J Vaccines Vaccin 2015, 6:3
http://dx.doi.org/10.4172/2157-7560.S1.025

OMICS International
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5th Asia Pacific Global Summit and Expo on
Vaccines & Vaccination

July 27-29, 2015 Brisbane, Australia

Targeting antigenic site on RSV F protein associated with virus neutralization for vaccine design

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Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in infants and young children. RSV also causes serious illness in the elderly, immuno-compromised and persons with cardiopulmonary diseases.1 The significant morbidity and mortality associated with RSV infection emphasises the urgent need for vaccines against RSV infection. The failure of formalin-inactivated RSV clinical trials in the 1960s[2] directed researches towards finding new approaches for the development of RSV vaccines. In this study, a B cell epitope KNYIDKQLLPIVNKQS from the RSV F protein, known to be the target of neutralizing antibody, was chosen for vaccine development. The proposed vaccine strategy utilizes the lipid core peptide (LCP) delivery system with self-adjuvanting properties 3, 4 in conjunction with the B-cell peptide epitope and Pan DR (PADRE) as a T helper epitope (Figure 1). The vaccine candidates were designed, synthesized and their purity and identity confirmed by RP-HPLC and ESI-MS, respectively. The secondary structure analysis and potential of specific antibodies to recognize the synthetic vaccine candidates were studied. LCP delivery system as well as the coil-promoting sequence from yeast GCN4 protein was required to generate the native (desired) helical confirmation of the epitope. CD results and ELISA data indicated that candidates with helical confirmation could bind to specific antibodies. In addition, dynamic light scattering (DLS) and TEM showed that the GCN_4 construct formed small nanoparticles which are expected to induce strong immune responses.

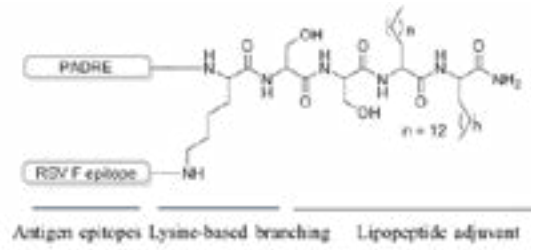

Figure 1: Schematic presentation of LCP construct.

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Lipid core peptide nanoparticles as effective delivery system to trigger humoral immune responses against Group A streptococcus (GAS)

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Group A streptococcus (GAS) infections result in a number of human diseases, including pharyngitis, rheumatic fever and rheumatic heart disease. There is no vaccine available on the market to prevent GAS. We designed and synthesized a self-adjuvanting lipopeptide (LP) GAS vaccine constructs. Each lipopeptide was composed of GAS B-cell epitopes (J14, 88-30 or their combination), an universal CD4+ T-cell helper epitope (P25) and an immunostimulant lipid moiety. The lipopeptides were synthesized using Boc-solid phase peptide synthesis (SPPS) and formulated into nanoparticles. The immunogenicity of the nanoparticles was tested in mice and antibody titres were analyzed using ELISA. Systemic IgG antibody response was elicited in outbred Swiss mice after intranasal immunization. 88/30 specific IgG response was higher in the construct containing both 88/30 and J14 epitope (LP-88/30-J14) than LP containing only 88/30 epitope (LP-88/30). All the compounds (and their formulation) were characterized with the help of dynamic light scattering (DLS), circular dichroism (CD) and transmission electron microscopy (TEM). LP-88/30-J14 formed nanoparticles of smaller size (9 nm) than LP-88/30 (50-100 nm) while LP-J14 particle size was 5 nm. The immune responses against vaccine candidates were size dependent, with the smaller particles eliciting higher antibody titers. Thus, this study showed that the choice of epitopes influenced both the particle size and the immune response against LPs.

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