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A tumor where the soul resides**World Brain Tumor Day: Interview with Professor Wolfgang Wick, head of the Clinical Cooperation Unit “Neurooncology” of the German Cancer Research Center (DKFZ) and Managing Director of the Neurology Department at Heidelberg University Hospital.**

Professor Wick, many people find brain tumors particularly scary. Why is that?

The brain is considered to be the place where the soul resides, it constitutes our personality. Patients who have been diagnosed with a brain tumor are afraid to experience personality changes. Or they fear to be perceived as having a changed personality. However, these changes occur only in very rare cases.

There are numerous types of brain tumor. How do these diseases differ from one another?

First of all: More than half of all tumors in the brain are not brain tumors in the true sense of the meaning but rather metastatic cancer that has spread to the brain from other parts of the body. Brain metastases are treated in completely different ways than “genuine” brain tumors. Of the true brain tumors, another half of the cases are usually benign tumors of the membranes surrounding the brain. These so-called meningiomas can be cured by surgery in most cases. The other half are the difficult cases: diffusely growing gliomas, mostly glioblastomas, which are extremely aggressive.

What makes glioblastomas so dangerous?

Glioblastomas have many characteristics that make it really hard to fight them successfully. First, they pervade the brain in a very diffuse manner so that they are impossible to remove completely by surgery or to irradiate precisely. Our own current results have revealed that the cancer cells even form a network structure that links them among each other throughout the brain. We therefore think that a glioblastoma infiltrates the whole central nervous system at the microscopic level. The tumor that we can see on the X-ray image is just the tip of the iceberg!

In addition: Glioblastoma cells are extremely resistant against all types of treatment and they are very varied at the molecular level. In addition, they have skilful ways of exploiting surrounding healthy tissue for their growth.

That sounds as if there is little we can do so far to combat this disease?

Surgical removal of the visible tumor without causing damage, radiotherapy, and a drug called temozolomid – these are the standard therapy options at present. Even after receiving these therapies, an average of much less than ten percent of glioblastoma patients survives the first five years after diagnosis.

But this is a mean value. Major advances in molecular tumor diagnostics, which have been achieved particularly in Heidelberg at the DKFZ and the NCT, have enabled us to categorize many patients into molecularly defined subgroups that are much better treatable. In these cases, we know the altered cell structures that fuel tumor growth. We are already able, or will be in the future, to precisely attack these structures with novel, targeted drugs that are often substantially more effective than standard therapies. Patients who have received this

treatment often have a much more favorable prognosis and in some cases survive without symptoms for many years.

To which patients can you offer a molecular tumor analysis?

We offer a comprehensive molecular examination already when the cancer is first diagnosed to glioblastoma patients at all partner sites of the German Cancer Consortium (DKTK). As molecular diagnostics is becoming more common and also with the enormous progress in imaging technology, we expect that we will be able to categorize significantly more tumors more precisely in the future. This will enable us to help more patients more effectively. Even though we will not overcome glioblastoma altogether this way, individual patients will benefit from this approach.

In Heidelberg, a lot of research on brain cancer is being done. Is there a prospect of any novel treatments?

We are currently testing, mainly in the laboratory, a combination of proton precision therapy with targeted drugs. We expect that glioblastomas will respond better to it than to conventional radiotherapy. I also think that the much discussed methods to activate the immune system against the tumor are promising.

In addition, we have seen a number of exciting and promising developments of completely new treatment approaches in recent years. For example, the agent APG101 from the DKFZ spin-off company Apogenix is already at an advanced stage. APG101 inhibits growth signals to glioblastoma cells – a mechanism that was initially discovered by researchers at the DKFZ. In a phase II trial, we were able to show that APG101 in combination with radiotherapy could significantly prolong overall survival times in a particular group of glioblastoma patients.

Another method that was developed at the DKFZ uses parvoviruses to fight glioblastomas. This viral therapy has proved to be safe in a first clinical trial and will now be further explored.

