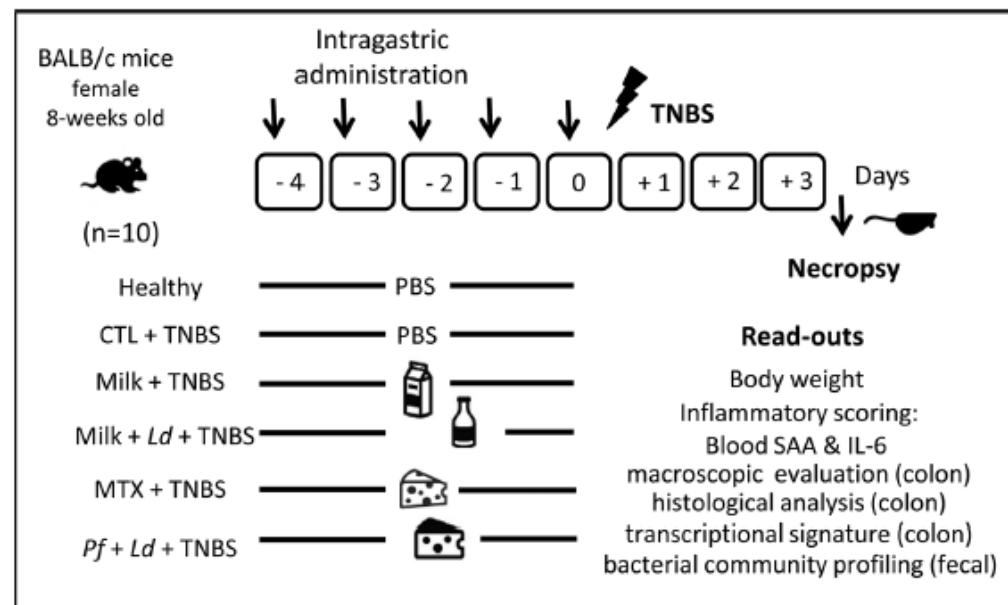
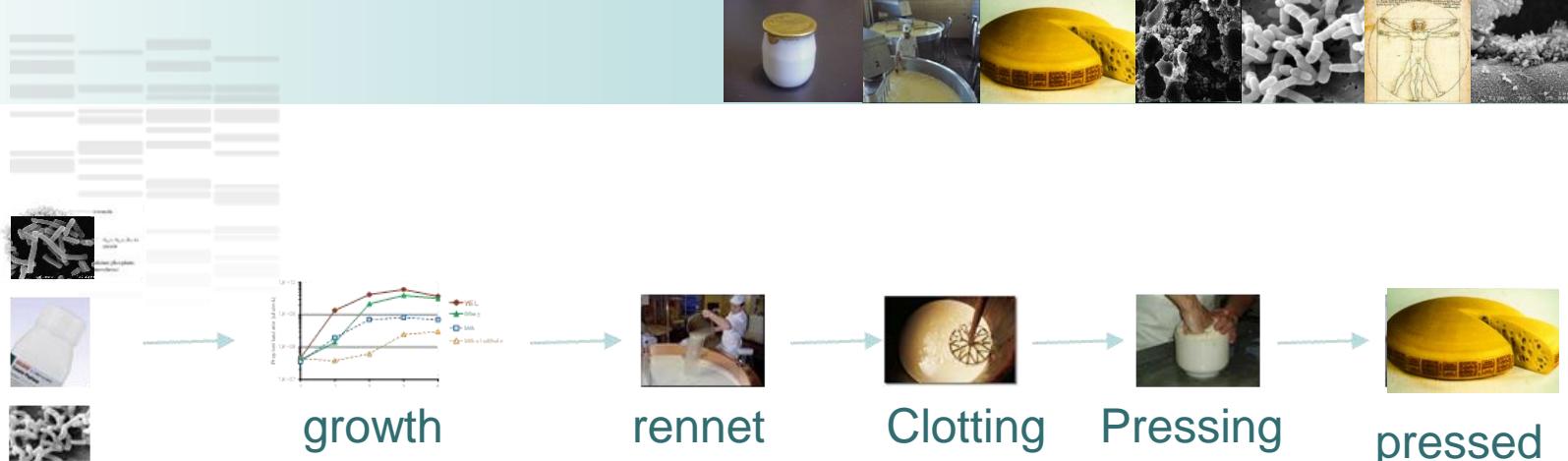
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PLOS ONE

