Structures discovered in brain cancer patients can help fight tumors

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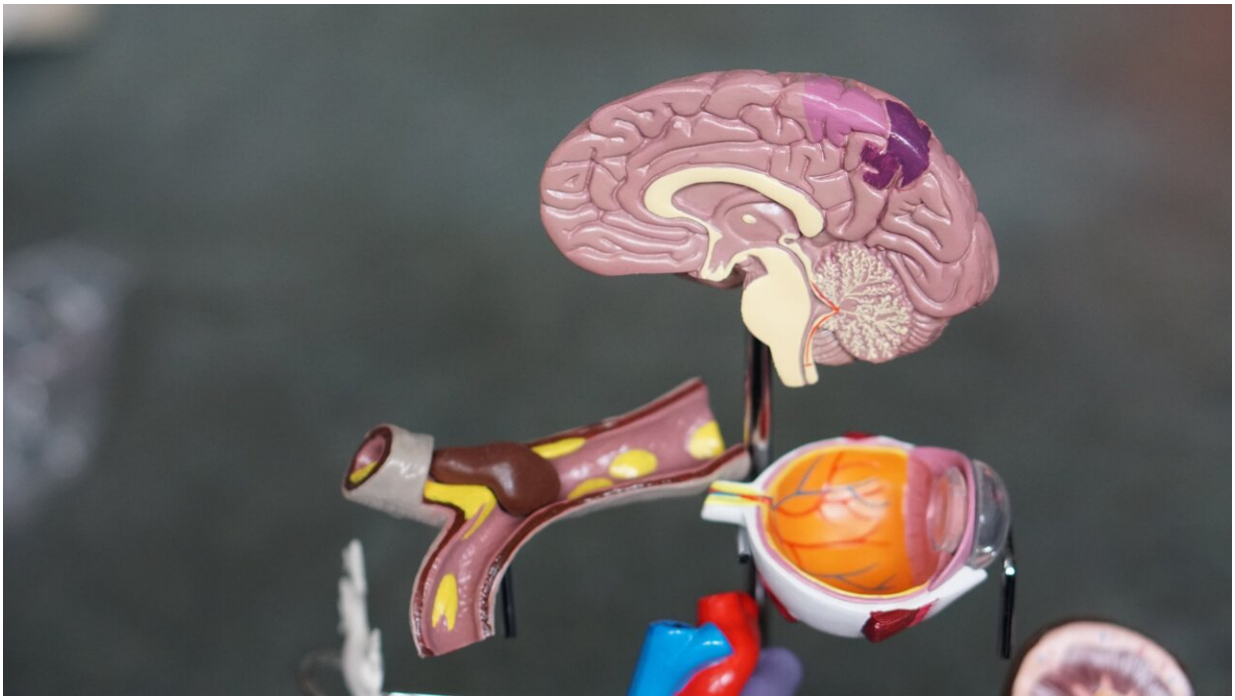

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Researchers at Uppsala University have discovered lymph node-like structures close to the tumour in brain cancer patients, where immune cells can be activated to attack the tumour. They also found that immunotherapy enhanced the formation of these structures in a mouse model. This discovery suggests new opportunities to regulate the anti-tumour response of the immune system.

Glioma is a deadly brain tumour with a dismal prognosis. One reason why brain tumours are very hard to treat is that our immune system, which is designed to detect and destroy foreign cells including cancer cells, cannot easily reach the tumour site due to the barriers that surround the brain.

To fight a developing tumour, killer immune cells such as T lymphocytes must be activated and primed in our lymph nodes, before travelling to the tumour site to effectively kill the cancer cells. Because of the barriers around the brain, it is a challenging process for T lymphocytes to reach the tumour.

In the study now published in the journal *Nature Communications*, the researchers describe their discovery of structures similar to lymph nodes in the brain where T lymphocytes could be activated.

"It was extremely exciting to discover for the first time the presence of lymph node-like structures in glioma patients. These structures are known as tertiary lymphoid structures (TLS) and they are not found in healthy individuals. They have all the components needed to support lymphocyte activation on-site which means that they could have a positive effect on the anti-tumour immune response," says Alessandra Vaccaro, Ph.D. student at the Department of Immunology, Genetics and Pathology and shared first author of the study.

The researchers also showed that the formation of TLS in the brain can be induced by a type of immunotherapy in glioma-bearing mice. Indeed, when they treated the mice with immunostimulatory antibodies called αCD40, the formation of TLS was enhanced and always occurred in proximity to tumours.

"Learning that immunotherapies can modulate the formation of tertiary lymphoid structures in the brain offers exciting opportunities to find new

ways of regulating the anti-tumour immune response in glioma," says Anna Dimberg who has led the study.

αCD40 is currently being tested to treat brain tumours in a number of clinical trials. In the study now published, the researchers found that while αCD40 boosted TLS formation, it also counterproductively inhibited the tumour-killing ability of the T lymphocytes. The study has therefore provided important insights into the multifaceted effects of αCD40 therapy.

More information: Luuk van Hooren et al, Agonistic CD40 therapy induces tertiary lymphoid structures but impairs responses to checkpoint blockade in glioma, *Nature Communications* (2021). DOI: 10.1038/s41467-021-24347-7

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