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Mutations, Tissue Type Both Influence Cancer Metabolism

Like teenage boys, cancer cells are ravenous. To fuel their increased growth, proliferation, and metastasis, they alter metabolism of 2 essential nutrients, glucose and glutamine. Research shows that depriving cancer cells of these nutrients, or inhibiting their metabolism, may selectively kill cancer cells. Such findings suggest that targeting metabolic reactions could be a promising therapeutic strategy.

However, a study reported in *Cell Metabolism* cautions that, just as one genetically targeted therapy does not fit all tumors, one metabolically targeted therapy may not work for all types of cancer.

"Cancer researchers hope that genetic fingerprints will allow us to tailor therapy for individual patients," says J. Michael Bishop, MD, of the University of California, San Francisco. "We argue that to personalize therapy, you may need to have each tumor's 'metabolome' as well as its genome. But we don't know yet whether we can predict one from the other."

Bishop and Mariia Yuneva, PhD, a research specialist in his laboratory, looked at how metabolism varied with overexpression of the oncogenes *Myc* and *Met* in different tissues. Using mouse models that the Bishop lab had developed, they found that the metabolism of glucose and glutamine differed between liver tumors induced by the 2 oncogenes.

Lung and liver tumors with *Myc* overexpression also had different metabolism. "Different tumors with the same activating mutations may have quite different metabolisms," Yuneva concludes. "You cannot generalize."

Additionally, the authors showed that while human cells with *MYC* overexpression rely on glutamine catabolism, *MET*-induced cancer cells synthesize glutamine from glucose and thus may be unaffected by therapies targeting glutamine catabolism.

Still, Bishop comments, both glutamine and glucose metabolism are obvious druggable targets in cancer. "The state of preclinical research is about what it was for tyrosine kinase inhibitors right before imatinib was developed for clinical use," he says. "But drug development for metabolic inhibitors has yet to catch up."

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