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Invitation

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Context-specific ribosome protection by macrolide resistance ABCF proteins

by **Dr. Maxim Svetlov**

September 9th, 2025, 10:00-11:00

Lecture hall of the Institute of Physiology, Videnska 1083, Prague 4

ANNOTATION

ATP-binding cassette proteins of the F type (ABCFs) are critical components of the translational apparatus responsible for resolving ribosome arrests caused by various factors. Bacterial antibiotic-resistance ABCFs (ARE-ABCFs) confer resistance to drugs targeting the ribosomal peptidyl-transferase center (PTC) or the nascent peptide exit tunnel (NPET). The conventional view proposes that, by associating with an antibiotic-stalled ribosome, ARE-ABCFs dislodge the drug molecule from its binding site. However, the mechanistic basis for the ribosome protection by ARE-ABCFs has remained mysterious. Here, by integrating biochemical studies with genome-wide ribosome profiling, we demonstrate that MsrE, a macrolide resistance ABCF, does not globally restore translation of macrolide-treated cells. Instead, by selectively rescuing drug-associated ribosomes attempting to translate specific sequences, MsrE action preferentially resumes the production of a subset of proteins. We hypothesize that MsrE functions not by directly dislodging the drug molecule from its binding site but by diverting the path of certain polypeptide chains in the NPET to re-activate the PTC catalytic activity, allowing stalled ribosomes to resume translation. Our findings may suggest that some translation rescue mechanisms have evolved to selectively restore the production of a handful of factors necessary to avoid cell death.

Maxim S. Svetlov, Ph.D.*is a distinguished researcher with over 16 years of expertise in molecular biology and microbiology, specializing in bacterial protein biosynthesis and the mechanisms of antibacterial drug action. After completing his education in Russia, Dr. Svetlov joined the University of Illinois Chicago (UIC) in 2015 as a Postdoctoral Associate in the laboratory of Professor Alexander Mankin, advancing to Research Assistant Professor in 2019. His work at UIC has yielded important insights into how antibiotics interact with ribosomes, with findings published in top-tier journals including Science, Molecular Cell, and Nature Chemical Biology. Notably, he discovered that the slow dissociation of certain antibiotics from ribosomes underlies their bactericidal activity, rather than merely inhibiting bacterial growth—a breakthrough that has deepened our understanding of antibiotic efficacy.*