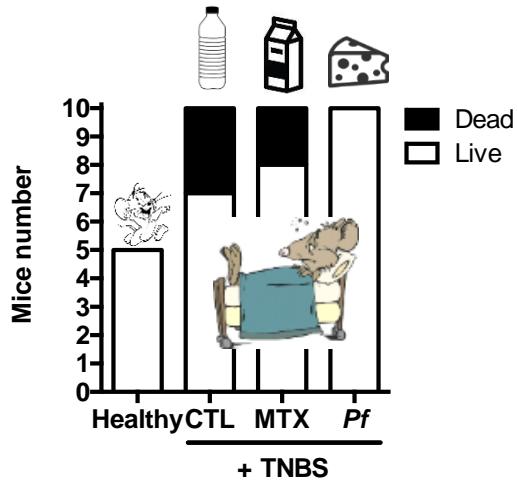
Local and Systemic Immune Mechanisms Underlying the Anti-Colitis Effects of the Dairy Bacterium *Lactobacillus delbrueckii*

Clarissa Santos Rocha^{1,3,4}, Ana Cristina Gomes-Santos², Thais Garcias Moreira², Marcela de Azevedo¹, Tessalia Diniz Luerce¹, Mahendra Mariadassou⁵, Ana Paula Longaray Delamare⁶, Philippe Langella^{3,4}, Emmanuelle Maguin^{3,4}, Vasco Azevedo¹, Ana Maria Caetano de Faria², Anderson Miyoshi^{1,9}, Maarten van de Guchte^{3,4,*}

