International Journal of Biomedicine | June 2021 - Volume 11, Issue Suppl_1: Abstracts from the Third Russian International Conference "Cryo-electron microscopy 2021: achievements and prospects"

POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: STRUCTURE AND FUNCTIONS OF THE TRANSCRIPTION AND TRANSLATION APPARATUS OF THE CELL

DOI: 10.21103/IJBM.11.Suppl_1.P25

Abstract P-25: High-Resolution Cryo-Electron Microscopy Structure of the *Staphylococcus Aureus* Ribosome Brings to Light New Possible Drug Targets

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Background: Antibiotic resistance is a growing worldwide problem. One of the major resistant bacterial pathogens is *Staphylococcus aureus*, which became a burden of healthcare systems around the world. To overcome the issue, more drug discovery studies are needed. One of the main antibiotic targets is a ribosome – the central hub of protein synthesis. Structural data of the ribosome and its features are a crucial milestone for the effective development of new drugs, especially using structure-based drug design approaches. Apart from many small structural features, ribosome possesses rRNA modifications that play a role in the fine-tuning of protein synthesis. Detailed species-specific structural data of the *S. aureus* ribosome is also a useful model for understanding the resistance mechanisms. This information could help with the design of new antibiotics and the upgrading of old ones. The data on *S. aureus* ribosomal RNA modifications and corresponding modification enzymes are very limited. Our aim was to improve the current models of the *S. aureus* ribosome by determining its structure with functional ligands at a much higher resolution -

thereby creating a foundation for structure-based drug design experiments and research of new drug targets.
Methods: The *S. aureus* ribosome complex consists of three components: ribosome, fMet-tRNA^{fMet}, mRNA and 70S ribosome. The complex from purified components was formed *in vitro* and applied to cryo-EM grids. Data was collected at Titan Krios with Gatan K2 detector (IGBMC, France). The data was processed and modeled in Relion 2.1, Chimera, Coot, and Phenix.
Results: We determined the cryo-EM reconstruction at 3.2 Å resolution of the *S. aureus* ribosome with P-site tRNA, messenger RNA. Based on the experimental map and existing bioinformatic data, we at the first time identified and assigned 10 modifications of *S. aureus* rRNA. We analyzed the positions of rRNA modifications and their possible functions.
Conclusion: In this study, we describe our structure of *S. aureus* ribosome with functional ligands. The present model is the highest resolution and most precise that is available at the moment. We propose a set of methyltransferases as targets for future drug discovery studies. The proposed methyltransferases and corresponding modifications may play an important role in protein synthesis and its regulation.

Key Words: ribosome • cryo-EM • rRNA modifications • *S. aureus*

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International Journal of Biomedicine. 2021;11 Suppl 1: S22-23.
doi: 10.21103/IJBM.11.Suppl_1.P25