

## Antibacterial properties of three newly identified recombinant *Staphylococcus aureus* phage endolysins

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### Abstract

*Staphylococcus aureus* causes serious infections in humans and animals. Controlling of staphylococcal infections is becoming very difficult to due to the emergence of multidrug-resistant strains. Therefore, search for novel antimicrobial alternatives has become of great importance. One of these new approaches is bacteriophage-encoded endolysin enzymes, which have exogenous lytic activity against multiple antibiotic resistant bacteria, especially in Gram positive bacteria. In this study, we described cloning, expression and functional analysis of three endolysins from temperate bacteriophages from three clinical isolates of *S. aureus* strains. Temperate phages were isolated from the host strains using the mitomycin C induction. The endolysin genes of the phages were amplified using PCR, cloned and over-expressed in *E.coli*. The lytic activity of endolysins were tested against a wide range of bacterial species using spot-on-lawn assay method. The combination of the three endolysins (LysSA10, LysSA14 and LysSA15) displayed activity against 222 of 239 (93%) of *S. aureus* strains including 67 MRSA and 6 ATCC type strains. In addition, endolysins showed lytic activity against other Gram positive bacteria including a number of clinical and type strains of *S. epidermidis*, *S. haemolyticus*, *Enterococcus faecalis*, *E. faecium*, *Streptococcus pyogenes*, *S. pneumoniae*, *S. intermedius*, *Bacillus subtilis*, and *B. atrophaeus*. No lytic activity was observed against 7 *Lactobacillus* and one *Listeria monocytogenes* ATCC type strains tested.

Overall, our results showed that the combination of the newly identified three recombinant endolysins exhibited a broad host range against several Gram positive bacteria. Thus, these endolysins are promising antimicrobial agents for combating bacterial pathogens.

### Introduction:

*Staphylococcus aureus* is a coccoid Gram-positive bacterium with a thick peptidoglycan layer (1), otherwise called a murein layer. This murein layer comprises of long ionic polymers involving the substituting amino sugars N-acetylglucosamine and N-acetylmuramic corrosive that make up the glycan chains and peptide linkers interfacing these glycan chains to a three-dimensional system. On account of *S. aureus*, these peptide linkers comprise of monitored stem peptides, which are interconnected through five back to back glycines, the purported pentaglycine connect. Another trademark highlight

of *S. aureus* peptidoglycan is O-acetylation at the C6-OH position of muramic corrosive, rendering the bacterium impervious to lysozyme. Teichoic acids covalently connected to the peptidoglycan work as controllers of cell development, as phage receptors, epitopes, for drawing in cations, and as devices for microbes to speak with the earth. *S. aureus* is known to be a piece of the ordinary microflora. This bacterium dwells fundamentally on the nares, skin, and mucosal films of people and creatures and represents no danger to the host species under ordinary conditions. The colonization rate in solid grown-ups is somewhere in the range of 5 and 30%, and 10 to 20% of people show changeless colonization. On the other hand, microscopic organisms from solid people can represent a danger of transmission to the immunocompromised populace, yielding unfavorable impacts on those contaminated. An assortment of illnesses can be brought about by staphylococcal strains, running from rather innocuous restricted skin contaminations to fundamental diseases upon the passage of microorganisms into the blood just as intense and interminable diseases of different organs, for example, heart, bones, and lungs. Sepsis, endocarditis, and harmful stun condition are instances of hazardous maladies brought about by *S. aureus*. One of the basic hazard factors for the advancement of emergency clinic obtained (HA) and network procured (CA) diseases is *S. aureus* nasal carriage. Expanded colonization rates have been accounted for to prompt expanded disease rates in the network and medical clinics.

Medication opposition in *S. aureus* can be procured by various components, including flat quality exchange by means of plasmids or other portable hereditary components just as unconstrained changes and determination. This prompted the rise of different strains that show protection from one or a mix of anti-toxins, for example, methicillin-safe *S. aureus* (MRSA), vancomycin-safe *S. aureus* (VRSA), and numerous medication safe *S. aureus* (MDRSA). In the course of recent years, there have been variances in the predominance of MRSA. Albeit by and large paces of *S. aureus* diseases may have balanced out and the predominance of MRSA is marginally diminishing in some Western nations, numbers are still alarmingly high on an overall scale. As indicated by U.S. what's more, Dutch predominance information, between 2 million and 53 million individuals are minimalistically assessed to convey MRSA around the world.

In spite of the fact that correlation of epidemiological information has demonstrated troublesome on account of contrasts in populaces tested and study structures, nations in North and South America and Asia just as Malta have been accounted for to have the most noteworthy MRSA rates, surpassing half. Particularly high rates have been accounted for Sri Lanka (86.5%), South Korea (77.6%), Vietnam (74.1%), and Taiwan (65.0%). Conversely, India and the Philippines have a lot of lower paces of 22.6% and 38.1%, separately. China, Australia, African nations, and some Southern and Eastern European nations, for example, Portugal, Greece, Italy, and Romania, have middle rates going from 25 to half. MRSA is commonly less predominant in numerous Western and Northern European nations, including The Netherlands and Scandinavian nations.

Anti-microbial of decision for the treatment of *S. aureus* contaminations at first was penicillin; be that as it may, penicillin opposition is amazingly normal in many nations. Accordingly, a penicillinase-safe  $\beta$ -lactam anti-infection, for example, flucloxacillin or oxacillin is normally utilized for first-line treatment; these anti-microbials have a similar instrument of activity as penicillin. *S. aureus* strains that are methicillin safe are likewise impervious to other  $\beta$ -lactam anti-infection agents, including penicillins (penicillin V, penicillin G, ampicillin, oxacillin, carbenicillin, and amoxicillin), carbapenems (imipenem-cilastatin [Primaxin]), cephalosporins (cephalothin), and monobactams.

Treatment of genuine contaminations may use blend treatment with different anti-infection agents; in any case, since this technique bears a high danger of harm to the kidneys, its utilization is disputable. Along these lines, meaning to battle MRSA, vancomycin, which is a glycopeptide anti-toxin, is usually utilized. Be that as it may, some treatment disappointments with vancomycin have been accounted for, even in patients contaminated with vancomycin-helpless MRSA. Linezolid, which has a place with the oxazolidinone class of medications, has been accounted for to have bacteriostatic movement against *S. aureus*. This anti-toxin is endorsed to treat confounded delicate tissue and skin contaminations and furthermore pneumonia in kids and grown-ups. It has oral and parenteral definitions, and its oral bioavailability is acceptable, however *S. aureus* strains that are impervious to this anti-toxin have been accounted for too.

Keywords: *Staphylococcus aureus*, glycopeptide anti-toxin, carbenicillin.