OLIGOMERIC ALPHA SYNUCLEIN: A HALLMARK IN PARKINSON'S DISEASE DIAGNOSIS

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PARKINSON'S DISEASE IN NUMBERS

- **10 million people** are estimated to have PD
- The risk of developing PD increases with age
- The global prevalence is expected to **double by 2030**

SOCIAL AND ECONOMIC IMPACT

- The annual European cost for PD was estimated to be **13,9 billion euros** (2011)
- **Burden of the disease**: dependency of patients in factors such as social, economic and family support

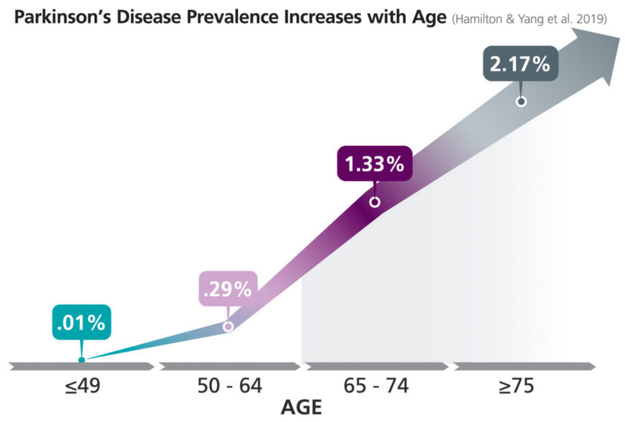


Figure 1. Increase in PD prevalence with age. ▲

CURRENT SITUATION

Clinical diagnosis relies on symptoms and detection of neurodegenerative damage through imaging techniques (MRI, PET, SPECT, TCS…)

Treatment includes:

- Levodopa
- Dopamine agonists
- MAO-B inhibitors

There is no cure for Parkinson's disease

BIOMARKERS

- Main driver of the disease (direct link to PD)
- Oligomeric species of α-syn are the culprits for neuronal degeneration

URATE, DL-1, Q10, HOMOCYSTEINE

- Indirect link to PD
- Not accurate

Figure 2. Summary of PD biomarkers and their strong or weak points. ▲

Quantification of o-α-syn is a more reliable indicator of the disease along with differentiation between soluble and oligomeric form in biological fluids

PROMISING BIOFLUIDS

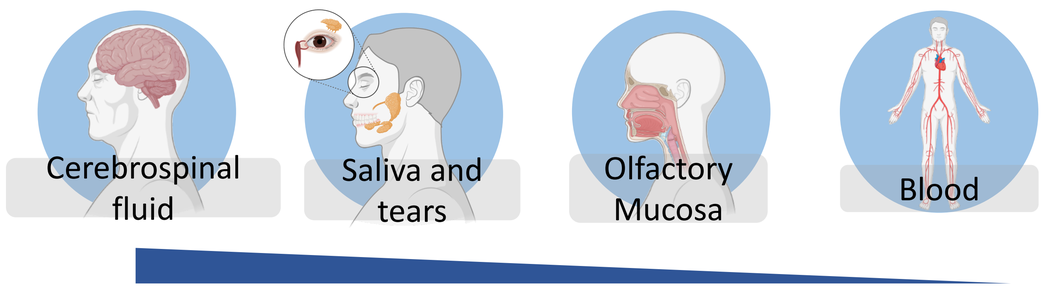
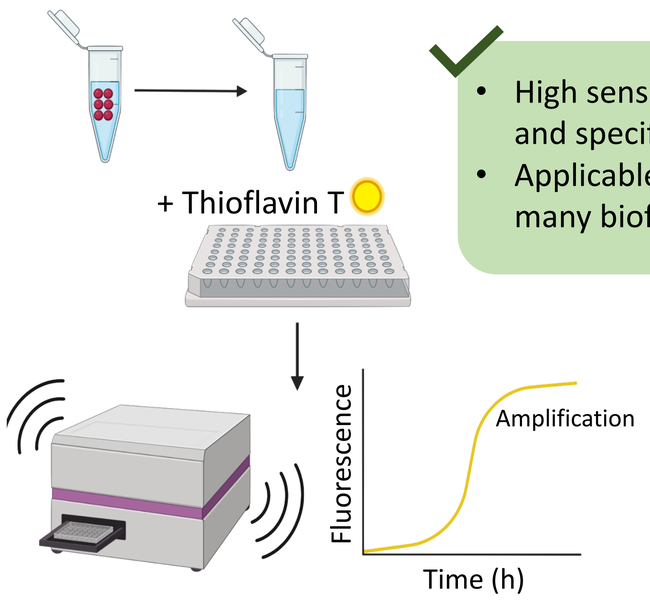


