Children's brain tumors more diverse than previously believed

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Paediatric brain tumours preserve specific characteristics of the normal cells from which they originate – a previously unknown circumstance with ramifications for how tumour cells respond to treatment. This has been shown by Uppsala researcher Fredrik Swartling together with colleagues in the U.S., Canada and England in a study that was published today in the distinguished journal *Cancer Cell*.

Every year, 80-90 children in Sweden are afflicted with brain tumours, a serious form of paediatric cancer. Today, three of four children who receive treatment survive.

The discovery improves the prospects for finding more effective treatments for forms of paediatric cancer that are currently very difficult to cure and has great significance for understanding how brain tumours arise. The next step is to carry out the clinical analyses necessary for developing drugs that target specific types of brain tumours.

Trials were carried out using immature cells, or stem cells, from such regions of the brain as the cerebellum, cerebrum and brain stem. The stem cells were then compared with tumour cells from more than 100 patients. Cellular origin showed itself to be at least as important a determinant of tumour malignancy as the genetic mutations underlying the transformation of normal cells to tumour cells. The point in time at which tumours arose was also of great relevance to the effectiveness of treatment.

"We can't focus exclusively on mutated genes when looking at cancer," says Fredrik Swartling, who directed the study jointly with paediatric neurologist William Weiss, who works at the University of California children's hospital and brain tumour research center in San Francisco, California, in the U.S. "The status of the cells of origin giving rise to cancer is at least as important from a treatment standpoint. Our study shows that tumours contain markers for these cells of origin."

Brain tumours most often arise on account of accidental genetic mutations. One gene that mutates readily and is well-represented in paediatric brain tumours is the MYCN cancer gene. Previous research has proposed that patients with high levels of a specific cancer gene like MYCN should be treated in the same way. The current study shows that this is not the case.

"The tumours are more diverse that we believed," Fredrik Swartling says. "It is very important, even for patients who exhibit the exact same mutation of a cancer gene, whether their tumours arose in the cerebellum, cerebrum or brain stem and whether these tumours arose during fetal stages or following birth."

The researchers showed in the study that normal stem cells are transformed into brain tumour cells in vitro following introduction of the MYCN cancer gene to the cells. Stem cells from an early fetal stage and from a later life juncture were both transformed into tumour cells. The effectiveness of treatment differed, despite the fact that the same cancer gene had caused the tumours in each case.

That tumours reflect their origins makes it relatively simple to determine the origin of the cancer represented in a tumour biopsy from a patient. The challenge ahead will be to identify reliable markers for tumour origin to enable better judgement about treatment options and ensure the effectiveness of treatment in diverse cases.

"The goal is to develop a range of different treatments for patients of different types," Fredrik Swartling says. "It may take some time before such treatments are available at hospitals, but clinical trials involving drugs similar to those used in the study are already under way, and we are keeping our fingers crossed that the drugs will work as anticipated."

More information: www.cell.com/cancer-cell

Provided by Uppsala University