[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT:

Barry Buchbinder, Ph.D., 240-627-3678; barry.buchbinder@nih.gov. Licensing information and copies of the U.S. patent application listed below may be obtained by communicating with the indicated licensing contact at the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD, 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished patent applications.

SUPPLEMENTARY INFORMATION: Technology description follows.

Glycan-masked Engineered Outer Domains of HIV-1 GP120 and Their Use

Description of Technology:

The VRC01-class of potent, broadly neutralizing antibodies (bnAbs) targets the conserved CD4-binding site (CD4bs) of HIV-1 Env which has been a major target of HIV-vaccine design. The current best priming immunogen to engage the VRC01-class germline precursors is the

eOD-GT8 60mer, which elicits VRC01-class precursors in multiple transgenic mouse models. However, a large proportion of the antibodies elicited by eOD-GT8 60mer are non-CD4bs or "off-target" antibodies, undermining its effectiveness in eliciting the VRC01-class bnAb precursors.

Researchers at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases introduced multiple N-linked glycosylation sites to mask non-CD4bs regions of eOD-GT8 60mer to focus the antibody immune response to the CD4bs.

Several glycan-masked mutants showed significantly decreased antibody binding to non-CD4bs "off-target" epitopes while maintaining strong binding to CD4bs-specific bnAbs. Furthermore, in vivo studies showed that immunization with the best glycan-masked eOD-GT8 mutants resulted in significant increases in the elicitation of CD4bs-specific serum antibodies, CD4bs-specific B cells in the spleen, and VRC01-class precursors, compared to immunization with the parental eOD-GT8 immunogen. In conclusion, because of their improved antigenic and immunogenic profiles, glycan-masked eOD-GT8 60mer mutants may serve as improved priming immunogens to elicit VRC01-class bnAbs in humans.

Potential Commercial Applications:

- HIV-1 vaccine- the priming component in a prime-boost approach.

Competitive Advantages:

- Reduced off-target immunogenicity.
- Improved efficacy in eliciting precursors for broadly neutralizing CD4bs antibodies.
- Facilitates the development of VRC01-class bnAbs in humans.

Development Stage: *In vivo* testing (rodents).

Inventors: John R. Mascola (NIAID), Hongying Duan (NIAID), Xuejun Chen (NIAID), Cheng Cheng (NIAID) and Jeffrey C. Boyington (NIAID).

Publications: Duan, H. et al., Glycan Masking Focuses Immune Responses to the HIV-1 CD4-Binding Site and Enhances Elicitation of VRC01-Class Precursor Antibodies. *Immunity* 49, 301 (2018).

Intellectual Property: HHS Reference Number E-083-2017 includes U.S. Provisional Patent Application Number 62/476,397 filed 03/24/2017 and PCT Application Number PCT/US2018/024330 filed 03/26/2018.

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