UT SOUTHWESTERN MEDICAL CENTER NEWS

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UT Southwestern researchers identify target for therapeutic drugs to fight most common adult brain cancer

DALLAS – Jan. 15, 2006 – A research team at UT Southwestern Medical Center has discovered a cell-signaling mechanism instrumental in the most common brain cancer in adults.

The study, published in today's issue of the journal *Cancer Research*, opens an avenue to develop therapeutic drugs to target the epidermal growth factor receptor genes that play a major role in the development of deadly brain tumors, researchers said.

The median survival of patients with glioblastoma multiforme (GBM), a cancer of the supportive tissue of the brain, currently is about one year after diagnosis with the best treatments available, said Dr. Amyn Habib, assistant professor of neurology at UT Southwestern and the study's senior author. GBM, which accounts for 60 percent of brain tumors in adults older than 50 years, can infiltrate the brain extensively and sometimes becomes enormous before turning symptomatic.

Researchers have known for years that tumor cells proliferate out of control by a mechanism characterized by an abnormally high number of copies of the epidermal growth factor receptor gene (EGFR). This overexpression of EGFR, Dr. Habib said, is a striking feature of glioblastoma multiforme, present in 40 percent to 50 percent of tumors and results in an uncontrolled multiplication of both normal EGFR and a mutant form called EGFRvIII.

While studying human brain tumor tissue and human brain tumor cells from cell lines grown in the laboratory, Dr. Habib and his colleagues discovered that EGFRvIII generates a unique pattern of signaling (distinct from normal EGFR) that causes brain cancer cells in GBM to grow and multiply unchecked.

"The better we understand the signaling mechanisms of the normal and the mutant EGFR, the better we can manipulate or control them," Dr. Habib said. "Our findings suggest that you have to target both the mutant and the normal EGFR based on the mechanism we described."

Current standard treatment of GBM consists of surgical removal of the tumor, followed by

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radiation and chemotherapy. Dr. Habib said he hoped the findings gained from the new study could eventually lead to therapeutic drugs that destroy brain cancer cells and spare healthy cells.

Other UT Southwestern researchers on the study were Dr. Deepti Ramnarain, postdoctoral researcher in neurology and lead author; Dr. Seongmi Park, postdoctoral researcher in neurology; Dr. Kimmo Hatanpaa; assistant professor of pathology; Dr. Jack Raisanen, associate professor of pathology; Dr. Raheela Ashfaq, professor of pathology; and Shane Scoggin, research assistant in the Harold C. Simmons Comprehensive Cancer Center. Researchers from Beth Israel Deaconess Medical Center and Harvard Medical School also participated.

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