



Peripheral Alpha-Synuclein Alterations in Red Blood Cells in Dementia with Lewy Bodies

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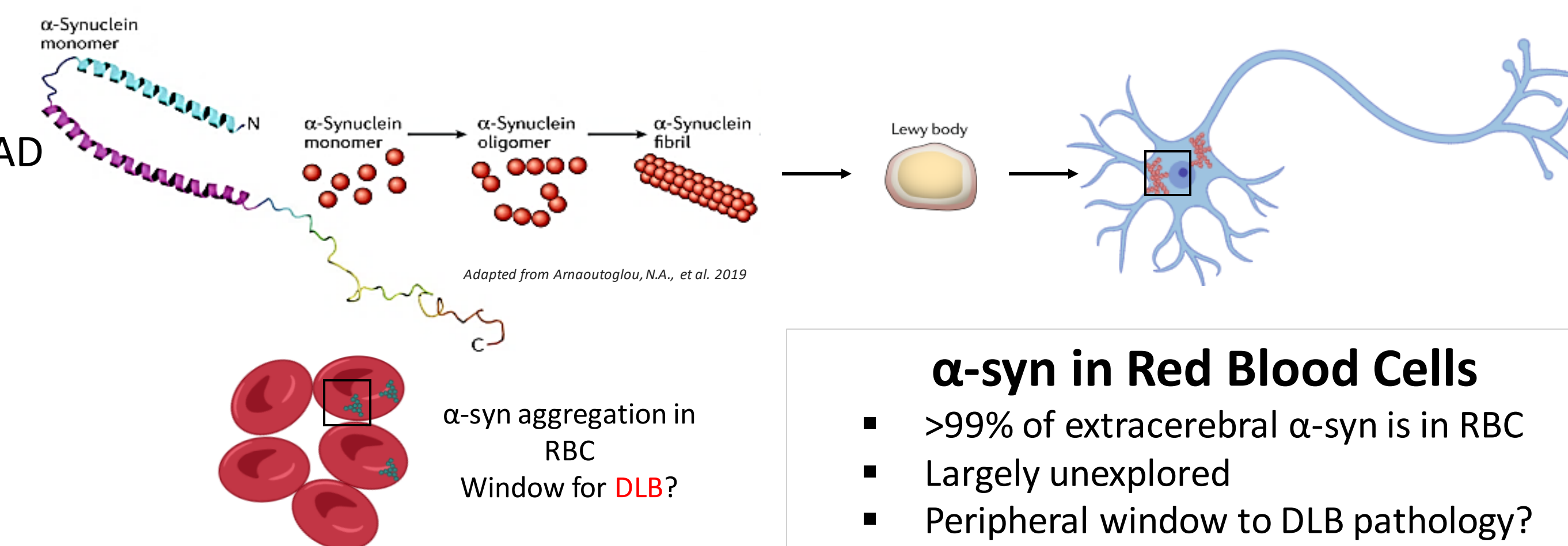
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INTRODUCTION

Dementia with Lewy bodies (DLB)

- 2nd most common cause of neurodegenerative dementia after AD
- Characterized by the abnormal accumulation of α -synuclein (α -syn) aggregates in neurons, nerve fibers or glial cells

Only one third of patients are correctly diagnosed
Pathophysiology not fully understood
No specific markers
No treatment



