Effects of AFN-1252 on In Vitro and In Vivo Staphylococcus aureus Virulence Gene Expression

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Abstract

Staphylococcus (S.) aureus is a Gram-positive pathogen that is responsible for a variety of infections across the human body, including skin and soft tissue infections, bacteremia, and endocarditis. One of the reasons for the plethora of disease types associated with S. aureus is its ability to rapidly change its pathogenesis in response to environmental cues through regulatory networks. Here, we describe an in vitro and in vivo evaluation of AFN-1252, a novel anti-staphylococcal antibiotic that was previously shown to reduce bacterial growth in murine models of infection and reduce virulence gene expression in laboratory strains of S. aureus.

Methods

In vitro experiments involved evaluating the impact of AFN-1252 on the expression of virulence genes in USA300 and Wood46 strains. The USA300 and Wood46 strains were obtained through the Network of Antimicrobial Stewardship and Resistance (NARSA) program supported under NIAID/NIH Grant #1R01AI106603. There are currently no marketed antibiotics that target the SaeR regulon, which is thought to be important during the infection process and resulting disease state in the host.

In vivo experiments involved inoculating 5-day old pouches of AFN-1252 treated and untreated CD-1 mice with USA300 and Wood46 strains, and then evaluating the impact of AFN-1252 on the expression of virulence genes in untreated samples.

Results

We found that AFN-1252 reduced the expression of virulence genes in USA300 and Wood46 strains. Additionally, AFN-1252 reduced the number of CFU in mouse pouches for up to 48 hrs.

Introduction

The ability to predict the impact of antibiotics on antibiotic resistance is a critical step towards developing new antibiotics. In this study, we evaluated the impact of AFN-1252 on the expression of virulence genes in laboratory strains of S. aureus. We found that AFN-1252 reduced the expression of virulence genes in untreated samples.

Methods and Materials

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Discussion

The results of our study demonstrate the potential of AFN-1252 as a novel antibiotic that could be used to treat S. aureus infections. This is the first study to evaluate the impact of AFN-1252 on the expression of virulence genes in laboratory strains of S. aureus. The results of our study suggest that AFN-1252 could be a promising new antibiotic for the treatment of S. aureus infections.

Summary and Conclusions

The results of this study demonstrate the potential of AFN-1252 as a novel antibiotic that could be used to treat S. aureus infections. This is the first study to evaluate the impact of AFN-1252 on the expression of virulence genes in laboratory strains of S. aureus. The results of our study suggest that AFN-1252 could be a promising new antibiotic for the treatment of S. aureus infections.