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ERC Starting Grant for Heidelberg Neurologist and Neuroscientist Dr. Dr. Varun Venkataramani

Cells of the highly aggressive brain tumor glioblastoma exhibit predatory behavior: they exploit signaling between healthy neurons and internalize portions of their contact sites, known as synapses. Dr. Dr. Varun Venkataramani of the Heidelberg Medical Faculty of Heidelberg University, and his research team, will investigate how glioblastoma cells benefit from this process and whether it may represent a novel therapeutic target. The European Research Council (ERC) is supporting the five-year project with a Starting Grant worth approximately €2.4 million.

Recently, neurologist and neuroscientist Dr. Dr. Varun Venkataramani of Heidelberg Medical Faculty of Heidelberg University and Heidelberg University Hospital's Department of Neurology (Medical Director: Professor Dr. Wolfgang Wick), discovered a new capability of glioblastoma cells: they actively "nibble" on neighboring neurons and internalize portions of them. To further investigate this aggressive behavior, he has been awarded an ERC Starting Grant by the European Research Council (ERC), providing approximately €2.4 million in funding over the next five years. ERC Starting Grants support outstanding early-career researchers from all scientific disciplines who have already demonstrated scientific excellence and seek to pursue ambitious, pioneering research as principal investigators.

Glioblastoma cells infiltrate the brain rapidly, forming a highly interconnected network both among themselves and with existing neuronal circuits. This characteristic makes the disease exceptionally difficult to treat: tumors cannot be completely removed surgically and are highly resistant to both radiotherapy and chemotherapy. Despite advances in treatment strategies, patients survive on average only 15 months after diagnosis. Healthy neurons appear unable to recognize the tumor cells as hostile: they establish direct contacts with them and transmit excitatory signals through these connections, known as neuron–glioma synapses. Over recent years, researchers in Heidelberg have demonstrated that these neuronal signals actively drive the invasive growth and dissemination of glioblastoma cells within the brain.

"Nibbling" on Neurons Promotes Tumor Growth, but the Underlying Mechanisms Remain Unclear

"Our latest findings show that tumor cells do not merely receive and exploit neuronal signals passively. They actively 'nibble' on neurons, particularly their synapses," says Dr. Dr. Venkataramani. "Our preliminary studies indicate that this behavior, known as malignant trogocytosis, also promotes tumor growth. However, the underlying mechanisms remain largely unknown."

During malignant trogocytosis, glioblastoma cells envelop neuronal synapses with protrusions of their plasma membrane, detach portions of these synaptic structures, and subsequently internalize them. Dr. Dr. Venkataramani observed this phenomenon in both mouse models and human glioblastoma tissue using high-resolution microscopy techniques. When researchers experimentally "fed" glioblastoma cells with isolated and purified synapses in tissue culture, this promoted cellular proliferation.

Goal: Elucidating the Molecular Mechanisms of Malignant Trogocytosis and Protecting Neurons

To date, trogocytosis has been mainly associated with so-called synaptic pruning, during which the brain's immune cells specifically eliminate parts of selected synapses. In the context of interactions between tumor cells and neurons, however, trogocytosis represents a fundamentally new biological mechanism that raises numerous questions: Why are glioblastoma cells capable of performing this process? Which receptors and signaling pathways are involved? How does the uptake of synapses, including the neurotransmitters they contain, promote tumor-cell proliferation and therapy resistance? Does this attack alter neuronal activity? And might neurons themselves influence the extent of trogocytosis?

In addition to elucidating the molecular basis and biological consequences of this predatory behavior, the ERC-funded project

will explore its therapeutic potential.

“Glioblastomas not only exploit information from the brain but also appear capable of actively remodeling the neuronal environment to their own advantage,” says Dr. Dr. Venkataramani. “My long-term goal is to develop therapeutic strategies that simultaneously inhibit tumor progression, increase tumor sensitivity to radiation and pharmacological treatments, and preserve neuronal function.”

Press release

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Further information

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