NeuTARGETS

Misfolding and progressive aggregation of disease-linked proteins in the nervous system and spatiotemporal spreading of pathological lesions through the brain is the common feature of neurodegenerative diseases (ND). Such diseases include Alzheimer (harboring accumulation of the beta-amyloid peptide (Aβ) and hyperphosphorylated tau) and Parkinson (with aggregates of α-synuclein).

The progressive spread of pathological lesions from region to region in patterns that match neuronal connectivity strengthened the concept of « Pathological Protein Propagation », a phenomenon in which pathogenic proteins might trigger a « prion-like templating » mechanism and spread in a toxic cascade following anatomical pathways.

The underlying mechanisms of this phenomenon are poorly understood, thus we aimed to identify common pathways of aggregation/toxicity and cell to cell transfer of pathogenic protein assemblies involved in different (NDs) in order to interfere with their stability, replication and spreading. We showed the involvement of tunneling nanotubes (TNTs) in transfer and spreading of pathogenic proteins and characterize the proteins involved in their formation, analyzed structural and functional properties of different α-synuclein strains, used antibodies to treat endogenous seeds in the mouse model of Alzheimer's Disease and established new methods (i.e: organotypic slice culture and amplification of protein deposits from patients) for future studies.