GUT MICROBIOTA INVOLVEMENT IN α-SYNUCLEIN PATHOLOGY AND PARKINSON'S DISEASE

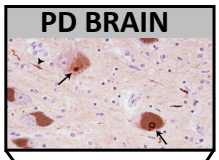
UAB Universitat Autònoma de Barcelona

Marc Moro Buendia, Biosciences Faculty, Microbiology

INTRODUCTION

Parkinson's disease

Parkinson's disease (PD) is a neurodegenerative disorder that involve non-motor and motor manifestations. The identified pathological hallmark are intracellular aggregates of **α-synuclein (α-syn)** found in the central and peripheral nervous system, forming **Lewy bodies** and **Lewy neurites**. [1]



α-Synuclein

α-Syn is a protein encoded by the SNCA gene. Its mutation and aggregation are the cause of PD. It is mainly expressed in the nervous system, with a high presence in the presynaptic terminals of the neurons and other subcellular compartments.[1]

PARKINSON AND MICROBIOTA

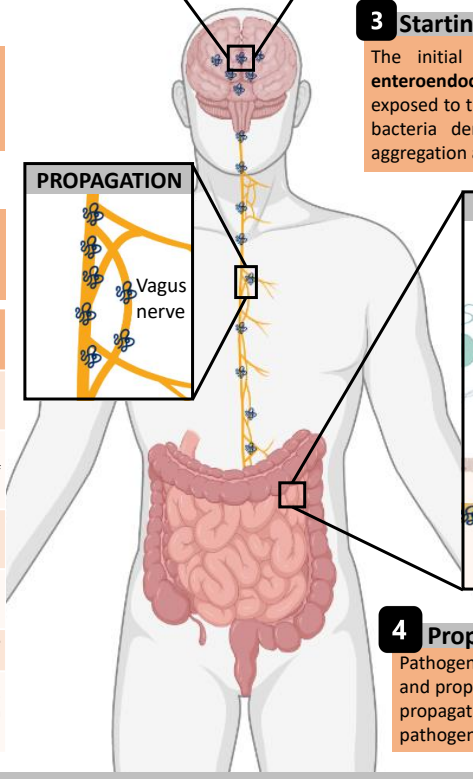
1 PD starts in the gut

Some studies have hypothesized that the gut is one of the first places where α-syn pathology starts. The idea is supported by clinical and empirical observations that have demonstrated a strong relationship between PD and the gastrointestinal system (GI).

2 Gut dysbiosis

PD patients present gut dysbiosis that might worsen PD or be the start point of the disease. *Romano and his colleagues* in 2021 characterized the gut microbiota of PD patients vs healthy patients.[2]

Genus2	Presence in PD vs Healthy	Function in healthy individuals	Consequences in PD
Roseburia	Lower	Butyrate producer.	Decreased SCFAs. Increased inflammation.
Fusicatenibacter	Lower	Butyrate producer.	Decreased presence of SCFAs. Correlated to the degree of gut inflammation
Blautia	Lower	Butyrate producer.	Decreased SCFAs. Increased inflammation
Anaerostipes	Lower	Butyrate producer.	Decreased SCFAs. Increased inflammation.
Lactobacillus	Higher	Enhance the integrity of the intestinal barrier.	Some genus can degrade Levodopa.
Akkermansia	Higher	Fortify the integrity of the epithelial cell layer and modulate the immune system.	Ability to degrade mucin, increasing gut inflammation and permeability.



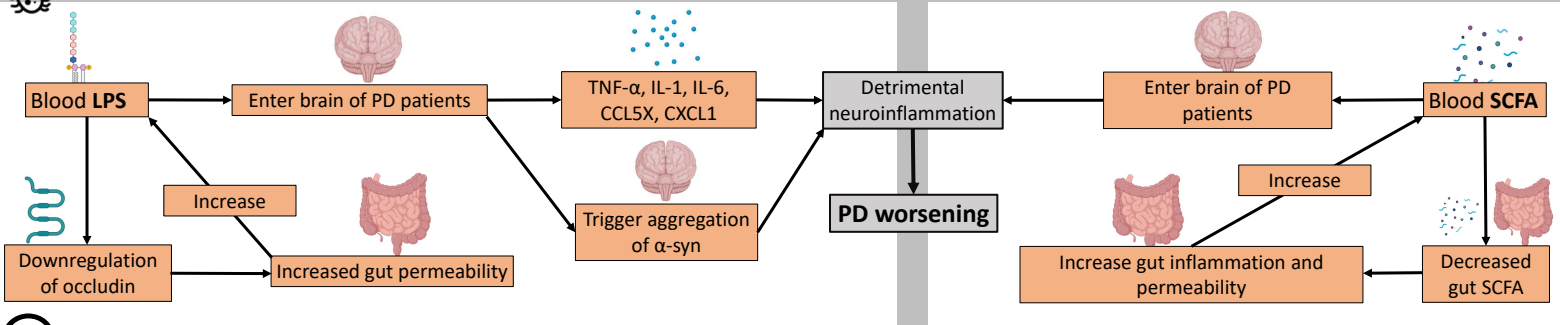
3 Starting point of the pathology

The initial start of α-syn aggregation and propagation occurs on **enteroendocrine cells (EECs).** EECs are found in the mucosa of the GI tract, exposed to the gut lumen and connected to the ENS. Toxins, pathogens and bacteria derived molecules present in the lumen can trigger α-syn aggregation and accumulation in EECs. [3]

4 Propagation gut to brain

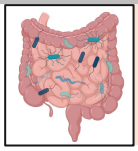
Pathogenic α-syn form originated in the EECs, can act as a pathogen and propagate from the ENS to the brain through the vagus nerve. The propagation is in a time dependent manner and depends on the pathogenic form of α-synuclein.[1]

BACTERIA DERIVED MOLECULES



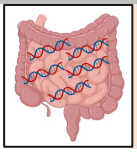
FUTURE APPROACHES

Future non-invasive early PD detection methods



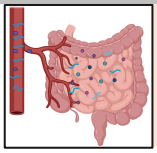
GUT DYSBIOSIS

16S rRNA study from faecal samples to detect dysbiosis



METAGENOMICS

Gene markers obtained from faecal samples.



SCFA/LPS

Levels of SCFA and LPS in faecal samples.

These methods are on an early stages of development and have shown a potential tool for early PD detection. The future idea is to build a machine learning algorithm that compromise these different factors and allow detection from simple faecal samples study.

CONCLUSION

In a conclusion, α-syn is able to start pathogenic aggregation in the EECs of the gut and is able to spread to the brain through the vagus nerve. It has been established that gut microbiota plays an important role in the starting and the outcome of the disease.

As an overall personal point, it has been shown that the detection methods involving gut microbiota are in early stages of development but have demonstrated a potential tool for early PD detection. They do not require invasive methods and their application could be easily implemented in hospitals.

REFERENCES

1. *Fitzgerald E, Murphy S, Martinson HA. Alpha-Synuclein Pathology and the Role of the Microbiota in Parkinson's Disease. Front Neurosci. 2019 Apr 24*
2. *Romano S, Savva GM, Bedarf JR, Charles IG, Hildebrand F, Narbad A. Meta-analysis of the Parkinson's disease gut microbiome suggests alterations linked to intestinal inflammation. NPJ Parkinsons Dis. 2021 Mar 10*
3. *Latorre R, Sternini C, De Giorgio R, Greenwood-Van Meerveld B. Enteroendocrine cells: a review of their role in brain-gut communication. Neurogastroenterol Motil. 2016 May;28*