Antibodies show effectiveness for HIV prevention and promise for treatment and cure

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David Margolis, M.D., leads the UNC HIV Cure Center. Credit: David Kinton, UNC School of Medicine

The ability of HIV to mutate has been a major challenge to vaccine

development. As the body produces antibodies to target the outer HIV envelope protein, this protein changes, thwarting the circulating antibodies' ability to neutralize it. Yet recent studies testing multivalent combinations of three broadly neutralizing antibodies, or bnAbs, have yielded promising results in animal models of HIV prevention. Two investigators at the University of North Carolina at Chapel Hill describe the potential of bnAbs to inform HIV prevention, treatment and cure strategies in a recent article in the *New England Journal of Medicine*.

"BnAbs are thought to be akin to signposts - that they point to a path that might be followed by a future HIV vaccine strategy through induction of bnAbs capable of preventing HIV infection," said David Margolis, M.D., article co-author and director of the UNC HIV Cure Center.

No single bnAb can protect against all the variants of HIV present in infected individuals. However, combinations of multiple bnAbs provide increased efficacy. The development of trispecific multivalent antibodies combine the best attributes of each into a single molecule capable of recognizing and neutralizing multiple viruses not recognized by the individual bnAbs.

"Trispecific antibodies engage a broader range of viral particles than do monospecific and bispecific antibodies," said J. Victor Garcia, Ph.D., article co-author and a professor of medicine at UNC. "Trispecific antibodies may also block infection more efficiently at mucosal surfaces and within deeper tissue as well as neutralize a wider range of viral particles."

The authors also detail how bnAbs could change HIV treatment and cure research. Broadly neutralizing antibodies may contribute to the deployment of long-acting antiretroviral therapy, which would be an attractive alternative for people who currently take daily medication to control their HIV. In the cure arena, bnAbs could be paired with latency

reversing agents to target and clear the virus.

J. Victor Garcia, Ph.D., is a professor of medicine at UNC. Credit: David Kinton, UNC School of Medicine

"Broadly neutralizing antibodies capable of recognizing HIV-infected cells could direct effector cells to clear the latent reservoir," Margolis said. "In the case of the evasive HIV envelope, three may be the charm."

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