RESEARCH ARTICLE

IN SILICO ANALYSIS OF VACCINE TARGET AGAINST MULTIDRUG RESISTANT *STAPHYLOCOCCUS AUREUS*

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ABSTRACT

Staphylococcus aureus (*S. aureus*) is a common bacterium that lives on the skin and in some people's noses. *S. aureus* can cause a range of mild to severe infections. Excessive use of antibiotics has led to drug-resistant strains of *S. aureus* (MRSA). The ancient practice of vaccine designing was being evaluated in the present study for the *in silico* development of preventive measure against multidrug resistant *Staphylococcus aureus* infections. Multiple sequence alignment revealed various conserved regions in mecA protein. We predicted one such type of multi-epitope peptide which was having very good potential to induce B cell response and a very good candidate for binding to MHC II molecule. Structure prediction of this sequence by PSIPRED revealed that 22 helix are present in this sequence. The identified peptide can be a suitable target for induction of both T_H cell and B cell. This peptide was designed from conserved regions of *mecA*, so it can be a preventive measure for MRSA infections after suitable experimental analysis. This data can be very helpful for generating antigenic candidate by wet lab researchers.

INTRODUCTION

The genus "*Staphylococcus*" is common inhabitant of the skin and mucous membrane. Staphylococcus gets its name from its appearance under the microscope: *staphyle*, the Greek word for a bunch of grapes, combined with *kokkos*, meaning berry. Illness results when staph bacteria are somehow able to overcome the body's natural defense mechanisms. Staph-related sicknesses range from skin infections to food poisoning or toxic shock syndrome, and severity ranges from mild to fatal. Approximately 20–30% of the general population is "staph carriers"[1]. It is still one of the four most common causes of nosocomial infections, often causing post-surgical wound infections. The emergence of antibiotic resistance in this microorganism and their spread is threatening the medical community. The resistance development in *Staphylococcus aureus* dates back to 1940s. Multiple drug resistance of *Staphylococcus aureus* is due to the presence of *mecA* gene coding for penicillin binding protein (PBP2a) with a low affinity for β- lactam antibiotics.

This gene is carried on Staphylococcal Cassette Chromosome (SCC) *mec,* a unique mobile genetic element that harbors the methicillin resistant gene (*mecA*) and other antibiotic resistant determinants[2]. Although it's usually treatable, when MRSA enters the bloodstream, the infection is life-threatening. This is why it is important to be aware of how staph infections develop and how to prevent them. Once someone contracts a staph infection, anyone in close contact with them can contract it from them. No effective vaccine is generally available that stimulates active immunity against staphylococcal infections in humans. However, vaccine therapies represent a new and innovative approach in broadening the available clinical tools against the global health problem of community and healthcare-associated *S. aureus* bacterial infections[3]. So, it is cardinal to focus over mecA protein to design a multi-epitope antigenic target specific against multidrug resistant *Staphylococcus* that may provide protection from variety of infections caused by this deadly bacterium. Thus, we investigated the possible vaccine candidate for the test organism using bioinformatics tools.

MATERIALS AND METHODS

An effort was made to analyze preventive measure against *Staphylococcus aureus*. So we performed *in silico* prediction of vaccine candidates of *mecA* through bioinformatics approach. In this context, we have done multiple sequence alignment of *mecA* sequences using database. The target which can be suitable for B-cell as well as T-cell epitope prediction is considered to be good[4]. We therefore search for the same and tried to find the possible targets as B-cell epitope by Bepipred method. The T-cell targets were predicted by using EpiJen server[5, 6]. Structural prediction was done by PSIPRED.

RESULTS AND DISCUSSION

The threat to the human population is that reservoirs of drug-resistant bacteria is abound. Even though pharmaceutical companies have produced a number of new antibacterial drugs

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over the years, resistance to these drugs by *Staphylococcus aureus* has increased manifold and has now become a global concern. Beginning in the 1940s, penicillin was produced and used to treat Staph aureus. Alarmingly, within just ten years, a drug resistant strain emerged. By 1960, methicillin was introduced, but less than twenty years later; Australia reported the first methicillin-resistant strain of staph. Methicillin-resistant Staphylococcus aureus (MRSA) was born, and in a few years it had cropped up all over the world[7, 8]. Athletes and prisoners fall into the category of high-risk for contraction of MRSA infections, and so do family members and coworkers. There is a special designation for MRSA contracted by those who have not been in a healthcare-related environment - community-associated MRSA (CA-MRSA). The Centers for Disease Control (CDC) estimates that around 12% of MRSA cases now fall within this category. But the vast majority of MRSA cases appear in healthcare settings[9]. The National Institute for Occupational Safety and Health (NIOSH) reports "5 Cs" that make it easier for the disease to be transmitted: Crowding, frequent skin-to-skin Contact, Compromised skin, contaminated items and surfaces, and lack of Cleanliness[10].

