

CEIPEX MU TOPIC 15

Položka / Field	Obsah / Content
NAME	doc. RNDr. Mgr. Jozef Hritz, Ph.D.
CEIPEX RESEARCH TOPIC LEVEL2	Structural Biology: Protein-protein interaction
NAME OF THE RESEARCH GROUP	Protein Structure and Dynamics
TOPIC	Structural Basis of Pathological Tau Recognition and Early Aggregation in Tauopathies
ABSTRACT	The pathological conversion of the intrinsically disordered tau protein into β-sheet-rich amyloid assemblies is a defining feature of Alzheimer's disease and several related neurodegenerative disorders collectively known as tauopathies. Despite extensive research on mature tau fibrils, the molecular events that initiate tau misfolding and drive the formation of disease-specific aggregation pathways remain poorly understood. Recent studies suggest that transient conformational states sampled during the earliest stages of tau aggregation expose unique structural epitopes that can be selectively recognized by disease-associated monoclonal antibodies. Such antibodies offer a unique opportunity to probe aggregation-prone tau conformations that are otherwise difficult to capture experimentally. The recently characterized conformational antibody DC11 represents an excellent example of this concept, as it specifically recognizes pathological truncated tau species and appears to interact with pre-aggregational tau conformations. The candidate will study conformational transitions within tau proteins, antibody-induced structural rearrangements, and the molecular basis of disease-relevant epitope formation. Special emphasis will be placed on identifying transient intramolecular interactions and partially folded states that precede amyloid formation, aiming to support the future development of mechanism-based diagnostic and therapeutic strategies for Alzheimer's disease and related tauopathies. The project will combine advanced biomolecular NMR spectroscopy, integrative structural biology, protein engineering, biophysical characterization, and molecular modeling. It builds on the Hritz laboratory's expertise in structural studies of intrinsically disordered proteins, protein aggregation, and protein-protein interactions. Close integration with ongoing research on conformational anti-tau antibodies and aggregation-prone tau fragments will provide access to cutting-edge biological systems directly relevant to the mechanisms underlying neurodegenerative disease. The project is expected to bridge structural biology, computational modeling, and neurodegeneration research, while benefiting from the interdisciplinary environment and state-of-the-art infrastructure available at CEITEC.
WEBPAGE OF THE RESEARCH GROUP	https://www.ceitec.eu/protein-structure-and-dynamics/rg110