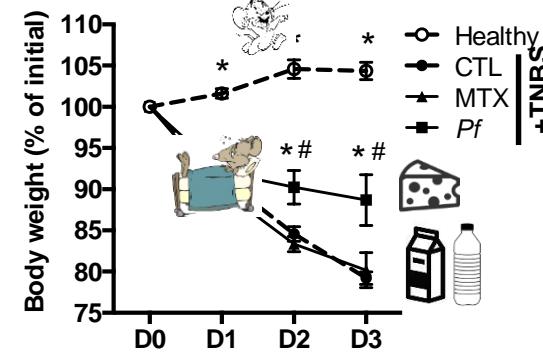




Cheese protects at the organism level



Survival

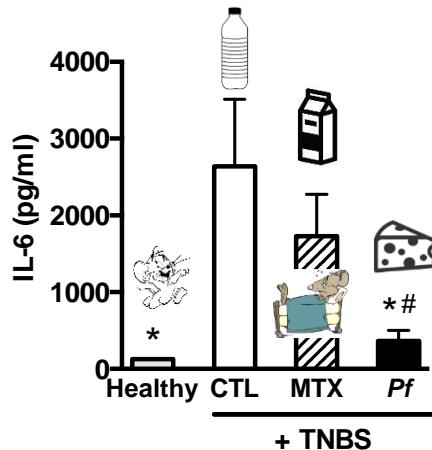


Body weight

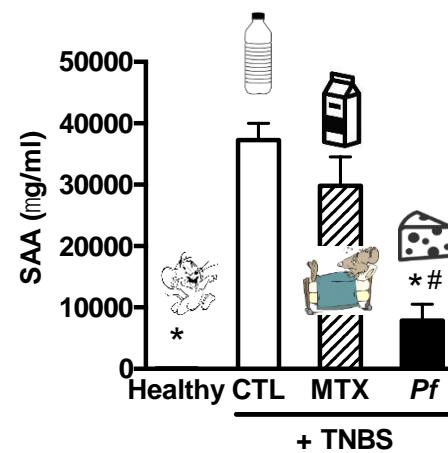
Cheese protects at the systemic level



Blood inflammation markers

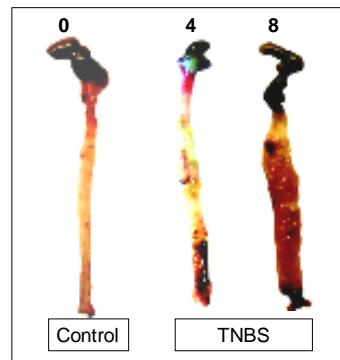
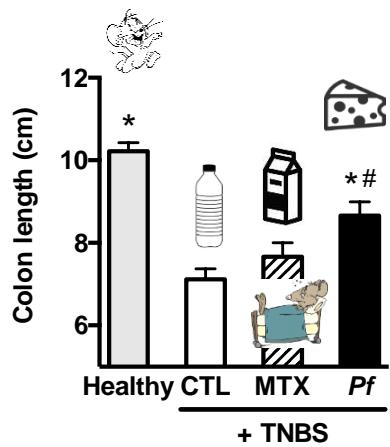


Interleukin 6

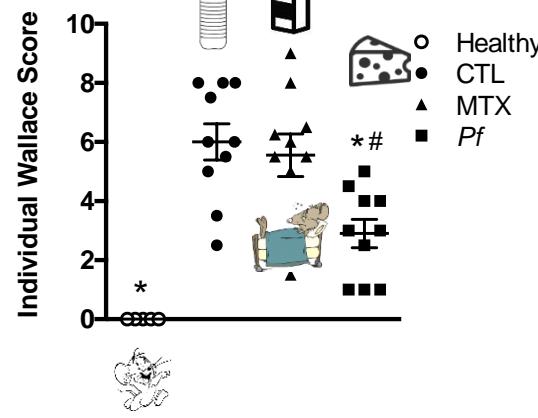
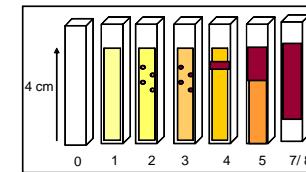


Serum Amyloid A

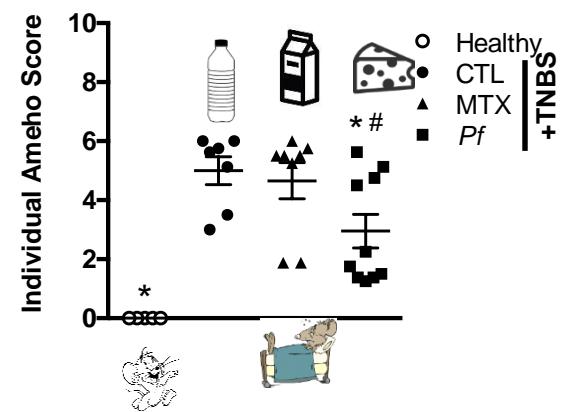
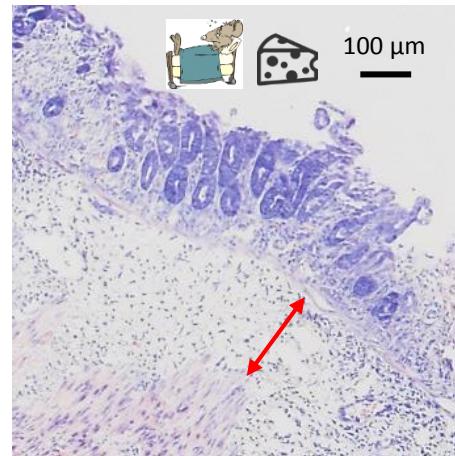
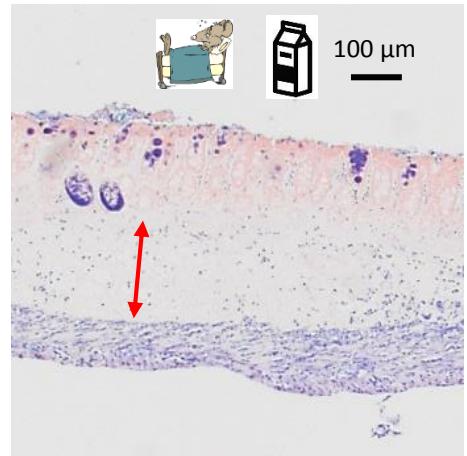
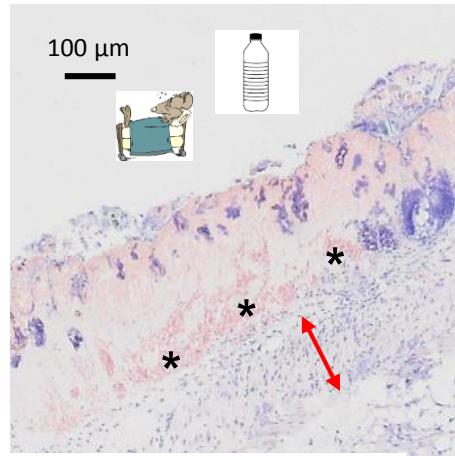
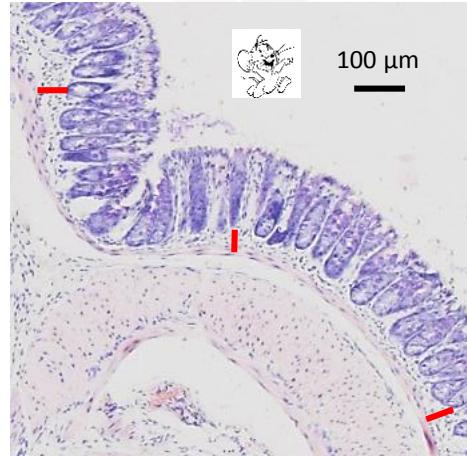
Cheese protects at the organ level



