Brain tumors in children: Cancer cells become less aggressive as they migrate within the tumor, finds study

January 8 2024

MRI image: In so-called medulloblastoma with extensive nodularity (MBEN), small tissue chambers are delimited within the tumor and are connected in a grape-like manner. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-023-44117-x

Certain brain tumors in small children contain cells that develop very similarly to normal brain cells and others that have already developed malignantly, depending on where they are located within the tumor.

By analyzing individual cells, a team of researchers from the Hopp Children's Cancer Center Heidelberg (KiTZ), the German Cancer Research Center (DKFZ), and Heidelberg University Hospital (UKHD) were able to characterize the genetic programs of the individual cells in detail and identify their developmental pathway within the tumor.

The study is published in the journal *Nature Communications*.

Medulloblastoma is among the most common solid tumors in children and the most common malignant brain tumor in children. The tumor grows in the cerebellum and can damage vital brain centers as it grows.

Based on tissue characteristics and genetic criteria, medulloblastomas are now divided into different risk groups, which can take a completely different course. While certain subtypes progress aggressively and form metastases, there are other forms that can usually be cured with an intensive combination therapy of surgery, chemotherapy, and radiotherapy.

A team of researchers has now used a novel method to investigate what

directs certain tumors in a more benign or malignant direction at the cellular level.

A certain type of medulloblastoma, which is characterized by its good chances of recovery and at the same time by the special structural properties of its tissue, served as a model for them: in so-called medulloblastoma with extensive nodularity (MBEN), small tissue chambers are delimited within the tumor, which are connected in a grape-like manner.

The study showed that tumor cells located in these nodules were no longer actively dividing, and their genetic program was similar to that of mature brain cells.

In the intermediate areas, however, the scientists identified different cell types: In addition to immune and connective tissue cells, there were also significantly more aggressive tumor cells that continued to divide uncontrollably and whose genetic program was more similar to those of fast-growing medulloblastomas and immature nerve cells.

However, during their migration into the nodes, the cancer cells matured back into nerve-like cells and no longer divided.

Kristian Pajtler, a pediatric oncologist at KiTZ, DKFZ, and UKHD and head of the study, explains the results as follows, "In some childhood tumors, the normal development process is blocked. The cancer cells thus become similar to immature precursor cells, which remain active in division due to a specific genetic program."

"In MBEN tumors, this apparently only works partially and many of the cells then go through the halfway normal development process of a cerebellar cell and stop dividing. This would also explain the mostly favorable course of this type of tumor."

For their analyses, the team dissected the tumors of nine young MBEN patients into their individual cellular components and analyzed the genetic program of the individual cells. Using a bioinformatic method, they could reconstruct where exactly these cells were located within the tumor.

The method, which was used in collaboration with Karsten Rippe's department at DKFZ, is of particular importance for medulloblastoma research, explains one of the two lead authors of the study, David Ghasemi, physician and scientist at KiTZ, UKHD and DKFZ.

"Until now, it has never been possible to develop laboratory models for this type of medulloblastoma. Only with this method was it possible to localize the individual cell types within the tumor and to understand how the various areas within the tumor differ from each other."

Blocking the maturation process is an important therapeutic tool that is already being researched in order to avert malignant progression in children and steer the cancer cells back in a benign direction.

"It is possible that MBEN tumors only need a little push here," says Kristian Pajtler. "Because even if most children with an MBEN tumor can be cured by surgery and, if necessary, further therapies, these are very intensive treatments for small children, which are often associated with severe, lifelong side effects."

More information: David R. Ghasemi et al, Compartments in medulloblastoma with extensive nodularity are connected through differentiation along the granular precursor lineage, *Nature Communications* (2024). DOI: 10.1038/s41467-023-44117-x

Provided by German Cancer Research Center