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Microbiota-gut-brain axis involvement in pain syndrome: biomolecular pathway and potential therapeutic strategies

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Abstract

Background
Several studies support the existence of a bidirectional communication between gut and brain. Indeed, it has been observed that the central nervous system (CNS) influences gut environmentactivity and function helping in the balance of intestinal homeostasis (Man AWC et al.).

Interestingly, Paclitaxel (PXT)and others antineoplastic agents alterthe physiological composition of the commensal microbiota that could lead to systemic exposure to bacterial metabolites and contribute to the pathogenesis of neuropathological conditions. (Ramakrishna C et al.). For examples, the dysbiosis is involved in the development and maintenance of chemotherapy-induced peripheral neuropathy (CIPN), a troubling condition among neuropathic pain syndromes (Mukaida N.).

Methods
In this study, we evaluated the efficacy of the oral intake of a new probiotic formulation, SLAB51(in drinking water for 45 days), in the prevention of dysbiosis and in the regulation of inflammation and neuropathic conditions, using an animal model of CIPN induced by the administration of PXT (8 mg/kg, intraperitoneally for 4 alternate days).

Results
Our results firstly showed that SLAB51 restored intestinal barrier integrity and permeability in mice treated with PTX.

In addition, significantly reduced systemic pro-inflammatory cytokines.

In vivo, SLAB51 was able to decrease allodynia and hyperalgesia in differentbehavioral pain tests. Ex-vivo experiments confirmed SLAB51 anti-nociceptive and anti-inflammatory activity, in fact, it increased opioid and cannabinoid receptors and peroxisome proliferator-activated receptor gamma (PPARγ) protein levels in PTX-micespinal cord.

Finally, immunohistochemistry analyses showed that probiotic prevented the PTX-induced loss of intra-epidermal fiber and decreased murine interleukin-8 (IL-8/CINC1) levels in the paw.

Conclusions
Our results confirm the correlation between intestinal homeostasis and pain, showing how a better response to antineoplastic therapy requires an intact and optimal commensal microbiota. SLAB51 could represent a valid adjuvant strategy tomitigate the acute and chronic pain symptoms associated with Paclitaxel treatment.

References

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Abstract
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