

University of Naples Federico II

Department of Pharmacy

PhD course in Pharmaceutical Sciences Cycle XXXVIII
(CRESCENDO PhD doctoral program)



CRESCENDO Welcome event

02/05/2023

High-fat diet shaped intestinal microbiota and risk for Parkinson's disease: pharmacological control by prebiotics

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UNIVERSITÀ DEGLI STUDI
DI NAPOLI FEDERICO II





Summary



01

**Context &
Prior research**

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**PhD project
objectives**

03

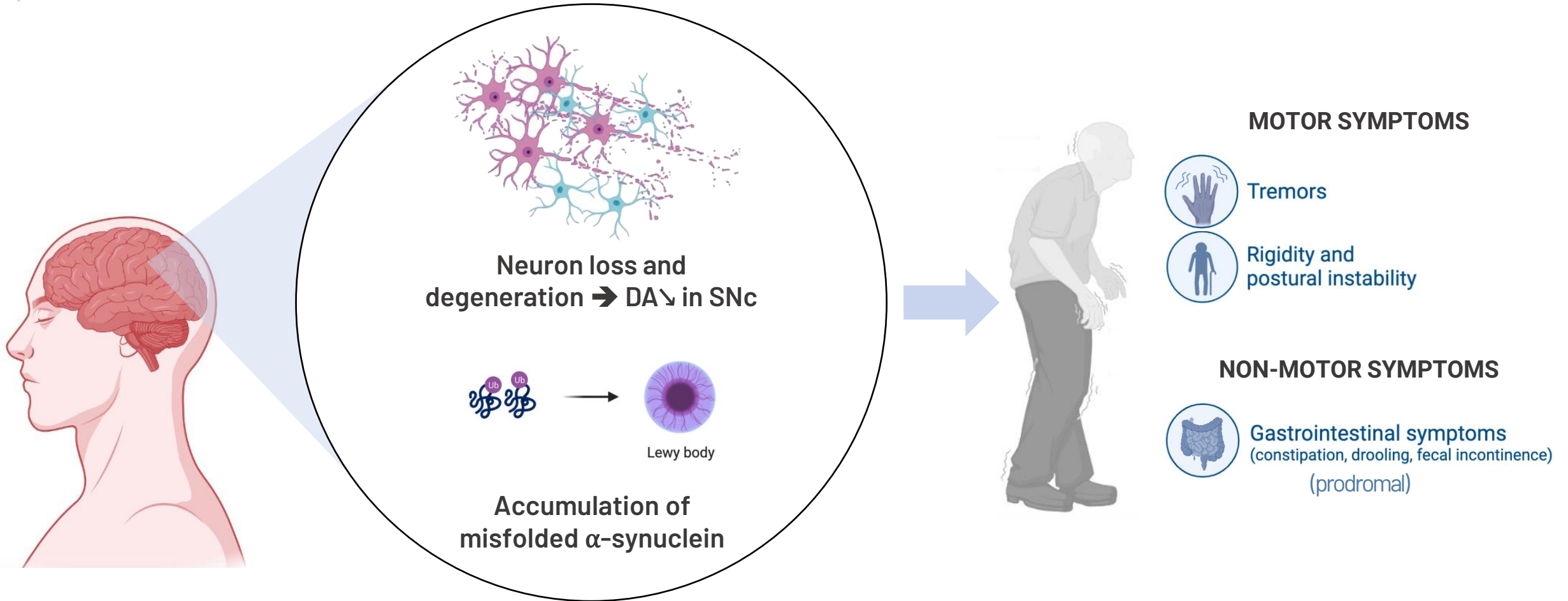
**Steps of the
PhD project**



01

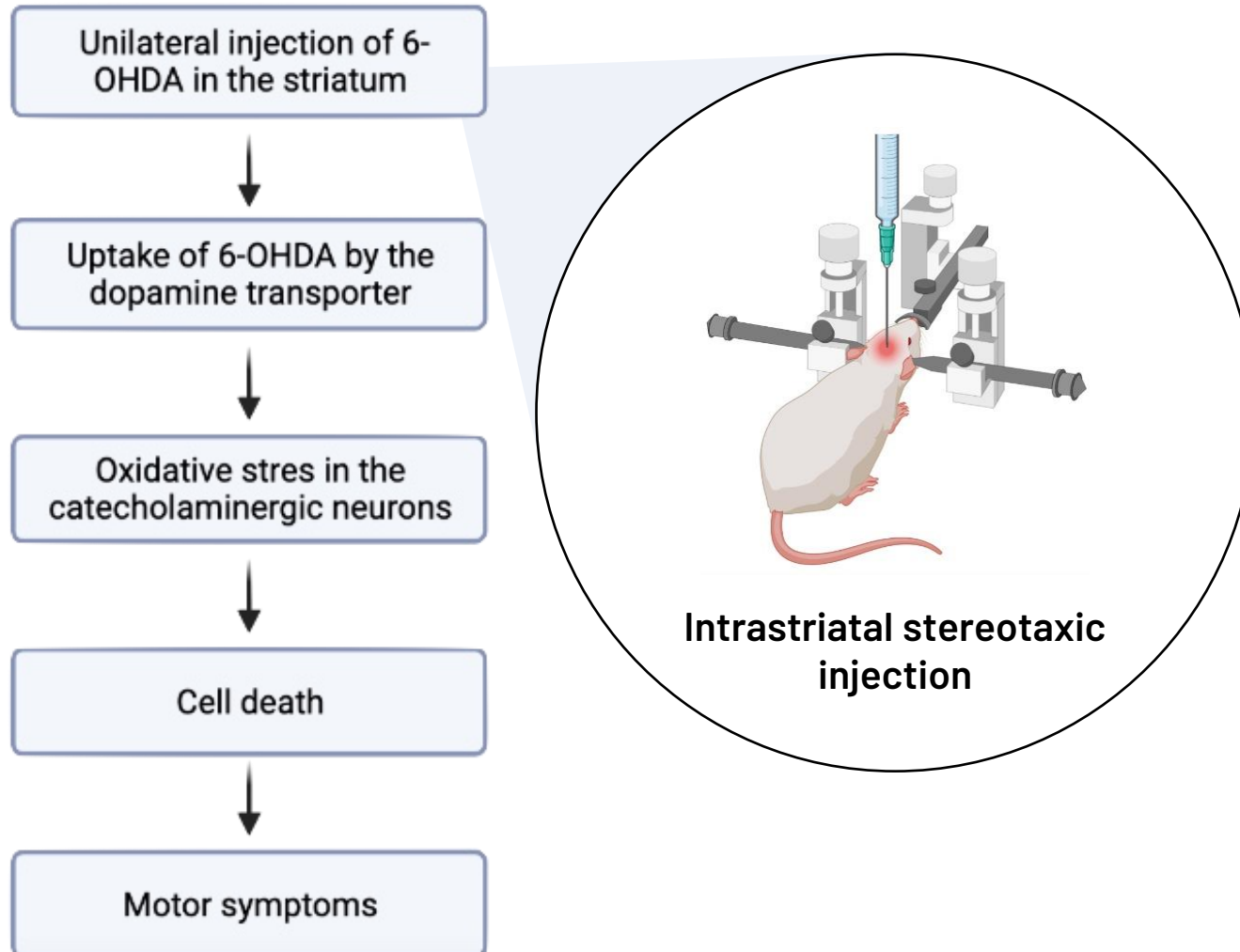
CONTEXT & PRIOR RESEARCH

Parkinson's disease (PD)



