Universität Basel

Research Project

Exploration of teichoic acids biosynthesis for the production of novel conjugate vaccines and antibiotics

Project funded by own resources

Project title Exploration of teichoic acids biosynthesis for the production of novel conjugate vaccines and antibiotics
Principal Investigator(s) Perez, Camilo ;
Organisation / Research unit
Departement Biozentrum / Structural Biology (Perez)
Project Website https://www.biozentrum.unibas.ch/research/researchgroups/overview/unit/pere z/
Project start 01.01.2020
Probable end 31.12.2021
Status Completed

Bacterial infections represent a major public health problem of broad concern to countries and multiple sectors, augmented by increasing occurrence of strains resistant to antibacterial agents. Pathogens such as the Gram-positive bacteria *Staphylococcus aureus,* commonly found in hospitals, are the cause of a great variety of infections that affect several parts of the human body, leading to death if the infection is not treated properly.The bacterial cell wall is a complex structure that exerts important protective functions against host defenses and antibiotics allowing bacterial survival and adaptation under adverse conditions. One of the most distinct features of the cell wall from Gram-positive bacteria is the presence of teichoic acids biopolymers. These polymers have been shown to be important for immune evasion, adhesion, biofilm formation and protection from antimicrobials. Despite the great importance of teichoic acids, mechanistic and fundamental biochemical aspects of membrane proteins participating in their assembly are poorly described. Understanding how such proteins work will have a tremendous impact on the design of novel vaccines against Gram-positive bacteria and to generate further antimicrobials. **In this project we seek to develop two strategies that will allow us to fight Gram-positive bacterial infections**. **The first strategy is to develop novel chemoenzymatic routes for the production of alternative conjugate vaccines derived from teichoic acids**. To do this, we first need to understand how the proteins involved in teichoic acids synthesis perform polymerization and assembly of these biopolymers. By understanding these processes, we will be able to engineer these proteins and to generate conjugate ensembles that will differ from classic capsular polysaccharide-derived vaccines, opening new alternatives for vaccination against *S. aureus* and other Gram-positive pathogens. **The second strategy is to characterize disaccharide inhibitors targeting the flippase LtaA, a central protein in lipoteichoic acids assembly pathway.** Recently**,** my lab found that LtaA is essential for survival of *S. aureus* under host niche conditions. We have generated preliminary data showing that some disaccharide molecules inhibit the activity of LtaA with high specificity. **We want to investigate the mechanism of LtaA inhibition by disaccharide molecules. We believe that by doing this, we will be able to discover novel alternatives for the treatment of *S. aureus* infections.** Our research will be of fundamental, groundbreaking impact to understand cell wall biology, activity modulation and inhibition of teichoic acids assembly pathways, and will reveal new routes for the design of conjugated vaccines. Our work will establish a framework that will allow development of treatments to counteract Gram-positive bacterial infections in the future.

Keywords Staphylococcus aureus, teichoic acids, conjugated vaccines, antibiotics
Financed by
Other funds

Add publication

Add documents

Specify cooperation partners