Patient's own infection-fighting T cells put late-stage melanoma into long-term remission

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Case is first to show safety and effectiveness of using cloned cells alone to kill tumors

Researchers describe the first successful use of a human patient's cloned infection-fighting T cells as the sole therapy to put an advanced solid-tumor cancer into long-term remission. A team led by Cassian Yee, M.D., an associate member of the Clinical Research Division at Fred Hutchinson Cancer Research Center, reports these findings in the June 19 issue of the *New England Journal of Medicine*.

Yee and colleagues removed CD4+ T cells, a type of white blood cell, from a 52-year-old man whose Stage 4 melanoma had spread to a groin lymph node and to a lung. T cells specific to targeting the melanoma were then expanded vastly in the laboratory using modifications to existing methods. The lab-grown cells were then infused into the patient with no additional pre- or post-conditioning therapies, such as growth-factor or cytokine treatment. Two months later, PET and CT scans revealed no tumors. The patient remained disease free two years later, when he was last checked.

"We were surprised by the anti-tumor effect of these CD4 T cells and its duration of response," Yee said. "For this patient we were successful, but we would need to confirm the effectiveness of therapy in a larger study."

Yee cautioned that these results, presented in the journal's "Brief Report" section, represent only one patient with a specific type of immune system whose tumor cells expressed a specific antigen. More studies are needed to confirm the effectiveness of the experimental T-cell therapy. If proven successful in more patients, Yee predicted this therapy could be used for the 25 percent of all late-stage melanoma patients who have the same immune-system type and tumor antigen.

Using a patient's own immune system to combat cancer, called immunotherapy, is a growing area of research that aims to develop less-toxic cancer treatments than standard chemotherapy and radiation.

The patient in the journal report was one of nine patients with metastatic melanoma who were being treated in a recently completed clinical trial to test dose- escalation of autologous CD4+ T cells. Earlier studies performed by Yee used CD8+ T cells, which do not persist in the body without the support of CD4+ T cells or growth factors such as interleukin 2. Yee and colleagues theorized that infusion of a massive dose of CD4+ T cells would persist longer in the body because they make their own growth factor, interleukin 2, while stimulating the anti-tumor effect of the patient's existing CD8+ T cells. However, until recently there was no feasible way to isolate and expand anti-tumor CD4+ T cells in the lab.

The researchers were successful in all of these areas. The patient received a dose of 5 billion cloned CD4+ T cells with specificity for the melanoma-associated NY-ESO-1 antigen. The cells persisted for at least 80 days in the patient's body. And, even though only 50 percent to 75 percent of the patient's tumor cells expressed the NY-ESO-1 antigen, the entire tumor regressed following the infusion. The scientists postulated that the patient's immune response was broadened to other antigens expressed by the tumor cells. Follow-up tests showed T-cell responses to two additional tumor antigens, MAGE-3 and MART-1.

Source: Fred Hutchinson Cancer Research Center