



## PROJECT

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### 1) Project title

#### **Role of gut barrier in the pathophysiology of extra-digestive diseases**

### 2) Abstract (max 500 words)

The intestinal barrier, which primarily consists of a mucus layer, an epithelial barrier, and a gut vascular barrier, has a crucial role in health and disease by facilitating nutrient absorption and preventing the entry of pathogens. The gut barrier is in close contact with gut microbiota on its luminal side and with immune/inflammatory cells and enteric nervous system (ENS) cells on its tissue side. Increasing evidence suggests that the intestinal barrier is compromised in digestive (both organic and functional) and extra-digestive disorders, including inflammatory bowel diseases, irritable bowel syndrome, visceral hypersensitivity, obesity, neurological and neuropsychiatric disorders. In this context, the nucleotide-binding oligomerization domain leucine-rich repeat and pyrin domain-containing protein 3 (NLRP3) inflammasome has been found to be involved in intestinal immune/inflammatory processes as well as in modulation of the gut barrier in both digestive and extra-digestive diseases.

The aim of the present study is to characterize the pathophysiological and pharmacological role of the gut barrier in the extra-digestive diseases, focusing on Alzheimer's disease (AD), Parkinson's disease (PD) and obesity. In this context, novel NLRP3 inflammasome inhibitor will be tested in animal models of obesity and brain disorders, including AD and PD. The following parameters will be evaluated: inflammatory/metabolic markers, disease markers, food intake, cognitive functions, intestinal permeability and transit.

The implementation of the present project will allow to better characterize the role of gut barrier in extra-digestive disease as well as to identify novel pharmacological entities acting on NLRP3 inflammasome to preserve enteric barrier integrity and counteract disease progression.