The Laboratory for Gut-Immuno-Brain Axis (GIBA) Research

VIB-UANTWERP CENTER FOR MOLECULAR NEUROLOGY

Universiteit Antwerpen

(I) Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the accumulation of misfolded α-synuclein, loss of dopaminergic neurons, and motor and non-motor symptoms. **While PD has long been viewed as a brain-centric disease, emerging evidence points to early involvement of peripheral systems, including the gut and immune system**, in disease initiation and progression.

(II) The Gut-Brain Axis

The gut–brain axis is a bidirectional communication system connecting the gut and the central nervous system (CNS) through neural, immune, and metabolic pathways. In PD, this axis may serve as a conduit for pathological signals, with α-synuclein aggregates potentially originating in the gut and spreading to the brain via the vagus nerve. **Our research explores how immune signals along this axis shape brain vulnerability.**
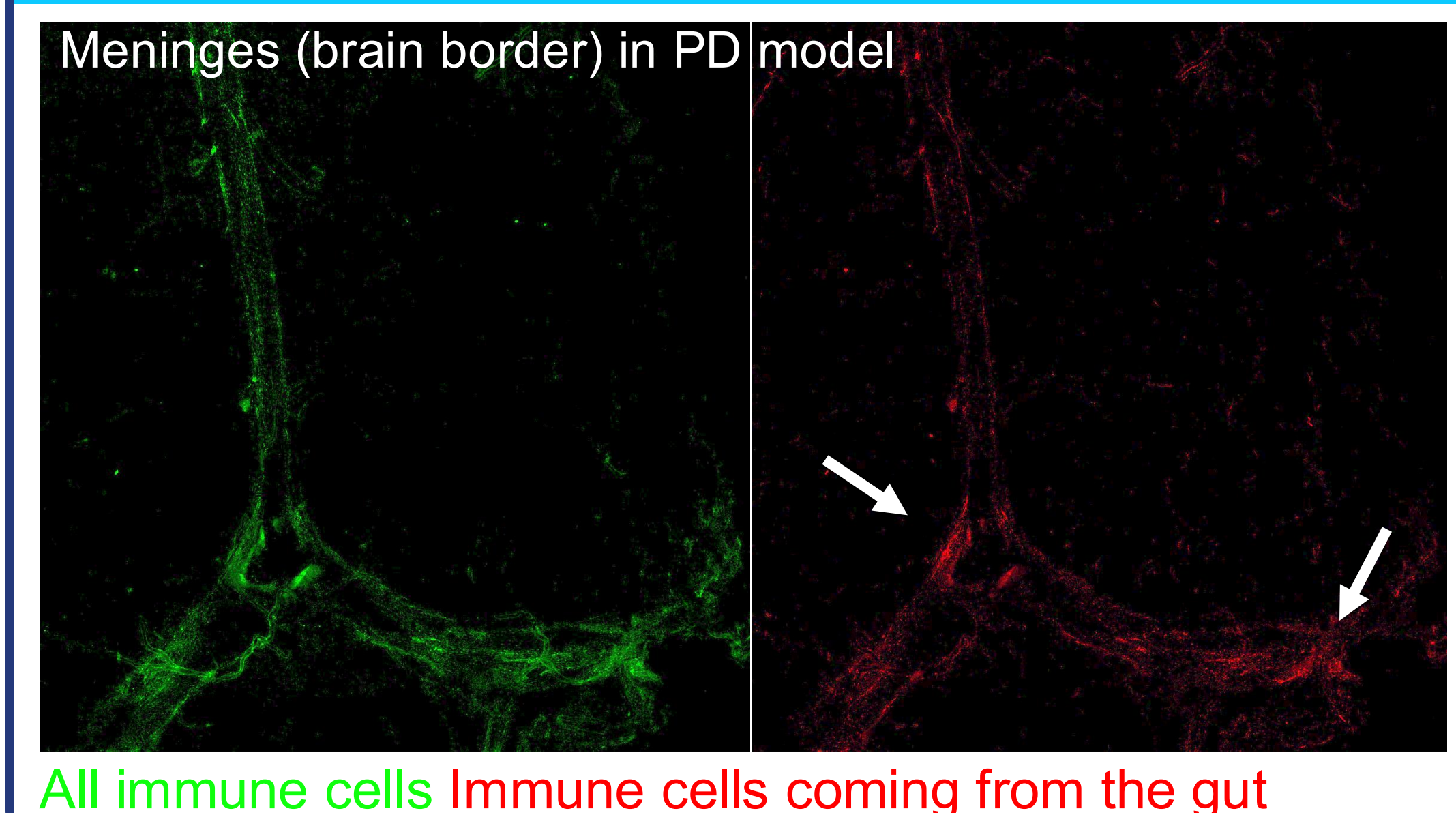
(III) Macrophages in the ENS

