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Brain cancer self-organizes into streams, swirls, and spheres

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Commonly, we think of cancer as anarchy, a leaderless mob of deranged cells, storming through the body. Pedro Lowenstein, Sebastien Motsch, and colleagues at the University of Michigan and University of Arizona think that cancer is highly organized—self-organized. In brain cancer, the Michigan and Arizona researchers report that glioma cells build tumors by self-organizing into streams,10-20 cells wide, that obey a mathematically predicted pattern for autonomous agents flowing together. These streams drag along slower gliomas, may block entry of immune cells, and swirl around a central axis containing glioma stem cells that feed the tumor's growth. The researchers will present their new work on tumor self-organization on Monday, December 14 at the 2015 Annual Meeting of the American Society for Cell Biology in San Diego, CA.

Lowenstein and Motsch mapped out this dynamic picture of glioma self-organization by building and comparing two model systems, one biological and one mathematical. The living model system was built in vivo using mouse and human glioma cells genetically tailored to express a deadly package of genes known to spur development and progression of brain tumors. The observed movement, distribution, and invasive nature of the resulting streams of elliptically shaped glioma cells were predicted by their mathematical model, they report. Assuming that the glioma cells were independent agents, the mathematical model took into account adhesion and repulsion dynamics between tumor cells. The results showed unmistakable signs of non-random, self-organization of brain tumors, say Lowenstein and Motsch.

Most striking, the presence of self-organizing structures was not related to any specific cancer mutation. These swirls eddied around cores of glioma stem cells that Lowenstein and Motsch describe as possible nucleating centers for brain tumor growth. The in vivo model also produced glioma cells organized as individual spheres, including some that slipped out of the tumor and set themselves adrift in the cerebrospinal fluid that surrounds the brain's ventricles, and may mediate tumor dispersion throughout the brain.

All this evident self-organization opens an exciting novel insight into brain cancer, say Lowenstein and Motsch, and makes disrupting tumor self-organization itself a new target for brain cancer treatment.

More information: Streams, swirls, and neurospheres: in vivo self-organization of brain tumors revealed by mathematical and biological modeling, ASCB 2015.

Provided by American Society for Cell Biology