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PRE-CLINICAL ASSESSMENT OF THE EFFECT OF *BIFIDOBACTERIUM LACTIS* CNCM-I-3446 ON MECHANISMS OF GASTROINTESTINAL AND SYSTEMIC IMMUNE DEFENSES: *IN VITRO*, *EX VIVO* AND *IN VIVO* APPROACHES

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Background and aims: The capacity of *Bifidobacterium lactis* CNCM I-3446 to improve immune defenses was previously suggested by its ability to confer benefit in the management of diarrhea. This health benefit ascribes, at least in part, to the capacity of *B. lactis* to impact on the intestinal mucosal immune system and/or the integrity of the intestinal barrier. The goal of the present work was to dissect at *in vitro*, *ex vivo* and *in vivo* levels the effects of this probiotic on mucosal as well as systemic host defenses mechanisms.

Methods: Co-culture systems were used to investigate the impact of *B. lactis* on barrier properties of polarized epithelial Caco-2 cells, on production by these cells of immune-related molecules, on bone marrow-derived dendritic and on T-helper cells functions. Effect of *B.Lactis* supplementation to young mice on the number of mucosal IgA-secreting cells (ELISPOTs) and response to subcutaneous tetanus toxoid vaccination was also assessed.

Results: We observed that *B. lactis* was able to potentiate the barrier properties of polarized epithelial Caco-2 cells, to stimulate production by these cells of the poly-immunoglobulin receptor or thymic stromal lymphopoietin, to induce maturation of bone marrow-derived dendritic cells and to efficiently drive T-helper cell differentiation. Moreover, supplementation of neonatal mice with *B.Lactis* significantly increased endogenous mucosal total IgA production and specific antibody response to vaccination.

Conclusions: Altogether, these data support the capacity of *B. lactis* to reinforce gut defenses by strengthening the epithelial barrier, stimulating the mucosal and systemic immune systems and improving specific responses to immunization.