α-synuclein and deficits of membrane trafficking in Parkinson's Disease

Alessia Sarchione*[1], Antoine Marchand[1], Francesca Filippini[2], Sebastien Nola[2], Thierry Galli[2], Jean-Marc Taymans[1], and Marie-Christine Chartier-Harlin[1]

[1]Centre de Recherche Jean-Pierre AUBERT Neurosciences et Cancer – Institut National de la Santé et de la Recherche Médicale : U1172, Université Lille 2 - Faculté de Médecine – France
[2]Institut de Psychiatrie et Neuroscience de Paris – Université Paris V - Paris Descartes – France

Résumé

Introduction: Parkinson's Disease (PD) is a neurodegenerative disorder characterized by defects in membrane trafficking. LRRK2 and SNCA, encoding α-synuclein (α-syn), are the two major genetic determinants of PD pathogenesis involved in membrane trafficking. α-syn has recently emerged as regulator of SNARE (*Soluble N-ethylmaleimide-sensitive-factor Attachment protein Receptor)*-dependent vesicle fusion. LRRK1, a homolog of LRRK2, has been also shown to interact with the SNARE protein VAMP7. Here we proposed to investigate the potential interactions between α-syn and the candidate interactors and modulators of vesicular trafficking such as other SNAREs, VAMPs and LRRK2 as well as the aggregation profile of α-syn and its release in cell medium.
Methods: The co-localization and interaction between α-syn and the SNARE proteins has been analyzed by immunocytochemistry and Proximity Ligation Assay, respectively. The released α-syn exocytosis has been measured at different time points upon α-syn overexpression in cells. Pharmacological treatment has been performed in order to analyze the clearance of VAMPs, upon lysosomal inhibition with Bafilomycine A1 in cells.

Results: We present preliminary results of PLA and co-localization testing the interaction between α-syn and proteins involved in vesicular trafficking VAMPs and LRRK2. Inhibition of lysosomal activity and effects on both VAMPs and α-syn levels are also tested. The α-syn release in cell medium is detectable up to 48h after transfection.
Conclusions: α-syn and VAMPs are both involved in vesicular and membrane trafficking and our preliminary results may suggest an involvement of the same pathway in their clearance. In our perspectives, we will evaluate the effect of VAMPs on the α-syn aggregation and exocytosis in order to evaluate if the α-syn homeostasis could be modulated by SNARE proteins.

Mots-Clés: α, synuclein, VAMPs, vesicular trafficking

*Intervenant