Brain cancer: Study focuses on forgotten cells

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Glioblastoma is a guileful enemy. While most of the brain tumor can often be removed surgically, in virtually every case the tumor reappears. One reason for this is that sporadic, infiltrative tumor cells will remain in the brain even after most careful surgery. Researchers at the University of Bonn have now subjected these 'forgotten' cells to closer scrutiny for the first time. While doing this, they were able to show that many of the fundamental properties of these tumor cells were substantially different from the cells in the midst of the tumor mass. The findings could offer an opportunity to explain why radiation or chemotherapy cannot entirely prevent this deadly disease to reoccur. The study will now be published in the *Annals of Neurology*.

Patients with a glioblastoma generally undergo surgery as quickly as possible. During the process, starting from the center of the tumor, the neurosurgeon gently removes diseased tissue until the tumor appears to be removed entirely. Unfortunately, the cancer cells are hard to get hold of. They often migrate far into adjacent, healthy brain tissue. That is why there are basically always some malignant cells remaining after every surgery, from which then new tumors are formed.

The Bonn scientists have now taken a closer look at these residual cells for the first time.

Apart from being provided with samples from the main mass of the tumor for their research, the scientists were also provided with small diagnostic samples from adjacent tissue from 33 patients by the

University of Bonn Department of Neurosurgery. 'From the small samples we then extracted and enriched the few tumor cells that would have normally remained in the patient.' Professor Björn Scheffler from the Institute of Reconstructive Neurobiology explains.

Astonishing discovery

While examining these residual cells, the researchers made an astonishing discovery. 'The cancer cells in the vicinity of the tumor have different properties compared to those from the center of the tumor,' Björn Scheffler's colleague Dr. Martin Glas from the Department of Neurology's Clinical Neurooncology Unit explains. 'For instance, they are more mobile, they form other receptors, they react differently to radiation therapy or chemotherapeutic substances.'

These findings may offer an intriguing explanation for the yet meager therapeutic success against the most frequent malignant brain cancer. Although there has been intensive research on this case for more than half a century, a cure is currently not available. On average, glioblastoma patients survive for only about 15 months from the time of initial diagnosis. Although radiation and chemotherapy both are aimed for complete destruction of residual tumor cells after surgery, these weapons apparently remain blunt. There is no other way of explaining that basically every glioblastoma patient will experience a relapse.

The new results could help medicine to upgrade its weapons arsenal against the remaining cancer cells. Up to now, therapies were only tested on the extracted tumor tissue. But even if medication could destroy the actual tumor, this does not have to be true for the malignant residual cells. 'At least, it is worth keeping an eye on this aspect,' Martin Glas and Björn Scheffler say. But at the same time they warn against exaggerated hopes. 'We still have a lot of work to do. For new approaches to therapy we first need to understand the biology of these cells even better.'

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