The ENS (enteric nervous system) is the gut's autonomous nervous network and the potential origin of α-synuclein pathology
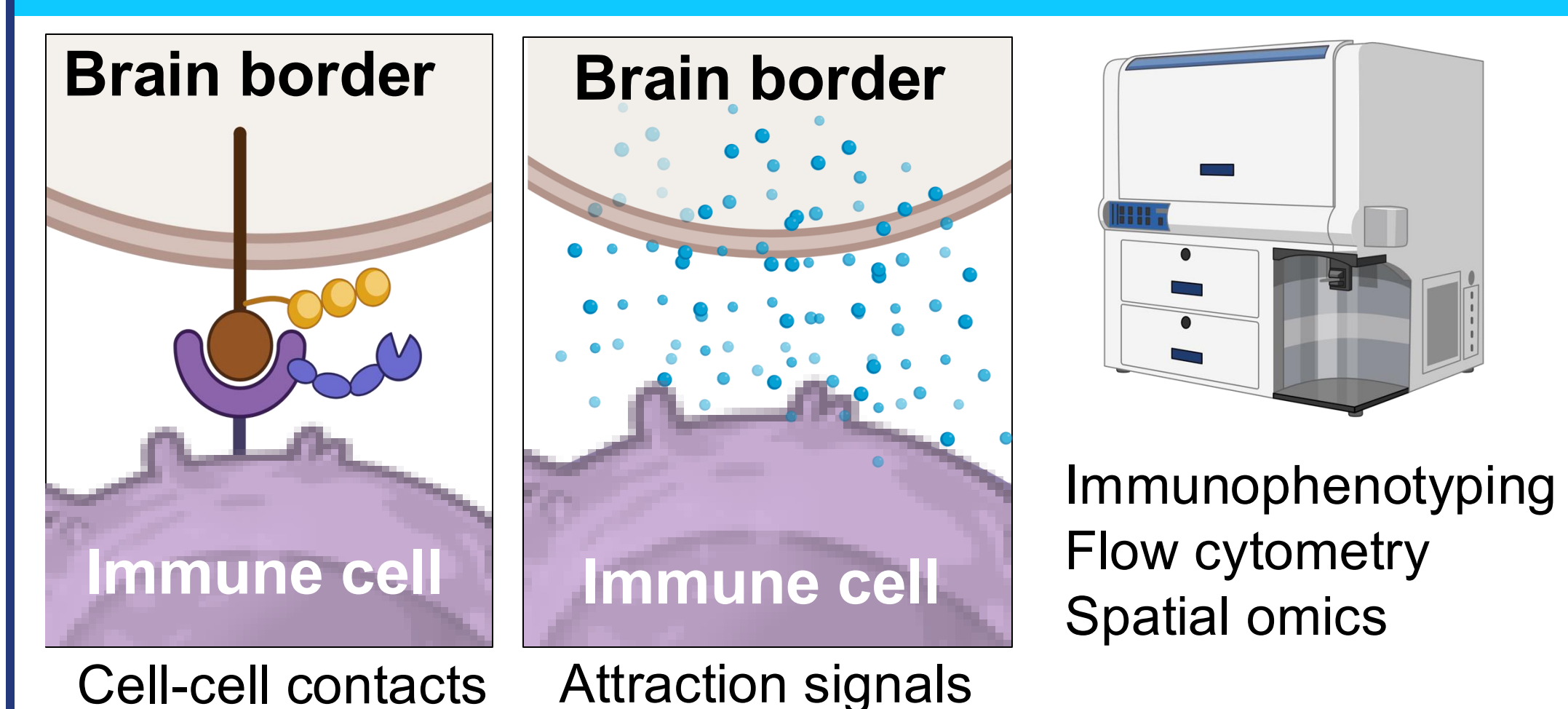
