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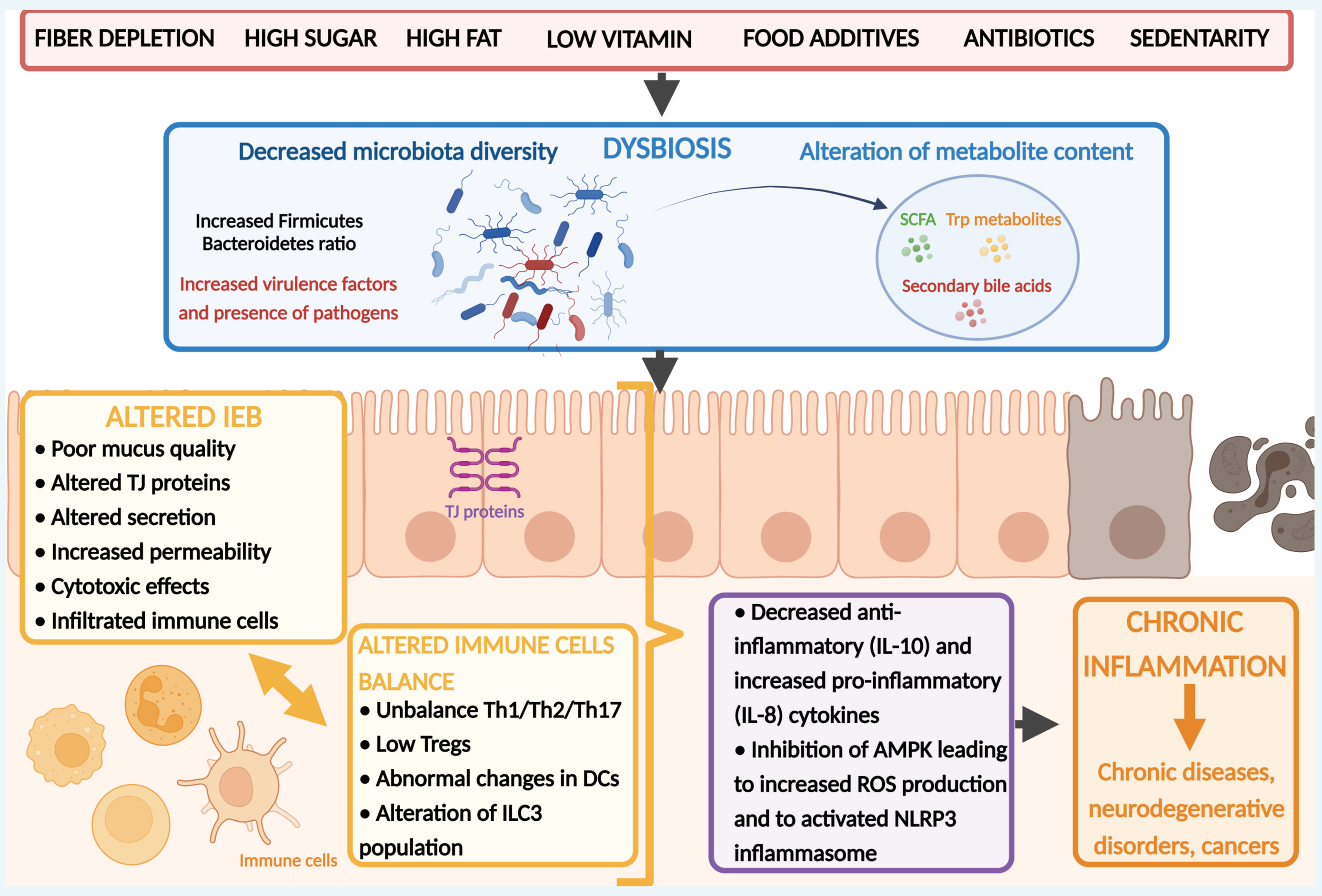
CONTEXT

