The study of familial forms of Parkinson’s disease is a key to understand the cause of the disease and to find new treatments. Parkinson’s Disease (PD) is the second most common neurodegenerative disorder, affecting more than 1% of the elderly population. Clinical manifestations include bradykininesia, resting tremor, muscular rigidity, and postural instability. The essential neuropathological features are the loss of dopaminergic neurons in the substantia nigra and the presence of eosinophilic intracytoplasmic inclusions termed Lewy bodies. Our group discovered in 1998 one of the first mutations involved in hereditary forms of PD: a missense mutation located in the SNCA gene and coding for a modified alpha-synuclein protein. These results were confirmed by multiple studies in which other missense mutations or multiplication of the SNCA loci were identified. Characterizing the role of the alpha-synuclein protein and its implication in PD has driven important knowledge about the marks and the development of the disease. Until now, targeting alpha-synuclein degradation is the most promising therapeutic strategy existing.

Role of the gut microbiome in the development of Parkinson’s disease
Parkinson’s disease patients frequently manifest early gastrointestinal disorders. These are reflected by increased intestinal permeability and high intestinal levels of inflammatory cytokines. Recent studies suggest that the gut microbiome (organisms that inhabit the gastrointestinal tract) is modified in Parkinson’s disease patients. Despite that these changes are related to the motor phenotype, its importance in the origin and development of the disease is unknown. We generated transgenic rodent models developing a gastrointestinal phenotype and we aim to understand changes of microbiome that are directly related to the phenotype observed. We are also testing if the gut flora is playing a protective role in the development of the pathology by housing our rodent models in a sterile environment (also termed germ-free).

Pharmacogenomics of anti-parkinsonian drug treatment
Intake of dopaminergic agonists is the most efficient therapy to limit symptomatic effects resulting from the loss of dopaminergic neurons observed in Parkinson’s disease. However, these pharmacological treatments are also associated with major adverse effects. We aim to better understand genetic factors influencing the inter-individual differences by studying associations between frequent polymorphisms in genes involved in the dopaminergic pathway and the apparition of levodopa-induced adverse effects in Parkinson’s disease.

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