they do not contain the amide group of Gln185 (Seit Nebi et al., 2000). In contrast to Q185 mutations, the G183G184 mutations cause complete abolishment of eRF1 activity (Frolova et al., 1999), indicating the essential role of these amino acid residues in termination reaction. However, the mechanism of this reaction remains unknown.

Apart from the termination reaction itself, the signal transduction from the stop codon to the peptidyl-tRNA is not understood at all. Here, a resemblance of this process to signal transduction in aminoacyl-tRNA synthetases from the anticodon-binding site to the catalytic site is remarkable (Kisselev et al., 2000). In synthetases, one domain recognizes the stop codon and induces a conformational change in the other domain, which carries the catalytic site. It seems highly probable that a similar mechanism operates in eRF1: when the N domain binds to mRNA containing stop codon, it induces a conformational transition in the M domain which contacts peptidyl-tRNA. This active conformation triggers the hydrolytic reactions. In the absence of the stop codon the eRF1 remains in non-active conformation.

The second release factor of eukaryotes, termed eRF3, is entirely different from eRF1 both structurally and functionally (reviewed in Buckingham et al., 1997; Kisselev and Buckingham, 2000). It is a GTP-binding protein possessing GTPase activity, which is entirely independent from the mRNA and peptidyl-tRNA but requires the presence of the ribosome and eRF1.

In addition to eRF1, eRF3 binds to polyA-binding protein (Hoshino et al., 1999). Although this interaction involves a variable N domain of eRF3 contrary to the conservative C domain which binds eRF1, its functional role remains unclear. Moreover, eRF3 in vitro stimulates the activity of eRF1 at low stop codon concentrations and this effect has not been reasonably explained, either. Therefore, eRF3, although being encoded by an essential gene, still remains mysterious from the functional viewpoint. In contrast, the function of the prokaryotic analog of eRF3, RF3, is understood much better: it facilitates the release of RF1/2 from the ribosome (Freistroffer et al., 1997). Various hypotheses have been put forward regarding the biological role of eRF3 (Buckingham et al., 1997), but none of them were justified experimentally.

Recently, it became evident that the translation termination machinery is composed of more factors than was thought before. In yeast and probably in humans, Upf1 and Upf2 proteins seem to take part in this process (Czapinski et al., 1998), though the mechanism of their participation in termination is a subject of speculations rather than demonstrated experimentally.

Clearly, the story of translation termination in eukaryotes could be taken as an illustration of a general tendency of molecular biology: “From simplicity to complexity”.

However, genuine knowledge requires that after this stage a third phase has to be reached, which is “From complexity to clarity”. This has not yet been achieved in translation termination and therefore makes this topic quite attractive for researchers even in the next century.

References


Grenzmann, G., Brechemier-Baey, D., Heurgue, V., Mora, L., Buckingham, R. H. (1994) Localization and characterization of the gene encoding release factor RF3 in