✓ **The gut microbiota plays a crucial role in the regulation of mucosal immunity and of the function of the intestinal barrier. Dysbiosis is accordingly associated with rupture of mucosal immune homeostasis, leading to inflammatory intestinal diseases. In this context, probiotic bacteria, including a new generation of intestinal probiotics, can maintain intestinal homeostasis and promote health. Surprisingly, little is known about the impact of fermented dairy products in this context, while they represent our main source of live and active bacteria. Indeed, they provide, through our daily diet, a high number of bacteria whose effect on mucosal immunity deserves attention. Among bacteria ingested in fermented dairy products, *Streptococcus thermophilus*, *Lactobacillus delbrueckii*, *Lactobacillus helveticus*, *Lactococcus lactis* and *Propionibacterium freudenreichii* are on top, as they are ingested in high concentrations (close to 10^9 ufc per gram of product) in fermented milks or cheeses.**

THE PROBLEM OF MODERN LIFESTYLE



SCFA: short chain fatty acids; *TJ*: tight junction; *IEC*: intestinal epithelial cells; *DCs*: dendritic cells; *ILC3*: type 3 innate lymphoid cells; *AMPK*: Adenosine monophosphate-activated protein kinase; *ROS*: reactive oxygen species; *NLRP3*: Nucleotide-binding Oligomerization Domain-like Receptor Protein 3.

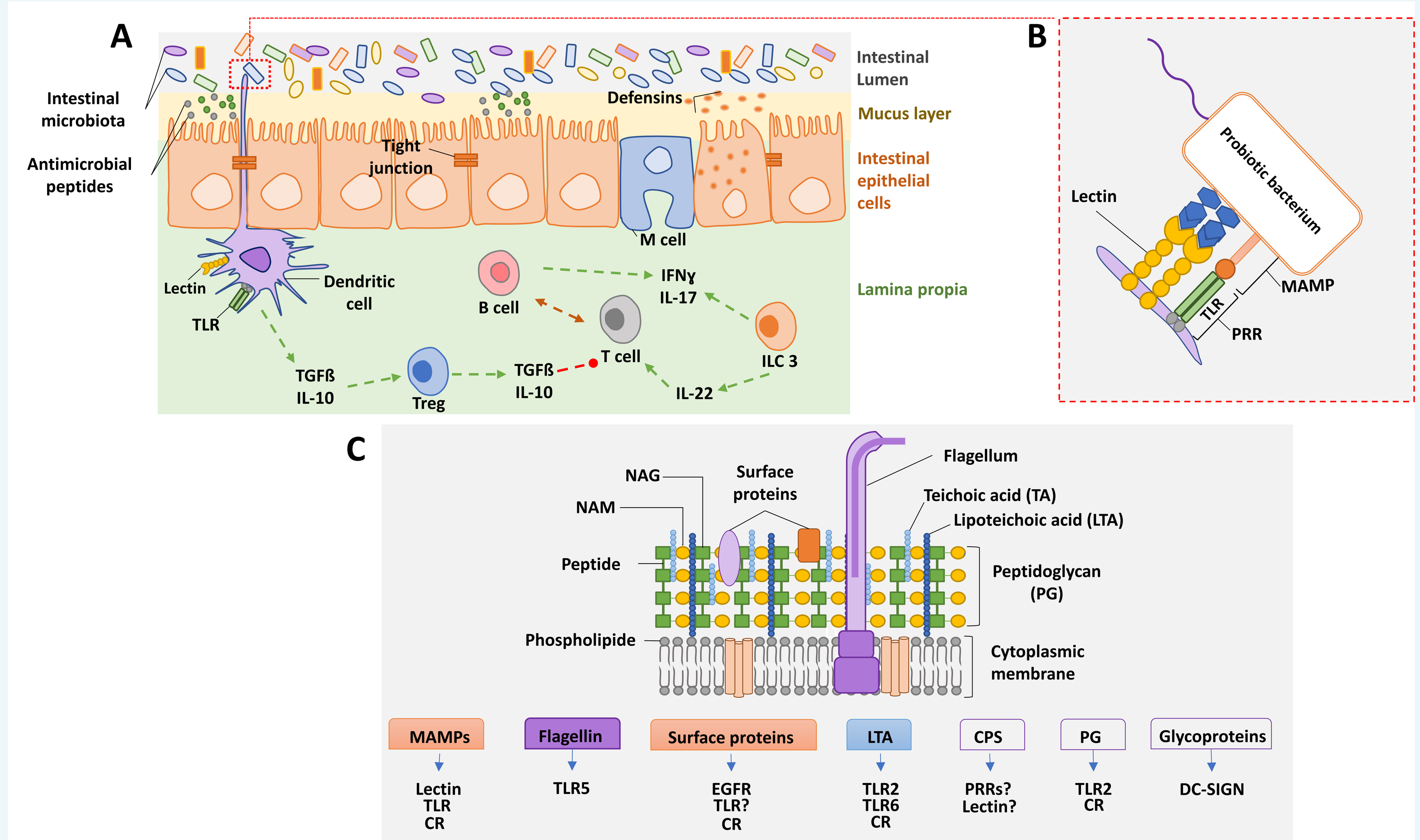
Consequences of changes in modern lifestyle on the gut dysbiosis, intestinal epithelial barrier (IEB) and immune system.

