A Method to Enhance Immunogenicity and Immunological Memory for Viral Envelope Protein Vaccines

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Technology description

Researchers at the UI have identified that RNA viral envelope proteins contain small peptide sequences that interfere with T cell receptor (TCR) signaling, leading to reduced antigen presentation, T cell proliferation, and thus reduced immunogenicity and memory. This invention involves altering this region of the viral envelope protein, but not the remainder of the protein. The altered protein will be used as a vaccine immunogen to enhance vaccine potency and memory. This applies to a wide range of RNA viruses, including hepatitis C virus, yellow fever virus, HIV, and animal pestiviruses.

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Background:

Viruses evolve to contain mechanisms that help them evade host immune defenses. By interfering with T cell activation pathways, a virus increases the likelihood that it will cause persistent infection. By interfering with antigen presentation this impairs the ability to elicit memory T and B cell responses or high titers of antibodies. The reason that subunit vaccines are poorly immunogenic has not been previously understood and this technology will improve a large number of vaccines.

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Approximately 10 basepair sequences from hepatitis C virus E2 protein, HIV gp120/160, influenza envelope protein, west nile virus envelope protein and other RNA viruses have been shown to inhibit T-cell signaling, which improves their ability to infect hosts and may limit the efficacy of candidate vaccines against those microbes. These sequences all contain a tyrosine residue and have been shown to interact with and block the pro-T-cell activation signaling of Lck. Lck phosphorylates the intracellular chains of CD3 and zeta-chains found in the MCH-bound TCR complex on tyrosine residues. These phosphorylations promote ZAP-70 binding, which Lck also phosphorylates to promote activation of

the T-cell. The tyrosine residues found in the viral envelope proteins serve as surrogate phosphorylation targets of Lck, thus limiting its ability to phosphorylate pro-activation cytoplasmic proteins. The original peptide sequences can be used as a therapy to limit T-cell activation in cases such as autoimmune disorders and can be mutated to inhibit this effect in potential vaccine formulations in order to augment the immune response to the antigen.

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