

Memorial Sloan Kettering Cancer Center

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#### On Cancer

# Researchers Discover Stem Cells That May Drive Aggressive Behavior in Glioblastoma

By Julie Grisham, Thursday, February 20, 2020



#### VIDEO 00:24

This video shows the division in cells within organoid-like structures. A cell with a jumping nucleus is highlighted in yellow, and the cell bodies

are tracked by a yellow arrow. The cells dividing in place with and without long processes, or tails, are indicated in green and blue. Credit: Wang et al./Stem Cell Reports

Video Details >

### Summary

Radial glia cells are a type of stem cell important for building the brain during fetal development. They appear to be very similar to cells found in brain tumors taken from patients.

For the past several years, researchers have recognized that the brain tumor **glioblastoma** is powered by cancer cells called tumor stem cells. Figuring out how tumor stem cells function is important because their ability to survive likely explains why glioblastoma is so hard to treat.

A multicenter team led by scientists at Memorial Sloan Kettering recently reported discovering a likely identity for these tumor stem cells. The leading contenders are called radial glia cells. Radial glia cells play a key role in building fetal brains but were previously thought to disappear after birth. The **findings** were published January 30 in *Stem Cell Reports*.

"We can't say with certainty that radial glia cells are the same as tumor stem cells, but they are now very high on the candidate list," says physician-scientist **Viviane Tabar**, Chair of MSK's Department of Neurosurgery, who was the study's senior author. "The look and behavior of brain stem cells in the developing brain and the tumor stem cells that we have identified are so similar to each other. This is the first time we've seen these features in cells from a human tumor."

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Viviane Tabar physician-scientist

## An Unexpected Finding

The first clues about the identity of these tumor stem cells were uncovered by **Rong Wang**, a research associate in **Dr. Tabar's lab**. Dr. Wang was studying tumor tissue that had been removed from patients. She was using the tissue to grow organoid-like structures in petri dishes. Organoids are miniature organs that look and behave very much like their full-size counterparts. They are an increasingly important tool across cancer research for studying tumor development as well as for testing drugs.

Dr. Wang noticed that some cells in the organoids had an unusual shape and exhibited unusual behavior. They had very long processes, or tails, and when they divided, their daughter cells had the same shape. Additionally, when these unusual cells divided, their nuclei jumped over long distances. Dr. Wang recognized that these features are also seen in radial glia.

Further analysis confirmed that these unusual cells also were present in the tissue taken from patients: The team studied samples from dozens of tumors. "Radial glia cells previously were not thought to persist in adulthood," Dr. Tabar explains. "If glioblastoma tumors arise from them, that may mean that humans retain some radial glia cells in our brains as adults. The other possibility is that the genetic changes in the cancer turn some of the brain cells back into cells that look very much like radial glia cells."

### A Valuable Collaboration



#### VIDEO 00:03

This video shows a mother cell with a long process dividing into two daughter cells. One daughter cell retains the long process, or tail, and the other daughter cell later grows one. Credit: Wang et al./Stem Cell Reports

#### Video Details >

To learn more about these cells, the Tabar lab collaborated with **Dana Pe'er**, Chair of the Sloan Kettering Institute's **Computational** 

and Systems Biology Program, as well as with computational biologists at the Wellcome Sanger Institute in the United Kingdom.

They performed studies called single-cell RNA sequencing to look at which genes were expressed, or turned on, in individual cells. The patterns of gene expression observed in the samples taken from patient tumors and those grown in the lab were very similar to what's seen in radial glia cells from embryos.

"This was a very challenging study to pull together. We took advantage of MSK's wide range of tumors and access to fresh surgical tissue, as well as the resources of the Computational and Systems Biology Program here," Dr. Tabar says.

## A Potential Explanation for a Cancer's Aggressive Behavior

Additional research is needed to confirm whether these cells are indeed the same. Another focus of future work will be the role of inflammation. "Inflammation may help bring radial glia-like cancer cells out of dormancy," Dr. Tabar explains. "This could explain why inflammation can sometimes lead to the worsening of brain tumors."

Dr. Tabar hopes that the publication of the findings will encourage further analysis and that "as technology advances, there will be easier ways to identify and study these cells," she concludes.

MSK's Brain Tumor Center brings together researchers and clinicians for the scientific discovery and development of truly

effective brain tumor therapies. Learn more.

This study was funded by National Institutes of Health grants (RO1 CA208405 and P30 CA 008748), the W. M. Keck Foundation, the Scientific Research Fund of Hunan Provincial Education Department, the Chinese Scholarship Council, the Chan Zuckerberg Initiative, the Wellcome Trust, and the New York Stem Cell Foundation.

