Progesterone could become tool versus brain cancer

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(Medical Xpress)—The hormone progesterone could become part of therapy against the most aggressive form of brain cancer. High concentrations of progesterone kill glioblastoma cells and inhibit tumor growth when the tumors are implanted in mice, researchers have found.

The results were recently published in the *Journal of Steroid Biochemistry and Molecular Biology*.

Glioblastoma is the most common and the most aggressive form of brain cancer in adults, with average survival after diagnosis of around 15 months. Surgery, radiation and chemotherapy do prolong survival by several months, but targeted therapies, which have been effective with other forms of cancer, have not lengthened survival in patients fighting

glioblastoma.

The lead author of the current paper is Fahim Atif, PhD, Assistant Professor of Emergency Medicine at Emory University. The findings with glioblastoma came out of Emory researchers' work on progesterone as therapy for traumatic brain injury and more recently, stroke. Atif, Donald Stein and their colleagues have been studying progesterone for the treatment of traumatic brain injury for more than two decades, prompted by Stein's initial observation that females recover from brain injury more readily than males. There is a similar tilt in glioblastoma as well: primary glioblastoma develops three times more frequently in males compared to females.

These results could pave the way for the use of progesterone against glioblastoma in a human clinical trial, perhaps in combination with standard-of-care therapeutic agents such as temozolomide. However, Stein says that more experiments are necessary with grafts of human tumor cells into animal brains first. His team identified a factor that may be important for clinical trial design: progesterone was not toxic to all glioblastoma cell lines, and its toxicity may depend on whether the tumor suppressor gene p53 is mutated.

Atif, Stein, and colleague Seema Yousuf found that low, physiological doses of progesterone stimulate the growth of glioblastoma tumor cells, but higher doses kill the tumor cells while remaining nontoxic for healthy cells. Similar effects have been seen with the progesterone antagonist RU486, but the authors cite evidence that progesterone is less toxic to healthy cells. Progesterone has also been found to inhibit growth of neuroblastoma cells (neuroblastoma is the most common cancer in infants), as well as breast, ovarian and colon cancers in cell culture and animal models.

More information: Fahim Atif, Seema Yousuf, Donald G. Stein,

"Anti-tumor effects of progesterone in human glioblastoma multiforme: Role of PI3K/Akt/mTOR signaling," *The Journal of Steroid Biochemistry and Molecular Biology,* Available online 28 April 2014, ISSN 0960-0760, dx.doi.org/10.1016/j.jsbmb.2014.04.007.

Provided by Emory University

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