Abstract

Control of gene expression in eukaryotes is regulated at various steps such as transcription, translation and protein degradation. Translation repression of mRNA regulates protein levels and maintains cell homeostasis. Translation control allows for spatiotemporal regulation of gene expression which is required for development and differentiation in organisms. Deregulation of translation can result in disease conditions like cancer and neurodegenerative diseases. In yeast *Saccharomyces cerevisiae*, the RGG-motif protein Scd6 (Suppressor of Clathrin Deficiency 6) represses translation by binding eIF4G1 via its RGG domain and prevents formation of 48S pre-initiation complex. Scd6 consists of N-terminal Lsm domain, central FDF domain and C-terminal RGG domain.

In this study, we assessed the contribution of other domains of Scd6 in its translation repression ability. Overexpression of Scd6 causes growth defect as a result of global translation repression. We observed that overexpression of Lsm domain deletion mutant could partially rescue the growth defect phenotype suggesting that Lsm domain might be contributing in Scd6 mediated translation repression. Deletion of FDF domain did not result in any significant change in the growth defect phenotype of Scd6 overexpression. Interestingly, both Lsm and RGG domains are necessary but insufficient to repress translation on their own. Lsm domains are conserved RNA binding domains. By mutating the putative RNA binding motif within the Lsm domain we observed a rescue from the growth defect phenotype of Scd6. Also, our preliminary results indicate that the RNA binding motif mutant of Lsm domain is defective in binding poly(U) RNA. We analyzed the translation repression ability of Lsm domain mutants by observing RNA granule formation under stress and non-stress conditions. We observe that the mutants are defective in localizing to granules. In addition, the mutant containing only Lsm domain localizes to nucleus like structure in non-stress condition and forms fewer RNA granules in the cytoplasm upon stress. Since Scd6 binds eIF4G1 to repress translation we analyzed the ability of Lsm domain lacking Scd6 mutant to interact with eIF4G1 *in vivo*. Our preliminary observations suggest that Scd6 mutant lacking Lsm domain is deficient in binding eIF4G1 *in vivo*. Considering all the observations from our studies, we propose a model in which Lsm domain of Scd6 helps in recognition of the mRNA target of Scd6 which is followed by eIF4G1-RGG domain interaction leading to translation repression.