Medical Xpress

Neural stem cells attack glioblastoma cells

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In their latest research, scientists of the Max Delbruck Center for Molecular Medicine (MDC) Berlin-Buch, Germany, have demonstrated how the brain's own stem cells and precursor cells control the growth of glioblastomas. Of all brain tumors, glioblastomas are among the most common and most aggressive. Dr. Sridhar Reddy Chirasani, Professor Helmut Kettenmann and Dr. Rainer Glass have now shown in cell culture and mouse model experiments just how the body's own protective mechanism they identified in an earlier study, actually works.

Glioblastomas are brain tumors that are most common in adults in their mid-fifties or early sixties. The causes for developing the disease are not yet known. Researchers assume that misdirected neural stem cells / precursor cells mutate into cancer cells and can form glioblastomas.

Several years ago the MDC and Charité researchers were able to show that normal stem cell/ precursor cells of the brain attack the tumor. Apparently, the tumor itself entices these stem cells to migrate over relatively long distances from the stem cell niches of the brain. Why this is so is unclear. Moreover, the researchers still do not know which substance attract the stem cells to the tumor. However, now they have discovered how the stem cells keep the tumor in check.

The scientists showed that the neural stem cells and neural precursor cells release a protein that belongs to the family of the BMP proteins (bone morphogenetic protein). This protein received its name for its ability to induce bone and cartilage tissue formation, the first characteristic that was known about it. However, BMP is active in the

entire organism - even in the brain.

Neural stem cells release BMP-7 in the brain in the vicinity of the glioblastoma cells. The protein influences a small population of cancer cells, the so-called tumor stem cells. The current consensus of researchers is that these tumor stem cells are the actual cause for the continuous tumor self-renewal in the brain. A small quantity of these cells is sufficient to form new tumors again even after surgery. BMP-7 induces signaling in the tumor stem cells, causing them to differentiate. This means that they are no longer tumor stem cells.

However, the activity of stem cells in the brain and thus of the body's own protective mechanism against glioblastomas diminishes with increasing age. This could explain why the tumors usually develop in older adults and not in children and young people.

The discovery of the tumor stem cells has led to new concepts in the therapy of glioblastomas. "Normal cancer cells" can be destroyed using conventional therapies (surgery, radiation, chemotherapy), which are seldom successful in tumor stem cells. The aim is therefore to develop therapy concepts to destroy these tumor stem cells. The findings from the mouse experiments of the researchers in Berlin could point to a new approach: reprogramming tumor stem cells into less harmful cells, which could then be destroyed with a therapy.

More information: Bone morphogenetic protein-7 release from endogenous neural precursor cells suppresses the tumourigenicity of stem-like glioblastoma cells, *Brain*, July 6, 2010, doi:10.1093/brain/awq128

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