Structure of the 80S ribosome from *Candida albicans* revealed by integrative structural biology approach

Y. Zgadzay[1,2], O. Kolosova[2], A. Stetsenko[3], K. Usachev[1], Sh. Validov[1], A. Rogachev[4], A. Guskov[3,4], M. Yusupov[1,2]

[1]*Laboratory of Structural Biology, Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan, Russia*

[2]*Department of Integrated Structural Biology, Institute of Genetics and Molecular and Cellular Biology, University of Strasbourg, Illkirch, France*

[3]*Groningen Biomolecular Sciences and Biotechnology Institute (GBB), University of Groningen, Groningen, the Netherlands*

[4]*Moscow Institute of Physics and Technology, Dolgoprudny, Russia*

a.guskov@rug.nl

Candida albicans is the most common commensal fungus colonizing humans, and normally it does not impact the human health. However under certain conditions, it can rapidly outgrow bacterial flora causing mucocutaneous or systemic (and potentially fatal) infections. In most (mild) cases the treatment with topical and oral medications works well, however the resistant strains of *C. albicans* appear at the alarming pace, requiring the prompt development of new medications targeting this pathogen. One of the most promising routes to fight pathogens is to interfere with their protein synthesis machinery, therefore the structural information on ribosomes from pathogenic organisms is essential.

In this research we used an integrative structural biology approach based on the combination of single-particle cryo-Electron microscopy and macromolecular X-ray crystallography to resolve the structure of *C. albicans* ribosome.

We obtained 2.4 Å resolution structure of the 80S ribosome from *C. albicans* with the bound antibiotic and 4.2 Å resolution structure of the vacant *C. albicans* ribosome by single particle cryo-EM and X-ray crystallography. The comparison with other available eukaryotic ribosomes revealed unique features of *C. albicans*. These results can be used as a structural basis to decipher the mechanisms of antifungal resistance in *C. albicans* and to design novel inhibitors.

.

Keywords: ribosome; Candida albicans; integrative structural biology; single particle cryo-electron microscopy; X-ray crystallography,

This work was supported by Russian Science Foundation grant 20-64-47041.