Structural organization of 3′UTR modulates the activity of PABP in translation termination

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It is assumed that in the process of translation, an mRNA structure with closely spaced 5' and 3' ends (so-called the closed-loop mRNA) can be formed. It forms via interaction of initiation translation factor eIF4G and poly(A) binding protein (PABP). Additionally, it was suggested that stop codon and poly(A) tail are also closely located in this structure as PABP is able to interact both with eIF4G and release factor eRF3. It is confirmed by the fact that PABP activates both initiation and termination of translation. We proposed that structure of 3’ untranslated region (3’UTR) can be critical for such activation, since the formation of hairpins in the 3’UTR can facilitate the physical convergence of the poly(A) tail and the stop codon. To reveal that, we determined the translation efficiency of mRNA with different structure of 3’UTR in the presence of PABP using in vitro reconstituted translation termination system. For this purpose, we used two alternative approaches of obtaining linear 3’UTR. First approach implied using long antisense oligonucleotide complementary to 3’UTR of mRNA. This oligonucleotide interacting with 3’UTR, prevented formation of hairpins in the 3’UTR. Second approach implies using repeated CA motive, unable to form secondary structure. As a result, we observed the dependence of the termination efficiency on the mRNA structure. In particular, when the stop codon is spatially distant from the poly(A) tail, PABP associated with poly(A) tail does not activate translation termination. Thus, the spatial coupling of stop codon and poly(A) tail, which may occur during the formation of a closed-loop structure, modulates the efficiency of in translation termination. The work was supported by Russian Science Foundation (grant No. 19-74-10078).