PD mouse model: 6-OHDA injection

(Dopamine analog)



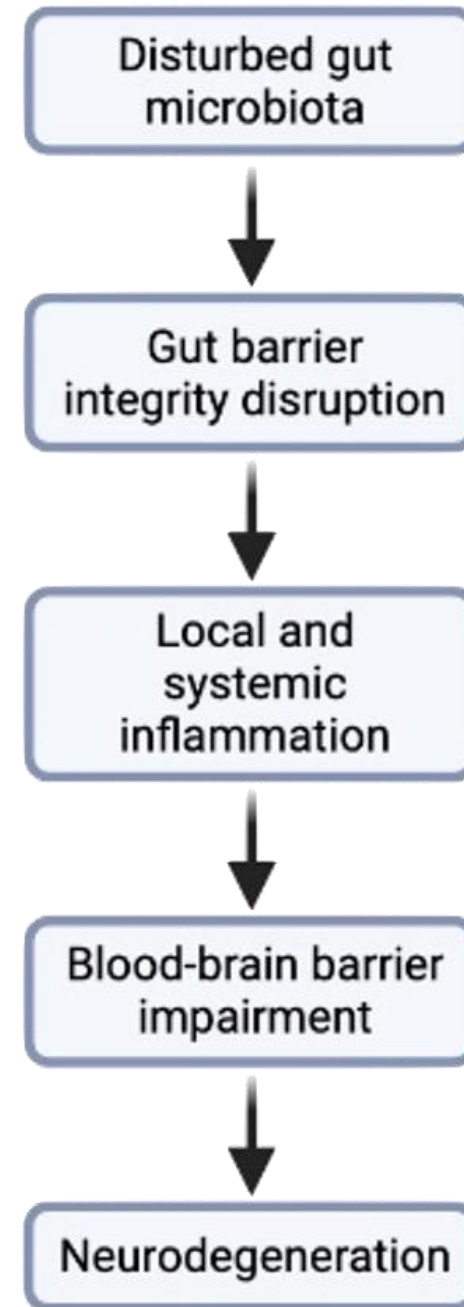
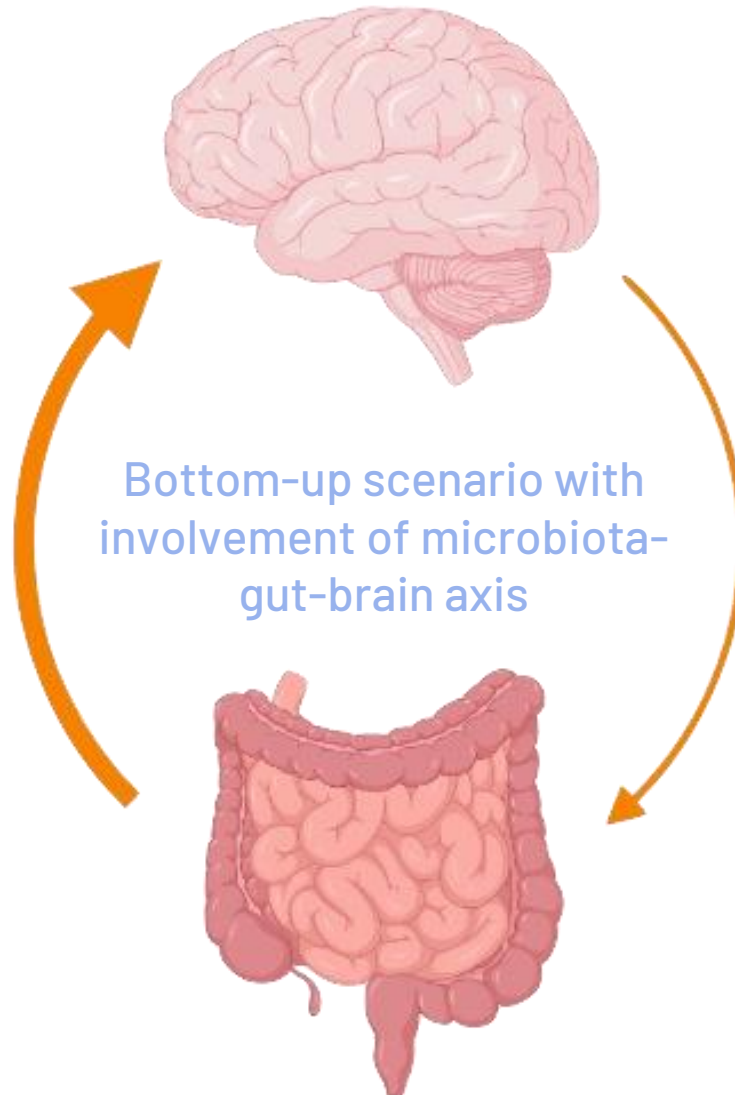
Advantages

