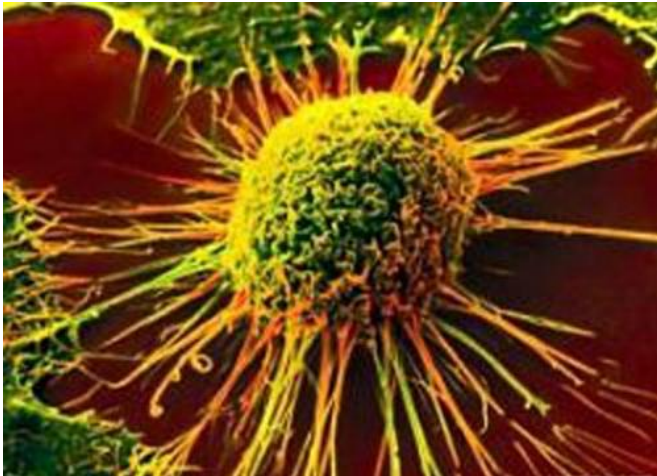


Researchers suss out brain tumors and therapy response with new metabolic PET tracer

22 October 2015, by Krista Conger



Locating a tumor hiding in a thicket of brain cells can be a tricky proposition. But doing so accurately is critical to removing the cancer via surgery, or for monitoring its response to therapy.

Now researchers at the School of Medicine have devised a new way to cause brain tumor tissue to stand out clearly during a type of imaging scan called [positron emission tomography](#).

They capitalized on the fact that rapidly dividing cancer cells require vast molecular stockpiles to create new cells. To meet this need, cancer cells express higher-than-normal levels of a protein called [pyruvate kinase](#) M2, or PKM2.

"Tumor cells do all kinds of things to survive and prosper in the body," said Sanjiv Sam Gambhir, MD, PhD, professor of radiology and director of the Molecular Imaging Program at Stanford. "One of the key things they modify is a master switch that

controls cell metabolism and allows the cell to make more of the building blocks necessary for cell division. But until now we've had no way to assess the presence or activity levels of the PKM2 protein involved in that switch."

Gambhir, who holds the Virginia and D.K. Ludwig Professorship for Clinical Investigation in Cancer Research, is the senior author of a paper describing the research. Former postdoctoral scholar Timothy Witney, PhD, and instructor of radiology Michelle James, PhD, share lead authorship of the paper, which was published Oct. 21 in *Science Translational Medicine*.

They developed a molecular tracer to track PKM2 activity that can tell researchers exactly where in the brain the cancer cells are hiding. Although the tracer has only been tested in mice to date, the researchers believe it could also give important, and speedy, information about how a tumor is responding to therapy. "This is the first time we can noninvasively interrogate the biochemistry of a tumor with respect to this [master switch](#) PKM2," said Gambhir. "If we treat a tumor with a drug, we now see whether the cancer cells' metabolic properties are changing. So we could know very quickly, possibly within a few days, whether the therapeutic approach is working. If it's not effective, we won't have to waste a month or more waiting to see if the tumor itself is shrinking."

FDA approval expected

Gambhir and his colleagues expect the new tracer, called [11C]DASA-23, to be approved by the Food and Drug Administration for use in humans within about a year or so.

All cells in the body face a kind of catch-22 as they metabolize energy sources like glucose. They can

either convert the energy into special storage molecules called ATP, or use it to generate cellular building blocks like amino acids. Pyruvate kinase is a key regulator of this process. When present as a complex of two pyruvate kinase molecules, called a dimer, it favors the accumulation of amino acids; when four molecules bind together, the cell generates more ATP.

The researchers knew that cancer cells tend to have higher levels of the dimer. They also knew that members of the molecule family called DASA bind to the dimer. They labeled one family member, DASA-23, with a radioactive carbon molecule, and they used PET scans to watch in laboratory mice as the labeled molecule sought out and bound to human glioblastoma cells implanted in the brains of the mice. Using the technique, the brain [cancer cells](#) stood out clearly against a background of normal, noncancerous cells.

"This new molecule, or tracer, works particularly well in the brain because normal [brain cells](#) have very low levels of PKM2 dimers," said Gambhir. "It's possible, though, that this tracer could also be used in cancers in other tissues like the prostate, or to even learn more about how normal tissues adjust their metabolism during development or in response to varied environmental conditions."

More information: "PET imaging of tumor glycolysis downstream of hexokinase through noninvasive measurement of pyruvate kinase M2" *Science Translational Medicine* 21 Oct 2015: [DOI: 10.1126/scitranslmed.aac6117](https://doi.org/10.1126/scitranslmed.aac6117)

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