Macroscopic score (Wallace)



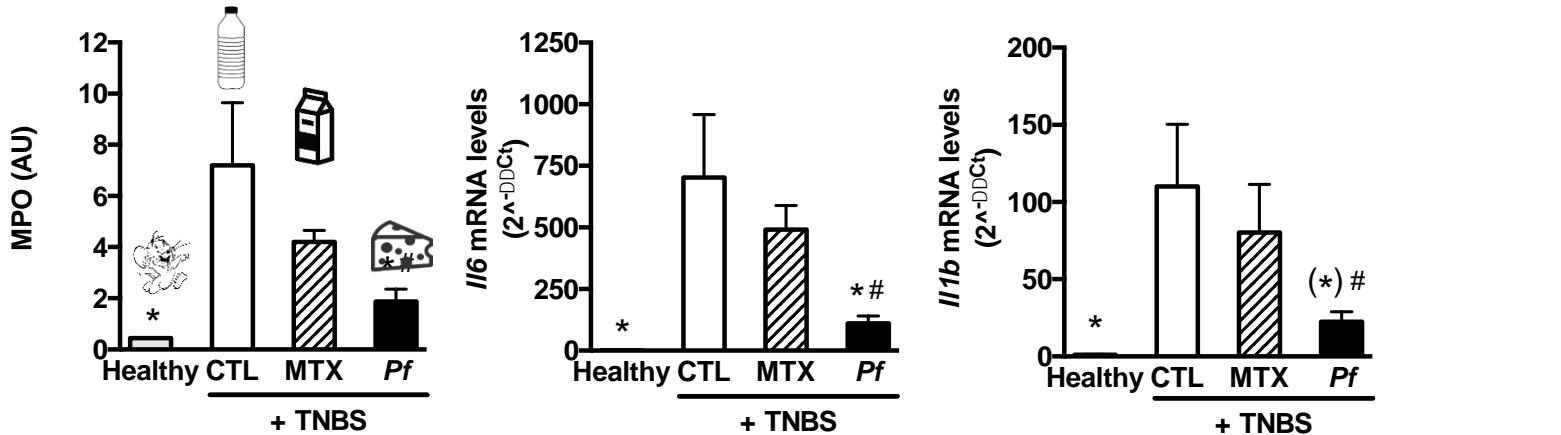
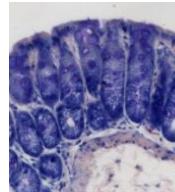
Cheese protects at the tissue level



