

Scientists Discover a Deadly Brain Cancer's Hidden Weakness

Common and cheap epilepsy drug stops tumor growth in mice

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The difficult-to-treat brain cancer glioblastoma steals a person's mental faculties as it spreads, yet the tumor's insidious ability to infiltrate neighboring networks in the brain could also prove its undoing.

Scientists at UC San Francisco have discovered that neural activity in these deadly tumors can restructure connections in surrounding brain tissue, causing the cognitive decline associated with the disease, and that the drug gabapentin, commonly used to prevent seizures, could block this growth-causing activity in mice with glioblastoma.

The findings, appearing in [Nature](#), provide a hopeful new direction for research on a disease that has defied even the most modern and sophisticated types of cancer drugs.

"Glioblastoma needs a win," said neurosurgeon [Shawn Hervey-Jumper](#), MD, who led the study along with postdoctoral scholar [Saritha Krishna](#), PhD. "This study opens the door to a whole world of treatment possibilities for these patients and a new way of thinking about brain cancer."

When Hervey-Jumper was beginning his study, scientists had recently discovered that brain tumors are fueled by a positive-feedback loop. It begins when cancer cells produce substances that can act as neurotransmitters. This "extra" supply of neurotransmitters spurs neurons to become hyperactive, which in turn stimulates the growth of the cancer cells.

Building on earlier studies done on mice and brain organoids (small bundles of neurons derived from human stem cells grown in petri dishes), Hervey-Jumper focused on what the feedback loop meant for human behavior and cognition in brain cancer.

The team recruited volunteers awaiting surgery for glioblastoma whose tumors had infiltrated the brain region controlling speech. Just before operating on the tumor, Hervey-Jumper placed a grid of tiny electrodes on the surface of the speech region, showed the volunteers pictures and asked them to name what they saw.

The research team then compared the results with normal-appearing non-tumor regions of the

brain from the same participants. They found that the tumor-infiltrated brain regions used a broader neural network of brain area in the effort to identify what they were seeing.

Cancer as a Conversation Between Cells

Hervey-Jumper attributes this to degradation of information-processing power in that region of the brain. He likens it to an orchestra where it's the musicians playing in synchrony that makes the music work.

"If you lose the cellos and the woodwinds, the remaining players just can't carry the piece the way they could otherwise," he said. The brain cells bound up in the tumor are so damaged that others must be recruited from farther out to perform the tasks that used to be controlled by a smaller area.

The study shows that it's this interaction between cells that causes the cognitive decline associated with brain cancer, rather than inflammation and pressure from tumor growth, as scientists had thought.

"A brain tumor isn't just sitting there dying," said Hervey-Jumper. "It's being regulated by the nervous system. It's having conversations with the cells around it and actively integrating into brain circuits, remodeling the way they behave."

We Haven't Thought About Cancer in This Way

Now, the researchers knew that the tumors were taking advantage of the brain's networks. So, they turned to gabapentin, which controls seizures by tamping down excess electrical activity in the brain, testing it in mice engrafted with human glioblastoma cells.

"Gabapentin actually kept the tumor from expanding," said Krishna. "This makes us hopeful that combining gabapentin with other glioblastoma therapies could stave off some of the cognitive decline we see in patients and perhaps extend their lives."

The findings will likely translate to other neural cancers, such as those of the spine, and may help explain why the brain is the first site of metastasis in many cancers.

Hervey-Jumper said the study encourages cancer specialists to consider communication networks between cells, like the positive-feedback loop in glioblastoma, as potential targets for treatments, along with genetic and immunological approaches.

"We haven't thought about cancers in this way before," he said. "The idea that there's conversation between cancer cells and healthy brain cells is something of a paradigm shift."

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