Abstract

Eukaryotic initiation factor 3 (eIF3) is a critical player involved in many steps of translation initiation, which ultimately result in the formation of the elongation competent 80S ribosome. With its 13 subunits (eIF3a – eIF3m) it is the largest and the most complex translation initiation factor composed of three mutually interconnected modules (i - iii), however, the role of individual subunits involved in its structural integrity and proper function is not fully explored. The eIF3e subunit was shown to be a part of the human eIF3 structural core and to help in the mRNA recruitment to the 43S pre-initiation complex by forming a molecular bridge between the 40S ribosomal subunit and the mRNA cap-binding complex. In this study, we employed siRNA-directed downregulation of eIF3e in HeLa cells and analysed its impact on the overall eIF3 integrity and function *in vivo*. The eIF3e knock-down ($eIF3e^{K.D.}$) led to the severe reduction of protein amounts of other three subunits (eIF3d, k and l), which together with the subunit eIF3c and e form module ii of the eIF3 complex. Remaining module i (composed of a, b, g and i) and iii (containing f, h and m) stayed partially bound perhaps thanks to a bridging effect of eIF3c, and showed reduced binding efficiency towards the 40S subunit compared to control cells. Furthermore, eIF3e-depleted cells exhibited decreased translation initiation rates and slow growth. The observed phenotype of the $eIF3e^{K.D.}$ indicates that e subunit of human eIF3 is important for the integrity of the complex, its ability to bind to small ribosomal subunit and thus to the overall fitness of cells.

Key words: eukaryotic translation initation, eIF3, eIF3e, siRNA-directed knock-down