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Editorial
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Epitope Driven Broad Spectrum Peptide Vaccines against MDR Pathogens

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Editorial

Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumonia have evolved as a group of co-existing multidrug resistant nosocomial pathogens spreading worldwide. Overuse of antibiotics has led to the emergence of pan drug resistant bacterial strains and has made all antimicrobial agents superfluous including carbapenems and even the last resort antibiotic-colistin, resulting in high mortality rates among the hospitalized patients. Vaccination is highly effective and successfully used strategy that reduces the incidence of infectious diseases, yet efforts towards development of vaccines for nosocomial infections are scant. In this direction, a broad spectrum vaccine is the futuristic need providing protection not only against *A. baumannii* but against the whole group of co-existing nosocomial pathogens.

The availability of complete bacterial genome and proteome sequences has revolutionized the approach of *in silico* vaccine prediction and development. Although there are a number of uncharacterized and putative proteins in the proteomes of the pathogens but the availability of genomic sequences and functional characterization of several genes involved in virulence has significantly increased our understanding of the molecular basis of pathogenesis and provides a wealth of information that can be used to design new approaches for effective vaccine development. Reverse vaccinology is a time effective technique that can predict potential epitopes as vaccine candidates by *in silico* analysis of bacterial proteomes and facilitates there *in vivo* validation [1], that ameliorates the treatment options against pathogens. In certain cases where natural immunogens do not induce optimal response and recombinant subunit vaccines become difficult to produce, epitope based approaches may solve the problem. Epitopes can be easily synthesized, formulated and validated in mouse models. Researchers are hopeful that in the near future synthetic peptide vaccine will be more effective, safe and long lasting compared to conventional ones. The ability of peptide vaccines to elicit both antibodies and cytotoxic T lymphocytes (CTLs) distinguishes them from conventional vaccines comprised of live attenuated or killed whole organism or purified antigen and makes them a promising vaccine approach to test on many pathogens.

The success of peptide vaccines may be attributed to the fact that peptides are selected by extensive *in silico* analysis using both sequence based and structure based screening methods. Because of their defined chemical nature and small size, synthetic peptides offer distinct advantages in terms of chemical characterization and manufacturing. The conventional method for T cell epitopes identification involves the experimental screening of overlapping peptides in the protein of interest which is a costly and time consuming task. Nevertheless, the development of various epitope predicting programs has facilitated the prediction of most promising epitope candidates and reduces the number of peptides selected for experimental validation. Outer membrane proteins conserved in different bacterial genera can be picked for prediction of identical epitopes prevalent in majority of bacterial proteomes. An important feature of epitope driven vaccine is epitope promiscuity that makes it a more relevant immunogen in genetically variable species such as human populations [2]. Therefore, an ideal peptide vaccine (peptope) could be designed by screening the complete pool of epitopes for most conserved, surface exposed ones that bind to majority of HLA alleles. These synthetic peptide vaccines can be conjugated with metalloprotein such as Keyhole limpet hemocyanin (KLH) [3] or can be used as such [4]. Examples of synthetic techniques used for their production involve the lipid core peptide vaccine delivery system, thioether ligation, multi-epitope vaccine prepared by polymerization approach, asymmetrical dendrimers produced with the help of copper-catalyzed azide-alkyne cycloaddition, multi-epitope construct produced by random polymerization of several acrylate modified B cell epitopes, recombinant polyepitope conjugated to adjuvant moiety with the help of intein and native chemical ligation and glycopeptides-based antigen synthesized in a mixed chemical/enzymatic approach [5]. The designed peptide vaccine when injected alerts the host's immune system to generate immunization memory cells. Although peptope is an acceptable approach for a candidate vaccine [4,6] however, its efficacy must be validated by clinical trials.

The reduced side effects, cost effectiveness and improved stability of epitope driven peptide based vaccines can provide a major breakthrough in the vaccine development against pathogens. Further, stitching prominent epitopes conserved in the proteomes of a group of nosocomial pathogens can lead to a promising vaccine candidate that can provide broad spectrum protection. We expect a quantum leap in treatment options by developing epitope driven vaccines in future.

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