Changes occurring during transition to a modern lifestyle include modification of the eating habits, with reduced intake of fibers, of vitamin, yet enhanced intake of sugar, of food additives, and of fat. These changes also include sedentarity and medication, including the use of antibiotics.

They favour dysbiosis, a dysregulation of the gut microbiota, with decreased microbial diversity and alteration of the content in microbial metabolites. This in turn leads to an altered intestinal epithelial barrier, which is involved in an altered balance of immune cells. All these changes finally favour chronic inflammation.

↳ Immunomodulatory bacteria may help

INTERACTIONS BETWEEN INGESTED BACTERIA AND THE HOST



Schematic view of possible interactions between ingested bacteria and the host.

A: Drawing of the key layers of the intestinal epithelial barrier. The intestinal barrier includes: (i) the intestinal lumen with the intestinal microbiota; (ii) the mucus layer that serves as a microbial and biochemical barrier; (iii) the intestinal epithelial cells (IECs) monolayer, maintained by tight junctions, forming a physical barrier; (iv) and the lamina propria which contains different immunological cells that interact together (DCs, T cell, or ILC3). Green arrows represent cytokine secretion or stimulation, brown represents interaction and red represents inhibition.

B: Focus on the interaction between a probiotic bacterium and dendritic cell (DC). Probiotic bacteria interact with DC via microbe-associated molecular patterns (MAMPs) and pattern recognition receptors (PRR).

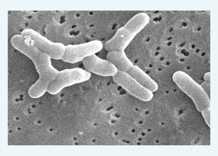
C: Schematic representation of the main surface components (MAMPs) of Gram-positive probiotic bacteria and the corresponding PRRs in IECs and DCs. Host pattern recognition receptors (PRRs) that recognize probiotic MAMPs include Toll Like Receptors (TLRs), C-type lectin DC specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN). CR, co-receptors; CPS, cell wall-associated polysaccharide; PG, peptidoglycan; TA, teichoic acid; LTA, lipoteichoic acid; EGFr, epidermal growth factor receptor; NAG, N-acetylglucosamine; NAM, N-acetylmuramic acid.

Examples of immunomodulatory starter bacteria are given below as ID cards

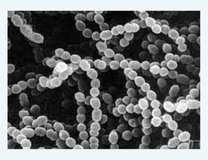
Table 1
Counts of some lactic acid bacteria and ripening flora in fermented dairy products.

Type of fermented milk products at the end of production	Species studied	Count range ($\log_{10}$ CFU.g $^{-1}$ of product)	Reference
Plain yogurt ($n = 5$) Flavored yogurt ($n = 5$) Liquid yogurt ($n = 5$) Fermented milk ($n = 5$) Biogarde®3 ($n = 5$)	S. salivarius subsp. thermophilus (*S. thermophilus*)	8.20–8.36 8.34–8.60 8.41–8.56 8.34–8.59 8.45–8.53	(1)
Commercial yogurt	*S. thermophilus* *Lactobacillus delbrueckii*	7.54 ± 0.05- 8.88 ± 0.06 6.90 ± 0.09 - 8.56 ± 0.01	(2)
Commercial Emmental cheeses (West part of France at 51 and 61 d of ripening)	Thermophilic streptococci including *S. thermophilus* Thermophilic lactobacilli including *Lactobacillus helveticus* Propionibacteria including *Propionibacterium freudenreichii*	Not detected 6.4; 5.7 8.0;8.6	(3)
Swiss Gruyère-type cheese manufactured with natural whey cultures (6-month ripening)	Thermophilic streptococci including *S. thermophilus* Thermophilic lactobacilli including L. *helveticus* *Lactobacillus helveticus* [2]	2.56 ± 0.07 –6.42 ± 0.01 3.0–7.86 ± 0.02 7.59 (±0.86)	(4)
Cantal cheeses (120 d of ripening)	Lactococci including *Lactococcus lactis* *S. thermophilus* Mesophilic lactobacilli Facultative heterofermentative lactobacilli Propionibacteria including *P. freudenreichii*	6.5 ± 0.5 6.3 ± 0.6 6.7 ± 0.3 7.4 ± 0.2 5.6 ± 0.3	(5)
Manchego cheese (150 d of ripening)	L. *lactis* subsp. *lactis* Commercial lactococci starter	~7 ~6	(6)