- Neuroinflammation and DA neuron loss
- Motor impairment

Disadvantages

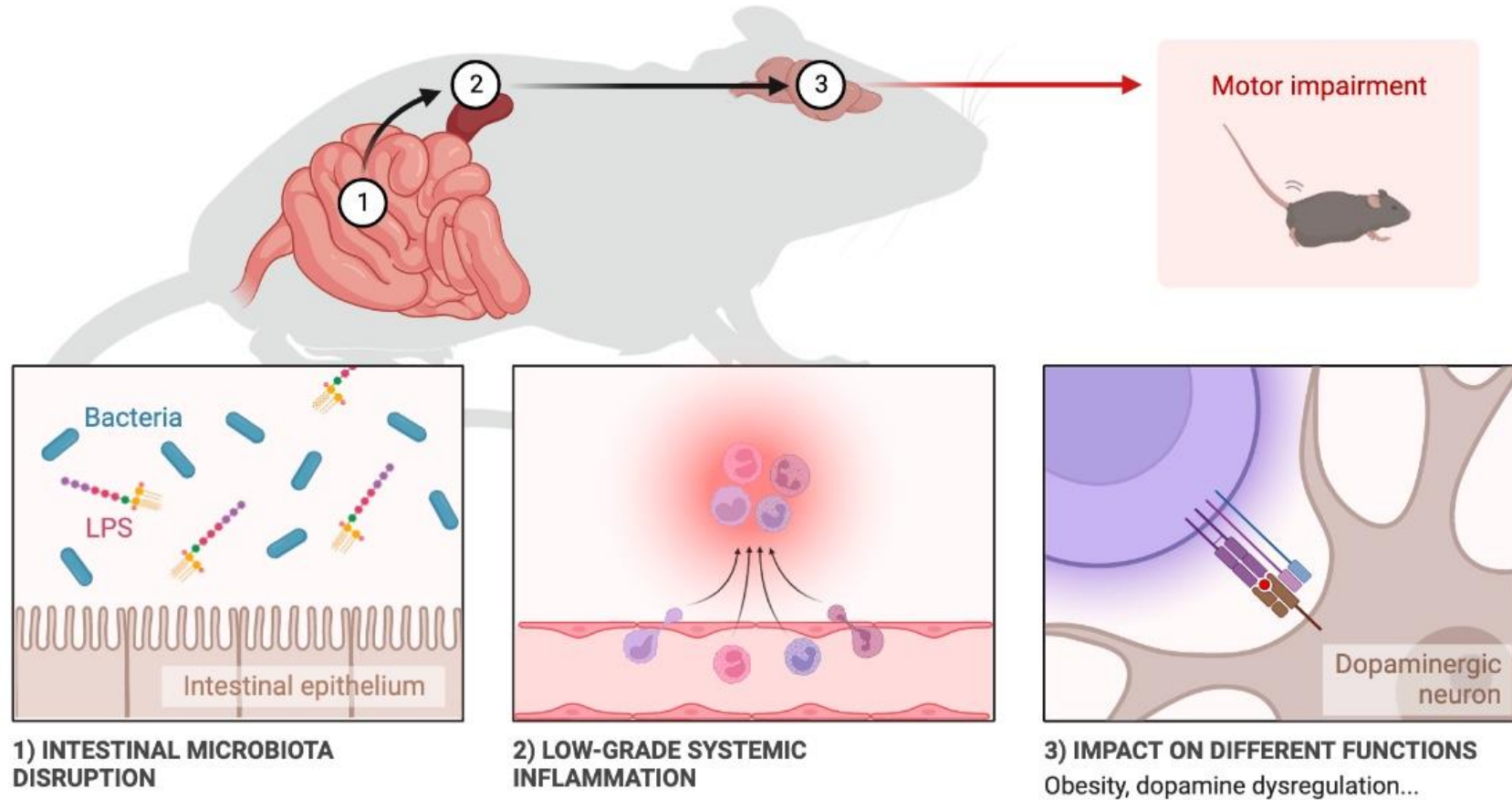
- No formation of Lewy bodies
- Damages other parts of the brain
- Only mimics the neuronal events of PD

Gut-brain axis



Dual-hit model of PD

Dysbiosis and striatal neurotoxin insult



Dual-hit model of PD by ceftriaxone-induced dysbiosis

6-OHDA

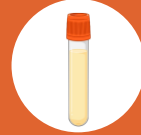


Brain



- ↓ Motor coordination
- ↑ Apomorphine-induced rotational behavior
- ↓ TH expression
- ↑ nNOS and iNOS expression
- ↑ COX-2 expression
- ↓ Bcl-2/ Bax ratio expression

Serum



- ↑ TNF- α and IFN- γ
- ↑ IL-1- β

Colon



- ↑ Histological structural abnormalities and inflammatory cell infiltration
- ↑ IL-1- β
- ↑ Ptgs-2
- ↓ ↓ IL-10

Feces



- ↑ *P. timonensis*
- ↑ *U.s. of Eubacteriales*
- ↓ *U.s. of Ligilactobacillus*

CFX + 6-OHDA



- ↓ ↓ Motor coordination
- ↑ ↑ Apomorphine-induced rotational behavior
- ↓ ↓ TH expression
- ↑ nNOS and iNOS expression
- ↑ ↑ COX-2 expression
- ↓ Bcl-2/ Bax ratio expression

- ↑ ↑ TNF- α and IFN- γ
- ↑ IL-1- β
- ↑ LPS

- ↑ ↑ Histological structural abnormalities and inflammatory cell infiltration
- ↑ ↑ IL-1- β
- ↑ Ptgs-2
- ↓ ↓ IL-10

- ↓ **Gut microbiota diversity**
- ↓ Keystone taxa
- ↓ *A. furcosa*
- ↓ *P.cinnamivorans*
- ↓ *D.saccarophila*
- ↑ *R.lactaris*

Western diet & PD

Western diet



Saturated and $\omega 6$
fatty acids



Refined sugars



Excessive salt
intake



Low consumption
of $\omega 3$ fatty acids
and fibers

Microbiota
dysregulation

↑ risk of PD, metabolic
syndrome / obesity, ...

02

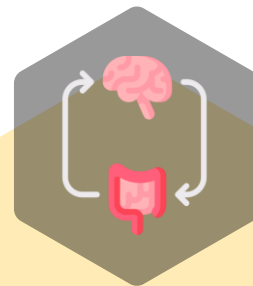
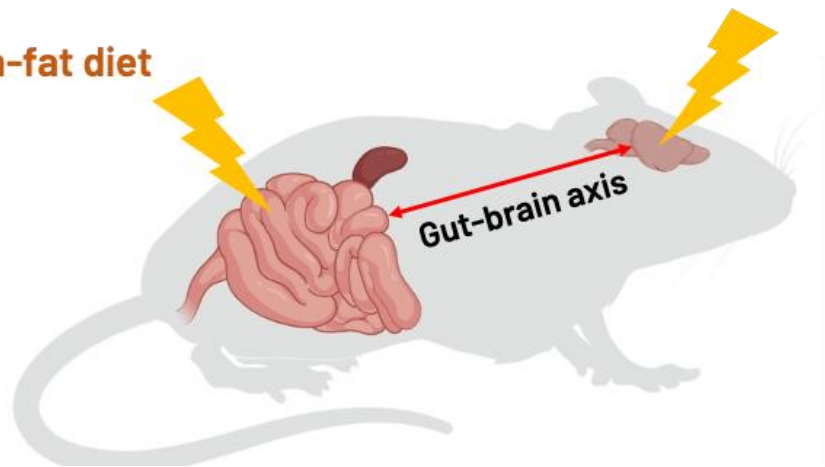
PhD project objectives

02 Objectives

PhD Project objectives

High-fat diet

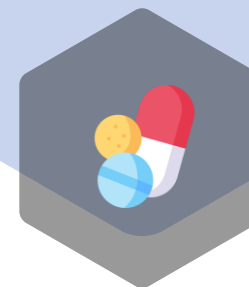
6-OHDA



Investigate the relationship between the **gut-brain axis** and the development of Parkinson's disease:

- Effect of High fat diet on:
 - Parkinson's disease progression
 - Gut microbiota and intestinal homeostasis in PD mice
- Identification of PD-associated bacteria

