Genetic mutations help brain tumors evade targeting by immunotherapy treatments

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Tumors of the brain and spinal cord, or gliomas, are among the most commonly occurring brain tumors. Although a majority of gliomas are classified as curable, these low-grade tumors have the potential to develop more aggressive traits and become resistant to tumor-targeting approaches, including immunotherapy.

In a study published this week in the *JCI*, Hideho Okada's lab at UCSF investigated whether acquired mutations in the enzyme isocitrate dehydrogenase (IDH), which are common in low-grade gliomas, help these tumors become resistant to immunotherapy.

In both human astrocytes and mouse models of glioma, the IDH mutations impaired immune responses in the tumor environment by reducing the recruitment of T cells. Thus, the IDH mutations may help gliomas avoid anti-tumor targeting by therapies that rely on immune system activation.

Importantly, inhibition of the mutant IDH enzyme enhanced the efficacy of a vaccine-based immunotherapy treatment in glioma-bearing mice. This finding suggests that combinatorial therapies may be able to counteract the effects of the IDH mutation to improve clinical responses to immunotherapy treatments for glioma.

More information: Gary Kohanbash et al, Isocitrate dehydrogenase mutations suppress STAT1 and CD8+ T cell accumulation in gliomas, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI90644