Metabolic profiles essential for personalizing cancer therapy

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One way to tackle a tumor is to take aim at the metabolic reactions that fuel their growth. But a report in the February *Cell Metabolism* shows that one metabolism-targeted cancer therapy will not fit all. That means that metabolic profiling will be essential for defining each cancer and choosing the best treatment accordingly, the researchers say.

The evidence comes from studies in mice showing that tumors' metabolic profiles vary based on the genes underlying a particular cancer and on the tissue of origin.

"Cancer research is dominated now by genomics and the hope that genetic fingerprints will allow us to guide therapy," said J. Michael Bishop of the University of California, San Francisco. "The issue is whether that is sufficient. We argue that it isn't because metabolic changes are complex and hard to predict. You may need to have the metabolome as well as the genome."

Just as a cancer genome refers to the complete set of genes, the metabolome refers to the complete set of metabolites in a given tumor.

The altered metabolism of tumors has been considered a target for anticancer therapy. For instance, tumors and cancer cell lines consume more glucose than normal cells do, a phenomenon known as the Warburg effect. There has often been the impression that such changes in metabolism are characteristic of cancers in general, but cancer is a genetically heterogeneous disease. The team led by Bishop and Mariia Yuneva wondered how metabolism might vary with the underlying genetic causes of cancer.

They found in mice that liver cancers driven by different cancer-causing genes (Myc versus Met) show differences in the metabolism of two major nutrients: glucose and glutamine. What's more, the metabolism of Myc-induced lung tumors is different from Myc-induced liver tumors.

"Our work shows that different tumors can have very different metabolisms," Yuneva said. "You can't generalize."

Bishop and Yuneva say their findings also highlight glutamine metabolism as a potential new target for therapy in some tumors, noting that the focus has been primarily on glucose metabolism. Interestingly, the data shows that a version of a glutaminase enzyme normally found in kidney cells turns up in cancerous liver cells. That means there might be a way to attack the metabolism of the cancer without damaging normal liver tissue.

"We shouldn't lose sight of the rather immediate therapeutic potential," Bishop said.

The researchers will continue to inventory metabolic variation in mouse models. Ultimately, they say it will be important to catalogue the metabolic variation in the much more complex, human setting.

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