

Gene therapy protocol activates immune system in patients with leukemia

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A research team at the Moores Cancer Center at University of California, San Diego (UCSD) reports that patients with chronic lymphocytic leukemia (CLL) who were treated with a gene therapy protocol began making antibodies that reacted against their own leukemia cells. The study will be published on line the week of February 11-15 in the online edition of the *Proceedings of the National Academy of Science*.

Researchers led by Thomas J. Kipps, M.D., Ph.D., inserted a gene with the potential to activate an immune response – a gene therapy protocol developed at UCSD – into six patients with CLL, the most common form of adult leukemia. Several of the patients started making antibodies that reacted against their own leukemia cells. When tested in the lab, the antibodies also reacted with the leukemia cells of other patients with the disease.

“The patient’s own leukemia cells were modified outside of their body and given back as a vaccine,” said Kipps. “The result raises hope that it may be possible to activate a patient’s immune system against their own cancer.”

The patients were shown to make antibodies reactive with a leukemia-associated antigen – a protein made by leukemia cells that can stimulate the body's immune system to produce antibodies – called ROR1. This antigen appears to be found only on the cell surface of the leukemia cells, but not on normal cells, and serves as a receptor that binds to a

ligand called Wnt5a, which activates a pathway important for the survival of the leukemia cells.

“The Wnt5a ligand interacts with ROR1 to enhance leukemia-cell survival. Antibodies that react with ROR1 can interfere with this survival signal and might also specifically target the leukemia cells for destruction,” Kipps said.

He also noted that because the ROR1 antigen is found only on leukemia cells, it could be developed as a very specific marker to monitor for the continued presence of leukemia cells after treatment or for identifying leukemia cells in patients with early disease, when the cancer otherwise might not be detected. It also provides a much more specific target for antibody therapy. Antibodies that target ROR1 would be unlike currently used antibodies, which bind antigens found not only on leukemia cells, but also on normal cells. Because they can destroy normal cells, the antibodies currently used to treat patients with this leukemia can cause side-effects and weaken the immune system.

The ROR1 antigen is ordinarily found on a few cells in early embryonic development and is not detected on adult human cells or tissues. However, high amounts of this antigen are found on all the leukemia cells of patients with CLL. In the PNAS paper, the UCSD researchers present data on the leukemia cells of approximately 70 patients, all of which expressed the ROR1 antigen.

Source: University of California - San Diego

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