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Novel prostate cancer vaccine taking aim at cancer cell 'sweet spot'

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Molecules of sugar sitting on the surface of cancer cells are keys to the development of a new vaccine aimed at both treating and stopping the spread of certain types of cancers called carcinomas, which include prostate, breast, ovarian and lung, among others. Armed with a new two-year grant for $600,000 from the Gateway for Cancer Research, an Illinois-based philanthropic foundation, immunologist Alessandra Franco, M.D., Ph.D., and her co-workers at the Moores Cancer Center at the University of California, San Diego are hoping to develop a low-cost immunotherapy for prostate carcinoma that may also have use against a variety of other carcinomas as well.

Franco, adjunct assistant professor of pediatrics at the UC San Diego School of Medicine, and her co-workers have spent the last decade proving that the immune system's destructive, or "killer," T-cells can recognize sugars on tumor cell surfaces. Her laboratory pioneered and developed the notion that conventional T-cells recognize not only peptides, or pieces of proteins, but also sugars, specifically small carbohydrates called tumor-associated carbohydrate antigens (TACA) expressed on carcinoma cell surfaces. Ideally, this recognition enables the T-cell to attach to and kill the cancer cell.

The researchers have designed "glycopeptides," compounds in which sugars are linked to peptides that are recognized by T-cells. When given as part of a vaccine therapy, these glycopeptides rouse immune system T-cells into recognizing TACA on tumor cell surfaces, attacking and killing the cancer cells. Her research team has already shown that both normal

mice and mice with tumors that were vaccinated could successfully generate carbohydrate-specific T-cells that could kill tumors expressing the same carbohydrate molecule.

Cancer vaccines have had a mixed record of success at best. Most immunotherapies have focused on revving up immune system antibodies to recognize proteins on tumor cells.

"A limitation with current immunotherapies is that every tumor expresses different protein antigens, which all need to be characterized," she explained. "It is difficult for the immune system to discriminate, to tell that cancer cells are 'non-self' and should be destroyed. What's nice about T-cells recognizing sugars and why it's so important in cancer is because the same molecules are uniquely expressed in a large variety of cancers." A cell that becomes cancerous begins making a variety of sugar molecules that are not expressed in normal adult cells, making this strategy potentially useful for wide-ranging treatments of different tumors. Her team is targeting a sugar that is expressed on all carcinomas, a type of cancer that begins in epithelial cells.

Studies in the first year of the grant are focusing on gathering further laboratory and preclinical data to show the vaccine's effectiveness. Franco is hoping to begin a clinical trial in the second year of the grant to test the vaccine on prostate cancer patients who have already had treatment but who are at extremely high risk for relapse. She sees the vaccine as being used to help prevent the spread of cancer (metastatic disease), and perhaps even in preventing cancer in healthy people.

"The beauty of this approach is that the same vaccine may prevent metastasis," she said, noting that tumor cells can use sugar or carbohydrate antigens to spread. "If ultimately proven successful, this could be used in a first attempt to try to address vaccination on a large scale to prevent cancer."

The same type of vaccine can potentially be used for breast, lung, liver, ovary and other carcinomas, Franco said. "If we can show that this system works in humans, we think that it can address a variety of tumors with the same sugar compounds." The vaccine's relatively simple formulation, stability and low production cost could make it ideal for use in developing countries, she added.

Source: University of California - San Diego