MedicalXpress

New vaccine extends survival for patients with deadly brain cancers

October 4 2010

A new vaccine added to standard therapy appears to offer a survival advantage for patients suffering from glioblastoma (GBM), the most deadly form of brain cancer, according to a study from researchers at Duke University Medical Center and The University of Texas MD Anderson Cancer Center.

The vaccine also knocks out a troublesome growth factor that characterizes the most aggressive form of the disease.

"About a third of all glioblastomas are fueled by a very aggressive cancer gene, called EGFRvIII; these tumors are the 'worst of the worst,'" said John Sampson, M.D., Ph.D., the Robert H. and Gloria Wilkins Professor of Neurosurgery at Duke.

"Our study showed that the vaccine eliminated all of the cancer cells carrying this marker in all but one of our study participants," said Darell D. Bigner, M.D., Ph.D., director of the Preston Robert Tisch Brain Tumor Center and the senior author of the study.

The EGFRvIII variant was co-discovered by Bert Vogelstein and Albert Wong at Johns Hopkins University and Bigner, at Duke.

The study, appearing in the Journal of Clinical Oncology, involved 18 patients newly diagnosed with GBM from Duke and MD Anderson and a matched set of 17 patients who served as controls. Patients in both groups received surgery, radiation and the chemotherapy drug

temozolomide. Patients in the vaccine group began receiving injections one month after completing radiation and stayed on the vaccine as long as it appeared to be working.

Adding the vaccine to standard therapy extended median survival time from an expected 15 months to 26 months. Patients in the vaccine group also experienced a much longer progression-free survival period, 14.2 months, compared to 6.3 months for those who did not receive the vaccine.

Glioblastoma is the most common form of brain cancer with roughly 10,000 new cases arising in the U.S. each year. The presence of EGFRvIII allows cancer cells to grow wildly out of control, seeding new tumors throughout the brain. Despite some advances in radiation and chemotherapy, the prognosis for patients with such tumors is grim; on average they live just over one year following initial diagnosis.

Sampson says new therapies are critical. Over the past decade he and his research team have been working on several new vaccine strategies. The particular vaccine used in this study is called a peptide vaccine and was designed to stimulate the patient's immune systems to respond to a particular part of a protein on EGFRvIII.

Other brain tumor vaccine studies are in progress at other institutions with peptides drawn from the tumors and with heat shock proteins.

Researchers found that the vaccine (variously known as CDX-110 by Celldex Therapeutics, and Rindopepimut (PF-04948568) by Pfizer) stimulated an immune response in approximately half of the patients who received it. Six patients developed EGFRvIII-specific antibodies and three developed T-cell responses.

The data suggest that these responses are linked to increased survival

time, "but the numbers are so small that we can not conclude this with any degree of certainty," says Amy Heimberger, MD, co-lead investigator, from MD Anderson.

Scientists were also able to examine pre- and post-vaccination tumor samples from 11 patients and found that when their tumors recurred, 82 percent lacked immunoreactivity, which Sampson says demonstrates that the vaccine had done its job in eliminating the most aggressive cells.

Sampson notes that the EGFRvIII vaccine may be worth further investigation because this growth factor is also found in other kinds of cancer cells, but not in normal tissue, making it a good target for intervention.

Bigner says that even though the study is small, the findings are intriguing and merit further study. "This appears to be a promising start, but the biological complexity of these tumors suggests that we may need multiple agents to attack additional markers of tumor growth or treatment resistance to be wholly successful."

Duke has a long history of vaccine design and Sampson says plans are already under way to couple the vaccine with another designed to strengthen T-cell responses.

Provided by Duke University Medical Center