New therapy strategy could help treat cancer that has spread from breast to brain

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(Medical Xpress)—Researchers at UCLA's Jonsson Comprehensive Cancer Center have successfully combined cellular therapy and gene therapy in a mouse-model system to develop a viable treatment strategy for breast cancer that has spread to a patient's brain.

The research, led by Carol Kruse, a professor of neurosurgery and member of the Jonsson Cancer Center and the UCLA Brain Research Institute, was published Aug. 1 in the journal *Clinical Cancer Research*.

Breast cancer is the most common form of cancer in women, and metastasis is a major cause of health deterioration and death from the disease. Managing metastasis is difficult for several reasons: The circulatory network known as the blood–brain barrier prevents many anti-cancer drugs from reaching areas of the brain to which cancer has spread, and metastases have a tendency to spring up in multiple brain locations simultaneously, making current treatments such as radiation challenging.

Cellular therapy is a type of immunotherapy that uses T cells, the foot soldiers of the immune system, that have been sensitized in the laboratory to kill breast cancer cells. These sensitized T cells are injected into the parts of the brain to which cancer has spread. The research shows that the T cells can move through tissue and recognize and directly kill the tumor cells.

With the gene therapy, genetically modified cancer cells are killed by a

drug called 5-flurocytosine (5-FC). To get the gene into the cancer cells, the researchers first insert it into a virus that can infect the tumor cells. After the virus has infected the cells, non-toxic 5-FC is given to the patient. Tumor cells infected by the virus convert the non-toxic drug to a toxic form that kills the cancer cells. Dr. Noriyuki Kasahara, a professor in the department of medicine at UCLA, developed the gene therapy method in his laboratory.

While the two methods alone each show efficacy in mouse models, the greatest reduction in metastatic brain tumor size occurred when the cellular and gene therapies were combined, the researchers said.

"There is a significant lack of federally funded research addressing translational studies on brain metastases of systemic cancers, even though metastatic brain tumors occur 10 times more frequently than primary brain tumors in humans," Kruse said. "These patients have a dismal prognosis because the brain represents a 'sanctuary site' where appropriate access by many chemotherapeutics is ineffective. Our research addresses this unmet need."

Both experimental therapies are being tested individually in ongoing clinical trials for primary malignant brain tumors; this presents a unique opportunity for the rapid translation of these technologies from the laboratory to the clinic for breast and other types of cancer that metastasize to the brain, the researchers said.

More information: clincancerres.aacrjournals.org/content/19/15/4137

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