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Extended Abstract

Vaccine against S. pyogenes

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Abstract

StreptInCor, a candidate vaccine against S. pyogenes is based on protective 55 amino acids residues of C-terminal portion of the M protein. Experimental assays have demonstrated that the StreptInCor peptide induces high titers of opsonic and neutralizing and protective antibodies in outbred immunized mice. Using HLA class II transgenic mice, it was possible to evaluate the immunogenicity and safety of the StreptInCor vaccine epitope for a period of one year. Specific and non-auto reactive antibodies were produced as well as no autoimmune or pathological reactions were observed in the heart or other organs of these animals. We also performed several studies in mini-pigs in order to evaluate the immune response and safety by submitting these animals to echocardiogram examination before immunization and after the four doses treatment. No alterations were observed. In addition, both repeated intramuscular-dose toxicity tests (28 days) with four doses and echocardiography procedure in mini pigs after 28 days were performed. No harmful effects to the tissues and organs studied were observed indicating that the vaccine is safe. StreptInCor vaccine also induces regulatory T cells (Treg) that strongly indicate that the vaccine peptide may have therapeutic potential to control both inflammatory and autoimmune response in RF/RHD patients. Streptococcus pyogenes causes severe, invasive infections such as the sequelae associated with acute rheumatic fever, rheumatic heart disease, acute glomerulonephritis, uncomplicated pharyngitis, and pyoderma. Efforts to produce a vaccine against S. pyogenes began several decades ago, and different models have been proposed. We have developed a vaccine candidate peptide, StreptInCor, comprising 55 amino acid residues of the C-terminal portion of the M protein and encompassing both the T- and B-cell protective epitopes. The present article summarizes data from the previous 5 years during which we tested the immunogenicity and safety of StreptInCor in different animal models. We showed that StreptInCor overlapping peptides induced cellular and humoral immune responses of individuals bearing different HLA class II molecules. These results are consistent with peptides that have a universal vaccine epitope. The tridimensional molecular structure of StreptInCor was elucidated by nuclear magnetic resonance spectroscopy, which showed that its structure is composed of two microdomains linked by an 18-residue α-helix. Additionally, we comprehensively evaluated the structural stability of the StreptInCor peptide in different physicochemical conditions using circular dichroism.

Additional experiments were performed with inbred, outbred, and HLA class II transgenic mice. Analysis of several organs of these mice showed neither deleterious nor autoimmune reactions even after a long period of vaccination, indicating that the StreptInCor candidate peptide could be considered as an immunogenic and safe vaccine.

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