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Title (English)

Interaction of inhibitory peptides with an aminoglycoside-3´-O-phosphotransferase by NMR spectroscopy

Title (Swedish)

Abstract

Antibiotic resistance against the aminoglycoside antibiotic kanamycin can occur due to kanamycin modifying enzymes, such as aminoglycoside-3´-O-phosphotransferase. The kanamycin modifying effect of this enzyme can be inhibited by the peptides indolicidin and protegrin. In this study, the interactions between aminoglycoside-3´-O-phosphotransferase and indolicidin respectively protegrin were investigated. SPR-based investigations revealed binding of both peptides. ^{1}H-^{15}N-TROSY-HSQC experiments were used in NMR titration studies to determine the amino acid residues of the enzyme, which were affected by the binding of indolicidin. The affected residues not only coincide with the kanamycin binding site, but are also found in its vicinity. Binding of indolicidin to the kanamycin binding site might unable a binding of kanamycin and thereby prevent antibiotic resistance against kanamycin. The aim of the study, was also to investigate the K_D constant of the interactions, however a determination was not possible during the time-span of the work.

Keywords

Aminoglycoside-3´-O-phosphotransferase (kanamycin kinase), Indolicidin, Protegrin, ^{1}H-^{15}N-TROSY-HSQC, Surface Plasmon Resonance (SPR), Biacore X

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