SOUTHWESTERN NEWS

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UT SOUTHWESTERN PHYSICIANS TRY GENE THERAPY ON BRAIN TUMORS

DALLAS — May 16, 1995 — If a new form of gene therapy currently being tested at UT Southwestern Medical Center at Dallas proves effective, physicians could have an important new alternative to radiation and chemotherapy in the battle against brain cancer.

The therapy might be seen as a form of medical espionage. After removing as much of the cancerous tumor as possible, doctors will plant their own agent, cells producing a viral vector, or carrier, that transfers to cancer cells the susceptibility to a particular drug. When that drug is injected — if the treatment works — it will kill the remaining cancer cells. The enemy will be wiped out.

If proven to be effective, the treatment, being tested at several medical centers around the country including UT Southwestern, would be especially attractive to physicians who previously relied only on radiation and chemotherapy to follow up brain cancer surgery. "This would be an easier treatment process in theory," said Dr. S. Clifford Schold Jr., chairman of neurology at UT Southwestern. Neither the vector nor the drug are toxic to normal cells, so patients would not have to endure the frequently debilitating side effects of radiation and chemotherapy.

Schold, holder of the Dorothy Rogers Cullum Distinguished Chair in Neuro-Oncology, leads the UT Southwestern research team, which also includes Dr. Hassan Fathallah-Shaykh, assistant professor of neurology, Dr. Bruce Mickey, associate professor of neurosurgery, and Dr. David Carbone, assistant professor of internal medicine.

Doctors are rarely able to remove all of the cancerous brain tumor during an operation. In this treatment, cells, which produce vectors that carry the thymidine kinase (tk) gene will get into the tumor cavity and the area surrounding it following the removal of the main part of the

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tumor. The vector and the tk gene will get into rapidly multiplying cancer cells but not the healthy cells, which are slow to multiply in the brain. Once the tk gene is incorporated into the cancer cell, the cell will produce thymidine kinase, which makes it susceptible to the antiviral drug, ganciclovir. Ganciclovir then will be injected intravenously to kill the cancer cells. The vector-producing cells also will be injected through a catheter left in the tumor cavity after surgery for retreatment subsequent to surgery. Gaithersburg, Md.-based Genetic Therapy Inc. produces the vector and is sponsoring the trial.

The National Institutes of Health, in collaboration with GTI, has performed similar research in the past few years and has had some success, Schold said. UT Southwestern expects to use the treatment on three to five patients over the next year, with 30 targeted for the trial nationwide.

The research project will involve only patients who have undergone treatment for tumors in the past and have had those cancerous tumors grow back. The patients also have to be in otherwise acceptable physical condition and able to withstand another operation. If the treatment proves successful, the method likely will be tested on patients in an earlier stage of the disease.

New brain tumors develop in about 15,000 adults in the United States each year. Brain tumors represent the third-leading cause of death from cancer in persons 15 to 34 years of age. The prognosis of patients suffering from glioblastoma multiforme, the type of tumor targeted in the current study, is grim, with a median survival of 9 to 10 months. When glioblastoma multiforme recurs, there is virtually 100 percent mortality within weeks to a few months.

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