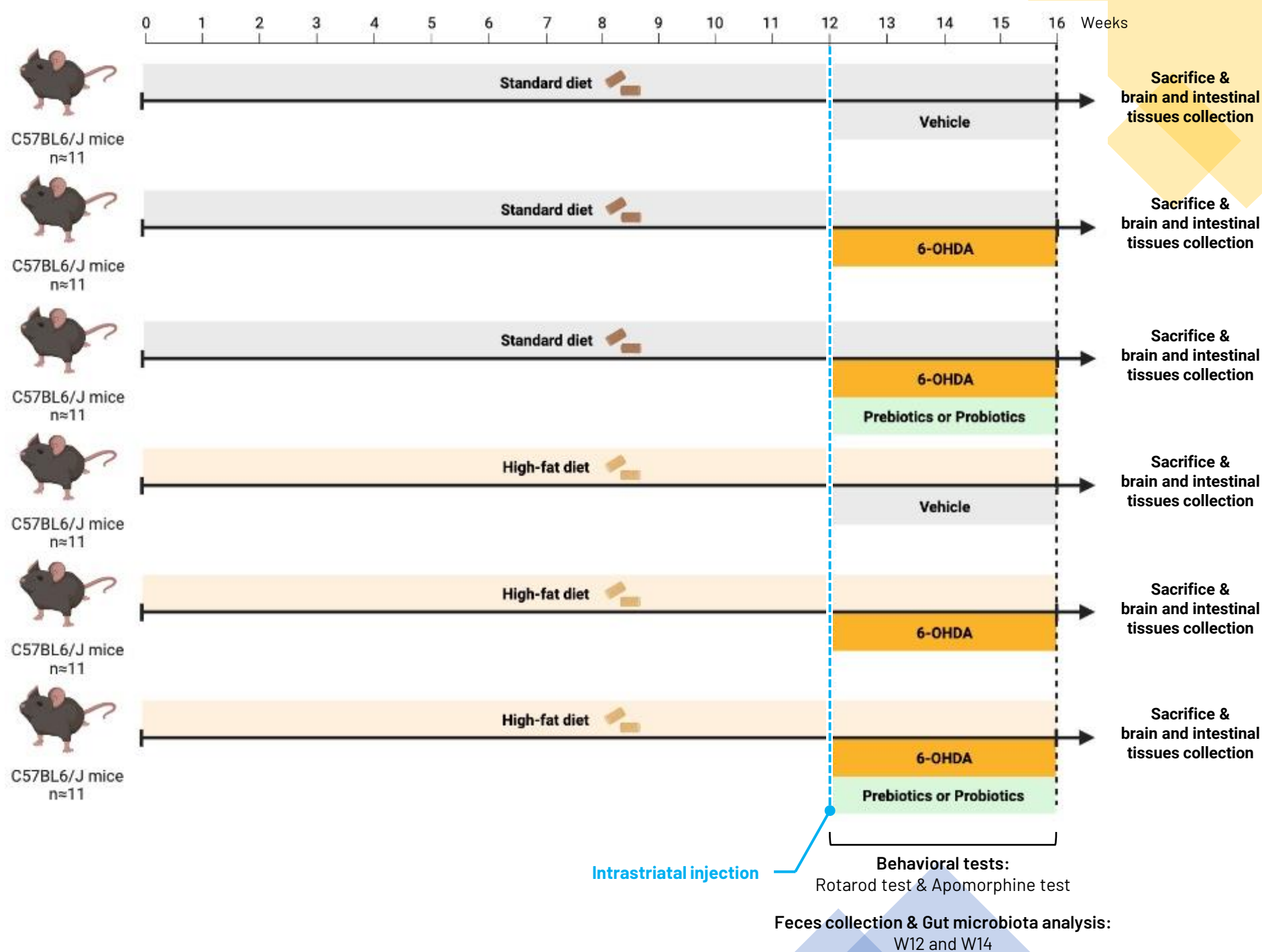
Examine the impact of altering gut microbiota on the disease's progression through the use of **prebiotics or probiotics**



