A double-barreled immune cell approach for neuroblastoma

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Adding an artificial tumor-specific receptor to immune system cells called T-lymphocytes that target a particular virus extended and improved the cells' ability to fight a form of childhood cancer called neuroblastoma, said researchers form Baylor College of Medicine and Texas Children's Hospital in a report that appears online today in the journal *Nature Medicine*.

"This is a way to convert a naturally occurring problem into a benefit in treating cancer," said Dr. Malcolm Brenner, director of the Center for Cell and Gene Therapy at BCM, TCH and The Methodist Hospital, and professor of pediatrics and medicine at BCM. He and his colleagues reported on using the new treatment in 11 patients with recurring neuroblastoma. "For the first time, we started to see tumor responses. We have one complete remission and others who have had stable disease for more than a year," said Brenner.

The patients responded after only the one infusion of cells because they last a long time in the body and their numbers can increase, said Brenner.

Previous attempted to use T-lymphocytes with an artificial receptor directed to tumor cells proved disappointing because they disappeared from the body too quickly to have an anti-cancer effect. However, cytotoxic T cells that already have a natural receptor for the Epstein-Barr virus are continually activated by the presence of the virus, which is never eliminated from the body.

Brenner and his group added to these T-lymphocytes a particular receptor for a protein called diasialoganglioside GD2, which is found in human neuroblastoma cells.

"We took the T-lymphocytes' with specificity for Epstein-Barr and added another receptor," said Brenner. "In effect they trampoline off the virus and onto the tumor."

Thus these cytotoxic T-lymphocytes remain in the body because they are constantly stimulated by the virus. Their artificial antigen receptor enables them to latch onto and kill the cancer cells.

When the researchers put the artificial receptor into both ordinary T-lymphocytes and those that are stimulated by the virus into the 11 patients, they found that the cancer directed cells stimulated by the Epstein-Barr virus lasted as long as 18 months and at higher levels than the other cells.

Neuroblastoma is a tumor of primitive cells that go on to form the sympathetic nervous system. Apart from brain tumors, it is the most common solid cancer of children, and accounts for 7 percent of the total. In two-thirds of cases, it is not diagnosed until it has already spread to other parts of the body.

He and his colleagues hope to improve the treatment to make the T-lymphocytes more potent cancer killers, he said. One way would be to add specific receptors for proteins that allow the T-lymphocytes to avoid the immune-dampening effects of the cancers. Another might be to give the treatment right after the patients receive a stem cell transplant. At that time, the number of tumor cells would be at its lowest and there would be a lot of signals telling the T-lymphocytes to increase in number.

Within the next year, they plan to add receptors for other cancers to the virus-specific T-cells and see if they get the same cancer-fighting effect.

Source: Baylor College of Medicine

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