Mystery solved of source of anti-cancer effects in pregnancy hormone

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(Medical Xpress)—University of Montreal scientists have identified a small molecule found in pregnant women's urine that apparently blocks the growth of several types of cancers, including AIDS-related Kaposi's sarcoma, which currently has no cure. Their study results will be presented Monday at the joint meeting of the International Society of

Endocrinology and The Endocrine Society: ICE/ENDO 2014 in Chicago.

These findings resurrect a nearly 20-year controversy over whether human chorionic gonadotropin (hCG), a hormone produced in high amounts during pregnancy, or its core fragments, or something else yields anti HIV and cancer-fighting activity against Kaposi's sarcoma tumors. Some researchers in the mid-1990s reported that "clinical-grade" hCG—crude or partially purified preparations of hCG extracted from pregnant women's urine—shrunk these AIDS tumors, but they later retracted their original claim that hCG itself was the active component responsible for activity against Kaposi's sarcoma.

"The real compound has been elusive," said principal investigator Tony Antakly, PhD, a biochemist at the University of Montreal, who said it has taken his small group of researchers more than 12 years to find the answer.

Early on, and shortly before this retraction, Antakly's group tested highly purified or recombinant hCG in Kaposi's sarcoma cells and found no anti-cancer effects. They concluded that the cancer-fighting compound, closely associated with the pregnancy hormone, must be removed when hCG is purified. Both clinical-grade and recombinant hCG are approved by the U.S. Food and Drug Administration as prescription medications for the treatment of select cases of female infertility and as hormone treatment for men.

The researchers narrowed their search to small molecular weight factors present in clinical-grade hCG that they called hCG-like inhibitory products, or HIP. To find the active molecule or part of a molecule, they used a biochemical approach involving systematically splitting the molecule (fractionation), repeatedly performing biological assays and chemical characterization.

Their results indicate that a small metabolite—the product of transformation of a larger molecule carried throughout blood and urine—into a potent bioactive metabolite that affects living tissue.

"We don't know if it changes only when needed," Antakly said. "Perhaps in cancer, it changes to fight the disease."

This HIP metabolite, they discovered, rides "piggyback" on the larger hCG molecule, which chaperones it to target cells. When hCG is extensively purified, the metabolite loses its ride and disappears, Antakly stated.

However, when he and his colleagues exposed human Kaposi's sarcoma cells in tissue cultures to hCG after purification from pregnant women's urine, he said the active HIP metabolite "wiped out the cancer cells completely."

Antakly said they do not yet know whether a synthetic replica of the HIP metabolite, which they are developing, is safe and effective to use at high doses in patients with cancer. However, in preliminary tests in cancer patients, they have shown that the "natural" HIP (purified from clinical-grade hCG) is safe and has anti-cancer activity.

Provided by University of Montreal