Crystal structure of the complex ribosomal silencing factor S and ribosomal protein L14 from Staphylococcus aureus

P-34-010

B. Fatkhullin[I,II], A. Gabdulkhakov[I], S. Validov[II], I. Khusainov[III], A. Bikmullin[II], K. Usachev[II], M. Yusupov[IV]

[I]Institute of Protein Research, Russian Academy of Sciences, Pushchino, Russia, [II]Institute of fundamental medicine and biology of KFU, Kazan, Russia, [III]EMBL, Heidelberg, Germany, [IV]IGBMC, Strasbourg, France

Staphylococcus aureus (*Sa*) is a pathogenic bacterium and the causative agent of different diseases: meningitis, pneumonia, sepsis and etc. Combating with *Sa* is complicated by the high viability of the bacteria and its potent resistance to different types of drugs. More than a half of them have a peptidyl-transferase center on a 70S ribosome as the target. The probable solution of this problem is searching the new targets for drugs not on the 70S ribosome, but in the 70S formation process. We focused on one of these steps: influencing a ribosomal silencing factor S (RsfS) to 50S ribosome subunit. This factor binds with L14 protein on the large subunit and takes out the 50S from a recycling process. This process is important to save energy and ensure survival in a starvation period. For a detailed analysis of the interactions between RsfS and the 50S ribosomal subunit in *Sa*, the crystal structure of the complex of recombinant *Sa*RsfS and *Sa*L14 was obtained at 2.27 Å resolution. Two heterodimers with the wide interface into each complex were found in the asymmetric unit: C-tail two α-helixes (α1, α2), loop 8, loop 10 from SaL14 and four of five β-strands of β-sheet (β2, β3, β4, β5), two α-helixes (α3, α4), loop 2 and loop 4 from *Sa*RsfS. The heterodimer is maintained by 14 H-bonds and hydrophobic interactions. Based on the number of hydrogen bonds on one amino acid we assume the stability of heterodimer is mostly provided by Arg97, Arg107 on *Sa*L14 and by Glu70, Asp81 on *Sa*RsfS. This correlates with published information about structures and functions of RsfS from *M.tuberculosis* and *E.coli*. Violation of these contacts by drugs is one of the ways to reduce the viability of *Sa*. The work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University.