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Assembling immunomodulatory strains of *Propionibacterium freudenreichii*, *Lactobacillus delbrueckii* and *Streptococcus thermophilus* to produce an anti-inflammatory Emmental cheese

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Introduction and Aims. Inflammatory Bowel Diseases (IBD), including Ulcerative Colitis (UC), coincide with alterations in the gut microbiota. Consumption of immunomodulatory strains of probiotic bacteria may induce or prolong remission in UC patients. Fermented foods, including cheeses, constitute major vectors for bacteria consumption. New evidences revealed anti-inflammatory effects of selected strains within the species *P.freudenreichii*, *S.thermophilus* and *L.delbrueckii*. We thus hypothesized that consumption of a functional cheese, fermented by selected strains of these three species, may exert a positive effect on IBD.

Methods. Strains of each bacterial species were screened based on the ability to induce regulatory IL-10 in human immune PBMC cells, or to downregulate nuclear factor kappa B (NF-κB) activation in a cultured HT-29 human intestinal epithelial cell line. We then investigated the effect of monostrain experimental cheese. We further investigated the impact two-strains experimental cheese. Finally, we produced in industrial conditions an Emmental cheese using one selected strain of each of the three species, i.e. *P. freudenreichii* CIRM-BIA 129 in combination with *Lactobacillus delbrueckii* CNRZ327 and *Streptococcus thermophilus* LMD-9. Consumption of all cheeses was investigated with respect to prevention of chemically induced colitis in mice.

Results. Consumption of the experimental cheeses, or of the industrial Emmental, reduced the severity of subsequent chemically induced colitis, weight loss, disease activity index and histological score, in mice. Furthermore, consumption of the Emmental cheese, in a preventive way, reduced small bowel Immunoglobulin A (IgA) secretion, restored occludin gene expression and prevented induction of Tumor Necrosis Factor α (TNFα), Interferon γ (IFNγ) and Interleukin-17 (IL-17).

Conclusion. Assembling immunomodulatory strains of both lactic acid and propionic acid starter bacteria leads to an anti-inflammatory Emmental cheese, as revealed *in vivo*. This opens new

perspectives for the development of functional fermented food products for personalised nutrition in the context of IBD.

Keywords: probiotic; colitis; cheese; inflammation; Propionibacteria; Emmental; intestine; Inflammatory Bowel Disease