α -syn in Red Blood Cells

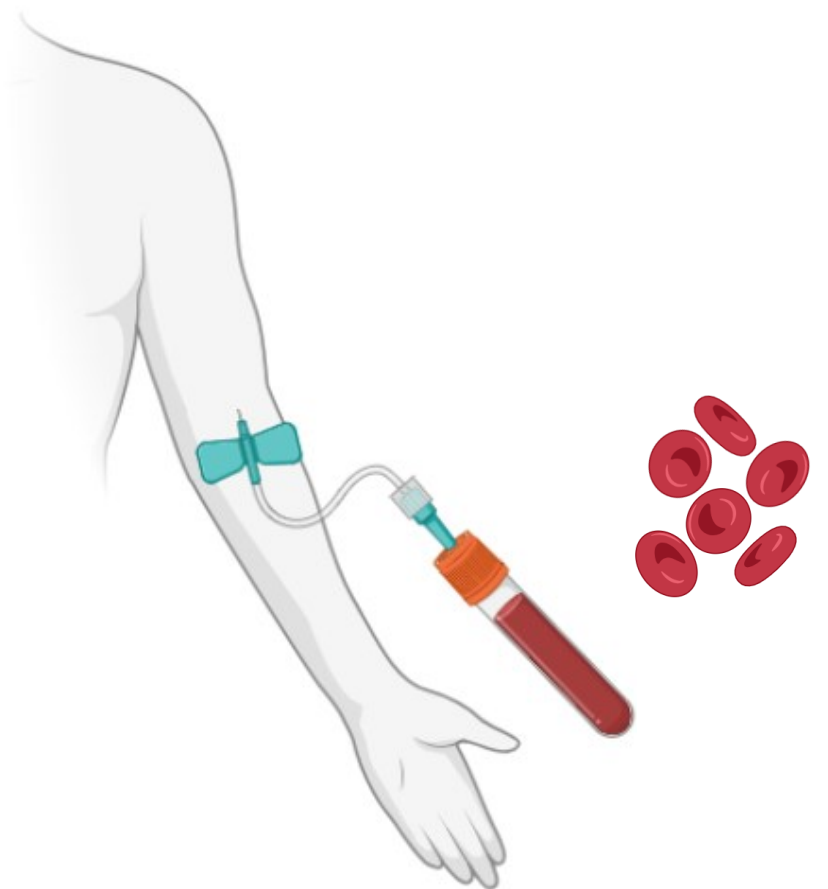
- >99% of extracerebral α -syn is in RBC
- Largely unexplored
- Peripheral window to DLB pathology?

OBJECTIVES

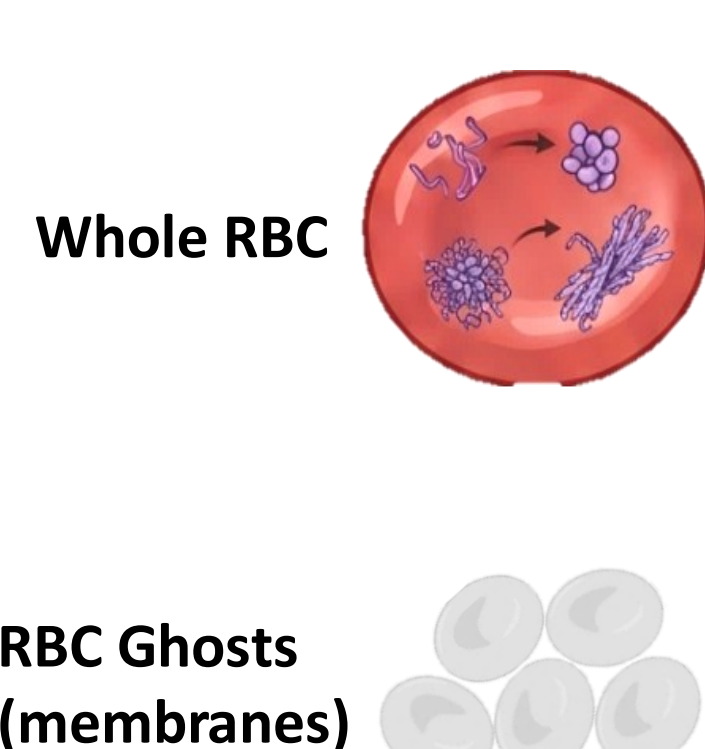
- 1 Characterization of α -syn in different RBC compartments of DLB patients
- 2 Examination of α -syn cargo in RBC extracellular vesicles

METHODOLOGY

RBC isolation



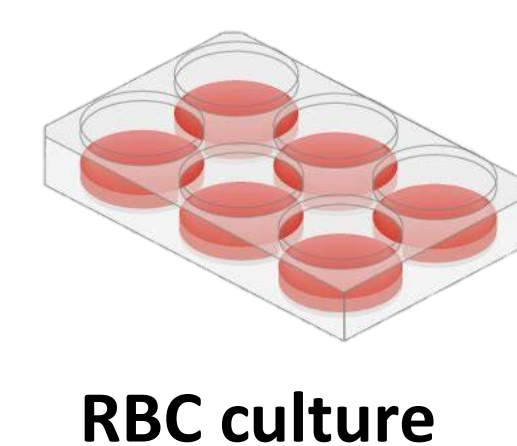
1. Quantification and characterization of α -syn in RBCs from DLB patients and controls