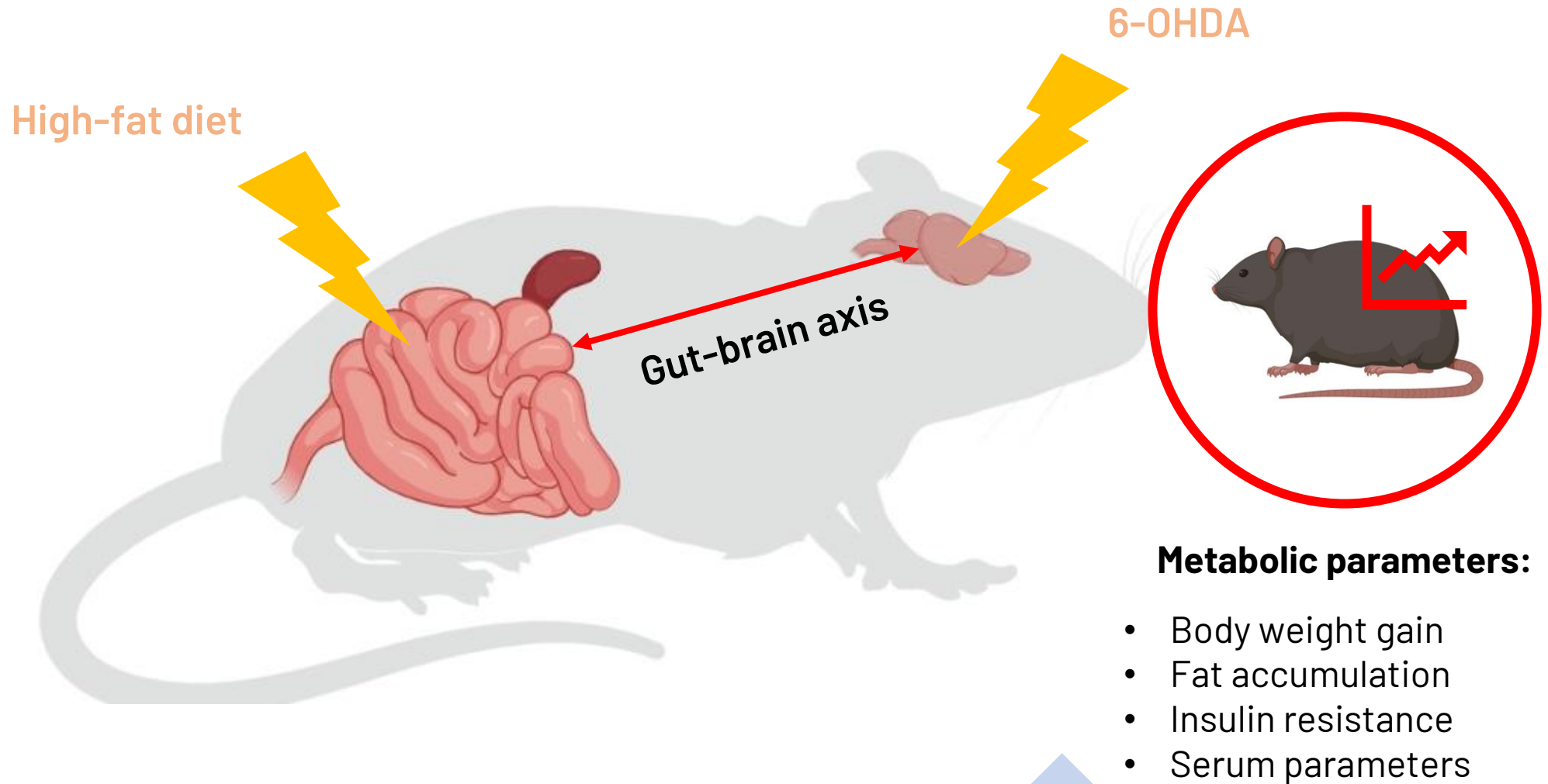
02

Objectives

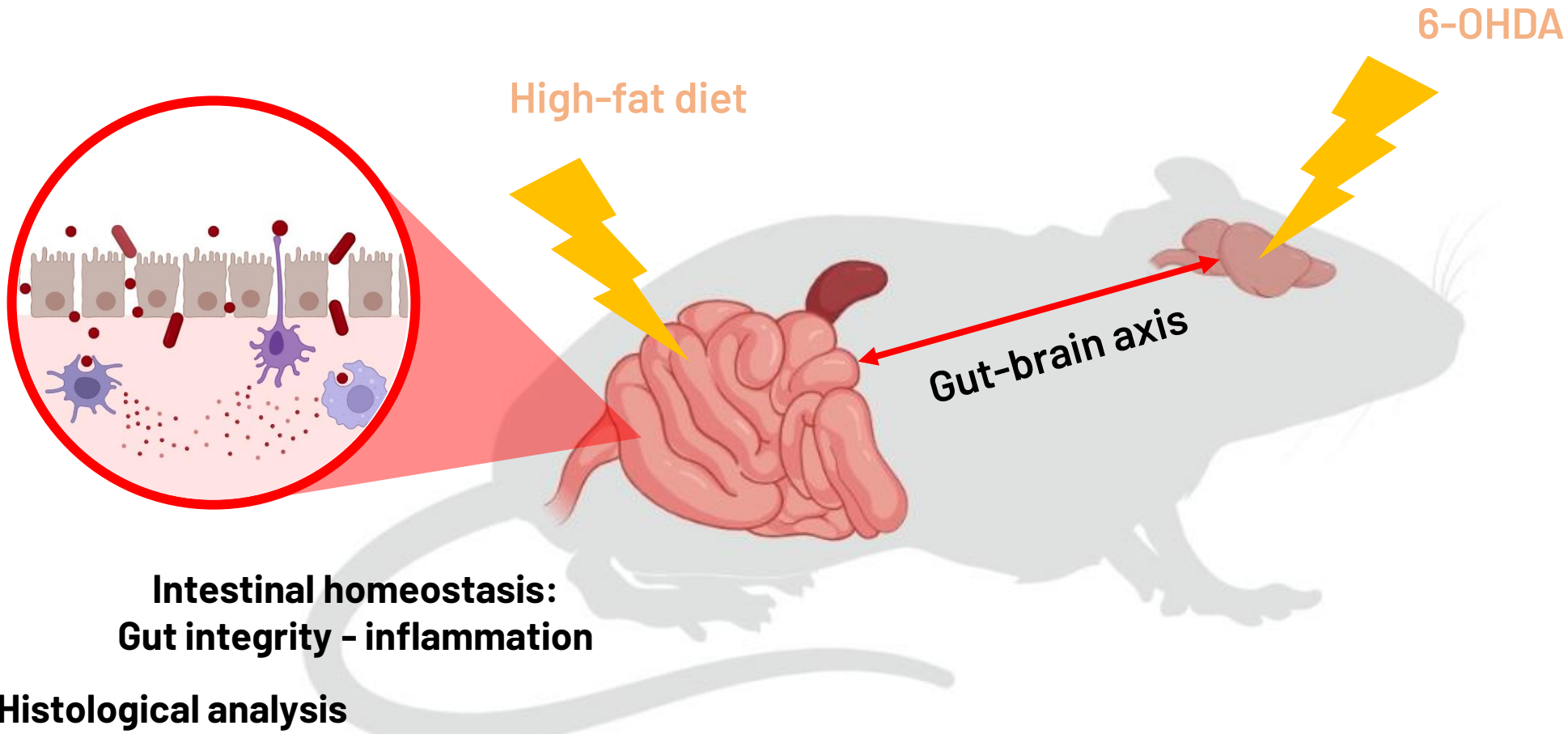
Experimental plan



Dual-hit model: analyzed parameters

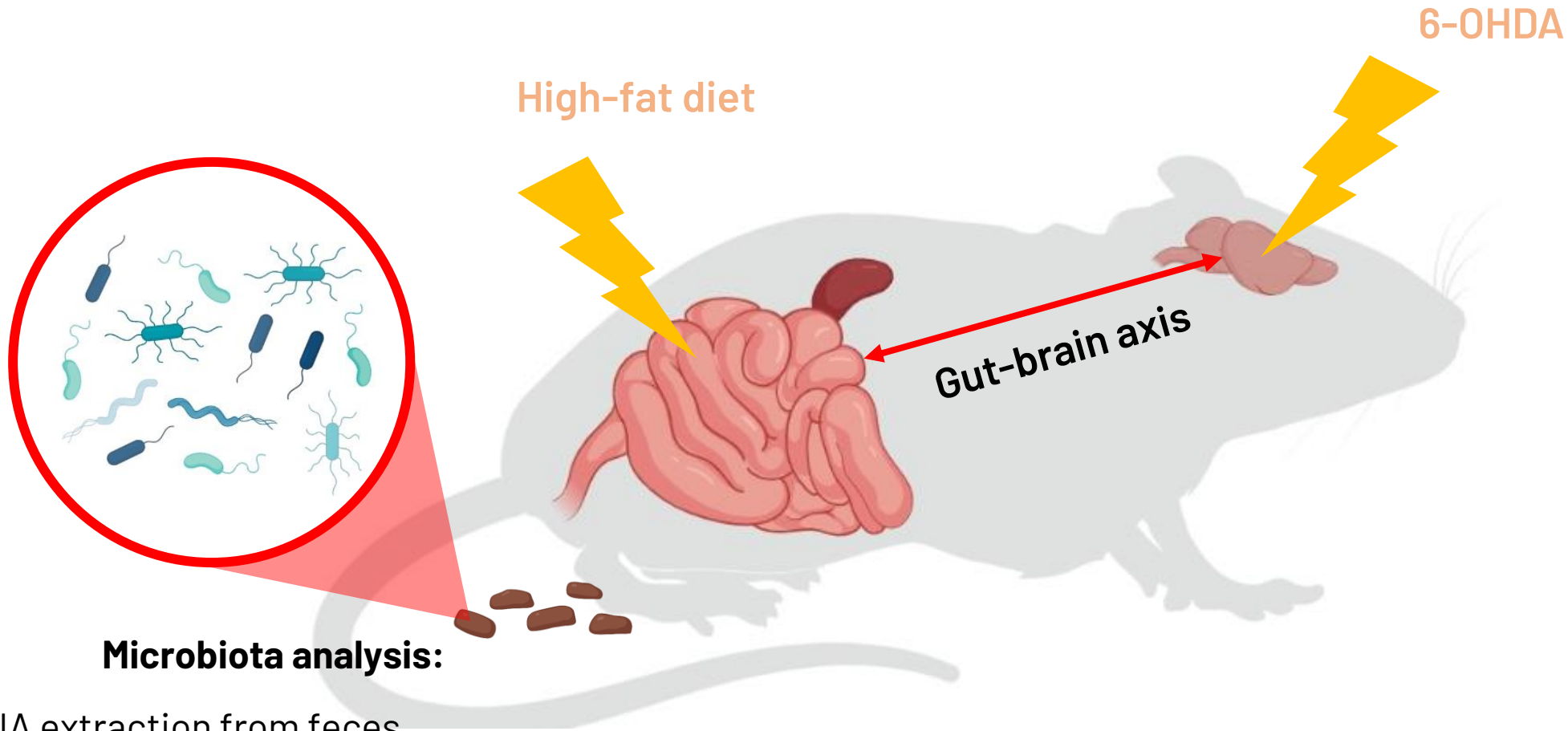


Dual-hit model: analyzed parameters



- **Histological analysis**
- **Tight junctions:** mRNA expression (*Real-time PCR*) and protein quantification (*Western blot*)
- **Cytokine** mRNA expression (*Real-time PCR*)

