UNIVERSITAT ROVIRA i VIRGILI

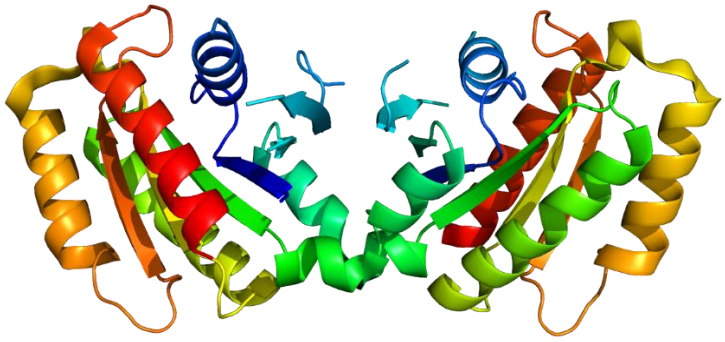
GÖTEBORGS UNIVERSITET

# STUDY OF THE EFFECT OF G2019S MUTATION IN LRRK2: UNDERSTANDING THE LINK BETWEEN PERIPHERAL INFLAMMATION AND NEURODEGENERATION IN PARKINSON'S DISEASE

**Laia Rivas Galvez**

**Double Bachelor's Degree in Biotechnology and Biochemistry and Molecular Biology**

## End of Degree Project in Biotechnology



**Academic Tutor: Mª del Carmen Portillo Guisado, Department of Biochemistry and Biotechnology, carmen.portillo@urv.cat**

**In cooperation with: University of Gothenburg**

**Supervisor: Dr. Anetta Härtlova, Department of Immunology and Microbiology, anetta.harlova@gu.se**

**Tarragona, September 1st 2023**

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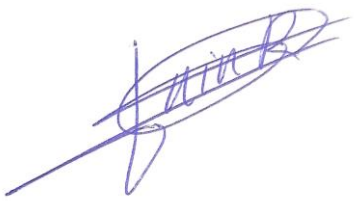

**This work is a confidential study**

# 1. Research Center's Information

This study was carried out during my curricular internship at the Department of Immunology and Microbiology of the University of Gothenburg from January to June of 2023.

The University of Gothenburg is a prestigious academic institution, known for its contributions to research and education. The Department of Immunology and Microbiology, within the university, is dedicated to advancing our understanding of immunological and microbiological processes, and it plays a crucial role in shaping the field's future.

Leading the research group I was in within the aforementioned department is Dr. Anetta Hartlöva, who has also served as my professional mentor during the internship period. The opportunity to collaborate with this institution has allowed me to apply the interdisciplinary knowledge I have gained throughout my studies.

University of Gothenburg

Address: Universitetsplatsen 1, 405 30, Gothenburg, Sweden

Phone: +46 31 786 00 00

# 2. Abstract

Parkinson's Disease (PD) is a neurodegenerative disorder characterized by the degeneration of dopaminergic neurons and the accumulation of protein aggregates in the brain. While current treatments focus on symptom management, the underlying disease mechanisms are complex and multifaceted.

This work explores the role of LRRK2 in the endolysosomal pathway, investigating how the G2019S gain-of-function mutation disrupt vesicle trafficking and protein degradation, contributing to PD pathology. Additionally, the study investigates the involvement of extracellular vesicles (EVs) in PD's inflammatory context, hypothesizing that dysfunctional lysosomal clearance of nucleic acids leads to intracellular buildup, prompting both cellular inflammation and the release of EVs.

Experimental methods include EV isolation from WT and G2019S LRRK2 mutant cells, their characterization through Western blot analysis, and assessment of the inflammatory signalling pathways using pattern recognition receptor (PRR) ligands as stimulation.

The findings contribute to our understanding of the interplay between LRRK2 mutations, lysosomal dysfunction, EVs, and inflammation in PD. These insights have implications for identifying new biomarkers and potential therapeutic targets, shedding light on PD's intricate mechanisms and offering avenues for disease management and intervention.

**Key words:** LRRK2, G2019S, extracellular vesicles, cGAS-STING, Type I Interferon, Parkinson’s Disease