IBA1 (Macrophage) ChAT (neuro) — 50 µm
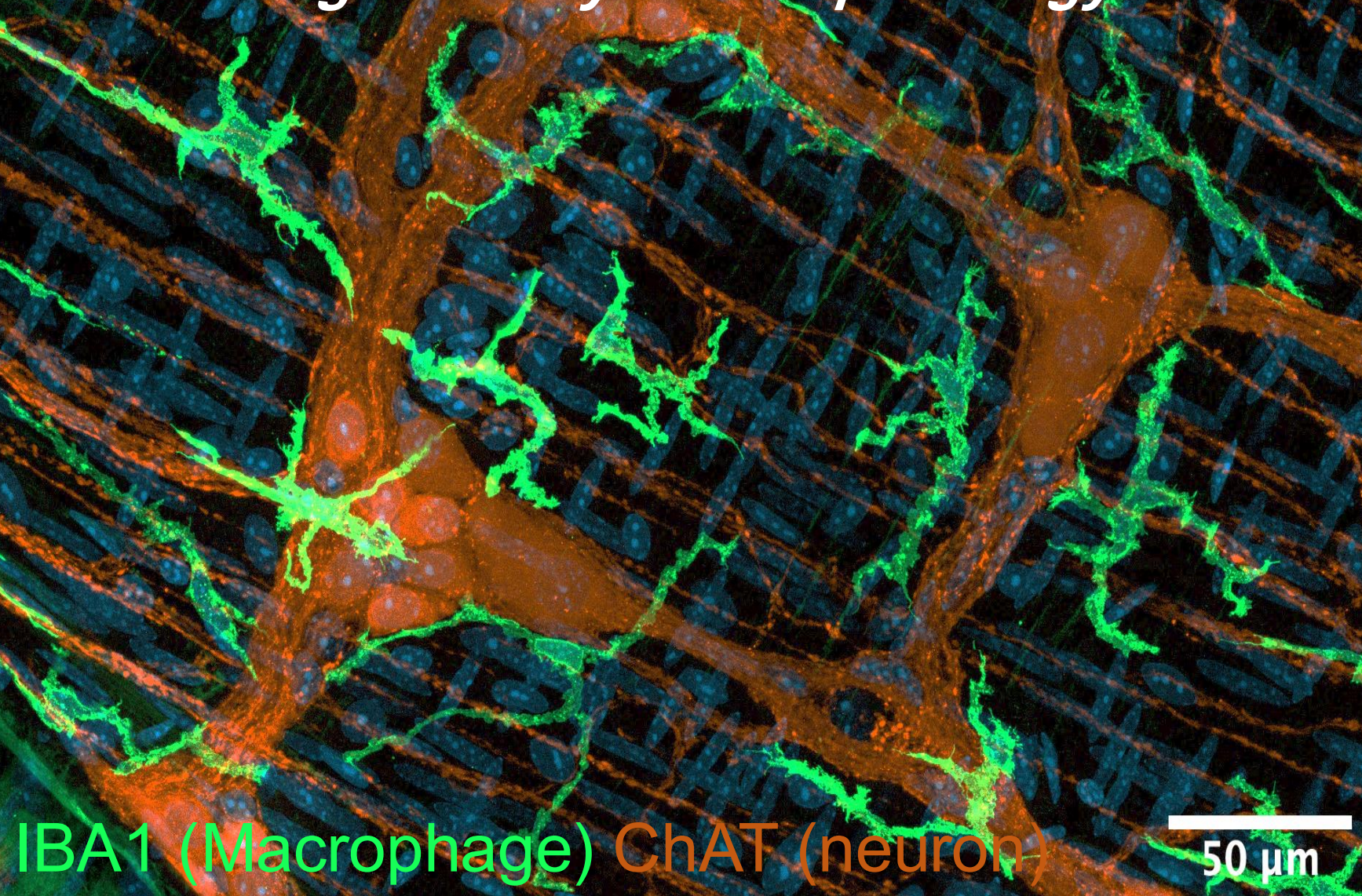
(IV) Intestinal Immune Activation and Immune Trafficking

