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HIGHLIGHTS

Researchers at Cedars-Sinai Medical Center's Maxine Dunitz Neurosurgical Institute in Los Angeles have combined a special protein (TRAIL) that targets cancer cells with neural stem cells (NSC) to track and attack malignant brain tumor cells. With its tumor-tracking capabilities and natural cancer-killing properties, the experimental NSC-TRAIL combination may offer new hope for treating gliomas, a particularly deadly type of brain tumor.

NEURAL STEM CELLS CARRY CANCER-FIGHTING PROTEIN TO TRACK AND DESTROY BRAIN TUMOR CELLS

LOS ANGELES (Dec. 15, 2002) -- Researchers at Cedars-Sinai Medical Center's Maxine Dunitz Neurosurgical Institute in Los Angeles have combined a special protein that targets cancer cells with neural stem cells (NSC) to track and attack malignant brain tumor cells. Results of their study appear in the Dec. 15 issue of *Cancer Research*.

Glioblastoma multiforme, or gliomas, are a particularly deadly type of brain tumor. They are highly invasive with poorly defined borders that intermingle with healthy brain tissue, making them nearly impossible to remove surgically without catastrophic consequences. Furthermore, cells separate from the main tumor and migrate to form satellites that escape treatment and often lead to recurrence.

Cedars-Sinai researchers recently published results of a study showing that neural stem cells have the ability to track glioma cells as they migrate. By engineering neural stem cells to secrete interleukin 12, they were able to elicit a local immune response that attacked cancer cells at the tumor site and in the satellites.

The current study used genetically engineered neural stem cells – cells that have the potential to differentiate into any of several types of cells of the central nervous system – to deliver a protein that is known for its cancer-fighting properties: tumor necrosis factor related apoptosis inducing ligand, or TRAIL. TRAIL has been shown to cause apoptosis, or cell death, in several types of cancers without causing toxicity to normal cells.

In vitro studies demonstrated that unmodified TRAIL cells quickly attacked human glioblastoma cells, with nearly all of the tumor cells being killed within 24 hours. TRAIL-secreting neural stem cells also resulted in significant cancer cell death, and the genetically engineered stem cells maintained their viability, strongly expressing TRAIL for as long as 10 days.

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Similar results were found *in vivo* when human glioblastoma cells in mice were treated with TRAIL-secreting NSC and controls. A week after treatment, strong secretion of TRAIL was visible in the main tumor mass and in disseminating tumor pockets and satellites, indicating that the engineered cells were actively tracking tumor cells. The tumors treated with NSC-TRAIL had also decreased significantly in size, compared with the controls. Furthermore, while the treatment was dramatically effective in killing glioma cells, it was not toxic to normal brain tissue.

With its tumor-tracking capabilities and natural cancer-killing properties, experimental NSC-TRAIL combination may offer a new approach for treating gliomas.

Moneeb Ehtesham, M.D., a postdoctoral fellow at the Institute, is the article's first author. John S. Yu, M.D., co-director of the Comprehensive Brain Tumor Program at the Institute, is senior author. The work was supported in part by National Institutes of Health grant NS02232 to Dr. Yu.

Cedars-Sinai is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, Cedars-Sinai has been named Southern California's gold standard in health care in an independent survey. It is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthrough biomedical research and superlative medical education. Named one of the 100 "Most Wired" hospitals in health care in 2001, the Medical Center ranks among the top 10 non-university hospitals in the nation for its research activities.

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