Does the existing standard of care supply energy sources to brain tumor cells?

EurekAlert

Chestnut Hill, Mass. (7/14/2010) The medical standard of care comprised of surgery, radiation and chemotherapy for the most common form of brain cancer triggers a number of biological responses that may actually feed the energy metabolism that supports the disease, according to Boston College researchers writing in the journal *Lancet Oncology*.

The deadly glioblastoma multiforme leaves the average patient a median survival of about a year from diagnosis. Just three percent of patients afflicted with the fast-moving brain cancer survive 36 months. The standard of care for the treatment of the disease has not changed markedly since it was established 50 years ago.

But the effects of surgery, radiation and chemotherapy produce a range of biochemical responses in the brain that can fuel tumor cell survival at the same time doctors are attempting to eradicate the disease, according to Boston College Professor of Biology Thomas Seyfried, whose lab has researched ways to deny energy to cancer cells.

"All tumors, regardless of where they are located, require two major fuels for survival: glucose and glutamine," said Seyfried, a specialist in lipid biochemistry. "As long as tumor cells have access to these energy molecules, they will survive. If you give them a lot of these molecules, they will survive even better."

The three components of cerebral cancer care may play a role in providing tumor cells with the metabolic fuels they need to survive. While these treatments reduce tumor growth over the short term, radiation and certain chemotherapies could actually contribute to the high recurrence of these deadly tumors.

A growing body of research over the past decade, according to Seyfried, now shows the processes of radiation and chemotherapy can serve to increase the supply of glucose and glutamine, leading to conditions favorable to tumor cell survival and growth.

Furthermore, infection-fighting tumor-associated macrophages and monocytes (TAMs) that flood the brain in an effort to battle tumor cells can indirectly support tumor growth through the release of agents that lead to inflammation and the growth of blood vessels.

"What develops then is an escalating situation of biological chaos, where the intrinsic properties of TAMs to heal wounds increase the capacity of brain tumor cells to proliferate, invade, and self-renew," writes Seyfried and his co-authors, researchers Laura M. Shelton and Purna Mukherjee. "High glucose concentrations

together with unrestricted glutamine availability will provide the energy necessary to drive this escalating situation."

Seyfried says this "perfect storm" of side-effects from the standard of care for glioblastoma should invite a broader discussion among researchers for potential alternative therapies. Through his past research, Seyfried has detailed the benefits of non-toxic metabolic therapies involving ketogenic diets that effectively restrict glucose-based fuels to brain tumors. By regulating glucose availability while simultaneously elevating fat-derived ketone bodies, which brain tumors cannot actively use for growth or survival, the ketogenic diet has been shown to control epileptic seizures, but there have been no human trials to test its therapeutic efficacy against brain cancer.

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