ENS macrophages become inflammatory in response to α-synuclein, and this promotes the recruitment of circulating immune cells, including T cells, **which are then trafficked to the brain.** We are interested in how these cells access the CNS via brain borders, where they interact with border-associated macrophages (BAMs) and contribute to neuroinflammation. **Understanding gut-initiating immune trafficking is central to uncovering how peripheral inflammation accelerates neurodegeneration in PD.**
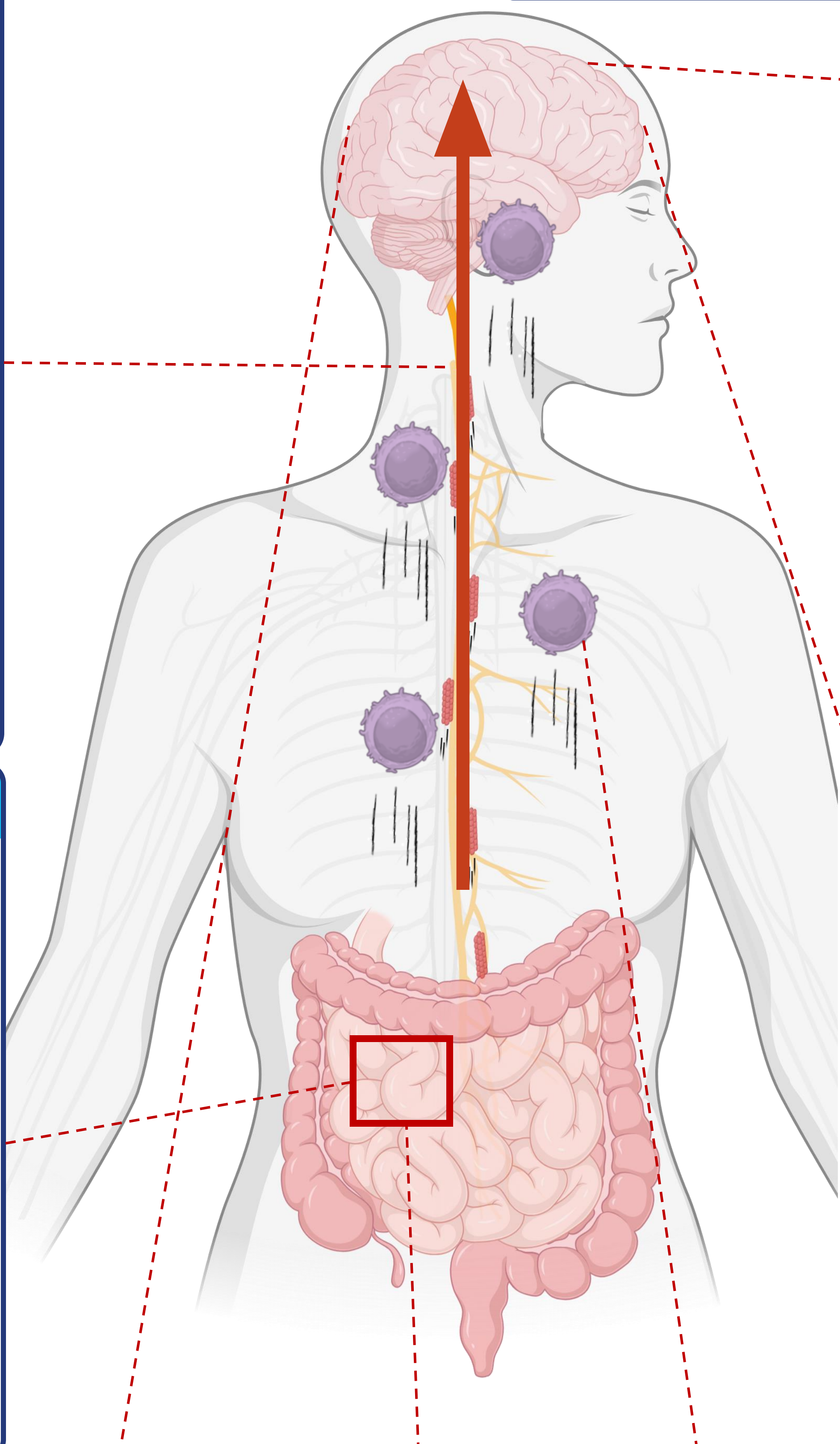
(v) Gut-derived immune cells accumulate at the meninges before they enter