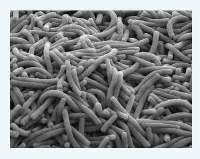
[1]CFU, colony forming unit.
[2] The quantitation of L. *helveticus* was performed by quantitative PCR, which specifically targets the *pheS* gene encoding the α-subunit of the phenylalanine-tRNA synthetase and expressed as $\log_{10}$ copies g^{-1}.



Genus: *Propionibacterium*
Species: *freudenreichii*
Description: rods, Gram+, pleiomorphic, non-pathogenic, food grade, mesophilic, propionic acid bacterium, heterofermentative
Residence: plants, digestive tract, mammary gland and raw milk
Workplace: cheeses
Profession: opening, flavour, texture
Mucosal immunity modulation (in a strain-dependent manner): prevention of colitis and mucositis in mice, may involve production of folate, surface layer proteins, induction of Treg, yet suppression of Th17 responses, modulation of several cytokines, mucus upregulation



Genus: *Streptococcus*
Species: *thermophilus*
Description: cocci, Gram+, in chains, non-pathogenic, food grade, thermophilic, lactic acid bacterium, homofermentative
Residence: mammary gland and raw milk
Workplace: yogurt and cheeses
Profession: acidification, clotting, proteolysis, flavour
Mucosal immunity modulation (in a strain-dependent manner): prevention of colitis and mucositis in mice, may involve production of folate, riboflavin, exopolysaccharides, teichoic acid, suppression of Th17 response, induction of IFNγ, TLR3 stimulation, mucus upregulation



Genus: *Lactobacillus*
Species: *delbrueckii*
Description: rods, Gram+, non-pathogenic, food grade, thermophilic, lactic acid bacterium, homofermentative
Residence: mammary gland and raw milk
Workplace: yogurt and cheeses
Profession: acidification, clotting, proteolysis, flavour
Mucosal immunity modulation (in a strain-dependent manner): prevention of colitis and colitis-associated cancer in mice, may involve surface proteins and exopolysaccharides, expansion of regulatory T cells, modulation of several cytokines

WHAT CLINICAL STUDIES SAY

- ✓ **deprivation of fermented foods from the human diet has strong impacts on the human immune system, including a fall in innate immune response (7).**
- ✓ **In obese women, yogurt consumption decreased serum LPS, lipids, and biomarkers of inflammation and oxidative stress (8).**
- ✓ **In overweight and obese people, yogurt reduced PBMCs expression of ROR-γt and serum levels of high-sensitivity C-reactive protein (hs-CRP)(9).**
- ✓ **In the same category of subjects, yogurt decreased plasma concentration of TNF-α, while increasing soluble TNF-α receptor-1 (s-TNFR-1), indicating an impact on low-grade systemic inflammation (10).**
- ✓ **consumption of yogurt reduced postprandial inflammation and markers of endotoxin exposure in healthy premenopausal women (11, 12).**
- ✓ **Yogurt consumption was further associated with lower levels of chronic inflammation, including serum levels of IL-6 and fibrin, in both normal weight and overweight volunteers, in the Framingham Offspring study (13).**
- ✓ **A randomized control trial evidence that fermented products cheese and sour cream reduced, while non-fermented products increased expression of genes related to lymphocyte activation, cytokine signalling, chemokine signalling, and cell adhesion (14).**

CONCLUSION & PERSPECTIVES

- **Modern lifestyle endangers gut barrier and favours gut inflammation**
- **Fermented food products are our main source of live and active bacteria**
- **Selected strains of fermenting bacteria exert an immunomodulatory effect**
- **This opens avenues for the development of functional fermented foods**

Read More :

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