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Scientists create army of tumor-fighting immune cells and watch as they attack cancer

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Researchers at UCLA's Jonsson Comprehensive Cancer Center created a large, well armed battalion of tumor-seeking immune system cells and watched, in real time using Positron Emission Tomography (PET), as the special forces traveled throughout the body to locate and attack dangerous melanomas.

The gene therapy work, done with melanomas grown in mice, employed a crippled HIV-like virus to serve as a vehicle to arm the lymphocytes with T cell receptors, which caused the lymphocytes to become specific killers of cancerous cells. A reporter gene, which glows "hot" during PET scanning, also was inserted into the cells so researchers could track the genetically engineered lymphocytes after they were injected into the blood stream, made their way to the lungs and lymph nodes and then specifically homed in on the tumors wherever they were located within the body.

"We're trying to genetically engineer the immune system to become a cancer killer and then image how the immune system operates at the same time," said Dr. Antoni Ribas, an associate professor of hematology/oncology, a researcher at UCLA's Jonsson Comprehensive Cancer Center and the senior author of the study. "We knew this approach of arming the lymphocytes with T cell receptors showed significant anti-tumor activity based on studies in humans. Now, by tracking the immune system's reaction to cancer and imaging it in real time, we can project how the same process that succeeded in mice might behave in people."

The study is published July 12, 2010 in the early online edition of the journal Proceedings of the National Academy of Sciences.

"The novelty of our work is that we were able to pack together the cancer specific T cell receptor and the PET reporter genes in a single vector and use it in mice with an intact immune system that closely resembles what we would see in real patients," said Dr. Richard Koya, an assistant professor of surgical oncology at UCLA's David Geffen School of Medicine and first author of the study. "We were also gladly surprised to see the targeted tumors literally melt away and disappear, underscoring the power of the combined approach of immune and gene therapy to control cancer."

The immune system generally does not recognize cancer cells in the body as enemies. The insertion of the antigen-specific T cell receptors - engineered to seek out a tumor antigen on the surface of the melanoma cells - in effect uncloaks the malignant cells, revealing them as deadly invaders that must be sought out and killed.

By imaging the genetically engineered T cells as they seek out and attack the cancer, the scientists can closely examine the processes of the immune system as it fights malignancies , which could then result in better monitoring response to therapy in melanoma patients.

In this study, the cells were injected into the bloodstreams of the mice and they had found and begun to fight the melanoma within two to three days. The mice were imaged periodically for 10 days to ensure the lymphocytes were indeed killing the cancer. The process to find and kill the malignant cells could take longer in people, Ribas said.

If a patient's tumor did not respond well to the administration of the genetically engineered T cells, scientists could determine by PET scanning whether the cells had not successfully made it to the tumor site

or, if they did arrive, whether or not they functioned as expected. Monitoring the immune response also could provide clues on ways to better engineer the lymphocytes to more effectively enter and attack the tumors.

In this study, about one million genetically engineered lymphocytes were created and injected into a mouse. In humans, the number of tumor-seeking cells needed to fight the cancer is about one billion, Ribas said.

Ribas and his team are working now on creating a vector, or vehicle, to insert the T cell receptors and reporter gene into the lymphocytes in a way that is safe to use in humans. If all goes well, human studies of the process could begin in about a year, Ribas said.

Provided by University of California - Los Angeles

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