Researchers use immune system to attack glioblastoma

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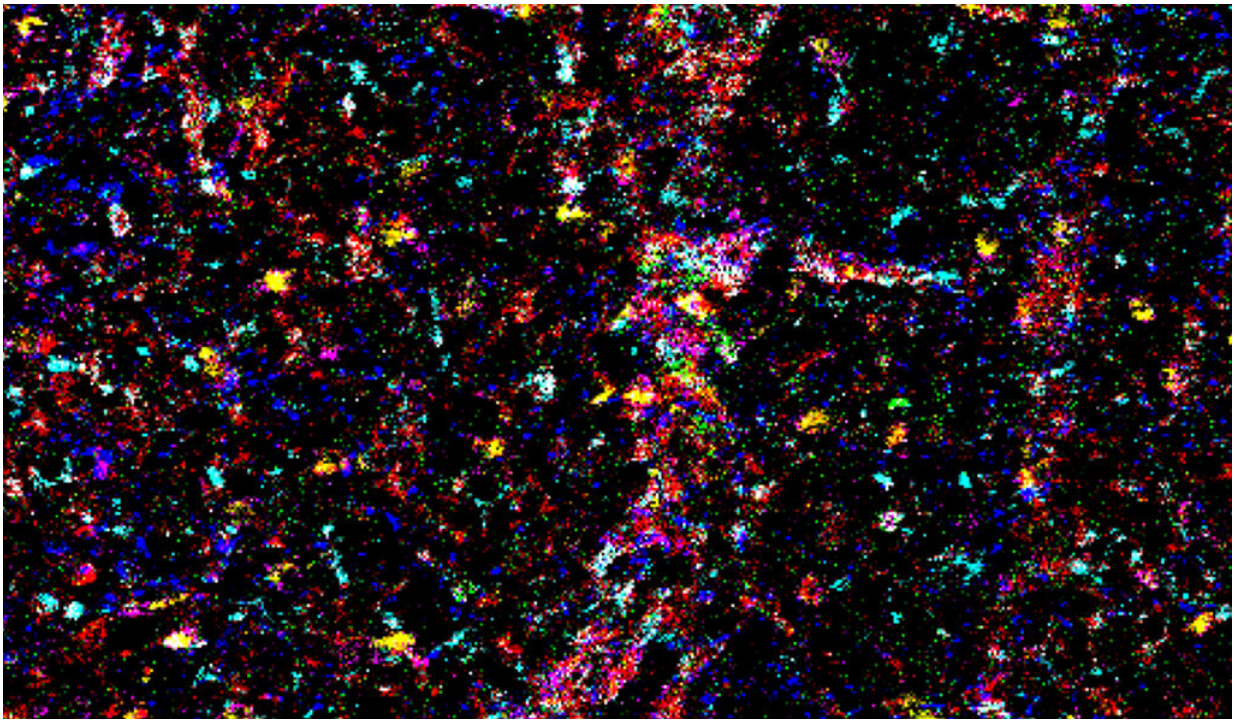

Multi-colored markers of the immune system are captured in glioblastoma tumors. Credit: Yale University

The Yale laboratory of Sidi Chen, assistant professor of genetics in the Systems Biology Institute and Yale Cancer Center, has developed advanced gene-editing and screening technology to find new targets for cancer immunotherapy.

In a new study published Sept. 23 in *Nature Biotechnology*, Chen and colleagues report that using T cells containing modifications of those gene targets reduced tumors in a mouse model of glioblastoma, a brain cancer that is especially difficult to treat.

The brain has a very limited immune system activity and therefore is not a particularly promising organ for immunotherapy, note the researchers. Chen's lab developed a sophisticated viral vector with an embedded transposon, or jumping gene, that facilitates the genetic screening capabilities of T cells.

Genomic screens of T cells uncovered one target, PDIA3, that when inhibited in T cells suppress glioblastoma tumor growth in mice. They also showed that knocking out PDIA3 in a specific type of T cells can enhance their cancer-killing properties in human glioblastoma cells.

Chen said similar techniques could be employed on different immune cells and other types of cancers that so far have been impervious to immunotherapy.

More information: Lupeng Ye et al. In vivo CRISPR screening in CD8 T cells with AAV–Sleeping Beauty hybrid vectors identifies membrane targets for improving immunotherapy for glioblastoma, *Nature Biotechnology* (2019). DOI: 10.1038/s41587-019-0246-4

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