In addition, we are currently focusing on an enzyme called IDH1, which has undergone characteristic and tumor-specific mutations in a few glioblastomas as well as in the majority of low grade gliomas. Colleagues from Heidelberg have recently succeeded in developing a mutation-specific vaccine that prompts an immune response against tumor cells that exhibit this altered protein. We are now conducting a phase I clinical trial to examine whether this vaccine can prevent that gliomas return in the wake of treatment. Additionally, DKFZ researchers in collaboration with Bayer Healthcare have developed an agent that blocks the typically altered variant of IDH1. Soon we will be able to test this substance for the first time in a clinical trial in Heidelberg.

The above mentioned malignant network of glioblastoma cells that we recently discovered has also given us clues to several new drug targets that were previously unknown to us. But presently this still is a dream of the future.

Are there ways to reduce one's personal risk of developing brain cancer?

Unfortunately, none are known. However, the data on the link between cell phone radiation and brain cancer still are too preliminary to allow a final evaluation of this risk.

But, on the other hand, this means that we can tell our patients: Do not blame yourself, you did not do anything wrong! Brain cancer is just fate.

World Brain Tumor Day: June 8, 2016

Images for this press release are available at:

<http://www.dkfz.de/de/presse/pressemitteilungen/2016/bilder/dkfz-mrt-2016-2a-down.jpg>

Caption: DKFZ radiologists are evaluating a brain tumor. Tobias Schwerdt, DKFZ

<http://www.dkfz.de/de/presse/pressemitteilungen/2016/bilder/Wick-Wolfgang-2014-2.jpg>

Caption: Prof. Dr. Wolfgang Wick. Image source: Heidelberg University Hospital

Facts about brain tumors

Primary brain tumors arise from cells of the central nervous system. According to the Robert Koch Institute, approximately **7,200 people** in Germany were newly diagnosed with tumors of the central nervous system in 2012. About 95 percent of these tumors occur in the brain. These figures are representative to the present day.

Primary brain tumors are rare and account for only about two percent of all cancers.

Invasion from inside the body: Metastatic brain cancer

Brain metastases are not primary brain tumors. The term refers to cancer that begins elsewhere in the body and spreads to the brain such as lung, breast, melanoma (skin cancer) cancers. Metastatic brain cancer accounts for more than half of all brain tumors.

Glioblastoma: The most common and most dangerous type of brain cancer

Approximately 50 percent of (non-metastatic) primary brain tumors arise from glial cells and are therefore called **gliomas**. Glial cells, such as astrocytes and oligodendrocytes, are part of the central nervous system and provide support, supply nutrients and insulate neurons.

The most common form of glioma is astrocytoma, which arises from astrocytes. The World Health Organization classifies astrocytomas in four groups. The most malignant group (WHO grade IV) is called **glioblastoma**. In Germany, about 3,400 glioblastomas are diagnosed each year.

Glioblastomas grow diffusely like corals and are therefore extremely difficult to remove by surgery. In addition, they tend to return very quickly after surgical treatment and are extremely resistant against radiotherapy and chemotherapy.

WHO grade II and III astrocytomas also grow in a diffuse manner and frequently re-grow after treatment. Only WHO grade I astrocytomas (pilocytic astrocytoma), which occur more often in children, can be cured by surgery alone.

Gliomas also include oligodendroglioma as well as ependymoma, a type of tumor that begins in the cells that line the ventricles of the brain.

Other brain tumors

Meningiomas are mostly benign (noncancerous) tumors of the membranous layers surrounding the brain. They represent about a quarter of all CNS tumors in adults.

Medulloblastomas, malignant tumors of the cerebellum, account for only about one percent of all brain tumors in adults. However, they are the most common malignant tumors of the brain in children.

There are several other tumor types that can occur in the brain. These include, for example, neurinomas, which are usually benign tumors of the peripheral nerves such as acoustic neuroma, and tumors of the pituitary gland.

Brain tumors in children

Brain tumors are the second most common cancer in children, following leukemia. Tumors of the central nervous system account for almost a quarter of the 2,000 newly diagnosed cancers in children and young adults under 18 years. Children are affected mostly by less malignant gliomas (pilocytic astrocytoma) as well as by medulloblastoma.

Further information:

<https://www.krebsinformationsdienst.de/tumorarten/weitere-tumorarten/hirntumoren.php>