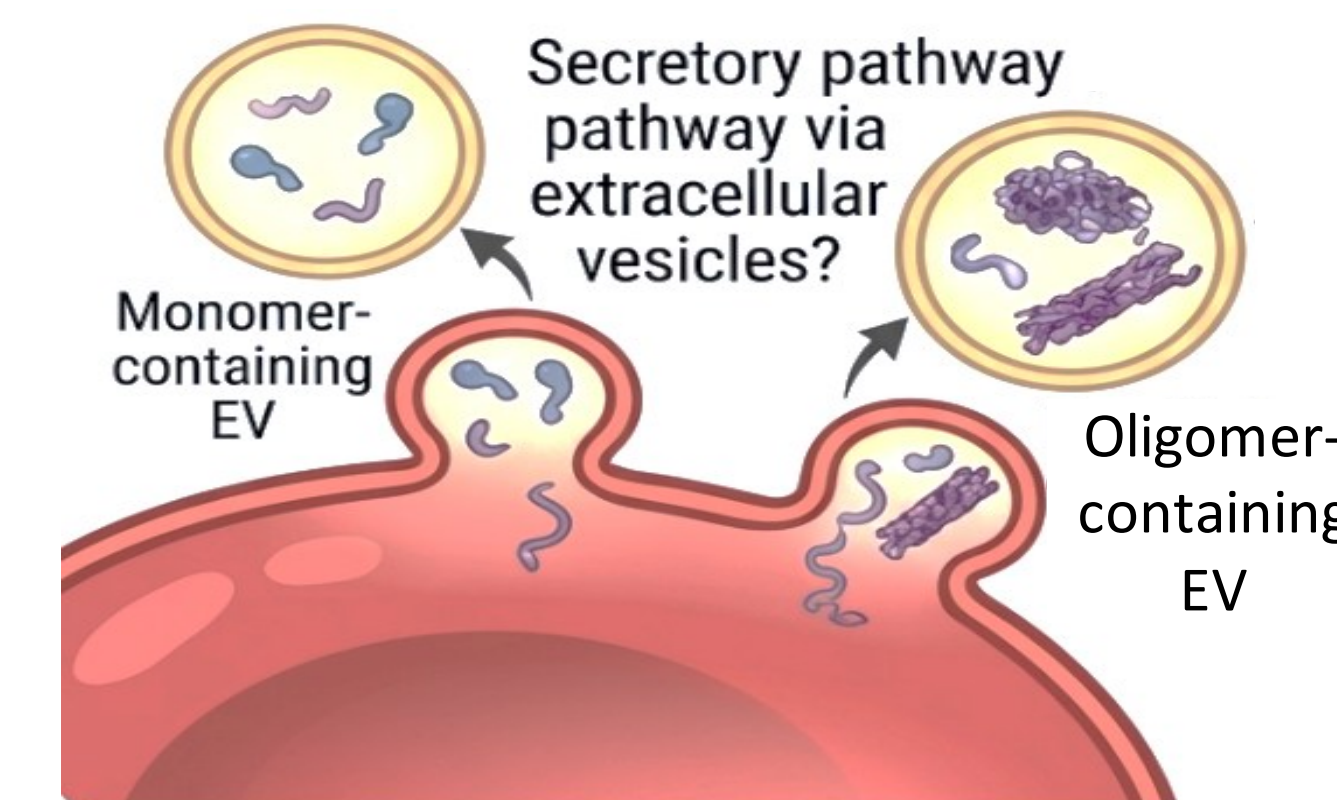
Studied α -syn forms:

