Investigation of interaction between SecM stop peptide and E. coli ribosome by MD

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The nascent peptide exit tunnel (NPET) participates the translation regulation. So-called stop peptides are able to bind NPET walls, arresting translation. SecM is a such kind of peptides that precedes the SecA translocase code in the mRNA: with SecA deficiency the arrest of the ribosome by SecM leads to unwinding of the mRNA hairpin hiding the SecA start codon and SecA synthesis. On the contrary, if SecA is abundant, the arrest of the ribosome by SecM is terminated by binding its N-terminus to the Sec translocon and the subsequent completion of SecM synthesis without initiating SecA translation. SecM is to contain the F_{150}XXXXWIXXXXGIRAGP$_{166}$ sequence to be able to arrest translation. Mechanism of SecM translation arrest was studied by MD simulations and cryoEM. Zhang et al. presented the structure of SecM complex with *E. coli* ribosome, in which the conformation of the critical GIRAG sequence contains two cis-peptide bonds. It is unlikely that anything in this region of the NPET is able to create such a conformation of the nascent peptide, although the published electron density indicates the general path of the peptide chain. Based on it, we modeled the structure of the SecM complex with the *E. coli* ribosome, which is characterized by stable interactions between the amino acid residues critical to SecM activity and NPET, such as A164 and R163 hydrogen bonds with U2585 and C2063 residues, hydrophobic contact of I162 and A2062 base, stacking interaction and hydrogen bonds of W155 with A789 residue. Thus, the structure simulated by us is consistent with the known experimental data. It can be assumed that these interactions enable SecM to bind strongly to NPET impeding translocation. But the external force pulling the peptide from the NPET is capable of breaking them, thereby translation arrest is reversible. All simulations were performed with the Lomonosov II supercomputer of Moscow State University using GROMACS 5 and PLUMED 2 packages and AMBER14SB force field.