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Novel immune system-based gene therapy induces strong responses in metastatic melanoma, sarcoma

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Researchers have found that a novel form of personalized therapy that genetically engineers a patient's own anti-tumor immune cells to fight tumors could treat metastatic melanoma and metastatic synovial cell sarcoma, representing a potentially new therapeutic approach against these and other cancers.

The technique, called adoptive immunotherapy, works with the body's immune system to fight cancer. Immune cells, called T lymphocytes, are removed, modified, expanded in large numbers, and given back to the patient. In this case, the process entailed genetically engineering T cell lymphocytes to express receptors directed against a specific antigen on the cancer cell.

"We believe that this approach of adoptive immunotherapy is the most effective means for using the body's immune system to combat cancer," said senior study author Steven A. Rosenberg, MD, PhD, chief of the surgery branch at the National Cancer Institute. "This paper represents the first time that adoptive immunotherapy using genetically modified cells has been successfully used to treat a solid cancer other than melanoma because we are targeting an antigen present on many types of cancer."

The treatment resulted in response rates of 45 percent and 67 percent in malignant melanoma and synovial cell sarcoma patients, respectively.

In earlier trials, Rosenberg and colleagues used adoptive immunotherapy on treatment-resistant patients with metastatic melanoma who had extensive prior therapy. Of 93 patients studied, they found that more than half had measurable responses, including 20 with complete disappearance of all melanoma metastases.

In the current study, 17 patients with treatment-resistant metastatic melanoma or metastatic synovial cell sarcoma received therapy with their own immune T cells. The cells were genetically engineered to express a T cell receptor that recognized the NY-ESO-1 cancer-testes antigen on cancer cells. NY-ESO-1 is expressed in one quarter to one third of common epithelial cancers such as those of the breast, kidney, esophagus and other cancer types, and in about 80 percent of synovial cell sarcoma.

Four of six patients (67 percent) with synovial cell sarcoma and five of 11 (45 percent) melanoma patients had measurable tumor regression. Two of the 11 melanoma patients had complete regression lasting for more than one year. The treatments had minimal toxicity.

"The effectiveness of this treatment in patients with synovial cell sarcoma may mean that this new approach can be used for patients with other cancers as well," Rosenberg said, "And potentially lead to new types of immunotherapy. "

Rosenberg's group recently reported the first example of using adoptive immunotherapy to treat a patient with non-Hodgkin's lymphoma, and continues to explore different ways to genetically modify a patient's immune system to treat cancer. They have also recently published results showing that immune cells could be genetically modified to target and destroy the blood vessels supplying nutrients to tumors in experimental models.