DESCRIPTION FOR THE GENERAL PUBLIC

The aim of the project is to elucidate what are the consequences of direct interaction between Tau protein and prion protein (PrP). Tau is a molecule responsible for stabilization of microtubules. Its oligomerization/aggregation leads to brain neurodegeneration and cognitive deficits. Accumulation of Tau amyloid aggregates in the brain is a hallmark of numerous tauopathies exemplified by Alzheimer's disease. Pathological assemblies of Tau such as amyloid aggregates and, in particular, soluble oligomers have been shown to be neurotoxic. Noteworthy, normal physiological form of Tau has been demonstrated to interact with PrP. Furthermore, co-deposition of aggregates of PrP and Tau has been frequently reported in another group of neurodegenerative diseases called prion diseases. Above mentioned, intriguing observations point to a potential role of PrP in tauopathies and cross-talk between these neurodegenerative diseases. Nevertheless, the studies aimed at unraveling the role of PrP-Tau interaction have not been reported to date. Interestingly, our preliminary experiments have shown that PrP binds to amyloid aggregates of Tau. More importantly, we have found that PrP influences process of amyloid formation (amyloidogenesis) of Tau. Hence, our working hypothesis is that PrP, by direct interaction with Tau, may inhibit amyloidogenesis and reduce cytotoxicity of Tau, and thereby impede progress of neurodegeneration in tauopathies. To verify above hypothesis and unravel the role of PrP-Tau interaction an inter-disciplinary approach combining protein biochemistry, cell biology and biophysical methods will be implemented. We aim to determine the effects of PrP binding on Tau structure, amyloidogenesis of Tau and ability of Tau assemblies to elicit neurotoxicity. These studies will be preceded by the comparison of the binding affinities of PrP for different Tau assemblies and identification of the binding sites on both molecules. Hence, the project should contribute to better understanding of the molecular mechanism of tauopathies. We speculate that PrP and its fragments retaining ability to protect neurons from cytotoxic forms of Tau may be used in designing drugs for effective treatment of tauopathies. Thus, the outcome of proposed research has also potential translational implications for therapy of numerous neurodegenerative diseases linked to Tau pathology.