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The role of the ABC-F proteins, Vga(A) and Msr(A), in antibiotics resistance in staphylococci

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Staphylococcal ABC-F proteins Vga(A)_{LC} and Msr(A) confer resistance either to lincosamides (L), streptogramins A (SgA) and pleuromutilins or to 14 and 15-membered macrolides and streptogramins B, respectively. All these antibiotics bind near peptidyl transferase centre in 50S ribosomal subunit and inhibit translation. Previous experiment has shown that 15 amino acid stretch of the Vga(A) inter-domain linker is important for the antibiotic specificity of Vga(A) proteins. Substitutions L212S, G219V, A220T and G226S, clustered in the stretch, were responsible for the changes in resistance to SgA and L and has been demonstrated *in vitro* that ABC-F proteins mediate antibiotic resistance through interaction with ribosomes. However, in our *in vitro* experiments, we confirmed that both proteins: Vga(A)_{LC}, Msr(A) co-localize with membrane fractions of the cells; therefore, it may be assumed that the proteins cooperate specifically with the ribosomes on the membrane or alternatively, the resistance mechanism is more complex, including also a cooperation of ABC-F proteins with a transmembrane partner. Vga(A)_{LC} and Msr(A) might influence binding of lincomycin and erythromycin to the ribosomes in a similar way. Therefore, the functional interference of these two proteins is expected. To test this hypothesis we determined the resistance to lincomycin and erythromycin in the strain expressing both proteins. We found that activity of Msr(A) was not inhibited by Vga(A)_{LC} as we expected but by the presence of sub-inhibitory concentration of lincomycin. Thus, usage of lincomycin may help in suppression of erythromycin resistance, conferred by Msr(A).

Biography

Jakub Lenart is currently a PhD student from Faculty of Science, Charles University in Prague. He works in the Laboratory for Biology of Secondary Metabolism, Institute of Microbiology of the Czech Academy of Sciences and Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University in Vestec. Since 2012, he is a Member of Czechoslovak Society for Microbiology.

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