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The Role of the Gut Microbiome on Neuroinflammation and Neurodevelopmental Disorders (mNeuroINF)

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Neurodevelopment results from a precise sequence of events, which, when disrupted by genetic defects or environmental insults, such as infections, provokes irreversible developmental alterations. Inflammation in the brain (neuroinflammation) is one of the hallmarks shared by various neurodevelopmental disorders, such as Down syndrome, Fragile X syndrome and Autism Spectrum Disorders.

Recent studies point to the existence of a gut-brain axis through which the intestinal microbiota is able to modulate inflammation and influence brain function and behaviour. The ***µNeuroINF*** project will explore the hypothesis that gut bacteria can trigger neuroinflammation, which in turn, affects metabolism and behaviour, and ultimately contributes to the progression of neurodevelopmental diseases. Using mouse models of Down syndrome, Fragile X syndrome and Autism Spectrum Disorders, we will study the gut bacteria, their genes, proteins and metabolites to identify which microbial metabolites shared by these diseases are absorbed in the gut and diffused into the bloodstream to reach the brain. The possible pro-inflammatory role of these metabolites will be investigated *in vitro* by screening their pharmacological targets in the host, and *in vivo* in the animal models of the disease.

Insights obtained from ***µNeuroINF*** will ultimately lead to novel therapeutic strategies for the treatment of neurodevelopmental diseases driven by gut microbiome. The project will not only demonstrate one of the most fundamental mechanisms by which gut bacteria affects behaviour, but it will also identify the microbial metabolites ("biomarkers") that can be used to better monitor brain inflammation or to lead to new drugs ("lead compounds") for the treatment of neuroinflammation.