Gene change identifies brain cancer patients that respond better to treatment

New research proves that a change in a particular gene can identify which patients with a specific kind of brain cancer will respond better to treatment. Testing for the gene can distinguis patients with a more- or less-aggressive form of glioblastoma, the most common and an often-fatal form of primary brain cancer, and help guide therapy, the researchers say.

Dr. Arnab Chakravarti: "Clearly, all glioblastomas are not the same. Rather, they are a collection of different molecular and genetic entities that behave uniquely and require personalised treatment."

The prospective study looked at a gene called MGMT in tumours removed from 833 glioblastoma patients It showed that when the gene promoter is altered by a chemical change called methylation, patients respo better to treatment.

"We show that MGMT methylation represents a new genetic test that can predict clinical outcomes in glioblastoma patients who have been treated with radiation combined with the chemotherapeutic drug temozolomide," says co-author Dr. Arnab Chakravarti, chair and professor of Radiation Oncology and co-director of the brain tumour program at the Ohio State University Comprehensive Cancer Centre - Arthur G James Comprehensive Cancer Centre and Richard J. Solove Research Institute (OSUCCC - James).

Not all the same

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Principal investigator Dr. Mark Gilbert, professor of neuro-oncology at M.D. Anderson Cancer Centre, will present the research June 5, 2011, at the 2011 American Society of Clinical Oncology annual meeting in Chicago. It comes from a prospective international phase III clinical trial sponsored by the Radiation Therapy Oncology Group (RTOG).

"Our study confirms the prognostic significance of MGMT gene methylation and demonstrates the feasibil of prospective tumour-tissue collection, molecular stratification and collection of patient outcomes in a larg

transatlantic intergroup trial," Gilbert says.

A tentative indication that MGMT methylation status might have prognostic importance emerged from an earlier retrospective study sponsored by the European Organisation for Research and Treatment of Canc (EORTC).

Current study validates finding

The current study (RTOG 0525) validates that finding. Patients with tumours carrying the methylated gene had an overall survival of 21 months versus 14 months for those with the unmethylated gene. The differen in progression-free survival - the period after treatment during which cancer does not worsen - was 8.7 months and 5.7 months for methylated versus unmethylated tumours respectively. The narrow difference, Chakravarti says, indicates that patients with the methylated gene had slower growing tumours.

About 18 500 new cases of glioblastoma multiforme are expected annually in the US, and 12 760 Americans are expected to die of the disease. Symptoms often include headache, seizures and motor or sensory changes. A brain scan detects the tumour. After a surgeon removes the tumour, it can be tested f MGMT methylation.

"Patients with the methylated gene could receive the standard treatment, radiation therapy plus the chemotherapeutic drug temozolomide," Chakravarti says. "Those with an unmethylated gene might receiv an experimental treatment through a clinical trial."

Research is now needed, he says, to learn whether MGMT contributes directly to tumour aggressiveness, whether it is just an indicator of other changes that cause tumour aggressiveness. "If the gene itself helps cause aggressive disease, MGMT or related DNA repair pathways might be important targets for novel therapies," Chakravarti says.

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The Ohio State University Comprehensive Cancer Centre - Arthur G. James Cancer Hospital and Richard Solove Research Institute (http://cancer.osu.edu) is one of only 40 Comprehensive Cancer Centres in the United States designated by the National Cancer Institute. Ranked by US News & World Report among th top cancer hospitals in the nation, The James is the 205-bed adult patient-care component of the cancer program at The Ohio State University. The OSUCCC-James is one of only seven programs in the country funded by the NCI to conduct both Phase I and Phase II clinical trials.