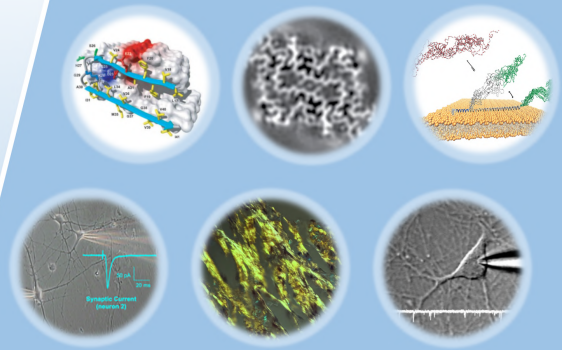


# *Protein misfolding and aggregation in disease*



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Organizers: Fabrizio Chiti, Mario Nuvolone, Stefano Ricagno.

## List of abstracts selected for oral presentation (order of appearance)

## Peripheral Biomarkers in $\alpha$ -Synucleinopathies: Unlocking Early Detection Through Olfactory Mucosa, Blood, and Urine Analysis

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### Abstract

This study leverages innovative technologies to identify peripheral biomarkers for Parkinson's disease (PD), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB) by analyzing olfactory mucosa (OM), blood, and urine. We aim to explore the distribution of disease-associated  $\alpha$ -synuclein ( $\alpha$ Syn<sup>D</sup>) and other key proteins to develop disease-specific biological signatures for these neurodegenerative diseases. Participants included patients with PD (n=20), MSA (n=20), DLB (n=15), other neurodegenerative diseases (OND, n=10), and age-matched healthy subjects (HS, n=10), all of whom underwent olfactory function testing prior to sample collection. The analyses employed a comprehensive approach: Seed Amplification Assay (SAA) for  $\alpha$ Syn<sup>D</sup> detection, Simoa SR-X for quantifying NfL, p-Tau231, and p-Tau181 levels, ELISA for measuring  $\alpha$ -synuclein and synapsin-3 levels, and nanoparticle tracking analysis (NTA) for evaluating extracellular vesicles (EVs) in urine and blood. Novel recombinant  $\alpha$ -synuclein proteins were also produced for protein-NMR studies of SAA reaction products. PD and DLB patients exhibited the most severe olfactory impairments. Preliminary SAA data detected  $\alpha$ Syn<sup>D</sup> in the OM of PD, MSA, and DLB patients, with higher sensitivity in PD and MSA than in DLB. Simoa analysis revealed significantly elevated plasma NfL levels in MSA patients compared to PD and HS, while p-Tau181 and p-Tau231 levels showed no notable differences. NTA of blood-derived EVs indicated higher particle concentrations and an increased concentration/size ratio in the PD, MSA, DLB, and OND groups compared to HS. These preliminary findings suggest that OM, blood, and urine represent valuable sources for identifying biomarkers, which can be easily and repeatedly collected. These biomarkers hold promise for enhancing clinical understanding of PD, MSA, and DLB. Ongoing analyses, combined with machine learning integration, will evaluate whether this approach can generate specific biological fingerprints for these neurodegenerative diseases.