Abstract

The staphylococcal protein VgaA belongs to ARE ABCF family, which confers resistance to ribosome binding antibiotics by the target protection mechanism. VgaA confers resistance to lincosamides, streptogramins A and pleuromutilins and thus provides the so-called LS_AP resistance phenotype. The expression of resistance genes often reduces fitness in the absence of an antibiotic, therefore the expression of resistance genes is often tightly controlled and triggered only in response to the presence of an antibiotic to which the protein confers resistance. The inducible expression has also been observed for the *vgaA* gene, nevertheless, its mechanism has not been elucidated.

In the diploma thesis, it was shown that the $vgaA_{LC}$ gene from *Staphylococcus haemolyticus* is regulated by ribosome-mediated attenuation. The mechanism is based on the detection of translation inhibitors via a ribosome translating a special regulatory open reading frame (uORF), which is part of an attenuator located in the 5' untranslated region of the mRNA. The $vgaA_{LC}$ gene is regulated at the transcriptional level in response to LS_AP antibiotics. Antibiotic specificity of induction is affected not only by the nature of the peptide encoded by uORF but also by the antibiotic specificity of the resistance protein. Fluorescence microscopy has shown that the protein regulated by its natural regulator is produced heterogeneously within the cell population.

Keywords

ARE ABCF proteins, $VgaA_{LC}$, *Staphylococcus haemolyticus*, antibiotic resistance, lincosamides, streptogramins, pleuromutilins, regulation of gene expression, r5'UTR element, ribosome mediated attenuation, SRC