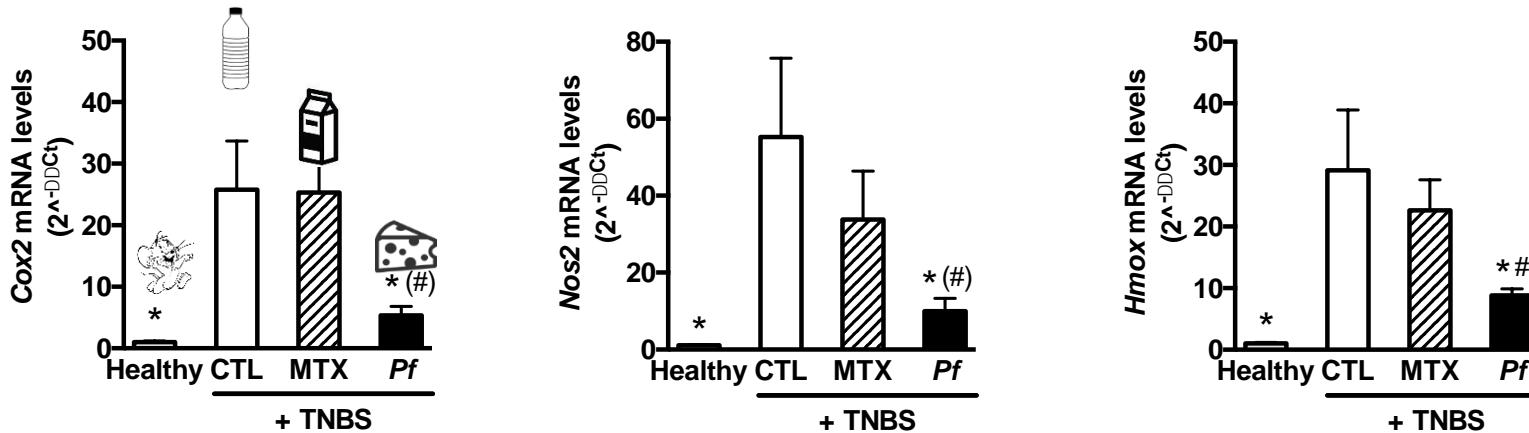
5

Cheese protects at the tissue level

Colonic inflammatory markers



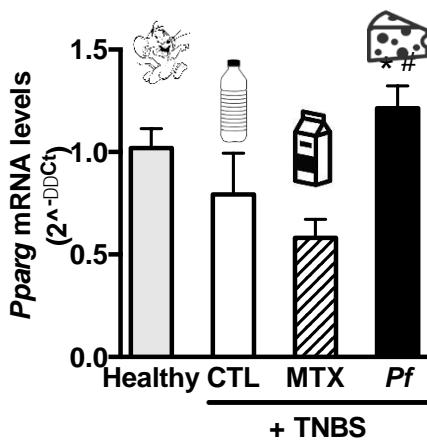
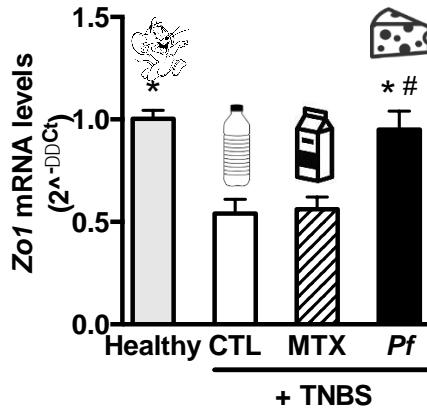
Colonic oxidative stress markers



