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LEAPS therapeutic vaccines as antigen specific suppressors of inflammation in four unrelated diseases

The L.E.A.P.S.™ Ligand Epitope Antigen Presentation system is a platform technology that has been successfully used to develop immunoprotective and immunomodulating small peptide vaccines for infectious and autoimmune diseases. Several specific products are currently in various stages of development, at the pre-clinical stage (in animal challenge efficacy studies). Vaccine peptides can elicit protection of animals from lethal viral (herpes simplex virus [HSV-1]; influenza A) infection or can block the progression of autoimmune diseases (e.g. rheumatoid arthritis as in the collagen induced arthritis model [CIA] and experimental autoimmune myocarditis [EAM]).

L.E.A.P.S. is a novel T-cell immunomodulating technology that enables the design and synthesis of non-recombinant, proprietary peptides as immunogens. Combination of a small peptide that activates the immune system (immune cell binding ligand (ICBL)) with a small peptide containing a T Cell epitope (8-25 amino acids, = epitope or nested limited set of epitopes) selected from a disease-related protein allows the L.E.A.P.S. vaccines to activate human monocytes or mouse precursors to differentiate and become dendritic cells (DCs) that can initiate appropriate T cell responses. As such, readily synthesized, defined immunogens can be prepared to elicit protective or therapeutic applications including modulation of inflammation, e.g. rheumatoid arthritis, and prevention of the cytokine storm associated with influenza A. In mice, the protective immune responses are associated with production of Th1 associated cytokines IL12p70 and IFN-γ, reduced inflammatory cytokines (TNF-α and IL-1, IL-17) and preferential synthesis of antigen specific IgG2a antibodies rather than a Th2 associated antigen specific IgG1 antibodies and elevated inflammatory cytokines (eg TNF-α IL1). These activities of modulation are by DCs and T cells activity as evidenced by both cytokines and viral activity. These J LEAPS conjugates have been used directly in vivo or as ex vivo activators of DCs which are then administered to the host. A model for the action of the J LEAPS conjugates, based on our findings, is presented to explain the action of J LEAPS vaccines on infectious diseases including viruses (HSV and Influenza) and intracellular bacteria (TB).

Characterization of mode of action of LEAPS therapeutic vaccines antigen specific suppressors of inflammation, as determined by cytokine profiles, antibody activity / isotype and ablation studies

The L.E.A.P.S.™ Ligand Epitope antigen presentation system technology platform can be used to develop immunoprotective and immunomodulating small peptide vaccines that can limit or stop the progression of autoimmune disease by acting on the initiating factor and modulating the subsequent host inflammatory process. Single epitope LEAPS vaccines prevent and block the progression of experimental autoimmune myocarditis (EAM) (a single epitope induced disease), block the progression of collagen induced arthritis model CIA (a single antigen but multiple epitope disease), as well as with multiple antigens with multiple epitopes, prevent or reduce disease by limiting viral activity (both HSV and H1N1), enhanced Th1 cytokines (HSV-1) and reduce the cytokine storm of inflammatory cytokines associated with H1N1 influenza A infection. These single epitope vaccines can also induce an isotype shift from a Th2 IgG1 dominant to a Th1 IgG2a dominant antibody response even after initial induction of IgG1 antibody. J LEAPS vaccines promote the development of unique type of DC that produces IL12p70 but not TNFα or IL-1 and promote production of IFNγ from T cells. Upon antigenic challenge with protein (free or viral), a polyclonal results isotype shift from Th2 (IgG1) to Th1 (IgG2a) occurs despite the use of a monoepitope containing J-LEAPS vaccine. These and other LEAPS conjugates are likely to be applicable for treating other autoimmune diseases in addition to RA as well as viral diseases such as HBV and HIV as well as TB.

Biography

Daniel H. Zimmerman, Ph.D. CEL-SCI's Senior Vice President of Research, Cellular Immunology since June 1998. He has over 30 years industry experience in researching and developing products for diagnosis, immunological status monitoring and vaccines. He has successfully developed commercial diagnostic products for Herpes Simplex Virus, Hepatitis B and HIV. Dr. Zimmerman was a Senior Staff Fellow at NIH and holds a Ph.D. in Biochemistry from the University of Florida's College of Medicine (1969). Dr. Zimmerman has over 50 publications and US patents in the fields of immunology, virology, L.E.A.P.S.TM and CEL-1000 technology.

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