# Blood test for brain cancer may be on horizon, research finds

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Glioblastoma (GBM) is the most common and deadliest type of brain cancer with a five-year survival rate of only 5%. Researchers at Penn State College of Medicine have identified a biomarker that can be used

in blood tests to diagnose GBM, track its progression and guide treatment. The researchers said that such a non-invasive liquid biopsy for GBM could help patients get the care they need more quickly.

"Patients normally receive imaging, such as MRI or CT scans, to diagnose and track the progression of brain tumors, but it can be difficult for physicians to tell from those scans if the patient is getting better or worse because they don't provide detail at the cellular or molecular level," said Vladimir Khristov, graduate and medical student, Penn State. "That is why we need a supplemental diagnostic test to help physicians determine if the tumors are responding to therapy and regressing, or if they are getting worse and need additional treatment."

Indeed, added Brad Zacharia, associate professor of neurosurgery and of otolaryngology, Penn State, a liquid biopsy for glioblastoma could be of tremendous value to patients suffering from this devastating tumor.

"A liquid biopsy may facilitate diagnosis and more importantly provide a better understanding of the tumor's response to treatment in a way that is lacking with our current technologies," he said.

The team studied a certain antigen receptor, called interleukin-13 receptor α2 (IL13Rα2), which is known to be elevated in the tumor tissue of more than 75% of GBM patients.

"Despite being significantly overexpressed in tumor tissue, no studies have explored the diagnostic and prognostic potential of IL13Rα2 circulating in patient biofluids," said James Connor, distinguished professor of neuroscience and anatomy, Penn State.

To investigate the utility of IL13Rα2 as a biomarker for GBM, the researchers examined the tumor tissue and blood plasma of 79 patients with primary GBM, along with the blood plasma of 23 control patients,

from two different health systems. The control patients had primary diagnoses of either spinal stenosis or arteriovenous malformation but did not have any malignancy or chronic inflammation.

In the patients' plasma, the researchers looked specifically at extracellular vesicles, which are small particles that are released by cells and carry material from those cells. They found that patients with GBM had significantly elevated levels of IL13Rα2 in their blood plasma compared to control patients and that the IL13Rα2 was likely concentrated on extracellular vesicles derived from tumor cells.

They also found that these IL13Rα2 levels in blood plasma were correlated with the IL13Rα2 levels in the patients' tumors. Their findings published in the *Journal of Neuro-Oncology*.

"The fact that we documented IL13Rα2 on tumor-derived extracellular vesicles and that we observed a correlation between plasma and tumor levels of IL13Rα2 suggests that plasma IL13Rα2 does indeed derive from GBM tumors," said Khristov. "This is important because previously it was difficult to tell if the IL13Rα2 in plasma came from the tumors, or if they came from the body's response to the tumors. Our findings suggest that IL13Rα2 does have utility as a biomarker for glioblastoma."

Connor noted that the finding is especially significant given that IL13Rα2 has been shown to have a patchy distribution in GBM tumors, raising the question of whether a needle biopsy or small sample of tumor tissue is representative of the tumor as a whole.

"Testing for IL13Rα2 circulating in plasma may provide an even better picture of the presence and extent of GBM than a tumor sample," said Connor. Additionally, he said, "the tumor-specific nature of IL13Rα2 implies that it can be used for tumor-targeted therapies without affecting

outside tissues."

Interestingly, the team found that elevated levels of IL13Rα2 in both plasma and tumors predicted longer overall survival. In fact, patients with high levels of plasma IL13Rα2 had a 6.5 month longer median overall survival compared to patients with low levels.

"It seems counterintuitive that high levels of plasma IL13Rα would confer a survival advantage since their presence indicates a tumor and, ultimately, we do not know why this is the case," said Khristov. "However, there is some evidence that increased IL13Rα2 is correlated increased fibrosis in the tumor, which indicates tissue healing. It's important for patients to know if they may have this survival advantage or not."

Zacharia noted that this work, and that of many other studies, relies on biological specimens, such as blood, tumor tissue and spinal fluid, from patients.

"Their generous and selfless gifts of these specimens to the Penn State Neuroscience Institute Biorepository make this work possible," he said, "and we are forever grateful to the patients and their families."

**More information:** Vladimir Khristov et al, Plasma IL13Rα2 as a novel liquid biopsy biomarker for glioblastoma, *Journal of Neuro-Oncology* (2022). DOI: 10.1007/s11060-022-04196-0

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