Computer model reveals cancer's energy source

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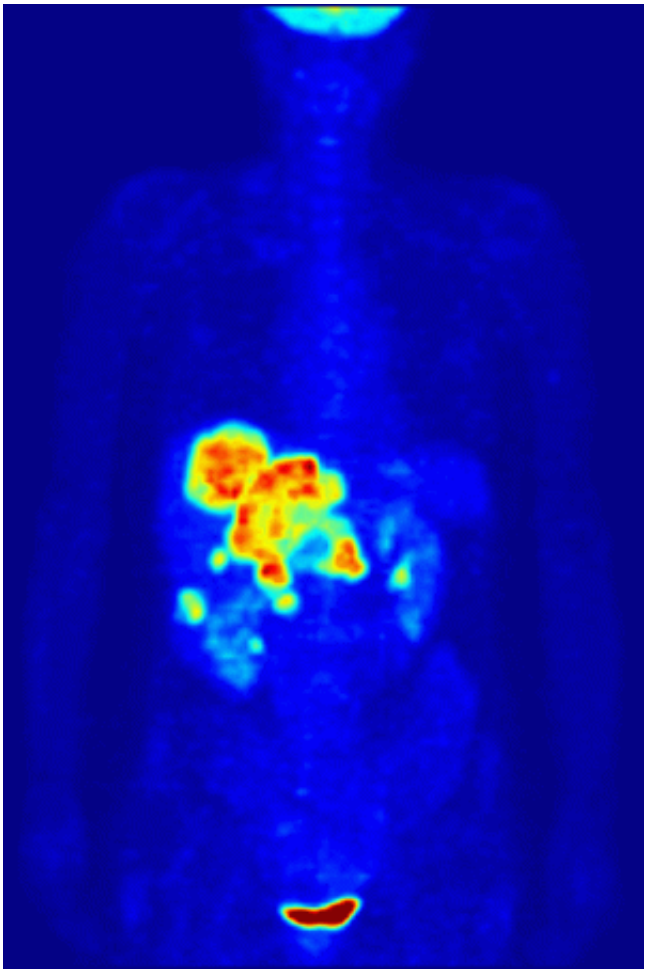

Whole-body PET scan using radioactive glucose to show liver metastases of a colorectal tumor. Doctors inject patients with radioactive glucose and then watch where it is consumed; tumors are a major source of consumption. Credit: Jens Maus

(Medical Xpress)—A computer model study reveals – for the first time – details of an energy-creating process vital and unique to cancer cells. The research holds promise for new interventions and for personalizing cancer treatments based on individual needs.

The findings, which will revise basic biochemistry textbooks, focused on the energy-making process in cancer cells known as the Warburg Effect.

The Cornell-led study, published July 9 in the journal eLife, revealed that some of the enzymes thought to have no effect on the Warburg Effect, in fact, play a large role: An enzyme called GAPDH influences many parts of a cancer cell's energy-making pathway.

"Our findings open opportunities for new ways to intervene in the Warburg Effect," said Jason Locasale, the paper's senior author and assistant professor of nutritional sciences in Cornell's College of Agricultural and Life Sciences. Alexander Shestov, a former senior research associate, and Xiaojing Liu, a postdoctoral fellow, both in Locasale's lab, are the paper's lead authors. The results also "provide glimpses into whether we have predictive capacity to discern if treatments might be working," Locasale added.

All multicellular organisms evolved pathways that take nutrients, sugars and oxygen and make energy through respiration and chemical processes. In normal cells, this energy-making process is known as oxidative phosphorylation. But when cells evolve cancerous properties and grow uncontrollably, they instead ferment their sugars to create energy even in the presence of oxygen. This process is called aerobic glycolysis, or the Warburg Effect.

The new findings are an important step toward developing a drug that affects only fermentation and not the normal metabolism of glucose, thereby depriving cancer cells of energy. The new model lays

groundwork for predicting whether treatments will be effective based on an individual's unique metabolism.

Still, very few details have been known about the Warburg Effect. "We can now systematically perturb anything in the [computer] model and identify important components" of the Warburg Effect, Locasale said.

Dating back to work by Efraim Racker, a Cornell researcher who made seminal discoveries in the area in the 1970s, followed by advances in cancer and genetic research, it is "known now that almost every cancer gene has some capacity to induce the Warburg Effect," making it fundamental to proliferative diseases, Locasale said.

Currently, the Warburg Effect is used in clinical practice to diagnose and monitor cancer. Doctors inject patients with radioactive glucose and then watch where it is consumed; tumors are a major source of consumption. Researchers are also exploring whether dietary interventions with less sugar and the use of diabetes drugs that lower glucose may impact the Warburg Effect to treat cancer.

Provided by Cornell University