**Comparison and interconversion of prion strains formed by Sup35 derivatives in yeast and mammalian cells**

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Self-perpetuating protein aggregation is a key factor in the development of a variety of neurodegenerative diseases in humans and other mammals, and a determinant of protein-based inheritance in lower eukaryotes. Translation termination factor Sup35 (eRF3) is one of the most extensively studied prionogenic proteins in yeast. Truncated form of yeast Sup35 (Sup35NM), including prion domain (Sup35N) can produce self-perpetuating aggregates of prion type when expressed in the mouse neuroblastoma cells. Moreover, different regions of Sup35N are necessary for prion propagation in the yeast and mammalian cells (Duernberger et al. 2018 MCB 38:е00111).

We have investigated prions formed in mammalian cells by the Sup35NM deletion derivative, lacking the region that is typically required for prion formation in yeast. These prions were transfected into the yeast cells. Successful transfection was detected for both yeast recipient bearing the full-length Sup35 protein (with high efficiency) and yeast recipient bearing the Sup35 derivative with a respective deletion (with much lower efficiency). Thus, Sup35 protein lacking a “classic” yeast amyloidogenic sequence can be converted into a prion state by a respective seed generated in a different environment. Notably, full-size Sup35 and its deletion derivative produced prion strains with different properties from one and the same seed. Moreover, full-length Sup35 produced multiple strains in these conditions. Our data confirm that different potentially prion-forming sequences are preferred in different organisms, and show that prion strain properties can be altered upon transmission to the substrate containing additional prionogenic regions. This phenomenon resembles strain adaptation detected when mammalian prions are infecting a different species.

This work was supported by Dmitrij-Mendeleev-Programme Scholarship from German Academic Exchange Service (DAAD) and St. Petersburg State University, Faculty Development Grant from Georgia Institute of Technology, the grants 19-34-51054 from Russian Scientific Foundation and 19-34-51054 from Russian Foundation for Basic Research. SPbSU Core Facilities Chromas, Molecular and Cell Technologies, and Biobank provided technical support.