Figure 3. Interesting biofluids from most (left) to least (right) promissing. ▲

RT-QuIC



- High sensitivity and specificity
- Applicable to many biofluids

Figure 4. Real time quaking induced converision (RT-QuIC).[2] ▲

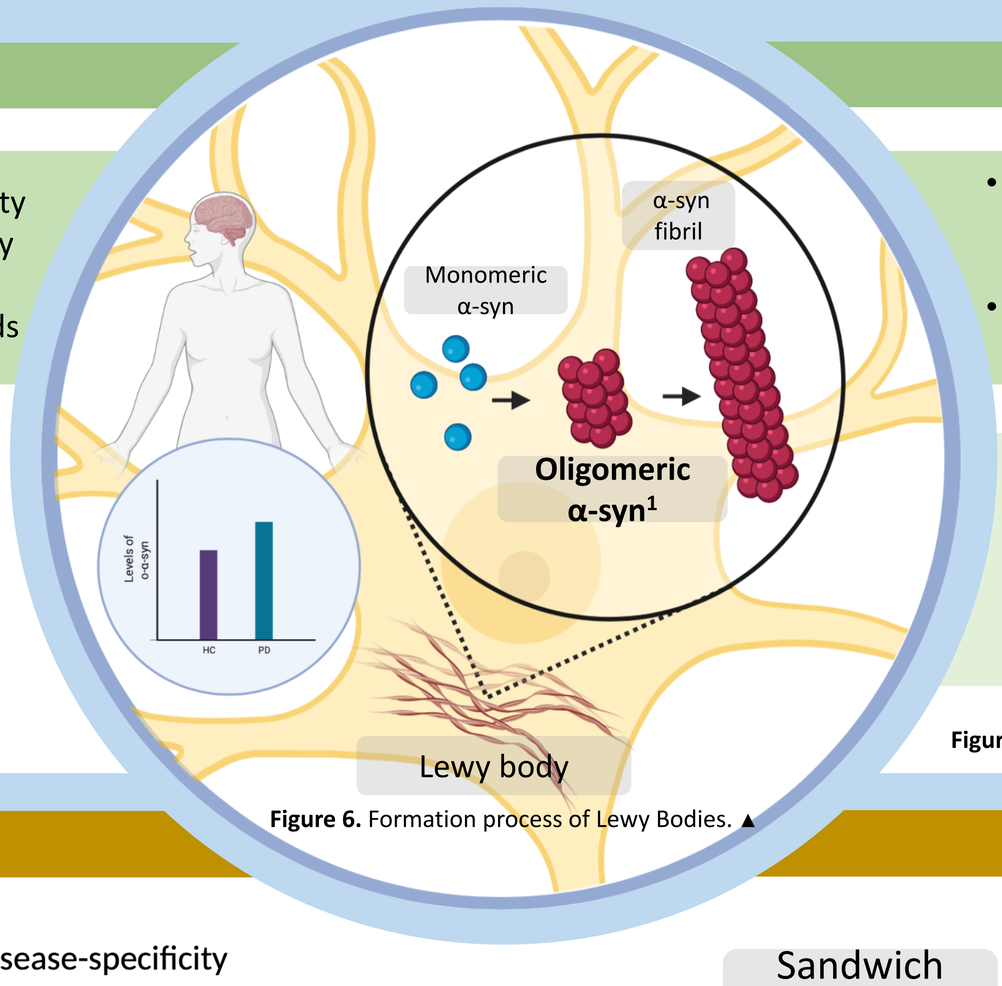
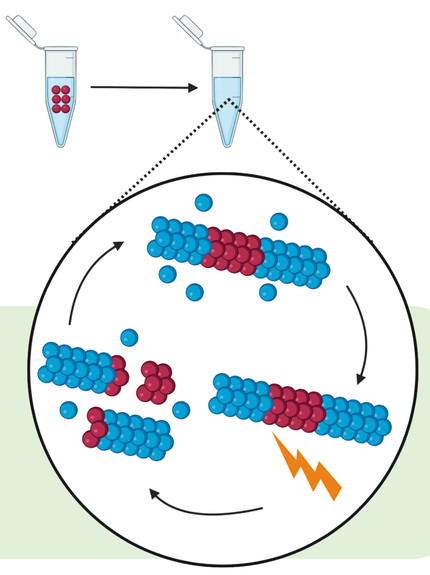


Figure 6. Formation process of Lewy Bodies. ▲

PMCA

- Dependent on highly trained professionals
- Further standardization



Combination of a suspected pathogenic sample with recombinant alpha synuclein

Figure 5. Protein misfolding cyclic amplification (PMCA).[3] ▲

ANTIBODIES

→ Native α-syn → Lacks disease-specificity

→ Aggregated α-syn
- Less reactivity for monomeric α-syn
- Cannot differenciate between aggregated conformations

