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Research targets way to stop brain tumor cell invasion

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Gliomas are brain invaders. A kind of malignant tumor cell, gliomas branch out like tendrils from a central tumor source, spreading cancer throughout the brain. Traditional therapies, such as cutting out the tumor surgically, can be ineffective if the cells have already spread. Researchers at the University of Alabama at Birmingham may have come upon a way to stop a glioma invasion in its tracks, using a drug already approved for use in Europe.

Much like early explorers of the Old West followed rivers and streams, depending on them to provide drinking water and food, gliomas spread through the brain by following the path of blood vessels, tapping into those vessels for the nutrients they need to survive. Cut that glioma off from the blood supply, and it starves.

"An explorer lost in the wilderness without food and water soon succumbs and dies," said Harald Sontheimer, Ph.D., director of the UAB Center for Glial Biology in Medicine and senior author on the paper. "A glioma that can't find and tap into a blood vessel will also die."

In a paper published March 30, 2011 in the Journal of Neuroscience, Sontheimer and co-author Vedrana Montana, Ph.D., discovered that bradykinin, a peptide that increases the size of blood vessels, is the mechanism glioma cells use to find blood vessels. Glioma cells carry a receptor for bradykinin, called the B2R receptor. Using that receptor to attract bradykinin gives the cell a navigator to lead it to blood vessels. Block the receptor from interacting with bradykinin and the cell will end

up lost in the wilderness.

The researchers introduced a B2R inhibitor known as HOE 140, a laboratory version of a drug approved for use in Europe for hereditary angioedema called Icatibant. HOE 140 bound to the B2R receptor on glioma cells, interfering with the receptor's opportunity to bind to bradykinin. The results were impressive.

"We found that 77 percent of glioma cells with bradykinin were able to locate a blood vessel and tap into its nutrients," said Montana. "However, when we blocked the B2R receptors from interacting with bradykinin, only 19 percent of glioma cells were able to find a blood vessel."

The researchers used human glioma cells transplanted into a mouse model and, using time-lapse techniques on a laser-scanning microscope, tracked the ability of the cells to navigate to blood vessels by means of fluorescent markers attached to the cells.

"Targeting the B2R receptors is an elegant and so far unexplored approach to treat gliomas, one of the most devastating types of brain tumor," said Sontheimer. "Icatibant, which is already in use in Europe, and its ability to block B2R receptors may prove to be very promising target for further investigation."

Provided by University of Alabama at Birmingham