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Aggregate formation by prionogenic proteins in yeast

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Cross-beta protein polymers (amyloids) cause diseases in mammals and control heritable traits in yeast. Initial amyloid formation is poorly understood. Amyloid (prion) form of the *Saccharomyces cerevisiae* protein Sup35 ([*PSI*$^+$]) is induced by overproduction of the Sup35 prion domain (PrD) either in the presence of the prion isoform of another protein (for example, Rnq1), or when Sup35 PrD is attached to another amyloidogenic protein, e. g. human Abeta peptide. This is accompanied by generation of various types of protein aggregates, among them filamentous structures representing intermediates of prion formation. We studied if filaments could be formed by Sup35 PrDs from other yeast species, or by chimeric constructs including both Abeta peptide and a fluorophore. Divergent Sup35 PrDs from various yeast species, or a chimeric protein composed of *S. cerevisiae* Sup35 PrD and human Abeta were tagged with fluorophores and expressed in the *S. cerevisiae* cells, either containing ([*PIN*$^+$]) or lacking ([*pin*$^-$]) the Rnq1 prion. Sup35 PrDs from various yeast species differed from each other by morphology of aggregates formed in the [*PIN*$^+$] cells. Some divergent proteins produced almost no filaments, although this did not necessarily correlate with the evolutionary distance. The Sup35 PrD-Abeta-CFP construct rapidly and efficiently formed dot-like aggregates in the [*pin*$^-$] cells. However, this aggregation did not result in [*PSI*$^+$] induction, indicating that either prion formation or immobilization of full size sup35 into a prion is inhibited by the attachment of fluorophore to the C-terminus of Abeta. Supported by SPbSU grant 1.50.1038.2014, RFBR 15-04-06650 and RSF 14-50-00069.

Biography

Anastasia V Grizel has received her PhD in Biophysics from Lomonosov Moscow State University in 2012, and performed postdoctoral studies at St. Petersburg State University. She currently is a Research Scientist at St. Petersburg State University (Russia). Her area of research includes genetic, cytological and structural analysis of protein aggregation, primarily in the yeast model. She has published six papers in scientific journals.

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