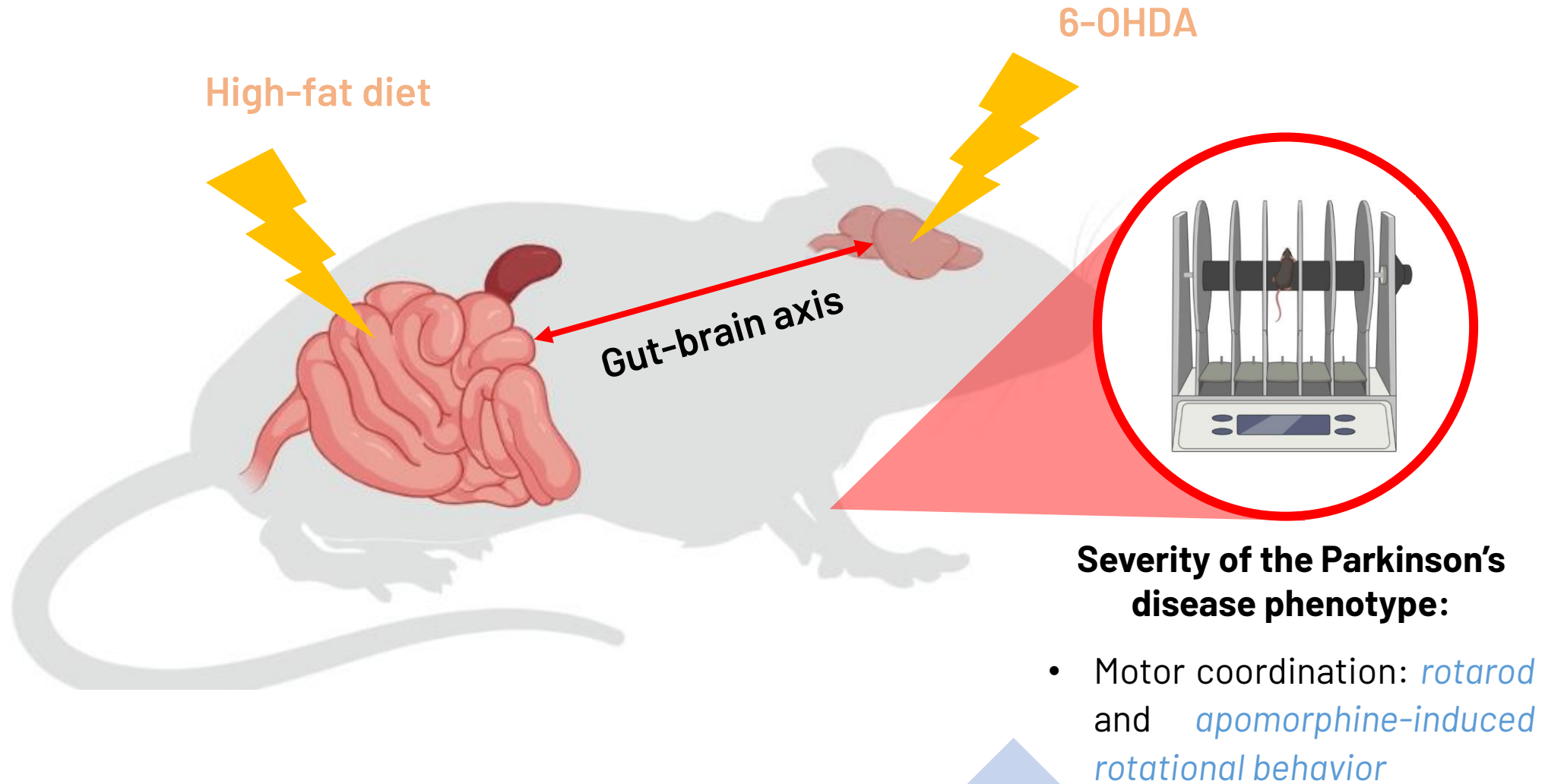
Dual-hit model: analyzed parameters



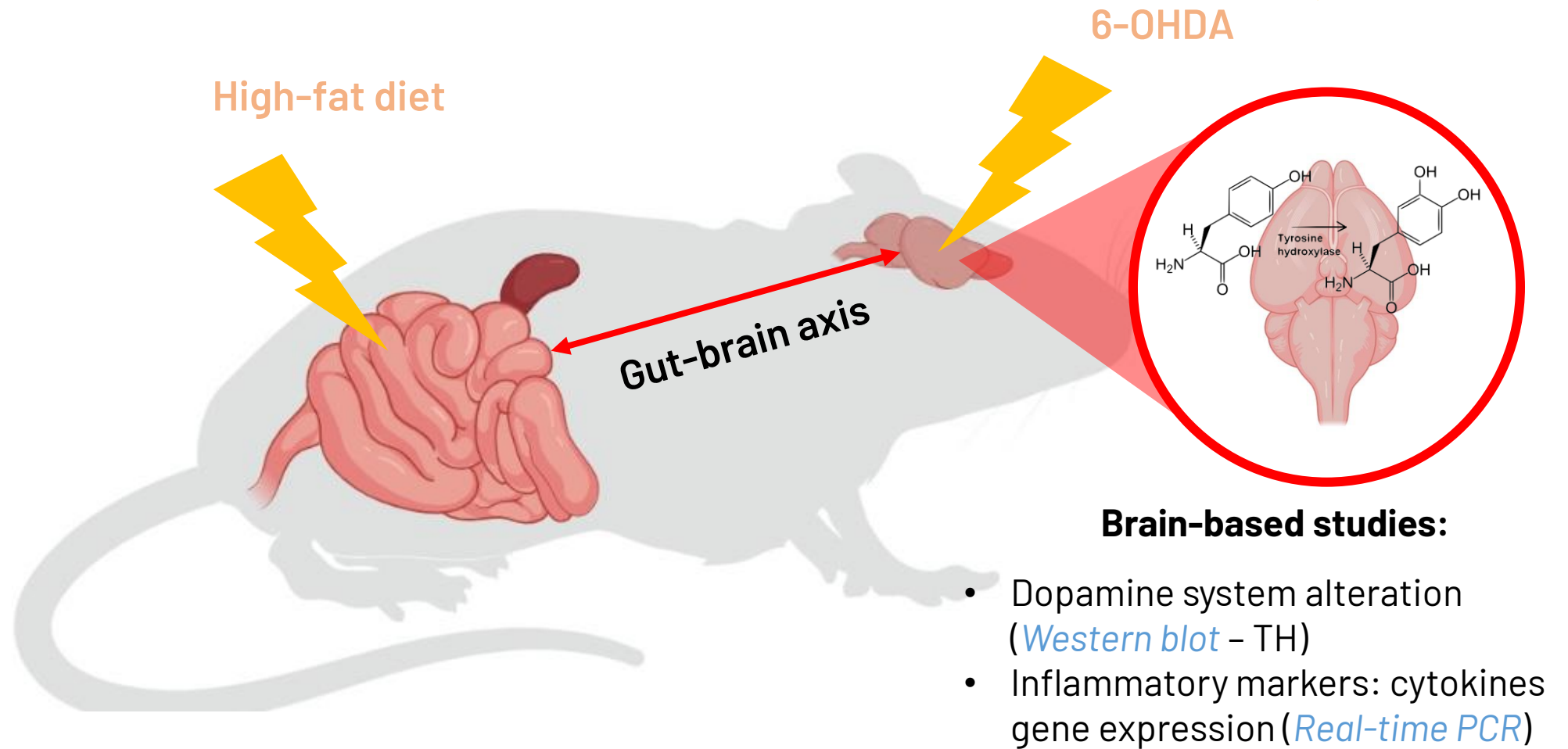
Microbiota analysis:

- DNA extraction from feces
- High-throughput NGS techniques
- Data analysis of microbiota sequences