- Total
 - Aggregated
 - Phosphorylated Ser129
-
- Total α -syn

2. Isolation and characterization of RBC extracellular vesicles (EVs)



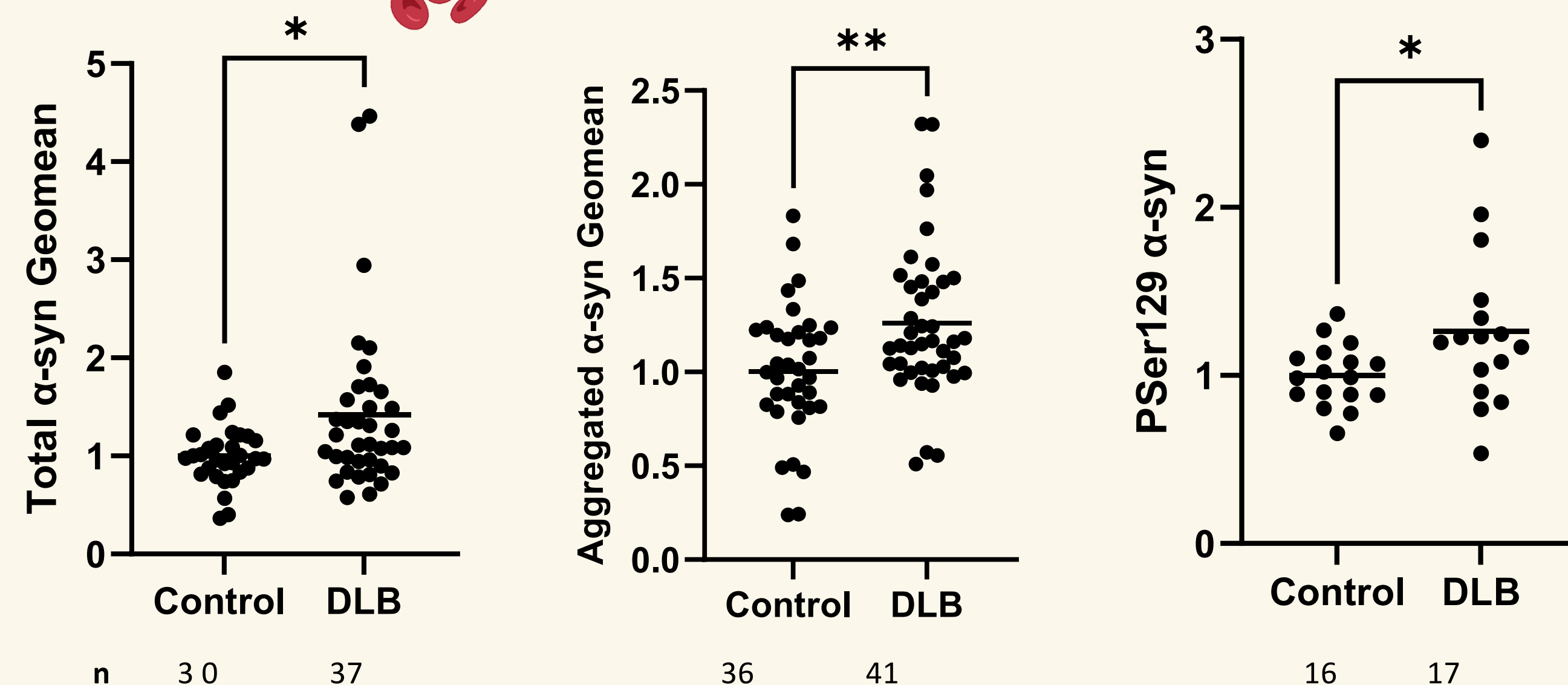
Isolation and characterization of RBC-EV



