NEW VACCINATION TECHNIQUE MAY WORK FOR DENGUE FEVER

WASHINGTON, APRIL 2 -- A new study funded by the U.S. National Institutes of Health (NIH) and the National Science Foundation suggests a new vaccination technique that would protect people against the four known dengue viruses.

Previous attempts to vaccinate against the four viruses have failed, and the solution might be injecting the vaccines at the same time into different places on the body, according to a March 29 press release from Rice University in Texas.

Dengue is a mosquito-born disease that kills tens of thousands of people every year and sickens 100 million more. It is called “bone-break disease" and is characterized by excruciating pain.

The U.S. Centers for Disease Control and Prevention called dengue "the most important mosquito-borne viral disease affecting humans" in 2005.

IMMUNODOMINANCE

The new study, by Rice University bioengineers and physicists, suggests the multisite vaccination strategy – called polytopic vaccination – might also be effective against other diseases, including HIV and cancer.

Dengue infection occurs from one of four closely related viruses. Previous exposure to one of the four – either by prior infection or by vaccination – makes people much more likely to develop a potentially lethal hemorrhagic infection if they are infected later by one of the other three viruses.

"This is a classic case of something called [immunodominance],” said lead researcher Michael Deem, “which happens when our immune system becomes overly reliant upon memory when recognizing diseases similar to those that it has seen before.”

The immune system's tendency with diseases like HIV, influenza and dengue is to "go with what it knows, Deem said, leaving people "more vulnerable to infection from a mutant strain or a related virus."

The immune system might respond less favorably in these cases than if it had never been exposed to the disease. Immunodominance arises from the way the immune system targets infection. When the immune system identifies infected cells, it takes pieces of them into the lymph node for targeting.

TARGETING INFECTION

Lymph nodes are any of the small structures located along the lymphatic vessels, particularly at the neck, armpit, and groin. Lymph nodes filter bacteria and foreign particles from lymph fluid.

During infection, lymph nodes can become swollen with activated lymphocytes – or kinds of white blood cells, along with T-cells, that are part of the body's immune response.

Within a few days of infection, the immune system completes a massive scan of the 100 million available T-cells in its arsenal. Through a complex trial-and-error process, it identifies three to five T-cells that best recognize and attack the components of the sickened cells. Once the cells are chosen, they are produced by the millions and sent out to clear the infection. When the infection is gone, thousands of the pre-programmed T-cells stay in the body in case the disease returns.

In recent years, public health officials have documented the co-existence of four dengue viruses in Brazil, Cuba, Thailand and other tropical and subtropical countries.

Because infection by multiple dengue viruses one after another can lead to an increased likelihood of deadly infections, public health officials have developed a vaccine that was supposed to fight all four versions at once.

But doctors found that patients who got a four-component vaccine wound up only being protected against one or two versions at most, because of immunodominance.

A NEW TECHNIQUE

To find out why the vaccine did not protect against all four viruses, Deem and graduate student Hao Zhou developed a computer model of the immune system's biochemical scanning process to see if they could recreate the effect and find out what caused it.

They conducted trillions of calculations and gradually built up a bigger picture of what occurs in dengue immunodominance.

In a person who has been exposed to all four versions of the dengue virus, the immune system produces T-cells specific to each version.

But when the immune system is presented with more than one version of the virus, Deem said, it might respond only against the version of the virus for which it has T-cells with the strongest affinity, or attraction, to the virus.

In this way, the immune system responds to only one (dominant) version of the virus, protecting against that version and none of the others. That is immunodominance.

Deem said giving the four vaccines at the same time at different places on the body could help overcome immunodominance by taking advantage of the relative isolation of lymph nodes in the body.

Each person has hundreds of lymph nodes at different places around the body. Deem believes that vaccinating someone at four different sites, served by four different lymph nodes, would allow the body to develop immune responses against all four versions of dengue at the same time.

"There may be other factors at work," Deem said, "but we appear to be explaining a significant portion of the effect that occurs in dengue immunodominance."

Immunodominance is also a problem for researchers who work on vaccines for the AIDS virus and cancer, each of which mutate quickly and occur in multiple strains.

The full text (http://media.rice.edu/media/NewsBot.asp?MODE=VIEW&ID=8381&SnID=376845526) of the press release is available on the Rice University Web site.

For related information, see Science and Technology (http://usinfo.state.gov/gi/global_issues/scitech.html).

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