→ Oligomeric, protofibril, and fibril α-syn
- Less reactivity for monomeric α-syn
- Specifically recognize each aggregated conformation

Figure 7. Summary of antibodies designed against different conformations of alpha synuclein. ▲

IMMUNOASSAYS

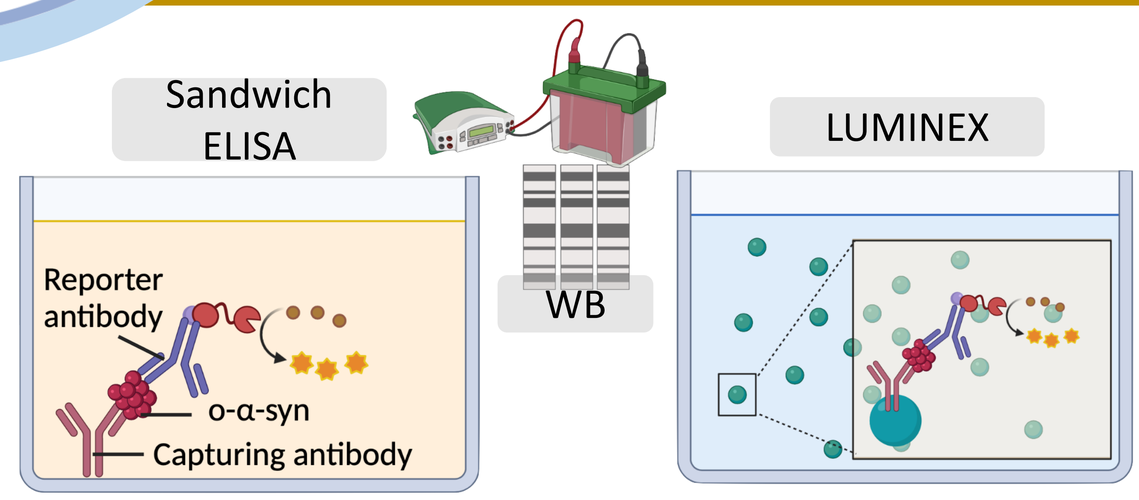
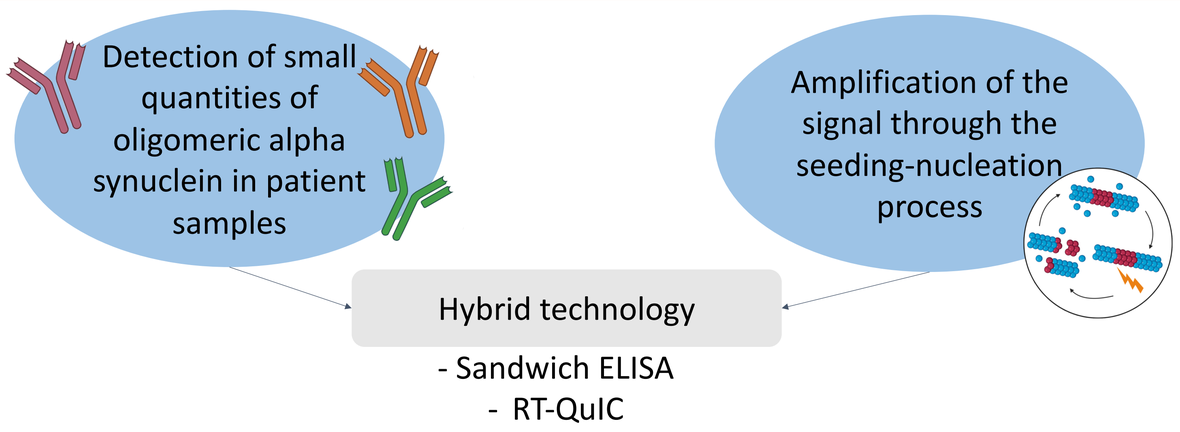


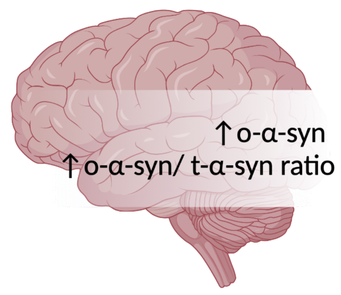
Figure 8. Immunoassay technologies, from left to right, Sandwich ELISA, WB and LUMINEX.[4] ▲

FUTURE PERSPECTIVES



CONCLUSIONS

- Current diagnostic method relies on symptoms and imaging techniques → incorrect diagnosis
- There is still a lack of reliable diagnostic method for PD
- An important goal is the detection of the early stages of the disease → New approaches of oligomeric alpha synuclein detection (quantification of o-α-syn and o-α-syn/ t-α-syn ratio)



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