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Blood stem cells deliver drugs to brain tumours

The brain is the central switchboard in our body. Professor Ghazaleh Tabatabai's work focuses specifically on the brain and the fight against uncontrolled proliferation of brain tumours. In May 2014, she was appointed professor in the newly established Interdisciplinary Division of Neuro-Oncology at the University of Tübingen and head of the Clinical and Experimental Neuro-Oncology research group at the Hertie Institute for Clinical Brain Research.

Prof. Dr. med. Dr. rer. nat. Ghazaleh Tabatabai
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Glioblastoma is one of the most common and most aggressive brain tumours. Glioblastoma cells are often found in adjacent healthy brain tissue, where they form tumour islets that are difficult to remove. Standard-of-care therapy involves surgery, radiation and chemotherapy. However, medial survival is only 18 months. "We urgently need new therapies that specifically attack infiltrating tumour cells," says Prof. Dr. Dr. Ghazaleh Tabatabai, director of the Interdisciplinary Division of Neuro-Oncology in the Department of Neurology at Tübingen University Hospital.

Blood stem cells could potentially be used as a drug shuttle. When she did her PhD in the Department of Neurology, Tabatabai and Prof. Dr. Wolfgang Wick, who was back then the medical director of the department, observed that human blood stem cells injected into the blood stream of mice migrated towards glioblastomas in the animals' brain. "Tumour cells release similar attractants to bone marrow cells, so the blood stem cells believe that they are returning home," says Tabatabai.

A Trojan horse against brain tumours

In order to destroy tumour cells, the 41-year-old researcher and Prof. Dr. Ulrich Lauer from Tübingen

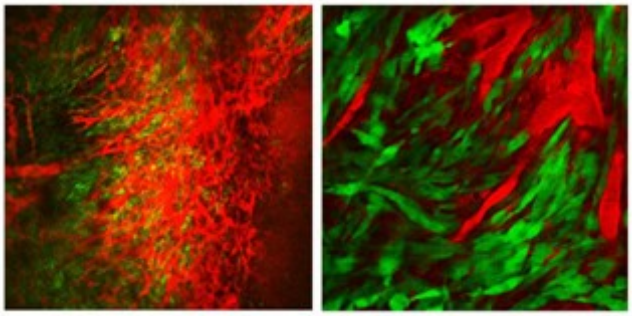


Image of blood vessels (red) in an experimental brain tumour (green).

University Hospital have loaded blood stem cells with attenuated measles vaccine viruses, which quickly multiply in tumour cells. The tumour cells burst and release new infectious virus particles that infect other tumour cells. This type of virus is known as oncolytic virus. Healthy cells have an intact virus defense system, which is why the measles vaccine viruses do not multiply in healthy cells.

The blood stem cells are used as a kind of Trojan horse, which helps the measles vaccine viruses bypass the body's immune system guards. "We know from cell and animal experiments that using blood stem cells as virus shuttles effectively infects and destroys glioblastoma cells," says Tabatabai. In order to enhance this effect, Tabatabai's group of researchers is currently investigating whether this approach can be combined with established therapies such as radiation and chemotherapy. However, it will probably take several years before the approach can be tested in human patients.

