

## Study on the preventive action of physical activity and probiotics in response to brain trauma in an elderly mouse model

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### Background:

Traumatic Brain Injury (TBI) is a devastating condition leading to structural damages and long-term cognitive impairments. Aging correlates with increased susceptibility to injuries, chronic inflammation and reduced resilience (collectively known as Inflammaging), likely due to profound gut dysbiosis. Consequently, modulating the microbiota is considered a viable tool to positively contribute to counteract Inflammaging.

### Methods and Results:

In this project, aged mice were orally administered probiotics (*L. Farmicinis* enriched) for 15 days and/or given access to a running wheel for 4 weeks before being subjected to moderate TBI. Molecular and behavioral evaluations to test the inflammatory/neuro-reparative as well as neurocognitive responses were performed at both 24 hours and 30 days post-trauma. Our preliminary results indicate a specific effect of probiotic and running in modulating the neuro-inflammatory response and, more importantly, the long-term cognitive improvement 30 days post-injury. These data suggest that a healthy lifestyle contributes to promoting neurorepair processes even in elderly subjects.

### Conclusions and Significance:

These data strongly indicate that a healthy lifestyle contributes to promoting neurorepair processes in elderly subjects. In particular, it is evident that the modulation of the intestinal microbiota following the administration of a probiotic is able to increase immune defenses in a post-traumatic context.

**Keywords:** aging, Traumatic Brain Index, Gut-Brain axis, probiotic, inflammation

### References:

- 1) Chiani F, Mastrorilli V, Marchetti N, Macioce A, Nappi C, Strimpakos G, Pasquini M, Gambadoro A, Battistini JI, Cutuli D, Petrosini L, Marinelli S, Scardigli R, **Farioli Vecchioli S**. Essential role of p21<sup>Waf1/Cip1</sup> in the modulation of post-traumatic hippocampal Neural Stem Cells response. (2024) *Stem. Cell Res Ther.*; 15(1):197.
- 2) De Santa F, Strimpakos G, Marchetti N, Gargari G, Torcinaro A, Arioli S, Mora D, Petrella C, **Farioli-Vecchioli S**. Effect of a multi-strain probiotic mixture consumption on anxiety and

- depression symptoms induced in adult mice by postnatal maternal separation. (2024), *Microbiome*. 12(1):29.
- 3) Battistini JI, Mastrorilli V, Nicolis di Robilant V, Sarauli D, Marinelli S, **Farioli Vecchioli S**. Role of Running-Activated Neural Stem Cells in the Anatomical and Functional Recovery after Traumatic Brain Injury in p21 Knock-Out Mice. (2023) *Int J Mol Sci.*;24(3):2911.
  - 4) Petrella C, Strimpakos G, Torcinaro A, Middei S, Ricci V, Gargari G, Mora D, De Santa F, **Farioli-Vecchioli S**. Proneurogenic and neuroprotective effect of a multi strain probiotic mixture in a mouse model of acute inflammation: Involvement of the gut-brain axis. (2021) *Pharmacol Res*. 2021; 172:105795.
  - 5) Petrella C, **Farioli-Vecchioli S**, Cisale GY, Strimpakos G, Borg JJ, Ceccanti M, Fiore M, Monteleone G, Nisticò R. A Healthy Gut for a Healthy Brain: Preclinical, Clinical and Regulatory Aspects. (2021). *Curr Neuropharmacol.*;19(5):610-628.