Researchers design unique method to induce immunity to certain STDs

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Chlamydia trachomatis is the most common bacterial agent of sexually transmitted disease, accounting for more than a million reported infections in the United States each year.

Researchers at the California NanoSystems Institute (CNSI) at UCLA and the David Geffen School of Medicine at UCLA have now designed a unique method for inducing immunity to the infection. The findings could accelerate progress toward the development of a vaccine against *Chlamydia trachomatis* infections, which can lead to reproductive dysfunction and profound local inflammation requiring medical attention.

The researchers were able to uncover a surprising connection between vault nanoparticles and mucosal immunity. Vaults are barrel-shaped nanoscale capsules found in the cytoplasm of all mammalian cells that can be engineered to serve as potential therapeutic delivery devices.

"The primary goal of vaccines is to generate robust cell-mediated immune responses at mucosal surfaces while reducing overall inflammation caused by infection," Kelly said. "We found that vault nanoparticles containing immunogenic proteins can act as 'smart adjuvants' for inducing protective immunity at mucosal surfaces while avoiding destructive inflammation."

Adjuvants are molecular triggers that initiate vaccine responses.

Mucosal immune responses provide superior protection against disease, but there are currently no adjuvants approved by the Food and Drug Administration that are capable of stimulating cell-mediated immune responses within mucosal tissues. Mucosal surfaces are hostile environments, and immunogenic proteins require added protection for delivery to cells in order to induce immunity.

The team produced recombinant vaults through a process that involved the molecular engineering of these naturally occurring cellular structures to test the concept that vaults can have a broad nanosystems application as malleable nanocapsules.

"Our research team wanted to find out if recombinant vaults could provide such protection by encapsulating an antigen and preserving its functional characteristics, even within the cells," Kelly said.

The internal cavity of the recombinant vault nanoparticle is large enough to hold multiple immunogenic proteins, and because vaults are the size of small microbes, a vault particle containing such proteins can be easily absorbed by the targeted cells.

Vaults are being studied for use in the delivery of a range of potential therapeutics, including synthetic and natural compounds, nucleic acids, and proteins. Recombinant vaults containing proteins are easily produced, making vaults a viable vaccine delivery platform.

"Adjuvants provide the necessary assistance to vaccine preparations for promoting immunity or protection from infection by combining the vault with a part of the Chlamydia organism," Kelly said. "We were able to design a vaccine that prevented Chlamydia infection better than other designs."

The research team found that when they immunized female mice with

recombinant vaults containing a component of Chlamydia and then exposed the mice to a vaginal challenge with live Chlamydia, their reproductive tracts were protected from severe bacterial infection.

The results suggest that vaults are superior adjuvants for immunization against infections largely limited to mucosal tissues.

"We are encouraged that our findings could accelerate progress toward developing a vaccine to guard against this infection," Kelly said.

The study appears in the April 30 edition of the peer-reviewed online journal *PLoS ONE*, published by the Public Library of Science, and is available at http://dx.plos.org/10.1371/journal.pone.0005409.

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