Journal of Vaccines & Vaccination
ISSN: 2157-7560
Rapose, J Vaccines Vaccin 2012, 3:1
DOI: 10.4172/2157-7560.1000e103
Editorial Open Access

Development of Antimicrobial Antibodies: A Novel Line of Attack in the Battle Against Infection

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Staphylococcus aureus is a common cause of severe infections in hospitalized patients [1]. The spectrum of disease varies from necrotizing skin and soft tissue infection to bacteremia, endocarditis and pneumonia [2]. Staphylococcal infection is also a feared complication in patients with prosthetic materials like artificial joints [3], cardiac support devices [4] and hemodialysis catheters [5].

In addition, *S. aureus* is now commonly associated with skin infection as well as pneumonia in patients in the community [6-8].

Staphylococcus infections are caused either by methicillin sensitive *Staphylococcus aureus* (MSSA) in which case treatment options include the use of beta lactams, or methicillin-resistant *Staphylococcus aureus* (MRSA) in which case the "gold standard" for treatment of severe infection is the drug vancomycin. Other antibiotics used in the treatment of staphylococcal infection include clindamycin, bactrim, quinolones, tetracyclines and rifampin.

There is now an increasing incidence of failure in spite of optimized dosing of the "gold standard". This can be attributable to increased vancomycin minimum inhibitory concentrations (MICs) of *S. aureus* [9,10]. Along with this, potential adverse effects including nephrotoxicity attributable to vancomycin, has resulted in research into new antibiotics against MRSA and development of products like linezolid [11], daptomycin [12], tigecycline [13] and ceftaroline [14]. Linezolid is considered a bacterostatic agent, while daptomycin is considered bactericidal. As expected, with increasing use of these products there are now reported cases of treatment failure even with high dose daptomycin [15] as well as linezolid [16] and ceftaroline [17].

The use of systemic antibiotics targeting *S. aureus* is also associated with "collateral damage". These antibiotics act against not only the *S. aureus*, but also cause disruption in host bacterial flora resulting in secondary infectious complications. The most common example of this is the development of *Clostridium difficile* infection and diarrhea [18].

Therefore there is an urgent need for development of new antimicrobial products against *S. aureus*.

In this issue of the Journal of Vaccine and Vaccination, Vaillant et al present very important research into "non-antibiotic" therapy for staphylococcal infections. *S. aureus* synthesizes protein A (SpA) which plays an important role in bacterial adhesion and has been demonstrated to be responsible for a cascade of reactions that help bacterial invasion of host tissue [19]. The authors used chicks to develop antibody to SpA. They showed that the antibody was able to inhibit the growth of *S. aureus*, thus demonstrating the antimicrobial properties of this product. This novel approach – targeted antibodies - in the battle against *S. aureus* infections is very important for a number of reasons: there is increased incidence of antibiotic resistance as mentioned above, there are significant side effects associated with high dose and prolonged antibiotic therapy for resistant infections, and increasing number of patients who present with allergies to multiple antibiotics. In addition, targeted therapy will hopefully reduce risk of collateral damage and hence *C. difficile* infection.

The use of the immune system in the prevention of infection is not a new concept. Oral typhoid and polio vaccines are examples of the use of agents in the prevention of bacterial and viral infections respectively. Use of monoclonal antibody targeting bacterial toxin is one of the new modalities in the treatment of *C. difficile* infection [20]. Important advantages of the authors' research include oral route of administration and non-live nature of this product.

One cautionary note is worth bringing up at this time. There are a number of patients who claim egg allergy, and though safety of vaccines has been demonstrated [21], this has been a stumbling block in the use of a number of vaccines in these patients. This may also prove to be a limiting factor in terms of human use of a product developed using chick embryo.

However we look forward for further developments and standardization of this exciting potential antimicrobial product. I convey to the authors wholehearted wishes for successful outcomes into this translational research.

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Received March 25, 2012; **Accepted** March 26, 2012; **Published** March 28, 2012

Citation: Rapose A (2012) Development of Antimicrobial Antibodies: A Novel Line of Attack in the Battle Against Infection. J Vaccines Vaccin 3:e103. doi:10.4172/2157-7560.1000e103

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