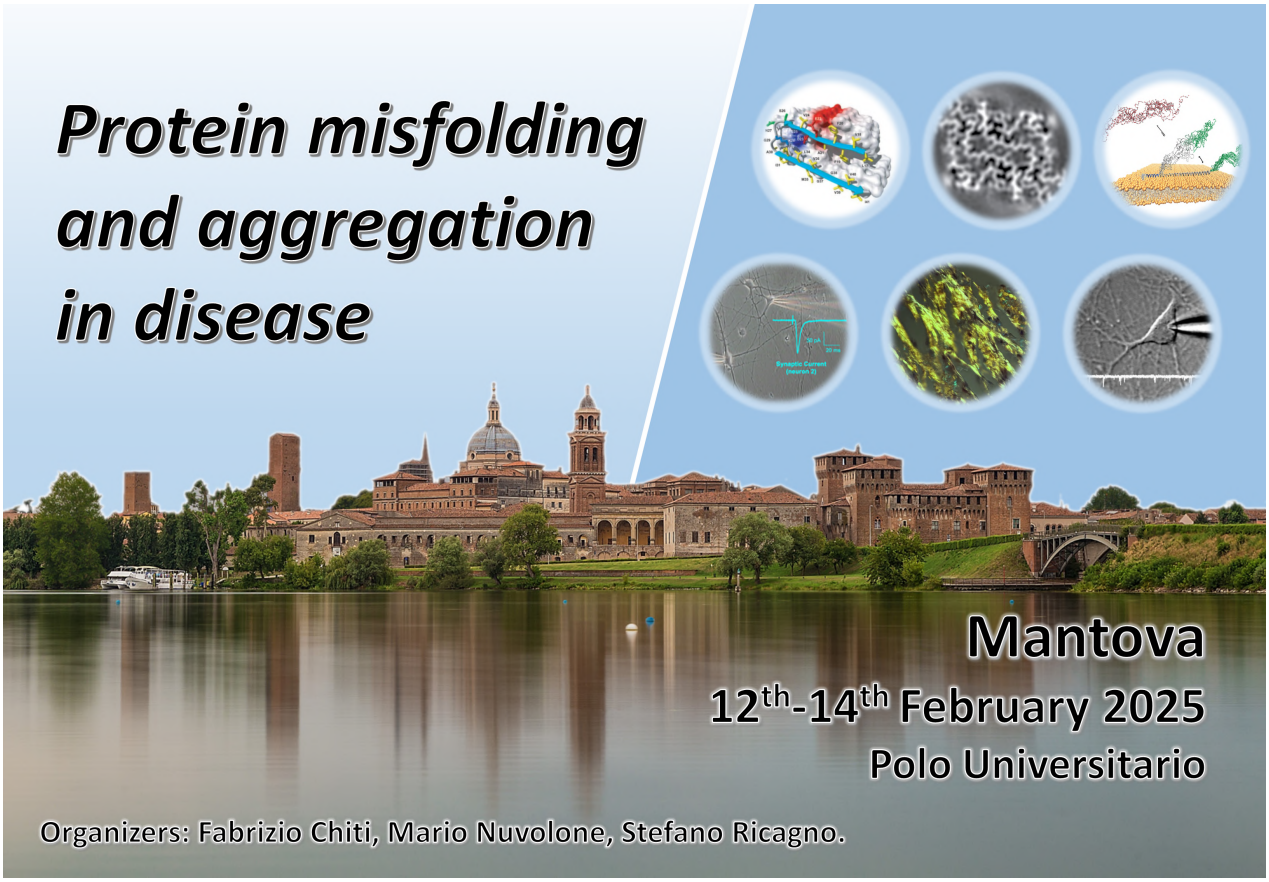

List of abstracts selected for oral presentation
(order of appearance)

Detection of misfolded α-synuclein in the skin of patients with Parkinson's disease and multiple system atrophy by seed amplification assay

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OBJECTIVE α-synucleinopathies, including multiple system atrophy (MSA) and Parkinson's disease (PD), are characterized by the accumulation of misfolded α-synuclein (αSyn^D) in the brain. Up-todate, *intra-vitam* diagnosis remains elusive; moreover, the invasiveness of cerebrospinal fluid collection together with the lack of reliable biomarkers, prompt the research for alternative approaches. Growing evidence suggests that αSyn^D can also be identified peripherally, using innovative and ultrasensitive techniques grouped as seed amplification assays (SAAs), thus offering a promising weapon for biomarker detection (De Luca et al., 2019). This study explores the potential of skin samples as a minimally-invasive and viable source for identifying αSyn^D in patients affected by PD and MSA, exploring the feasibility of this analysis as a valuable tool for the accurate clinical diagnosis of α-synucleinopathies.

MATERIALS AND METHODS Participants included patients with PD (n=10), MSA (n=10) and agematched healthy subjects (HS, n=5), all of whom underwent skin biopsy procedure to collect skin samples. The biopsies were taken proximally (C7 paravertebral) and distally (ankle). After the collection, skin samples had been homogenized following an optimized and published protocol (Mammana et al., 2021). We then performed the SAA analyses of the skin samples obtained. Furthermore, biochemical analysis of final SAA products will also be conducted.

RESULTS Preliminary results showed a satisfactory seeding activity in skin samples collected from MSA (7/10) and PD (8/10) patients. In contrast, no seeding activity was observed in HS samples, except for one subject (1/5). Overall, the results obtained are promising, however further validation, together with an increase in the cohort of patients tested, is required to corroborate these findings. Preliminary biochemical analyses revealed no relevant differences between SAA products generated by PD and MSA.

CONCLUSIONS These preliminary results demonstrate the potential of SAA analysis of skin sample as a minimally-invasive source of αSyn^D. Further research with larger cohorts is indeed needed to validate these results and explore the clinical utility of skin αSyn^D as a biomarker for αsynucleinopathies. The correlation of these findings with the conventional immunohistochemical data might be useful to improve the clinical diagnosis of PD and MSA.

REFERENCES De Luca CMG, Elia AE, Portaleone SM, et al. Efficient RT-QuIC seeding activity for α-synuclein in olfactory mucosa samples of patients with Parkinson's disease and multiple system atrophy. *Transl Neurodegener*. 2019;8:24. Published 2019 Aug 8.

Mammana A, Baiardi S, Quadalti C, et al. RT-QuIC Detection of Pathological α-Synuclein in Skin Punches of Patients with Lewy Body Disease. *Mov Disord*. 2021;36(9):2173-2177.