Deconstructing glioblastoma complexity reveals its pattern of development

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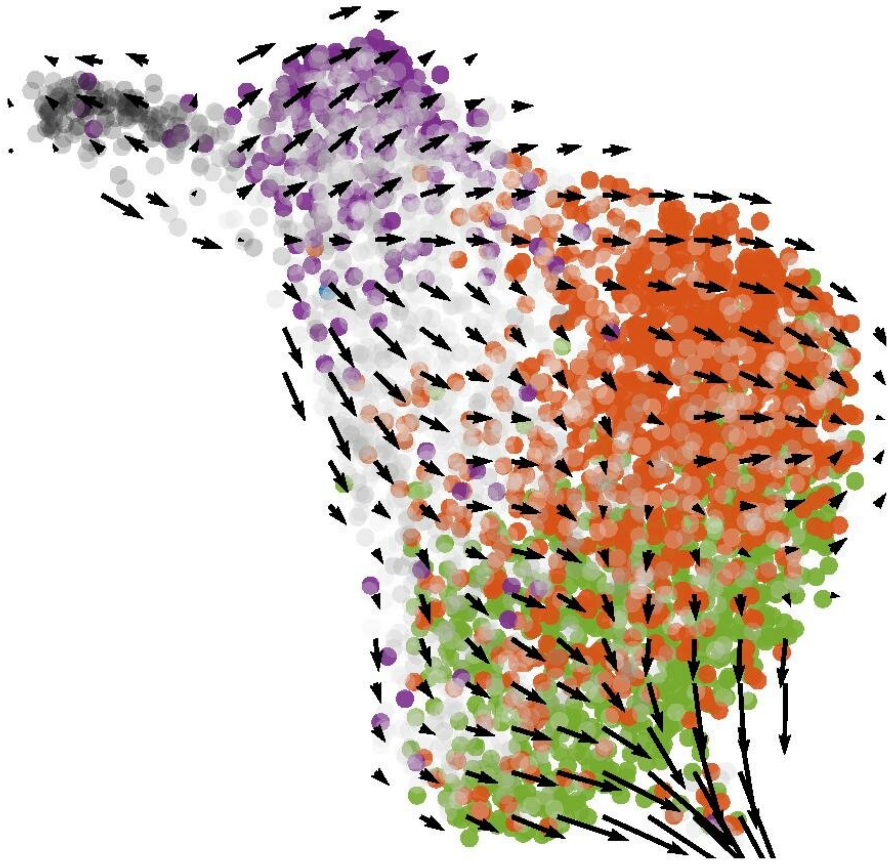

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Brain cancers have long been thought of as being resistant to treatments because of the presence of multiple types of cancer cells within each tumor. A new study uncovers a cancer cell hierarchy that originates from a single cancer cell type, which can be targeted to slow cancer growth.

The research was led by Dr. Kevin Petrecca, a neurosurgeon and brain cancer researcher at The Neuro (Montreal Neurological Institute and Hospital) of McGill University, part of the McGill University Health Centre.

The study, which is the largest ever single cancer cell RNA sequencing project, included 55,000 glioblastoma cells and 20,000 normal brain cells. The team found that there are five main cancer cell types within each tumor, and these cancer cell types are similar to the cell types that are in the normal human brain.

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The team found that progenitor GSCs divided much more than the mature cancer cells and make up the vast majority of dividing cells in the tumour, despite making up a relatively small proportion of the total tumor. These rapidly dividing cells are the earliest detectable cancer cells in the hierarchy and so make a promising target for therapy.

After identifying molecular vulnerabilities in progenitor GSCs, the researchers then targeted these and found that progenitor GSC survival and proliferation decreased as a result. In preclinical disease models, this reduced tumour growth and increased survival.

"Our work has gone a long way to resolve the complexity of glioblastoma heterogeneity, and provides a new framework to reconsider the nature of glioblastoma," says Dr. Petrecca "As part of this work, our study also shows, in contrast to decades long dogma, that glioblastoma stem cells are the most rapidly dividing cancer cells in the tumor, and we identified new ways to target these cells. There is still much work to be done. Understanding how these cancer cells interact with the cancer microenvironment is not well understood in this disease, but this study serves as a good starting point to begin to understand how glioblastoma originates and evolves prior to treatments."

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