Progesterone inhibits growth of neuroblastoma cancer cells

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High doses of the hormone progesterone can kill neuroblastoma cells while leaving healthy cells unscathed, scientists at Emory University School of Medicine have found in laboratory research.

The results, published in the journal Molecular Medicine, suggest that progesterone could be used to fight neuroblastoma, the most common form of cancer affecting small children.

More research is necessary to determine the optimal dose, how long progesterone treatment should last and if it should be used alone or in combination with radiation or chemotherapy. Emory scientists are also exploring whether it can stop the growth of other brain cancer types such as glioblastoma and astrocytoma. Progesterone has also been reported to slow growth of several other types of cancers in the laboratory, but has not been used clinically against neuroblastoma.

The first author in the team of researchers is Fahim Atif, PhD, instructor in emergency medicine, with senior author Donald G. Stein, PhD, Asa G. Candler professor of emergency medicine and director of Emory's Department of Emergency Medicine Brain Research Laboratory. Daniel Brat, MD, PhD, professor of pathology and laboratory medicine in Emory School of Medicine was a collaborator on the research team.

The discovery grew out of studies of progesterone's protective effects in brain injury. Based on Stein's pioneering work, medical centers across the country are now testing progesterone in the setting of acute traumatic

brain injury in a phase III clinical trial. While investigating how to enhance progesterone's effectiveness, Atif and his colleagues observed that it could protect healthy neurons from stress but caused cells from a tumor cell line to die.

In a mouse model, progesterone treatment cut tumor growth in half over eight days, while no drug toxicity was seen with healthy neurons or in live animals. The researchers showed that progesterone can decrease the levels of proteins produced by tumor cells that attract new blood vessel growth and help tumor cells invade other tissues.

"This fits with what we know about one of progesterone's roles during pregnancy, which is to regulate the growth of placenta," Atif says. "Placental cells behave in a way that resembles tumor cells, invading the uterine wall and tapping into the mother's blood vessels."

In studies performed elsewhere, doses of progesterone that were lower than the most effective dose in the Emory study actually accelerated cancer growth. Based on their results, the Emory researchers propose that for fighting certain types of cancer, high doses of progesterone may be better than low doses.

Progesterone's effects on cancer are known to be complex. There may be differences between progesterone, the natural hormone, and synthetic progestins. The National Institutes of Health's Women's Health Initiative study showed that women who received hormone replacement therapy with combined estrogen and progestins had an increased risk of heart disease and breast cancer, although some studies have identified a potential "safe period" if hormone replacement therapy lasts less than two years.

Progesterone has a long history as a treatment designed to prevent preterm birth. If progesterone is to be used with small children, any

potential effects on development must be weighed against the risks of standard treatments.

More information: F. Atif, I. Sayeed, S. Yousuf, T. Ishrat, F. Hua, J. Wang, D.J. Brat, D.G. Stein. Progesterone Inhibits the Growth of Human Neuroblastoma: In Vitro and In Vivo Evidence. Mol. Med. doi: 10.2119/molmed.2010.00255 (2011).

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