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FOR RELEASE March 22, 2006

TREATMENT FOR DEADLY BRAIN TUMORS AND INFECTIONS DISCOVERED BY RESEARCHERS AT BOARD OF GOVERNORS' GENE THERAPEUTICS RESEARCH INSTITUTE AT CEDARS-SINAI MEDICAL CENTER

LOS ANGELES (March 22, 2006) – In a study published in the March 15 issue of *The Journal of Immunology*, researchers at Board of Governors' Gene Therapeutics Research Institute at Cedars-Sinai Medical Center have developed a way to overcome immune privilege in the brain to eradicate potentially deadly brain tumors such as glioblastoma multiforme and other types of brain infections.

Brain tumors account for 85 to 90 percent of all primary central nervous system tumors. Of those tumors, almost 40 percent are either the deadly glioblastoma multiforme or anaplastic astrocytomas. Each year about 19,000 people in the United States are diagnosed with primary brain cancers, and close to 70 percent of those diagnosed will not survive more than five years. In addition, approximately 150,000 Americans a year are diagnosed with metastatic brain tumors, cancer that has spread into the brain from another part of the body.

“We have developed a novel gene therapy strategy to modify the brain microenvironment which will allow us to overcome immune privilege in the brain and improve the lives of those who are suffering with life-threatening diseases such as brain cancer or brain infections,” said Maria Castro, Ph.D., co-director of the Board of Governors' Gene Therapeutics Research Institute at Cedars-Sinai Medical Center and the principal investigator of the study.

The brain's blood-brain barrier and lack of a drainage system means that the organ has immune privilege and therefore cannot mount a defense against cancer or other infectious diseases localized in it. Once activated, immune cells can cross the blood-brain barrier and attack pathogens or tumors; however, it is not possible to mount an effective immune response from the brain itself because it lacks antigen presenting cells. In the study published in the *Journal of Immunology*, researchers lead by Dr. Castro and Dr. Pedro Lowenstein found a way of engineering the brain's microenvironment to induce the migration of antigen presenting cells to the brain itself and mount an effective immune response against deadly tumors and other brain infections.

In a prior study published in *Cancer Research* in 2005, the same Cedars-Sinai researchers tested two genes, one that killed cancer cells and a second that elicited the production of immune cells in a large brain tumor model in laboratory mice. Now, building upon that study, these scientists, using a viral vector that delivers the protein Flt3 Ligand into the brain, have demonstrated that it attracts immune cells which can take up tumor antigens and present them to the immune system. These dendritic cells, also referred to as antigen presenting cells, which normally are absent from a healthy brain, can destroy tumors as well as combat any other type of brain infections.

“Our previous work in the lab has shown that Flt3 Ligand could be used to eradicate large brain tumors,” said Pedro Lowenstein, M.D., Ph.D., director of the Board of Governors' Gene Therapeutics Research Institute at

Cedars-Sinai Medical Center and the co-senior author of the study.” Now through the outcome of our most recent study, we have developed a delivery system to produce this protein and we know how it works.”

Through the pre-clinical trial, researchers used a viral vector to encode the Flt3 Ligand gene and deliver it safely into the brain. They discovered that this molecule can overcome the brain’s immune privilege and was able to elicit a very potent anti-glioma immune response. The discovery on the mechanisms to overcome the immune privilege in the brain will open up very exciting therapeutic opportunities to treat primary and metastatic brain cancers and deadly brain infections.

The high levels of Flt3 Ligand molecules recruited an elevated influx of antigen presenting cells to the site of the brain where Flt3 Ligand had been generated. The conclusion was that Flt3 Ligand is capable of regenerating a component of the immune system which otherwise is absent from the brain; opening the door to treating a number of devastating brain disorders such as cancer and other infections.

“We are extremely excited by the results of this study; our approach actually killed glioblastoma multiforme tumors in a period of just two weeks,” Dr Castro said. “Needless to say, we are anxious to start the next phase of the process, our phase one clinical trials, so that we can quickly move on to improving the quality and even saving lives of patients afflicted with these devastating diseases.”

The study, *Fms-Like Tyrosine Kinase 3 Ligand Recruits Plasmacytoid Dendritic Cells to the Brain*, was funded by the National Institutes of Health, the Linda Tallen and Paul Kane Foundation, and the Board of Governors at Cedars-Sinai Medical Center.

For more information about the work of the physicians and researchers at the Board of Governors’ Gene Therapeutics Research Institute at Cedars-Sinai Medical Center, please visit: <http://www.csmc.edu/3255.html>.

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The first of eight hospitals in California whose nurses have been honored with the prestigious Magnet designation, Cedars-Sinai Medical Center is one of the largest nonprofit academic medical centers in the Western United States. For 18 consecutive years, it has been named Los Angeles’ most preferred hospital for all health needs in an independent survey of area residents. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities and was recently fully accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP). Additional information is available at www.cedars-sinai.edu.

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