

Animal study identifies promising new target for brain tumor therapy

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A drug that targets the body's immune cells may be effective in treating malignant brain tumors, according to a new study led by researchers from Duke's Preston Robert Tisch Brain Tumor Center. In animal models, the drug re-engaged the body's cancer-damaged immune system.

"We were effectively targeting 'bad' T cells that can damage the immune system if their numbers are too high, and 'good' T cells that help create an immune response to things like infections and tumors," said John Sampson, M.D., Ph.D., a neurosurgeon at Duke and senior investigator on the study. "We found that this drug was able to stop the bad cells in their tracks by giving the good ones a type of bulletproof jacket."

The researchers speculate that patients with a restored immune system will be better equipped to fight off brain tumors. They hope to start a clinical trial soon.

The results of this study hold promise for the development of vaccines that can work against tumors by eliciting the help of the body's immune system, Sampson said. The researchers published their findings in the April 1, 2007 issue of the journal *Clinical Cancer Research*. The study was funded by the National Institutes of Health, the Brain Tumor Society and Accelerate Brain Cancer Cure.

T cells are white blood cells that play an important role in the body's immune system. Regulatory T cells help maintain immune balance, so they are responsible for toning down an immune response after the body

has fought off a foreign invader, such as an infection, Sampson said. But patients with brain tumors often have too many regulatory T cells, rendering their immune systems ineffective in fighting off tumors.

In contrast, cytotoxic T cells, which act to destroy infection and tumor cells, are often depleted in people with brain tumors, enabling the tumor cells to grow and spread unchecked. Those cytotoxic T cells that remain can be insufficient because of the increased number of regulatory T cells, Sampson said.

"We speculated that this drug, which has been used successfully to treat other types of cancer such as melanoma and prostate cancer, might be effective in treating tumors that originate in the brain as well," said Peter Fecci, Ph.D., a medical student at Duke and lead investigator on the study.

The identification of T cells as targets for this drug was first made by study co-author James Allison, Ph.D., of Memorial Sloan-Kettering Cancer Center, who then went on to demonstrate the effectiveness of the drug in pre-clinical models of other types of cancer.

For this study, the researchers found that the drug, which targets a molecule called CTLA-4 that is found on both types of T cells, could halt the effects of the bad T cells, which stunt immune response, by making the good T cells more resistant to them, thereby helping the immune system combat the brain tumor, Fecci said.

"Brain tumors can be especially challenging because these patients have such high levels of regulatory T cells and also because many drugs are not able to permeate the blood-brain barrier," Fecci said. "We are encouraged by these results because this drug has a restorative effect on the immune system and doesn't need to get into the brain to be effective." Animal subjects also did not demonstrate symptoms of

autoimmunity, a condition in which the immune system attacks the body, which can be a side effect of drugs that target immune cells, Fecci said.

Duke researchers are in the process of launching a clinical trial to test the effectiveness of the drug in humans.

"This dual-pronged approach that targets both types of cells holds great promise," Sampson said. "We hope that it will soon lead to more effective treatments for people diagnosed with these deadly brain tumors."

Source: Duke University Medical Center

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