MedicalXpress

Brain tumor growth linked to lowered expression of hundreds of immune function genes

April 26 2010, by Emily Caldwell

A new study links progression of a lethal type of brain tumor with reduced expression of more than 600 immune system genes, suggesting how complex the immune response is to the cancer and the resulting difficulty in targeting specific immune system proteins for treatment.

Previous research found that people with allergies were less likely to be diagnosed with this type of brain cancer, called glioblastoma multiforme. However, it was not clear whether allergies reduce brain tumor risk or whether the growing tumor "cures" allergies.

To further explore the relationship between these two conditions, scientists examined almost 1,000 genes associated with allergies, immunity and inflammation to learn how they were affected once these tumors were present in the brain.

The researchers expected to see that allergy gene function was low in brain tumor tissue, which would be consistent with the known immune system suppression that is associated with these tumors.

What they found was a surprise: Allergy genes were not the only immune function genes suppressed during tumor growth. Instead, in almost 70 percent of the 919 genes examined, the genes' activity was decreased as the brain tumors progressed.

"This result provides evidence that there is a relationship between glioblastoma and allergies - specifically, high tumor aggressiveness is associated with low allergy-related gene function," said Judith Schwartzbaum, lead author of the study and an associate professor of epidemiology at Ohio State University. "But it still does not tell us whether allergies inhibit tumor growth or tumors block allergies."

The findings also show that immune function in the brain continues to change as these tumors grow.

"As the tumor progresses, the majority of the immune-function genes express themselves at lower levels," Schwartzbaum said. "So we know that with progression there is less immune function, but we don't know which came first, the lowered immune function or the cancer."

The cause of this kind of cancer remains unknown, and there is no cure. The complexity of the immune response to this tumor suggests that it will be difficult to identify key immune function proteins that inhibit tumor growth. Schwartzbaum said that in addition to using information about the immune system to treat tumors, researchers must also study the immune system to find ways to prevent these aggressive tumors.

The study is published in a recent issue of the journal *Neuro-Oncology*.

Glioblastomas constitute up to 60 percent of adult primary brain tumors in the United States, affecting an estimated 3 in 100,000 people. Patients who undergo surgery, radiation and chemotherapy survive on average for about one year, with fewer than a quarter of patients surviving up to two years and fewer than 10 percent surviving up to five years.

The researchers used publicly available data from genetic analysis of 142 brain tumor tissue samples collected from patients with glioblastoma multiforme tumors as part of the National Cancer Institute's The Cancer

Genome Atlas project.

The scientists used levels of expression of the CD133 gene as an indicator of tumor progression. Previous studies had suggested that activation of this gene is related to tumor aggression and a poor clinical outcome.

With these data, Schwartzbaum and colleagues then plotted expression of immune function genes against levels of CD133 expression in these tumors.

Gene expression refers to the switching on or activation of genes. Schwartzbaum and her colleagues analyzed mRNA expression data in their study; mRNA synthesis is the first step in gene expression and may lead to creation of functional proteins.

The analysis showed that higher levels of CD133 expression were associated with lower levels of immune function gene expression in 69 percent of the genes examined.

There were, however, immune function genes whose expression increased with CD133 expression, including a cytokine gene called interleukin-17 that is linked to inflammation, and a gene related to suppression of immune function called NCAM-1.

The genes whose function was lowered with tumor progression included most of those associated with allergies, as well as, paradoxically, many of those that counteract allergy genes. In another surprising finding, many genes known to suppress immune function were also expressed at lower levels as the tumor progressed.

"That was a surprise because you'd think that genes that suppress the immune system would be more active in these tumors, which may be

lethal, in part, because they are immunosuppressive. But we didn't see that," Schwartzbaum said.

Schwartzbaum is planning to focus her subsequent research on the end products of genetic activation, immune function proteins or cytokines.

She plans to analyze 1,200 samples from the Janus Serum Bank in Norway, which were collected on average 10 years before brain tumor diagnosis, to find out whether the presence of certain cytokines in those samples might offer clues that will help identify people at high risk for brain tumor development.

Provided by The Ohio State University