Meninges (brain border) in PD model

All immune cells — Immune cells coming from the gut

Project 1: Investigate how immune cells infiltrate the brain: where, how, when?

Brain border — **Brain border**

Immune cell — Immune cell

Cell-cell contacts — Attraction signals

Immunophenotyping
Flow cytometry
Spatial omics

Using innovative tools and models, we track **the timing, routes, and molecular cues** that guide peripheral immune cell entry into the brain and their ultimate cellular targets.

Project 2: How do macrophages respond to α-synuclein aggregates? What factors influence their response?

Macrophage

Specialized vacuum cleaner

…But appears to break down in response to α-syn

Mapping of macrophage functional states and interactions in PD

We study how macrophages in the gut, bladder, and skin, tissues affected early in PD, respond to local α-synuclein accumulation. We further investigate how **intestinal inflammation**, a risk factor for PD, promotes this pathological immune crosstalk.

Project 3: Characterize the circulating immune profiles in high-risk individuals as predictors of PD Risk

High-risk PD patient

Immunophenotyping
Functional assays

Disease progression prediction
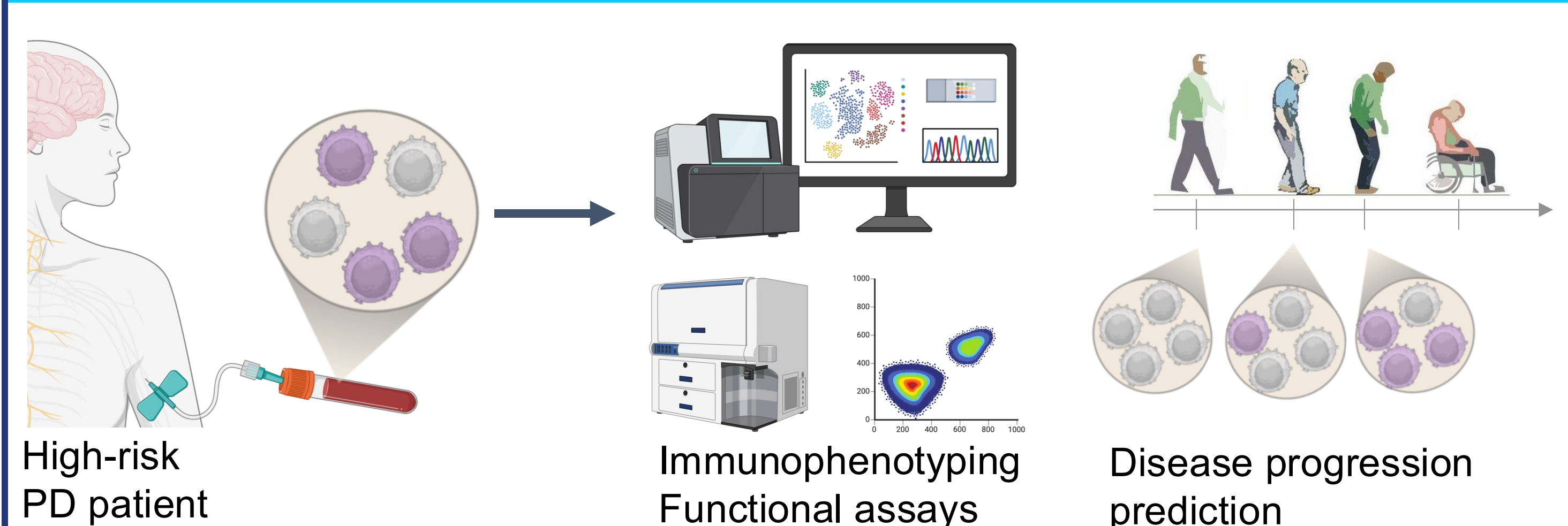
In collaboration with clinical cohorts, we profile PBMCs from high-risk patients and use humanized mouse models to test their disease-promoting potential. We aim to discover predictive immune biomarkers and define functional immune phenotypes linked to PD.

The lab (May 2025): Dr. Seppe De Schepper, Dr. Alanna Spiteri, Dr. Wen Peng, Andriana Lygeraki, Ruben Hellemans

A) Immune trafficking across the gut-brain-border axis in PD (Alanna)
B) Understanding the role of macrophage origin and inflammation in PD (Andriana, Wen)
C) Contributes to everything and everyone (Seppe, Ruben)

Tools and focus: Tissues: gut, brain, bladder, skin; **Models:** gut injection models, PD models, intestinal inflammation; **Focus:** macrophage function, immune crosstalk, systemic priming **Tools:** spectral flow cytometry, CITE-seq, spatial proteomics,…

These are only brief overviews of the main projects. **Interested in finding out more?** Talk to us or reach out: sebastiaan.deschepper@uantwerpen.be Website: https://deschepperlab.sites.vib.be/en

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