The CDC states that it's critical to maintain a clean environment "by establishing cleaning procedures for frequently touched surfaces and surfaces that come into direct contact with people's skin."
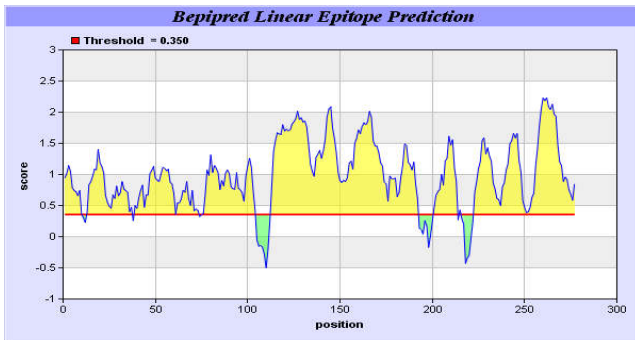

Figure1. Predicted B-cell epitope by BepiPred Epitope prediction method

In the present study, it was found that mecA protein of *Staphylococcus* can be used as an effective candidate for the development of preventive measures against drastic diseases by blocking its resistance efficiency. In fact *in silico* approach of vaccine target prediction is definitely less labor intensive, rapid and economic in relation to search for a lead antigenic molecule against mecA protein[11]. Multiple sequence alignment revealed various conserved regions of this protein. Analysis was done for finding out the potential of these conserved regions to work as B cell epitope and we found 41 potential B cell epitopes among the conserved sequence. For any predicted epitope, it is cardinal that it should induce T and B cell response[12]. Such type of multi-epitope vaccine is a very recent experimental technique for predicting vaccine targets against HIV and Influenza virus[13]. We predicted one such type of multi-epitope peptide which was having very good potential to induce B cell response as well as a very good candidate for binding to MHC II molecule as found by Kohler (2000)[14] also in his study. (Fig. 1) Among 51 MHC II alleles analyzed, the conserved region of protein *mecA* showed binding affinity with all the 51 alleles with one or more than one paratope found in each. As per the results of ProPred, 47 sequences were found to bind with MHC I alleles. During the last step of study, this

protein sequence was also analyzed for its binding affinity with T-cell receptors using the EpiJen server[15]. Structure prediction of this sequence by PSIPRED revealed that 22 helix are present in this sequence (Fig. 2). This data can be very helpful for generating antigenic candidate by wet lab researchers.
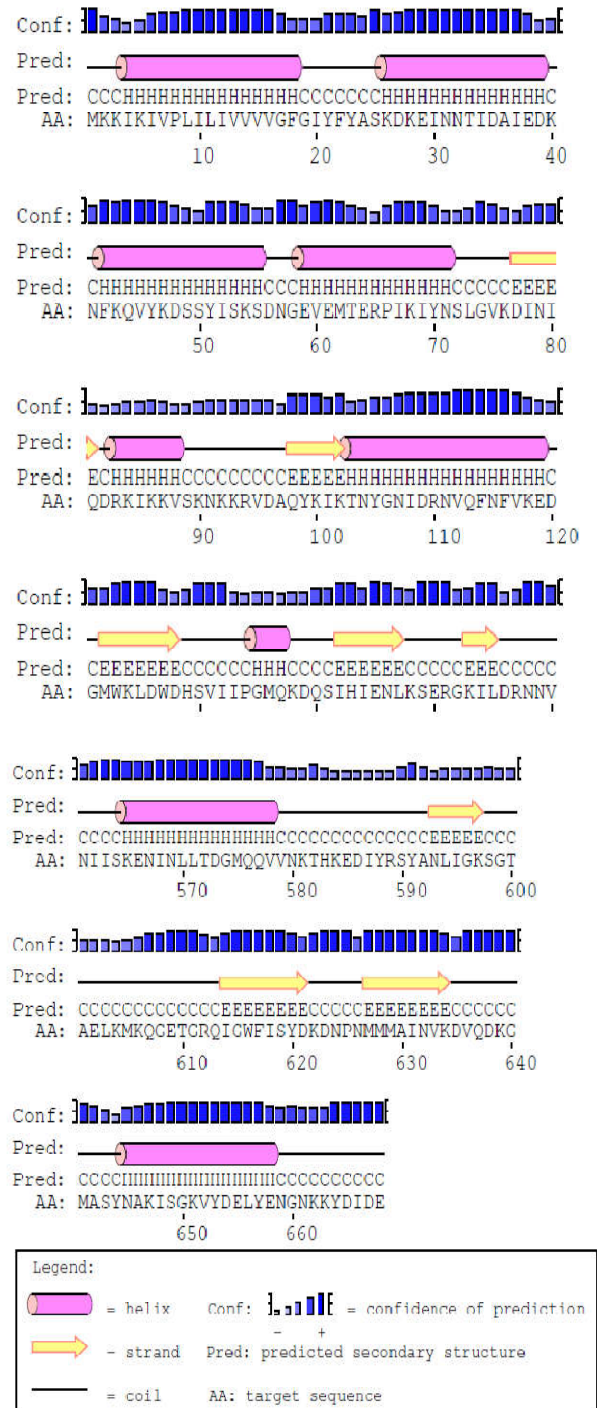

Figure 2. A part of the structure of proposed vaccine target against MRSA predicted by PSIPRED

Conclusion

The most important, all-encompassing matter in preventing staph infections like MRSA is cleanliness The results presented in this report were encouraging, although clinical controlled

studies are required to define the real efficacy and possible toxic effects *in vivo*. Also the focus of this study was on a bioinformatics based approach as a means to enhance the optimal selection of potential target of immune response that can then be validated by experiment that test the biological function of these antigen sequences in immune system based assays.

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