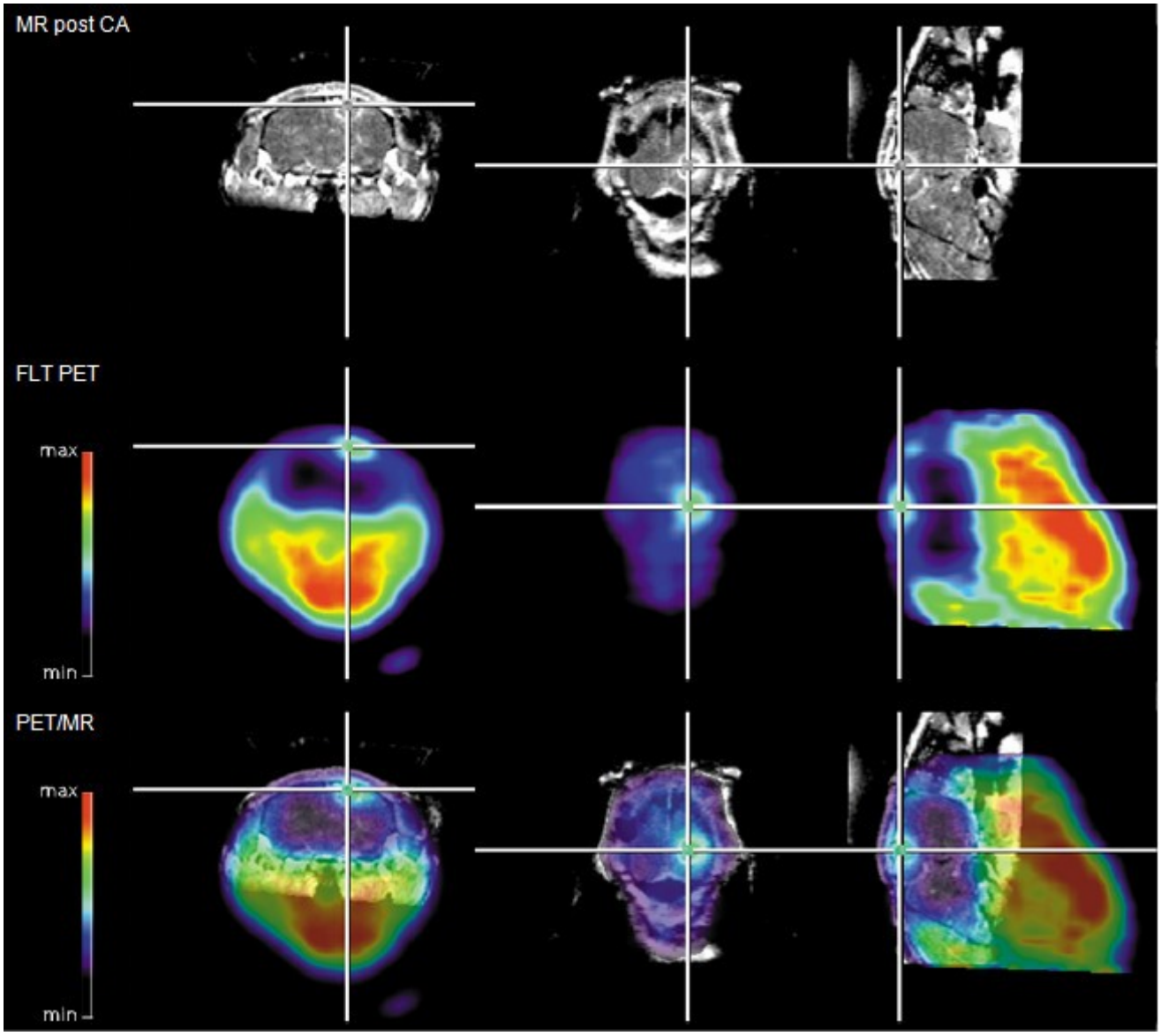
Patient benefit is paramount

In cooperation with stem cell researcher Dr. Olivier Raineteau from Lyon, France, Tabatabai is working on another approach for treating glioblastoma. The researchers have been able to prevent the transcription of tumour-promoting genes in the nuclei of glioblastoma cells, both in culture dishes and in animal models. They have used genetic engineering techniques to inactivate so-called E proteins, which normally help DNA-binding transcription factors called helix-loop-helix proteins to find their way into the nucleus. Usually, glioblastoma cells produce an excessive amount of these transcription factors.

"As a medical doctor, I am mainly interested in the benefit basic research has for patients," says Tabatabai whose decision to focus on tumour diseases goes back to a key event that happened when she was doing internship at the Harvard Medical School's Brain Tumour Center in Boston. "It was the first time that I had seen what it meant to suffer from glioblastoma, and I also realised that there were a large number of unsolved questions," recalls the neurologist. "This experience left a lasting impression," she says.

Personalised cancer vaccination

"The conditions in Tübingen are particularly well suited for turning laboratory findings into clinical practice," says Tabatabai pointing out that her research group works both within the Hertie Institute and the Department of Neurology at Tübingen University Hospital where she is a neuro-oncologist. Moreover, Tabatabai's team is involved in a European-wide clinical phase I trial called GAPVAC-101 (GAPVAC stands for Glioma Actively Personalised Vaccine Consortium), which is coordinated by the pharmaceutical company immatics Biotechnologies GmbH, also in Tübingen. The trial is seeking to



Magnetic resonance and positron emission tomography images of a glioblastoma in the brain.

assess the safety of a treatment concept that is based on drugs designed and manufactured for each patient individually according to the specific characteristics of their tumour and immune system.

Tabatabai does not appear stressed despite her full diary. She is a keen violinist and pianist who draws inner strength from her family and playing music. Music nourishes her soul and soothes her brain.

Article

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Further information

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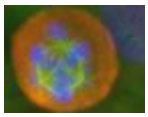

Cancer – basic research, successes and trends

New trends in the field of immunology