

ABSTRACT

Protein synthesis is a tightly regulated process of gene expression. Each gene has its start and its stop, which is determined by one of the three stop codons. Many recent articles describe ribosomes that purposely bypass stops on specific mRNAs to extend the nascent polypeptide to alter its properties. It is called programmed stop codon readthrough. Since over 15% of human genetic diseases are caused by so called premature termination codons (PTC) that halt translation and produce truncated proteins, this mechanism has a great potential implication in medical research. Numerous labs search for non-toxic drugs specifically increasing readthrough at PTCs; however, the success of this effort requires identification and understanding of all factors that are involved in this process. Here, we present one such factor eukaryotic initiation factor 3 (eIF3) and describe its ability to induce readthrough on stop codons in termination non-favorable context during programmed readthrough and also the consequences of its action on translation regulation. We additionally analyzed which near-cognate (nc) tRNAs are incorporated at UGA stop codons depending on the nucleotide that immediately follows them (so called +4 base). This way we established new rules for stop codon decoding and identified so called readthrough inducing tRNAs for each UGAN stop codon. We believe that the progress we have achieved in characterizing the regulation of translation termination will contribute to the overall intention of many researchers from the translation control field to fully understand the process of protein synthesis on a molecular level in order to improve human health.