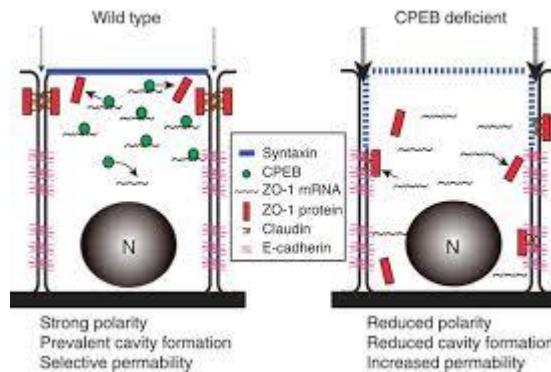
* p<0.05: vs CTL
p<0.05: vs MTX

Cheese protects at the cell level

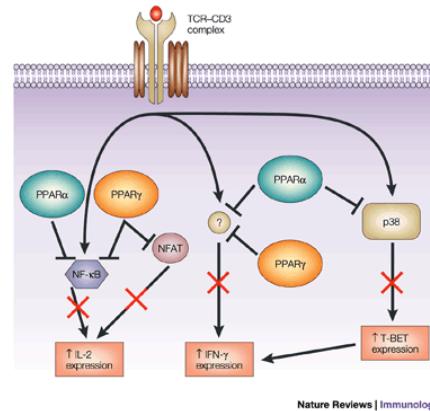
Colonic epithelial cell markers



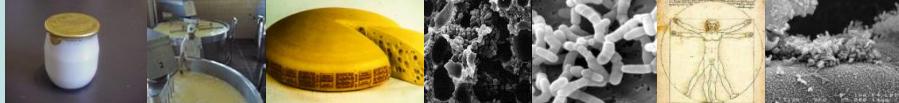
Nagaoka, Nature Communications, 2012



The zona occludens proteins (ZO-1, ZO-2 and ZO-3) : tight junction proteins that function as cross-linkers



Peroxisome proliferator-activated receptors (PPARs) regulate T-cell cytokine production.



Immunomodulatory properties identified in other dairy bacteria

S-Layer Protein Mediates the Stimulatory Effect of *Lactobacillus helveticus* MIMLh5 on Innate Immunity

Valentina Taverniti,^a Milda Stuknyte,^a Mario Minuzzo,^b Stefania Arioli,^a Ivano De Noni,^a Christian Scabiosi,^a Zuzet Martinez Cordova,^c Ilkka Juntila,^{d,e} Sanna Hämäläinen,^{c,d} Hannu Turpeinen,^c Diego Mora,^a Matti Karp,^f Marko Pesu,^{c,g} Simone Guglielmetti^a

Department of Food, Environmental and Nutritional Sciences, Università degli Studi di Milano, Milan, Italy^a; Department of Biomolecular Sciences and Biotechnology, Università degli Studi di Milano, Milan, Italy^b; Institute of Biomedical Technology, Biomeditech University of Tampere, Tampere, Finland^c; School of Medicine, University of Tampere, Tampere, Finland^d; Fimlab Laboratories, Tampere, Finland^e; Institute of Environmental Engineering and Biotechnology, Tampere University of Technology, Tampere, Finland^f

Clinical & Experimental Immunology
The Journal of Translational Immunology

British Society for
Immunology

Clinical and Experimental Immunology | ORIGINAL ARTICLE

doi:10.1111/j.1365-2249.2011.04408.x

Lactobacillus rhamnosus GG and Streptococcus thermophilus induce suppressor of cytokine signalling 3 (SOCS3) gene expression directly and indirectly via interleukin-10 in human primary macrophages

S. Latvala,* M. Miettinen,† R. A. Kekkonen,† R. Korppela† and I. Julkunen*

*Department of Vaccination and Immune Protection, National Institute for Health and Welfare (THL), †Valio Ltd R&D, Meijeritie, and

[†]Institute of Biomedicine, Pharmacology, University of Helsinki, Helsinki, Finland

Summary

In the present study we have characterized T helper type 2 (Th2) [interleukin (IL)-10]/Th1 (IL-12) cytokine expression balance in human primary macrophages stimulated with multiple non-pathogenic Gram-positive bacteria used in the food industry and as probiotic substances. Bacteria representing *Lactobacillus*, *Bifidobacterium*, *Lactococcus*, *Leuconostoc*, *Propionibacterium* and *Streptococcus* species induced anti-inflammatory IL-10 production,

