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Researchers one step closer to elusive cancer vaccine

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When cells become cancerous, the sugars on their surfaces undergo distinct changes that set them apart from healthy cells. For decades, scientists have tried to exploit these differences by training the immune system to attack cancerous cells before they can spread and ravage the body.

Now, researchers at the University of Georgia Cancer Center have synthesized a carbohydrate-based vaccine that – in mice – has successfully triggered a strong immune response to cancer cells. The finding, published in the October issue of the journal *Nature Chemical Biology*, brings the scientists one step closer to a much-sought-after "cancer vaccine."

"In mice we can elicit very strong antibody responses and we have shown that the antibody responses are functional – that they can kill cancer cells," said lead author Geert-Jan Boons, Franklin professor of chemistry.

Vaccines are currently use to prevent diseases by priming the immune system to recognize and attack a virus or bacteria. The vaccine that Boons and his team have developed, on the other hand, is a therapeutic vaccine that trains the body's immune system to fight an existing disease.

The discovery in the 1970s of unique sugars on cancer cells set scientists in search of a way to get the immune system to recognize and attack cells that express these cancer-associated sugars. Until now, however, the

results have been less than spectacular.

Cancer cells originate in the body, and the immune system leaves them alone because it distinguishes between the body's own cells and foreign invaders such as viruses and bacteria.

Boons explained that early cancer vaccines were created by linking the tumor-associated carbohydrate with a foreign protein. The immune system, perhaps not surprisingly, attacked the protein and the linker molecules, but generally left the carbohydrate alone.

"We needed to come up with a vaccine that does not give our immune system a chance to go after anything else but the tumor-associated carbohydrate," Boons said. "In other words, there should no junk that can induce an immune response to something other than the tumor-associated carbohydrate."

Rather than using naturally derived and purified proteins and linkers, Boons and his team created a vaccine synthetically from scratch by stacking molecules together and arranging them in the appropriate configuration. In 2005, they created a fully synthetic vaccine that stimulated an immune response to the tumor-associated carbohydrate alone. The vaccine stimulated only low antibody levels, however, so the researchers began optimizing the components of the vaccine to illicit a stronger immune response.

Their optimized vaccine includes a tumor-associated carbohydrate that triggers the immune system's B cells, a part of a protein that triggers the immune system's T cells and a linker molecule that stimulates the production of generalized immune components known as cytokines.

The results of their three-pronged approach were astounding, particularly with respect to a critical component of the immune system

known as IgG.

“When we tested our best vaccine we got really, really fabulous antibody levels that have never been seen before,” Boons said. “The levels of IgG antibody production were 100 times better than with conventional approaches.”

The vaccine has been successful in creating an antibody response that can kill cultured epithelial cells – those commonly involved in most solid tumors, such as breast and colorectal cancer – derived from mice and in stimulating an immune response in healthy mice. The researchers are currently testing the vaccine in mice with cancer, and Boons hopes to start phase I clinical trials in humans within a year.

Despite his enthusiasm for his work, Boons cautions that it’s too early to predict how the vaccine will perform in humans.

“There’s a very big step going from mice to humans,” he said. “Other cancer vaccines have worked in mice but not in humans.”

In addition to testing the new vaccine, Boon’s team is exploring the specific components of the immune response as they relate to cancer, determining the exact cytokines and antibodies that are most effective against cancer cells.

“We’re looking at which molecules are being upregulated at each level of immune response,” Boons said. “That gives us a road map to further optimize each component of the vaccine.”

Source: University of Georgia

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