Docket #: S18-206

A STRATEGY FOR CREATING VACCINES TO ELICIT ANTIBODIES TARGETING A SPECIFIC EPITOPE

Researchers at Stanford, funded in part by the Chan Zuckerberg Biohub, have developed PMD (Protect, Modify, Deprotect), an immunofocusing strategy that can be used in vaccine development for the generation of antibodies targeting a specific epitope.

Vaccine development is a ground-breaking accomplishment in the biomedical field, leading to the near eradication of several diseases. Many vaccines provide long-lasting protection against infectious disease by eliciting an antibody immune response against a particular antigen. However, the generation of an antibody immune response towards some infectious agents has proved difficult. For example, in the case of viruses like influenza and HIV, most of the antibodies generated by vaccination target highly variable regions of the virus surface. These immunodominant variable regions preclude the generation of an immune response against more constant, and therefore desirable, regions of an infectious agent. Thus, there is a need for immunofocusing strategies, or the creation of vaccines that focus the antibody response toward these more desirable epitopes.

Stage of Research

The inventors have developed an immunofocusing method called Protect, Modify, Deprotect (PMD), which directs the immune response towards a desired epitope of an antigenic protein. The method involves selecting an antigenic protein, comprising both target and non-target epitope regions. The target epitope is then protected by the introduction of a binding partner. The remainder of the protein is chemically modified while the desired antigenic region is shielded. After chemical modification, the shield for the desired epitope is removed. This immunofocused antigenic protein can then be used to generate a vaccine-induced response. The authors demonstrate

the utility of the PMD method by generating antibodies targeting desired regions of an influenza virus. This strategy has the potential to create high-specificity vaccines to formerly non-targetable regions of infectious agents.

Stage of Development
Research -

in vitro

Applications

- Generation of antigenic proteins with a desired epitope
- Antigenic protein complexes can be used for in vivo immunization

Advantages

- Facile and generalizable method for creating desired immunogenic proteins
- Preserves the target epitope while decreasing non-target antigenicity

Publications

- Weidenbacher PA and Kim PS. Protect, modify, deprotect (PMD): A strategy for creating vaccines to elicit antibodies targeting a specific epitope. Proc Natl Acad Sci USA. 116(20):9947-9952 (2019).

Patents

- Published Application: WO2019222674
- Published Application: 20210139542
- Issued: 12,304,928 (USA)

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