Popular science summary

Origins of amyloid disaggregation in double β-barrel J-domain protein family

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Most new proteins evolve from pre-existing once, however tracking a path from an ancestral one to a novel protein remains challenging. Double β-barrel J-protein family consists of two types of proteins (A and B), both of which control the stability of other proteins in human, yeast or bacteria cells. However, only cytosolic type B J-proteins are essential for the survival of yeast cells and maintenance of prions (misfolded proteins with the ability to transmit their misfolded shape). In humans type B J-proteins are involved in disaggregation of abnormal proteins called amyloids, thereby preventing Alzheimer's and Parkinson's diseases. The way in which they acquired their unique functionalities is not known. The results of our preliminary research show that these proteins evolved in cytosol from a type A J-protein ancestor.

The goal of our project is to track and investigate how these proteins acquired their unique capabilities. To answer this question, we plan to reconstruct type B J-protein ancestors on a molecular level, which will allow us to synthetize them. Function of ancestral proteins will be tested using biochemical assays, which will help us to understand how it has changed during evolution. Next, we will examine the effects of ancestral proteins on yeast cells. This approach will allow us to identify key sequence changes that lead to the emergence of the recognition of abnormal proteins.

This research will help us to better understand how proteins evolve from their pre-existing precursors and adapt existing biochemical features to recognize new types of fold architectures, such as abnormal protein aggregates.