Methods of Predicting the Functions of Intrinsically Disordered Proteins: The Functions of Tau Protein

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Tau protein is an intrinsically disordered protein (IDP) with essential roles in the assembly, stabilization, and modulation of microtubules, which play a critical role in the proper functioning of neurons. In pathological conditions, tau protein can form insoluble aggregates that accumulate in the extracellular space of neurons, leading to impaired neuronal function. These insoluble aggregates are the signals of the appearance of neurodegenerative diseases called tauopathies, among which is the Alzheimer's disease. The aim of this work is to predict the functions of tau protein, by using three computational methods that are based on the primary structure of the protein: DisoRDPbind, MoRFpred, and the method of sequence homology. Using the DisoRDPbind method, I concluded that the N-terminal region, the proline rich domain, and the microtubule binding domain (MTBD) have a very high probability to interact with other proteins. The MoRFpred prediction revealed that there might be several molecular recognition features in the MTBD, meaning that tau protein may suffer a disorder to order transition upon binding the microtubules. By aligning tau with the acetyl-CoA binding protein (ACBP), I identified the presence of sequence homology, which can indicate that tau protein has the capacity to bind acetyl-CoA. Together with a PhD researcher, I experimentally tested the prediction that tau binds to coenzyme A, and the results are positive. Being able to make predictions is very important, as they give us clues to what experiments we need to perform in order to discover new functions of IDPs.

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