- NTA analysis of EVs
- Characterization of α -syn cargo by WB and ELISA

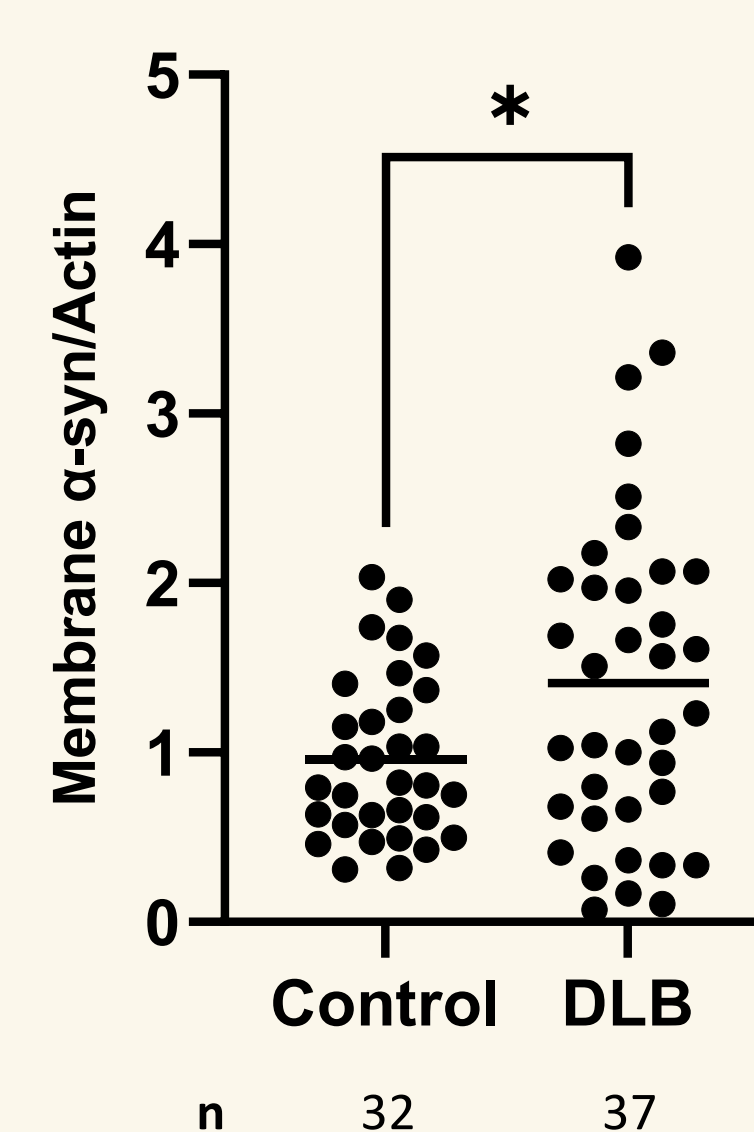
RESULTS

α -syn in RBC of DLB patients



Total, aggregated and phosphorylated α -syn in patients' RBC are significantly higher

Membrane-bound α -syn



α -syn relocalization at the RBC membranes in patients

CONCLUSION & PERSPECTIVES

- Deregulation, membrane relocalization, and higher aggregation of α -syn in patients' RBC compared to age and sex matched controls
- Preliminary data proved the liberation of α -syn from RBC by EV

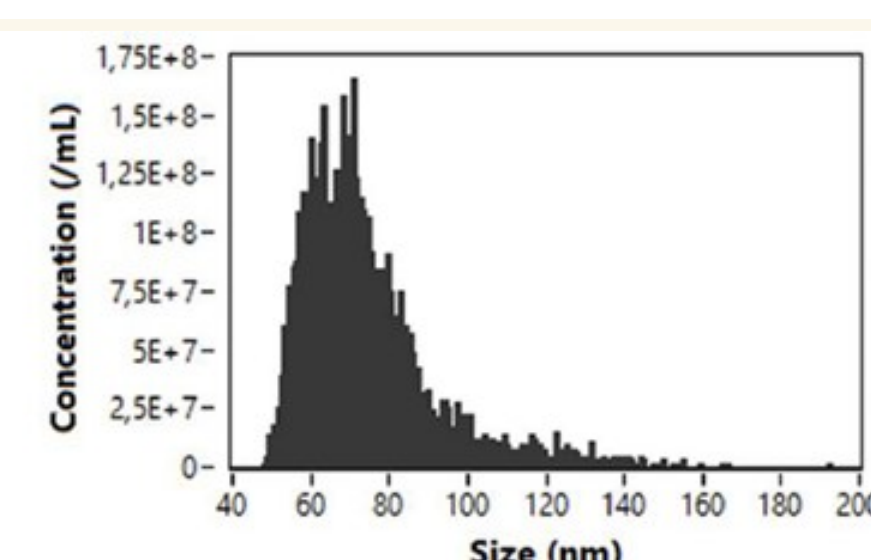
Next:

- α -syn seeding assays on RBC fractions
- Characterizing RBC-EV of patients and controls
- Testing the effect of RBC-EV on neurons and microglia in vitro

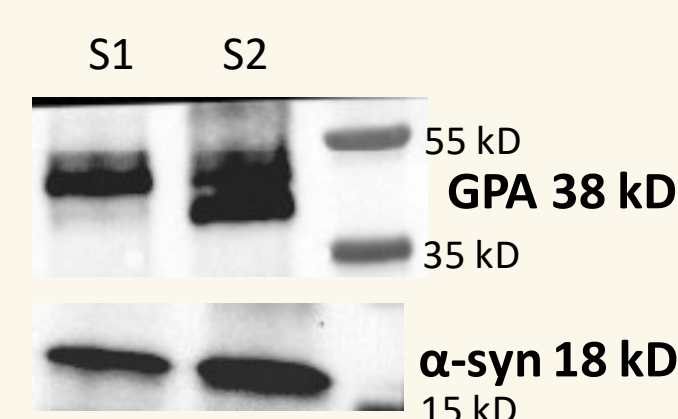
This study would provide

- ✓ Clearer understanding of the pathophysiological mechanisms at play in DLB
- ✓ Potential peripheral window for the central pathology of DLB
- ✓ Informing future therapeutic strategies

α -syn in RBC-EV
(ongoing)



RBC-EV characterization is ongoing by NTA



Detection of RBC-EV markers and α -syn

Proved isolation of RBC-specific EV and the detection of their α -syn cargo

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