

# Searching for an Achilles' Heel in Brain Cancer Cells

Damon Runyon researchers look at the metabolism of glioblastomas as a possible route to treatment for this aggressive brain cancer.

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Glioblastomas (GBMs) are the most common—and the most aggressive—type of cancer originating in the brain. Part of the reason these tumors are so hard to treat is that the cancer cells suppress the immune cells that enter their environment. Not only can they outcompete immune cells for critical nutrients, effectively starving the immune cells, but some GBMs can even adjust their metabolism to produce metabolites that directly inhibit immune cell activity. (Metabolism refers to the pathways by which a cell breaks down fuel and converts it into energy; metabolites are the intermediate or end products of these pathways.)

It makes sense, then, that targeting GBM metabolism has arisen as a therapeutic possibility. But first, Damon Runyon Clinical Investigator Daniel R. Wahl, MD, PhD, former Damon Runyon-Dale F. Frey Breakthrough Scientist Costas A. Lyssiotis, PhD, and their colleagues at the University of Michigan sought to answer an important underlying question: can brain tumors can be categorized based on their metabolism, and does their metabolic category influence patient survival?

To find out, the team profiled the metabolomes (the complete set of metabolites) of different types of brain tumors and compared this data with patients' clinical outcomes. They found that the GBM metabolome is indeed distinct from other brain tumors, such as astrocytomas and oligodendrogliomas, and that the non-glioblastoma patients experience better survival rates.

Glioblastomas, the researchers observed, can be separated further into metabolic subtypes with different survival rates. Patients with GBMs that produced amino acids as metabolites, for example, fared better than those whose tumors produced nucleotides and lipid metabolites.

These findings both validate the theory that metabolism is what drives the aggressiveness of GBMs and offer a means of prognosticating based on metabolic subtype. As efforts to develop glioblastoma treatments continue, this system of classification may be used to match patients with the metabolically targeted therapy that will most effectively curb their GBM growth.

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