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Study finds new targets for drugs to defeat aggressive brain tumor

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University of Pittsburgh Cancer Institute (UPCI) researchers have identified over 125 genetic components in a chemotherapy-resistant, brain tumor-derived cell line, which could offer new hope for drug treatment to destroy the cancer cells.

The results will be reported in the cover story of December's issue of the journal *Molecular Cancer Research*, to be published Dec. 18 and currently available online.

The potential drug targets were identified after testing more than 5,000 genes derived from glioblastoma multiforme, an aggressive brain tumor. The genes were evaluated for their role in responding to the chemotherapy drug temozolomide.

"The current standard of care for people with this type of cancer is to remove as much of the tumor as possible, and then treat with radiation and temozolomide," said lead author David Svilar, Ph.D., a student in the Medical Scientist Training Program at the University of Pittsburgh School of Medicine. "However, glioblastoma multiforme is highly resistant to this chemotherapy drug, so we need to find better treatments to improve the patient survival rate."

According to the National Cancer Institute, glioblastoma multiforme is the most common type of brain tumor in adults. It accounts for about 15 percent of all brain tumors, and typically occurs in people between the ages of 45 and 70 years.

Patients with glioblastoma multiforme usually survive less than 15 months after diagnosis, and there are no effective long-term treatments for the disease.

Temozolomide, also known by the brand name Temodar, works by modifying the cancer's DNA in a way that triggers cell death. It has been approved by the U.S. Food and Drug Administration for use in brain tumors and is in clinical trials for other cancers, such as melanoma and leukemia. It is well-tolerated in most patients.

"Unfortunately, some cancers - particularly glioblastoma multiforme – are able to repair the DNA damage done to the tumor by Temozolomide before the cancer cells are destroyed," said senior author Robert W. Sobol, Ph.D., a scientist at UPCI and an associate professor in the departments of Pharmacology & Chemical Biology and Human Genetics. "Clinical trials are underway to test drugs and chemotherapy dosing schedules to inhibit this repair, but none have proven effective to date."

Dr. Sobol and his colleagues identified multiple "druggable" targets that could make the cancer more sensitive to temozolomide, as well as the processes that allow the tumor to survive the onslaught of surgery, radiation and chemotherapy.

"Our hope is that drug companies will use our findings to develop adjuvant chemotherapy drugs that will vastly improve patient survival from this deadly cancer," said Dr. Sobol.

Provided by University of Pittsburgh Schools of the Health Sciences