Leaky Park

Gut barrier permeability: a modulator of Parkinson's disease?

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Its precise origin is still unknown, but recent research suggests that the gut might play a role in its development and/or progression. It has been suggested that in some people with PD, the pathology may begin in the gastrointestinal tract, and more broadly, that the gut may play a role in disease progression. To facilitate nutrient absorption and prevent the passage of toxic substances, the intestine acts as a selective barrier. Our driving hypothesis is that the intestinal barrier is too porous in some subjects with PD (a condition called leaky gut, hence the short name of the project) and that gut porosity occurs early and is associated with a more severe disease progression.

To test this hypothesis, we propose to perform a comprehensive clinical evaluation together with an analysis of the intestinal barrier in subjects with very early/early-stage/mid-stage PD at baseline and after a 3-year follow-up. Additional experiments will be carried out in two complementary animal models of PD. To achieve these objectives, we set up an international collaboration between 4 research teams with a complementary expertise on the gastrointestinal tract in PD.

This study will help us determine whether a leaky gut occurs (or not) in early-stage PD and if it is related with disease progression. Due to the strong interconnection between the gut and the brain (known as the gut-brain axis), a leaky intestinal barrier may allow factors from the gut lumen to affect neurons both in the intestine and in the brain. Conversely, restoration of intestinal barrier properties may represent a novel approach to change disease progression in PD, as already proposed in some gastrointestinal disorders. In addition, the evaluation of gut permeability might be used as a marker for early detection or management of disease progression.

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