Drugs to inhibit blood vessel growth show promise in rat model of deadly brain tumor

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In a landmark study, Medical College of Wisconsin researchers in Milwaukee report that drugs used to inhibit a specific fatty acid in rat brains with glioblastoma-like tumors not only reduced new blood vessel growth and tumor size dramatically, but also prolonged survival. The study is the featured cover story of the August, 2008 *Journal of Cerebral Blood Flow & Metabolism*.

"These rat model tumors were developed from human glioblastoma tumor cells and closely mimic human tumors in growth patterns and response to therapy," says lead researcher David Harder, Ph.D., Kohler Co. Professor in Cardiovascular Research. "The concept of targeting blood vessels that feed tumors as an approach to limit tumor growth is not a novel idea," he says. "However, blocking the specific fatty acid described in this study is novel, and holds great promise for use in humans."

Malignant gliomas are very aggressive tumors of the central nervous system, resistant to chemotherapy and radiation, and account for about half of the 350,000 brain tumors currently diagnosed in the U.S.

Dr. Harder is also professor of physiology, associate dean for research and director of the Medical College's Cardiovascular Research Center. He believes that further studies, demonstrating that such drugs work in humans may reveal that higher concentrations or infusions over longer periods of time may be more effective than the results reported in this study.

"If survival time could be extended, with a combination of surgical therapy and infusion with similar drugs, this could be a significant treatment option," he says.

Earlier studies from the Harder lab have shown that specific fatty acids generated in the brain induce new blood vessel growth known as angiogenesis. Harder and colleagues designed these studies on the premise that all cells, including cancer cells, require oxygen for growth and that blocking formation of specific fatty acids would decrease blood vessel growth and oxygen supply to tumors, retarding their growth.

In their current study, Dr. Harder and colleagues compared three sets of rats with induced tumors, two groups using either one of two inhibitor drugs, 17-ODYA or miconazole, to block the fatty acid CYP epoxygenase and a control group, receiving a placebo. Drugs were infused directly into the tumors over an extended period of time, using specially-designed miniature osmotic pumps and a very small burr hole in the skull. The pumps, similar to those used in humans, were buried just beneath the skin through a tiny incision.

Compared to the control group, tumor size in the drug-infused groups was reduced by an average 50 to 70 percent, and survival time increased by five to seven days, equivalent to three to four months in terms of human survival.

"These pumps have been used in humans for other diseases and can be designed for delivery of these drugs as well," says Dr. Harder. "We believe they can be used to deliver drugs to block angiogenesis in complex human tumors such as glioblastomas."

Source: Medical College of Wisconsin