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POSTER ABSTRACT PRESENTATIONS

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

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**Abstract P-15: Structural Insights of Dirithromycin Binding to the Bacterial
Ribosome**

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Background: Macrolide antibiotics bind in the nascent peptide exit tunnel (NPET) of the bacterial ribosome near the peptidyl transferase center. One of the second-generation macrolides, dirithromycin (DIR), differs from the parent erythromycin (ERY) by the presence of a hydrophobic (2-methoxyethoxy)-methyl side chain that has significantly increased the delivery of this antibiotic to tissues due to better lipophilicity. In this work, we present a cryo-EM structure of DIR bound to the functional complex of 70S ribosome from *E. coli*.

Methods: Ribosomal complexes containing deacylated tRNA^{fMet} in the P site and fMet-Phe-tRNA^{Phe} in the A site were incubated with 30 mM DIR for 10 min before application onto carbon coated grids (Quantifoil R 2/2) and freezing. Cryo-EM data was collected using cryo-TEM Titan Krios and processed using Warp, Relion 3.0 and CisTEM. Model building was performed in Phenix.real_space_refine and Coot.

Results: Preliminary analysis failed to reveal any significant differences in location of macrolactone ring of DIR (current work) and ERY (pdb: 4v7u). In both structures only one hydrogen bond is formed between antibiotic and residue A2058. However, in comparison to the crystal structure of the ribosomal complex with ERY, our cryo-EM map demonstrates additional rotation of A2062 of 23S rRNA towards desosamine of DIR.

Conclusion: Structural peculiarities of DIR binding to the *E. coli* ribosome determined by high-resolution cryo-EM overall coincide with the mode of ERY interaction with the *E. coli* ribosome revealed

by X-ray crystallography. Our results suggest a conformational lability of the (2-methoxyethoxy)-methyl side-chain of DIR, which is directed towards tunnel cavity and doesn't form any additional contacts with its walls.

Key Words: ribosome • antibiotics • structure • cryo-EM

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