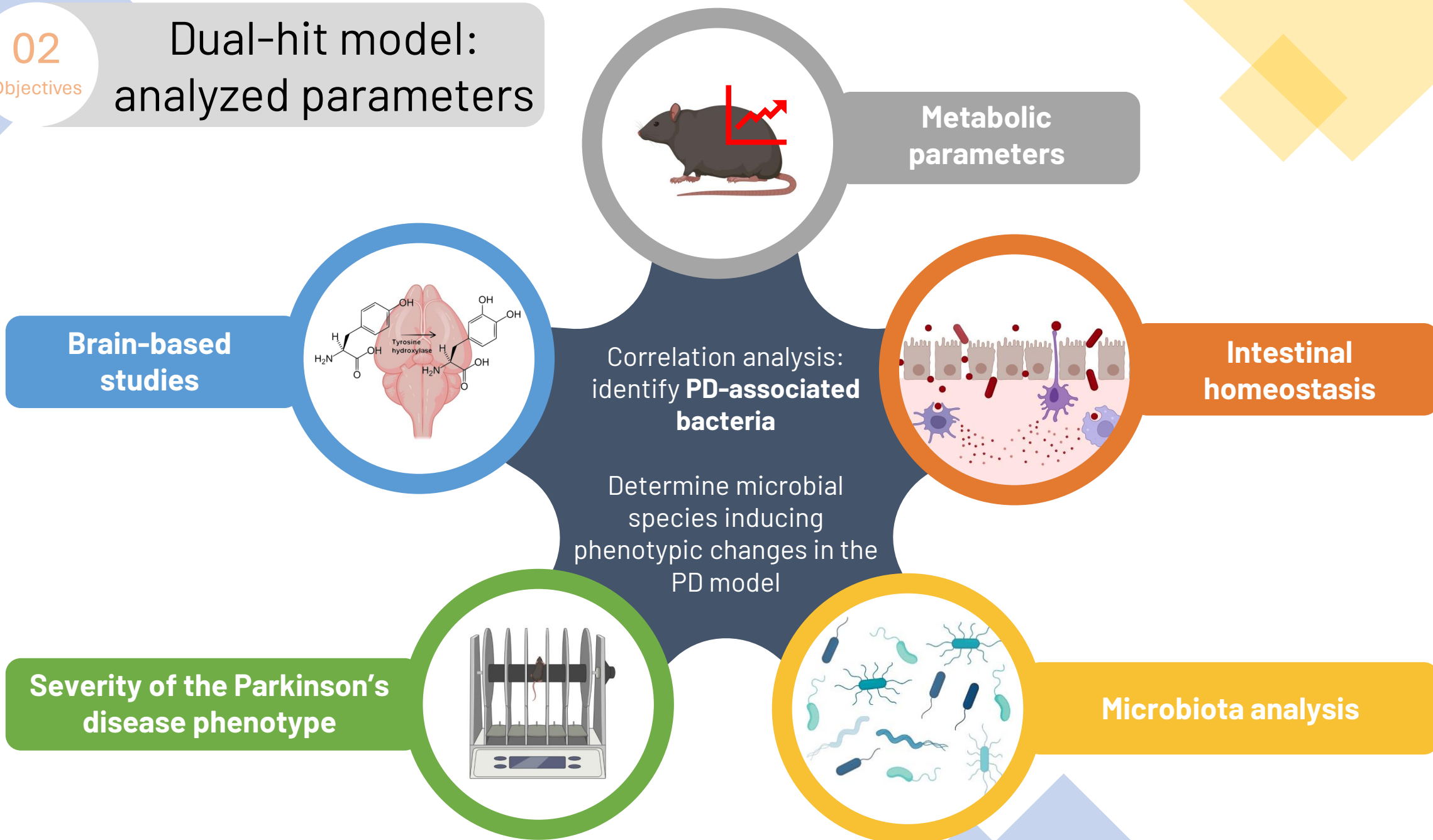
Dual-hit model: analyzed parameters



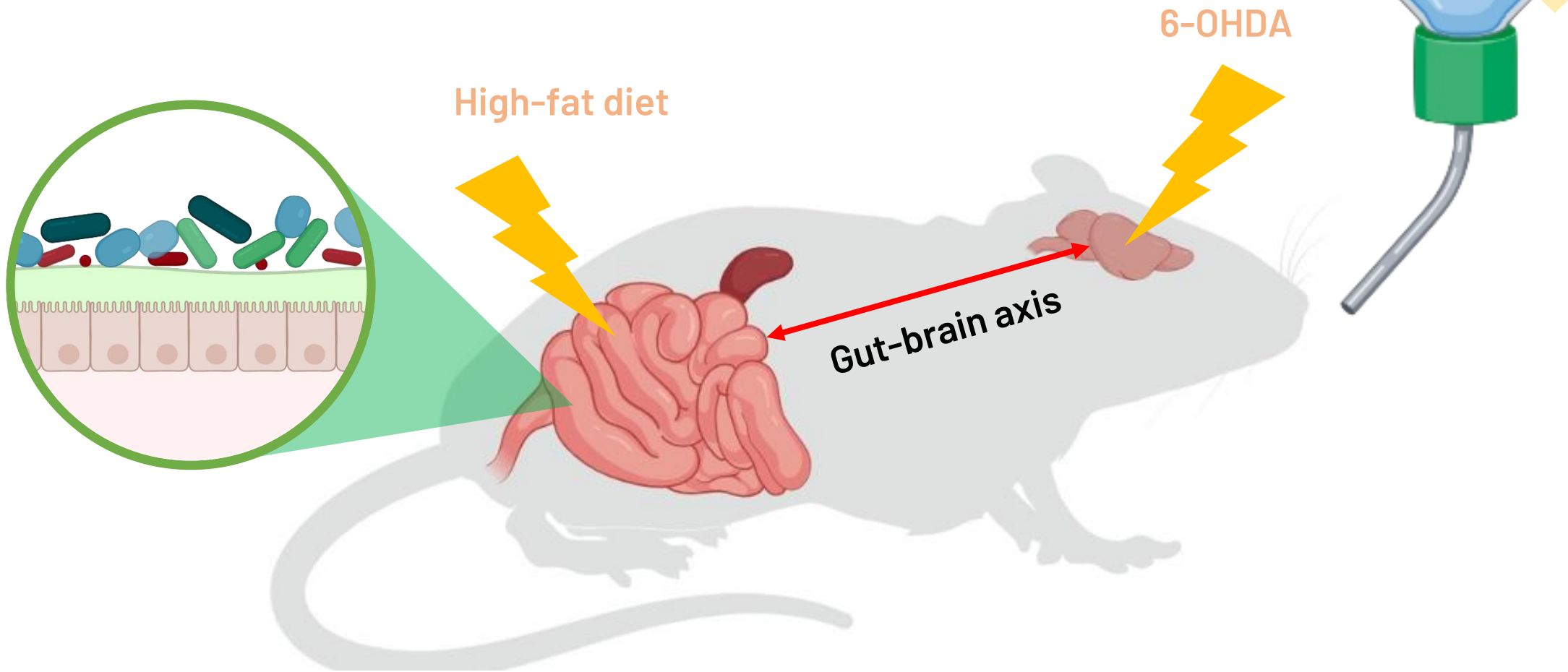
Dual-hit model: analyzed parameters



Dual-hit model: analyzed parameters



Microbiota-based therapeutic intervention

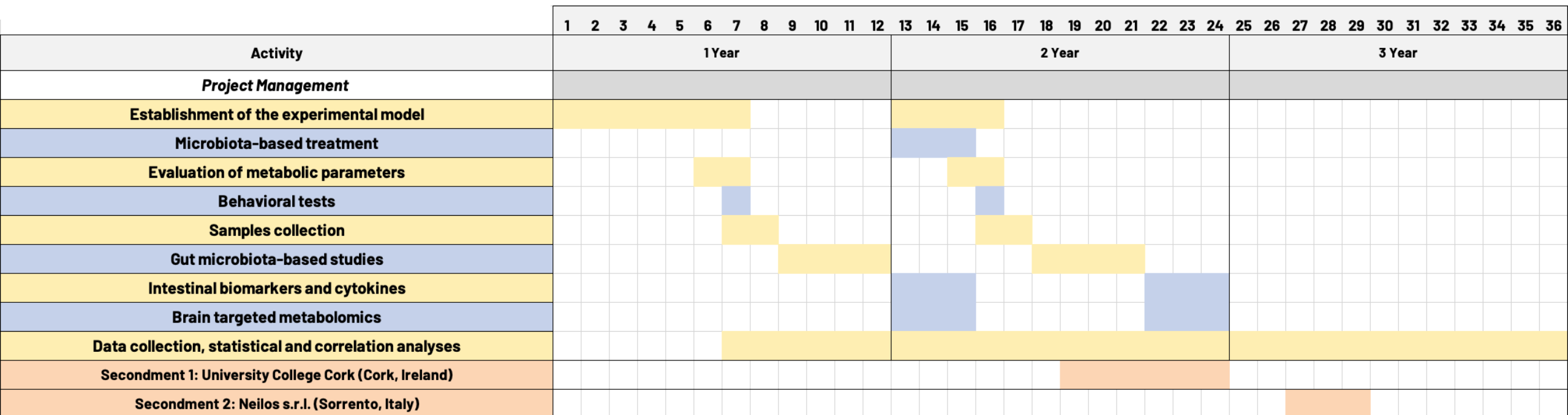


➔ Analysis of the impact on **PD phenotype** and on **microbiota composition**

03

Steps of the PhD project

Gantt diagram



Until now...

Lab training

- DNA extraction from feces and saliva
- Bacterial DNA amplification & quantification
- RNA extraction
- Study of gene expression through PCR
- Bacterial culture and manipulation
- Laboratory safety training

Animal training

- Certification for animal testing
- Mice handling & dissection training



Bioinformatics training

- Online course introducing the shell program and the basic bioinformatic tools for microbiota analysis
- Computed analysis of microbiota: bacterial diversity, relative abundance of species, correlation network

Congresses

- Gut Microbiota for Health – Prague (03/23)
- MicrobiotaMi – Milan (04/23)

The slide features a light blue background with several decorative geometric elements. In the top-left corner, there are overlapping blue squares and diamonds. In the top-right corner, there are overlapping yellow squares and diamonds. A central horizontal blue bar contains the text. On the right side of this bar, there is a blue square and a blue diamond. At the bottom center, there are overlapping blue squares and diamonds.

THANK YOU FOR YOUR ATTENTION