Genetically diverse cancer cells key to brain tumor resistance

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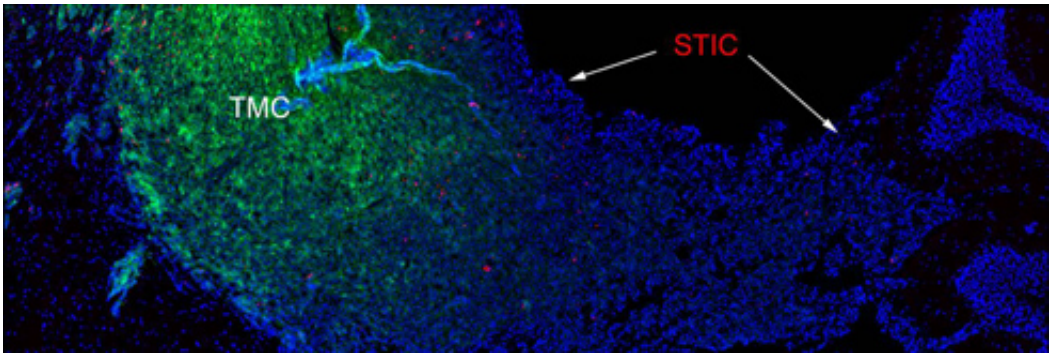

In this image of mouse brain tissue containing human brain tumor cells, red dye shows invasive, stem-like cells that carry two copies of chromosome 7, while green dye depicts non-stem-like cells that carry three copies of the problematic chromosome. The cells can change into one another by adding or deleting copies of of chromosome 7. Mathematical modeling suggested the involvement of chromosome instability helps tumor cells fend off treatment. Credit: Yi-Hong Zhou

(Medical Xpress)—For a cancer cell, it pays to have a group of eccentric friends.

Like X-Men characters, a group of cancer cells with diverse physical traits is safer, because it takes different strategies to kill each member.

The more diverse the group, the better the chances are for individual cells to survive and join forces as a cohesive tumor.

A multi-university research team, including researchers with the Fralin Life Science Institute at Virginia Tech, discovered that the unique physical differences among brain tumor cells were because of chromosomal abnormalities.

Understanding the biology behind diverse cell production in cancerous brain tumors may contribute to knowledge for better treatments, according to Jianhua Xing, an associate professor of biological sciences in the College of Science and a Fralin Life Science Institute affiliate.

Xing, with Yi-Hong Zhou, an assistant professor of neurological surgery in the School of Medicine at the University of California-Irvine, concluded that tumor cells with genes that have varying numbers of copies of chromosome 7 leads to cell diversity and survival of brain tumors.

Cancer cells bypass the surveillance systems that limit the number of copies of chromosomes in normal cells to produce an abnormal number of chromosomes.

Zhou, whose research program is devoted to developing novel drugs to treat brain cancer, led the experimental portion of the project, and Xing, an expert in mathematical modeling of biological systems, analyzed the results.

The discovery was published in November in *PLOS One*.

"Cancer is a biological entity that continues to evolve, where the cancer ecosystem, with its dynamic interactions among cancer cells and normal cells, selects the best cells to survive," Zhou said. "Our findings presented only one aspect, among many others, that cancer cells use to change, with mis-segregation of chromosomes clearly being the most powerful one. By applying this concept of cancer survivability, a

rewarding therapeutic approach might be developed through reducing random or chance development of tumor cells, which we are currently investigating."

The project involved 21 members from the University of California-Irvine, Virginia Tech, the Veterans Affairs Medical Center at Long Beach, the University of Arkansas for Medical Sciences academic health center, Ziren Research LLC, and the National Engineering Center for Biochip at Shanghai in China.

Key work was done by Yuanjie Hu, a graduate student at the University of California-Irvine; Hang Zhang of Hebei, China, a graduate student at Virginia Tech; Xiao-Jun Tian, a postdoctoral associate at Virginia Tech; and two research specialists—Ning Ru of the University of California-Irvine and Neil T. Hoa of the Veterans Affairs Medical Center at Long Beach.

"While it's unlikely that this finding is the only mechanism that controls cancer plasticity, it is a piece of the puzzle," said Xing. "Cancer cells are, unfortunately, very smart. That is why the battle against cancer is so difficult."

More information: Hu Y, Ru N, Xiao H, Chaturbedi A, Hoa NT, et al. (2013) "Tumor-Specific Chromosome Mis-Segregation Controls Cancer Plasticity by Maintaining Tumor Heterogeneity." *PLoS ONE* 8(11): e80898. DOI: 10.1371/journal.pone.0080898

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