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Neuroinflammation promotes neurochemical and hormonal changes, resulting in profound effects on motivational states (anhedonia), mood (depression and anxiety disorders) and cognitive functions (decrements in learning and memory). One of the processes mainly affected by the neuroinflammation is the hippocampal adult neurogenesis, the mechanism of production of new neurons in the adult mammalian hippocampus.

Indeed, injection of LPS triggers an inflammatory response leading to several dysfunctions in the hippocampal neurogenic niches: an increase of astrogliosis with a consequent depletion of the neural stem cells pool, a decrease of progenitor proliferation and an altered migration and arborization of neuroblasts. These events result in an impaired adult hippocampal neurogenesis with a consequent deficit of hippocampal memory tasks.

In this context, several studies have highlighted that gut microbiome not only contributes to the regulation of metabolism and immunity, but also plays a key role in regulating the neuro-inflammatory pathways through its interaction with gut-brain axis. During inflammation, several intestinal cell signaling pathways are persistently active and lead to the overproduction of pro-inflammatory mediators such as cytokines, which may cause intestinal injury, and interfere with the production of critical factors involved in brain functions, such as short chain fatty acids (SCFA), neurotransmitters and gut hormones, compromising neural functions and contributing to the development of brain disorders.

For this reason, the modulation of microbiota-gut-brain axis represents an appealing approach to develop novel therapeutic strategies for disorders characterized by cognitive decline.

Our research aims at evaluating the putative neuroprotective and proneurogenic role of a new probiotic mixture, called BP-002, in a mouse model of LPS-induced neuroinflammation.

BP-002 was administered to 3 month-old mice for 15 days and then the mice were treated with a single dose of LPS by ip injection. The sacrifice and the tissue collection was carried out at 2 and 24 hours after LPS injection. Before the sacrifice, we performed behavioral tests in order to analyze the sickness behavior.

Collected tissues were used to analyze the early stages of adult neurogenesis and microglia activation, the modulation of neuro-inflammatory patterns and intestinal homeostasis:

- The proliferation analysis clearly indicates that the treatment with BP-002 induced a significant increase in newly-generated neurons in the dentate gyrus mainly in DCX + neural progenitors.
- LPS induced a clear modification of the microglial population towards a state of activation, a symptom of an ongoing pro-inflammatory state in hippocampus and cortex. BP-002 prevents the LPS-dependent inflammatory activation of microglia both in Dentate Gyrus and Cerebral Cortex by maintaining the cells in a resting/surveillance state.
- The expression analysis of neuro-inflammatory patterns demonstrated that the treatment with BP-002 decreases the expression of proinflammatory genes in response to LPS.
- The analysis of the colonic inflammatory state showed that the high level of pro-inflammatory cytokines induced by LPS treatment, was reduced by BP-002 consumption. BP-002 alone was able to increase gut barrier integrity.

Collectively, our data clearly indicate that BP-002 exerts a powerful neurogenic stimulus in terms of increase of proliferation and differentiation of neural progenitor pool, independent of LPS treatment. The treatment with BP-002 could attenuate the inflammatory response under acute inflammatory condition and prevent the pro-inflammatory over-activation leading to neuronal damage.

This project is part of a wider IBBC-Actial Pharmaceutical collaboration, with a more general perspective of implementing public-private interaction aiming at expanding the scientific potentiality of the IBBC.

References:


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