Abstract

Eukaryotic translation initiation factor eIF4E1 (eIF4E1) plays a pivotal role in the control of cap-dependent translation initiation, occurs in P- bodies and is important for the formation of stress granules (SG). Human cells encompass two other non-canonical translation initiation factors capable of cap binding although with a lower affinity for the cap: eIF4E2 and eIF4E3.

Here, I investigated the ability of individual eIF4E family members and their variants to localize to SGs and P-bodies in stress-free, arsenite and heat shock conditions. Under all tested conditions, both eIF4E1 and eIF4E2 proteins and all their variants localized to P-bodies unlike eIF4E3 protein variants. Under both arsenite and heat stress conditions all tested variants of eIF4E1 and the variant eIF4E3-A localized to SGs albeit with different abilities. Protein eIF4E2 and all its investigated variants localized specifically to a major part of heat stress-induced stress granules.

Further analysis showed that approximately 75% of heat stress-induced stress granules contain all three eIF4Es, while in 25% of them eIF4E2 is missing. Large ribosomal subunit protein L22 was found specifically enriched in arsenite induced SGs. Heat stress-induced re-localization of several proteins typical for P-bodies such as eIF4E2, DCP-1, AGO-2 and depending on the temperature also DDX6, to SGs. Thus, severe heat stress in mammalian cells induces SG fusion with P-bodies, as was published previously in yeast´s cells.

Last, I searched for eIF4E2 interaction partners using immunoprecipitation followed by mass spectrometry. I detected eIF3, eIF4E-T, eIF4E-BP2, PABP in a complex with eIF4E2. The possible implications for the eIF4E2 involvement in translation repression or initiation are discussed.