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PLOS ONE

Lactobacillus helveticus SBT2171 Inhibits Lymphocyte Proliferation by Regulation of the JNK Signaling Pathway

Tomohiro Hosoya^{1,3}, Fumihiko Sakai^{1,3}, Maya Yamashita¹, Takuya Shiozaki², Tsutomu Endo³, Ken Ukibe¹, Hiroshi Uenishi¹, Yukio Kadooka¹, Tomohiro Moriya¹, Hisako Nakagawa², Yosuke Nakayama², Tadaaki Miyazaki^{2*}

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SHORT COMMUNICATION

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Lactobacillus bulgaricus OLL1181 activates the aryl hydrocarbon receptor pathway and inhibits colitis

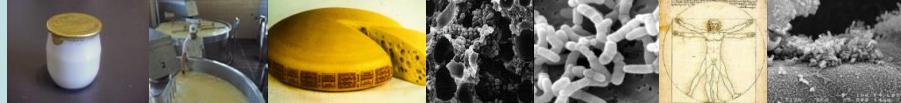
Takeyuki Takamura¹, Daisuke Hara¹, Suguru Fukumoto¹, Yuki Nakamura¹, Naomi Shimokawa¹, Kayoko Ishimaru¹, Shuji Ikegami², Seiya Makino², Masanori Kitamura³ and Atsuhito Nakao¹

PLOS ONE

L. plantarum, *L. salivarius*, and *L. lactis* Attenuate Th2 Responses and Increase Treg Frequencies in Healthy Mice in a Strain Dependent Manner

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Reverse engineering of cheese?

Molecular Nutrition
Food Research

Mol. Nutr. Food Res. 2016, 60, 935–948

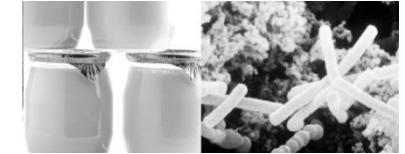
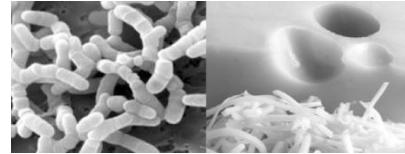
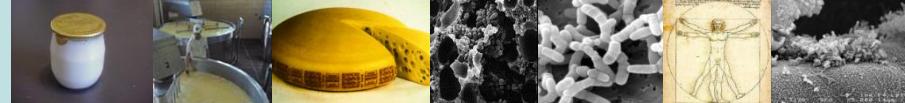
DOI 10.1002/mnfr.201500580

935

RESEARCH ARTICLE

Combining selected immunomodulatory *Propionibacterium freudenreichii* and *Lactobacillus delbrueckii* strains: Reverse engineering development of an anti-inflammatory cheese

Coline Plé¹, Jérôme Breton¹, Romain Richoux², Marine Nurdin², Stéphanie-Marie Deutsch^{3,4}, Hélène Falentin^{3,4}, Christophe Hervé⁵, Victoria Chuat^{3,4,6}, Riwanon Lemée⁵, Emmanuelle Maguin^{7,8}, Gwénaël Jan^{3,4}, Maarten Van de Guchte^{7,8} and Benoit Foligné¹



Conclusion:

- ✓ Fermented dairy products: a source of bioactive bacteria
- ✓ Molecules and strains involved are being identified

Perspectives :

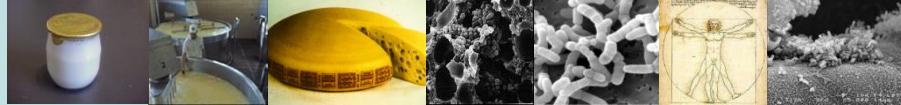
- ✓ Preclinical and clinical studies with fermented products
- ✓ Fermented food for specific populations



Fermented foods : 30% of our diet



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A major source of bacteria : 10^5 to 10^9 per gram

A huge variety of bacteria

