Classifying childhood brain cancers by immune response may improve diagnostics and treatments

by University of Pittsburgh

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Researchers and pediatric neurosurgeons at the University of Pittsburgh School of Medicine and UPMC Children's Hospital of Pittsburgh in USA, have developed a new way to profile brain cancers in children, paving the way for improved diagnostics and treatments.

In *Science Translational Medicine*, researchers describe a diagnostic platform that could classify brain tumors based on the body's cancer-fighting immune response. This approach, which is complementary to traditional microscopic and genetic cancer cell analyses, establishes an opportunity to tailor cancer therapies to each patient's unique immune response and harness the success of immunotherapies that revolutionized the treatment of childhood leukemias.

"Understanding how the repertoire of immune cells fits with the diverse landscape of brain cancer types can help us find new therapies in the future," said lead author Itay Raphael, Ph.D., research assistant professor of neurological surgery at Pitt.

Brain cancer is the second most common cancer in children after leukemia, and it is also the deadliest. This is due to a constellation of factors: brain tumors are diverse, resistant to treatments and often hard to access surgically.

On the other hand, the sharp reduction in deaths from leukemia over recent decades is due in part to the enormous success of immune-based therapies, which harness the body's intrinsic protective mechanisms by expanding the pool of cancer-fighting white blood cells called T cells.

T cells are precisely tuned to recognize molecules on the surface of cancer cells—called antigens—and use them as signals to attack and clear out tumor cells while leaving healthy cells intact. When T cells find a target on the tumor cell surface, they become activated and start rapidly doubling their numbers in a process called clonal expansion, aimed to clear the cancer.

Because of how varied brain tumors and their antigens are, understanding the tumor's molecular composition can help clinicians personalize each patient's treatment. Similarly, the new study's complementary approach can help pinpoint the best treatment option by identifying which T cell-surface receptors are most abundant in the environment surrounding the tumor.

"The success of T cell-based therapies for non-**brain tumors**, including childhood leukemias, suggests tremendous potential for brain cancers," said senior author Gary Kohanbash, Ph.D., assistant professor of neurological surgery at Pitt.

"Having access to an unprecedented dataset of pediatric tumors and new bioinformatic tools allowed us to investigate how T cell immune response and clonal expansion could be used as markers for treatment classification and prognosis independent of other diagnostic tools."

As part of the study, the researchers profiled nearly 1,000 pediatric brain tumor samples, which were collected through the Children's Brain Tumor Network (CBTN), a medical research consortium of 35 medical centers across the nation and globally. The study was the first to look at the T cell clonal repertoire and expansion in this sample group.

The group observed that very aggressive tumor types are associated with less T cell expansion than less aggressive ones, suggesting that clonality can inform patient outcomes across tumor types. On the other hand, studying T cell response can shed light on which antigens on the surface of cancer cells can be exploited therapeutically, offering avenues for the development of cancer-antigen peptide immunotherapy.

"Ultimately, we hope for a future where clonal T cell expansion is incorporated into pediatric cancer diagnosis," said co-author Ian Pollack, M.D., distinguished professor of neurological surgery at Pitt, and a founding institutional principal investigator of CBTN.

"UPMC Children's Hospital is committed to supporting brain tumor research and developing new life-saving treatments, and we think that this landmark study represents a foundational shift to how the field will be considering pediatric tumors in the future."

More information: Itay Raphael et al, The T cell receptor landscape of childhood brain tumors, *Science Translational Medicine* (2025). **DOI: 10.1126/scitranslmed.adp0675. www.science.org/doi/10.1126/scitranslmed.adp0675**

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