Different type of colon cancer vaccine reduces disease spread, Jefferson scientists show

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(Taking advantage of the fact that the intestines have a separate immune system from the rest of the body, scientists at the Kimmel Cancer Center at Jefferson in Philadelphia have found a way to immunize mice against the development of metastatic disease.

Reporting online Tuesday, June 24, 2008 in the *Journal of the National Cancer Institute*, Scott Waldman, M.D., Ph.D., professor and chair of Pharmacology and Experimental Therapeutics at Jefferson Medical College of Thomas Jefferson University and his co-workers have shown that mice immunized with an intestinal protein developed fewer lung and liver metastases after injection with colon cancer cells than did control animals that were not immunized. The work may portend the development of a different kind of cancer vaccine, the researchers say, that may help prevent disease recurrence.

One of the reasons that cancer vaccines have been disappointing in many cases is the lack of immune system-alerting protein antigens that are specific for tumors only. According to Dr. Waldman, mucosal cells, which line the intestines (colon cancer arises from mucosal cells, and mucosal cell proteins continue to be expressed even after they become cancer) are essentially compartmentalized and possess a separate and distinct immune system from the body's general immune system. He and his group thought that such proteins would be seen as foreign by the latter system and be useful for anti-cancer vaccines.

Dr. Waldman, postdoctoral fellow Adam Snook, Ph.D., and their colleagues engineered viruses – adenovirus, vaccinia and rabies – to express the protein guanylyl cyclase C (GCC), which is normally found in the intestinal lining (and in metastatic colon cancer). The researchers injected the animals with colon cancer cells before or after immunization.

They found that the vaccinated animals developed fewer metastases in the liver and lung – 90 percent and 75 percent, respectively – compared with control animals. Vaccination also prolonged overall survival, with a median of 38 days in immunized animals and 29 days in control animals.

"We think this identifies a novel class of vaccine candidate targets for tumors that originate and metastasize from mucosa, like colorectal cancer," Dr. Waldman says. "Mucosal cells turn into cancer, invade the wall of the intestine, breech the compartment and metastasize, carrying with them all the antigens that typically reside in the mucosal system. They continue to be expressed by tumors that originate in the mucosa even when those tumors metastasize into the systemic compartment where they don't belong."

Dr. Waldman sees GCC as "the poster child" for mucosal antigens. "Immunizing an animal or person systemically with GCC will be recognized to some degree as foreign, and the body will mount an immune response in the systemic compartment," he explains. "We think that the immune response will be effective against the cancer but it won't cross over into the intestines and cause autoimmune disease."

As a result, he says, the immune responses against GCC could be used both prophylactically and therapeutically. "The target populations for such a vaccine are patients who have had surgery and adjuvant chemotherapy and have no evidence of disease. If they have recurrence, it's from microscopic disease."

"This paper demonstrates the profile of a model cancer mucosal antigen class that can generate systemic immune responses," he says. "There is incomplete systemic tolerance to these antigens, as we predicted, and that the immune responses have anti-tumor efficacy and the animals are free of autoimmune disease."

The researchers suggest that this approach of using antigens from tumors originating in immune-restricted sites might be extended to other cancers that originate from mucosal cells, including cancers of the head and neck, lung, breast, vagina, and bladder. Adding mucosal antigens from the same tumor type might also enable the development of a "polyvalent" vaccine, Dr. Waldman notes.

Source: Thomas Jefferson University