aSynProtec
Alpha-synuclein pathology propagation in Parkinson's disease and quest for novel protective strategies

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Misfolding and aggregation of α-synuclein (α-syn) in the form of Lewy bodies and Lewy neurites are the major hallmarks of Parkinson's disease (PD). Available evidence shows that exogenous human α-syn fibrils can be taken up into neurons and inoculate aggregation of endogenous α-syn in the recipient cells. Up to date, it is still obscure on the origin and the molecular mechanisms leading to the development of α-syn amyloid aggregate formation, for example:

1. When, why and how are the endogenous α-syn aggregates formed; do they initiate in the brain or in the peripheral tissues and how do environmental factors, including the microbiome, contribute to this process?
2. What are the structural requirements for α-syn cell-to-cell propagation and spreading?
3. How do the aggregation state and structural properties of the aggregates influence conversion of endogenous α-syn and pathology spreading?
4. How, and through which route(s), is/are misfolded/aggregated α-syn transported and spread from one cell to another?
5. How does genetic susceptibility contribute to the propagation and aggregation of α-syn?
6. how do posttranslational modifications of α-syn impact on α-syn spreading, aggregation and cytotoxicity
7. Can small molecule compounds and biological reagents, such as specific antibodies, block α-syn spreading, seeding and aggregation?

In the last three years, the *aSynProtec* consortium teams have made great progresses on all the above mentioned issues and deepened our understanding of the interplay between genetic and environmental risk factors and their role in the initiation of α-syn aggregation and pathology spreading in PD and related synucleinopathies, which lead to the identification of novel targets and open new paths for the development of novel therapeutic preventive and therapeutic interventions, such as immune therapies with monoclonal antibodies.