New findings about the development of brain tumors could lead to more effective treatment

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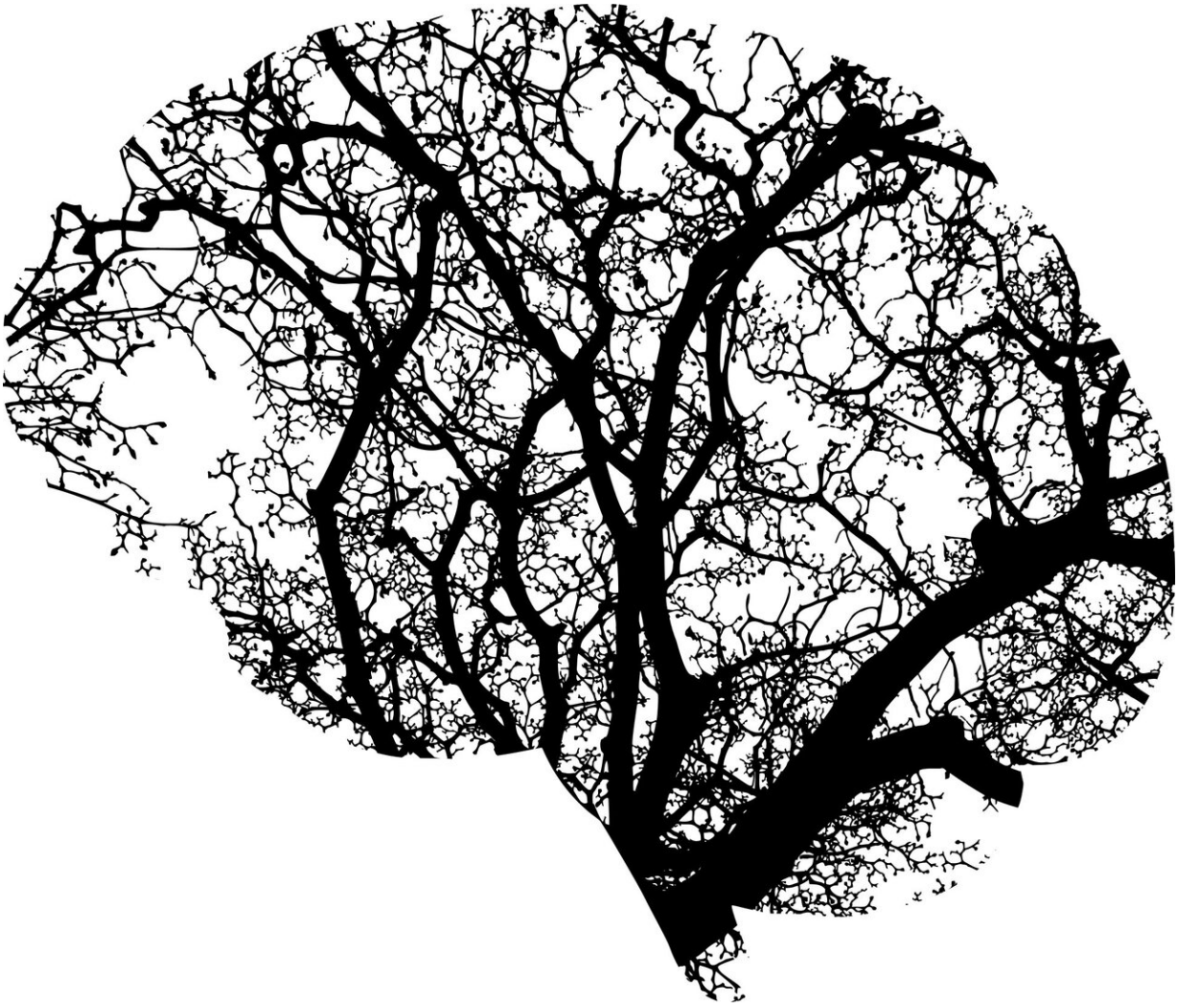

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For the first time, an international study team with substantial participation from researchers from the Comprehensive Cancer Center (CCC) of MedUni Vienna and Vienna University Hospital, has identified the molecular differences between individual tumor cells in ependymomas, which are an aggressive type of brain tumor. The researchers further demonstrate that ependymomas develop in a specific stem cell niche of the brain. These findings could explain why some ependymomas behave very aggressively and are difficult to treat, while others are associated with a better prognosis. The therapeutic approaches derived from the findings have proven highly promising in preliminary laboratory tests. The paper has now been published in the leading journal *Cancer Cell*.

Ependymomas are rare brain tumors that can occur in children and adults alike. Moreover, this group of tumors is heterogeneous and it has not been known until now why some have a good prognosis and some follow an extremely aggressive course, or why pediatric ependymomas are frequently associated with a poor prognosis.

The very latest analytical tools

The recently published study used cutting-edge methods, such as single cell sequencing, to conduct genome-wide analysis of individual tumor cells and to describe their molecular biological characteristics. The group found that ependymomas are very heterogeneous and consist of many cells with different characteristics, which complicates their treatment and might be the reason for chemotherapy resistance. In the course of their study, the research team examined both tumors with good and bad prognosis. A large proportion of the patients whose tumors were studied were recruited into the study at the MedUni Vienna (20 out of 28).

One of the important findings is that ependymoma cells develop from a specific stem cell niche of the brain. Hence, they often exhibit stem cell

characteristics. Stem cells have the ability to replace other cells in the body and to mature into body cells with different functions (e.g., nerve cells). This process is called differentiation. While they are still immature, that is to say undifferentiated, they are essentially capable of unlimited proliferation. If the cells maintain their stem cell characteristics, particularly aggressive forms of cancer develop.

Johannes Gojo, consultant and researcher at the Department of Pediatrics and Adolescent Medicine of MedUni Vienna and Vienna University Hospital and at MedUni Vienna's Institute of Cancer Research, member of the CCC and of the Comprehensive Center for Pediatrics (CCP) of MedUni Vienna and Vienna University Hospital and lead author of the study says, "We saw that the individual cells of ependymomas go through different stages of development inside the tumor. Those tumors with an aggressive course have many immature cells, so that they are very similar to stem cells. Tumors in which a majority of the cells were in a mature state, had a more favorable prognosis. This finding could provide us with a starting point for new treatment strategies."

It also explains why ependymomas often behave more aggressively in children than in adults: in children, the proportion of undifferentiated, stem-cell-like ependymoma cells is higher than in adults.

Gojo says, "Furthermore, we were able to obtain accurate information about the molecular biological characteristics of tumor cells, which likewise enables us to derive new therapeutic approaches. Initial tests in this direction are highly promising but still require more detailed investigation."

More information: Johannes Gojo et al. Single-Cell RNA-Seq Reveals Cellular Hierarchies and Impaired Developmental Trajectories in Pediatric Ependymoma, *Cancer Cell* (2020). DOI:

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