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P23 The transcriptional regulator Sfp1 forms aggregates under specific conditions

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Prions in yeast act as heritable traits. The most studied prion [*PSI*$^+$] is a heritable amyloid of the eRF3 (Sup35) protein which, in prion form, reduces stop codon readthrough accuracy. Sfp1 is a global transcriptional regulator. It is known to affect the Isp+/Isp- phenotype, which was previously thought to be caused by a prion or prion-like element.

We have shown that excess Sfp1 can lead to [*PSI*$^+$]-dependent lethality. The lethality was accompanied by elevation in *SUP35* mRNA levels in a [*PSI*$^+$] strain, suggesting transcriptional upregulation as the mechanism. However, *SUP45* overexpression, known to compensate for [*PSI*$^+$]-dependent lethality caused by excess Sup35, did not affect Sfp1-derived lethality. Search for the factors that influenced the lethality of excess Sfp1 led to identification of the Hsp40 chaperone Sis1 which alleviated toxicity caused by both excess of Sfp1 and Sup35 in [*PSI*$^+$] strains. We also showed that overproduced Sfp1 formed SDS-resistant aggregates, which colocalize with Sup35 and Sis1 in [*PSI*$^+$] cells. Sfp1 aggregation did not depend on the presence of the [*PSI*$^+$] or [*PIN*$^+$] prions in the cell, but, surprisingly, it occured only when the *SFP1* gene was expressed under the control of *CUP1* promoter. *SFP1* overexpression driven by *GPD*, *GAL1* or *SFP1* promoters did not lead to formation of Sfp1 aggregates. It is thus possible that Sfp1 aggregation occurs *in vivo* only under specific conditions which remain unknown. The work is supported by RC MCT SPbSU and by RFBR grants 16-04-00202 and 18-34-00536.