

ISALIAH SELMON-MILLER, MICHAEL WHABY, and DEANNA M. SCHMITT. Department of Natural Sciences and Mathematics, West Liberty University, West Liberty, WV 26074. Lipoprotein sorting as a potential target of resazomycins, a novel family of antibiotics.

The prevalence of antibiotic-resistant bacterial infection has increased, promoting a global health concern. The significance of this resistance pertains to the limitation it places on effective and available microbial agents, resulting in a predicament worsened by the small number of antimicrobial agents introduced over the last couple of years. Therefore, new antibiotics must be developed with unique targets that are not susceptible to rapid antimicrobial resistance. With this stated, it is known that the Lol system is responsible for transporting lipoproteins to the outer membrane in Gram-negative bacteria which play essential roles in a wide variety of bacterial physiological processes. We have identified a novel family of compounds, resazomycins, which exhibit antimicrobial activity against select Gram-negative bacteria including the human pathogens *Francisella tularensis* and *Neisseria gonorrhoeae*. A common feature of resazomycin-sensitive bacteria is possession of a unique lipoprotein sorting system, LolDF. This complex differs from the LolCDE sorting complex found in most Gram-negative bacteria like *Escherichia coli* that are resistant to resazomycins. We sought to determine whether LolDF is the target of resazomycins by cloning the genes that encode the *E. coli* LolCDE transporter into an *F. tularensis* plasmid and then electroporated this plasmid into an attenuated *F. tularensis* live vaccine strain (LVS) to see if these would render the bacterium resistant to resazomycins. Thus far, LolCDE-expressing LVS exhibits no difference in susceptibility to resazomycins compared to wild-type LVS. Therefore, we are investigating the role of other *F. tularensis* genes in susceptibility to resazomycins.