

Brain cells called astrocytes undergo reorganization and may engulf attacking T cells

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When virally infected cells in the brain called astrocytes come in contact with anti-viral T cells of the immune system, they undergo a unique series of changes that dramatically reorganize their shape and function, according to researchers at the Board of Governors Gene Therapeutics Research Institute at Cedars-Sinai Medical Center. Intriguingly, the new data indicate that astrocytes may defend themselves from attacking T cells by engulfing (gobbling up) the aggressors.

"Further studies into the cellular and molecular processes leading to these changes could have implications for understanding and treating brain infections, brain tumors and neurodegenerative disorders," said Pedro R. Lowenstein, M.D., Ph.D., director of the institute and holder of the Bram and Elaine Goldsmith Endowed Chair in Gene Therapeutics. Lowenstein is senior author of an article on the new findings, published on Aug. 20 in *PLoS ONE*, an open-access, peer-reviewed, online journal of the Public Library of Science.

Astrocytes play numerous roles in maintaining the structure, metabolism and function of the brain. They provide nutrients to neurons, are integral in the formation of the blood-brain-barrier, and have essential functions in controlling neuronal activity.

Normal astrocytes are star-shaped, with octopus-like tentacles extending outward to ensheath neurons and their synapses. When they are exposed

to trauma, stroke or neurodegenerative processes, they become enlarged symmetrically, generally retaining their original form.

But according to the new laboratory research, when T cells attack astrocytes that are infected with a virus or are recognized as foreign, the astrocytes undergo a major structural reorganization. The numerous "tentacles" withdraw and the cell changes from being multipolar to unipolar, displaying one single major protrusion that extends toward the "immunological synapse" where the T-cell has made contact onto its target astrocyte.

"Astrocyte polarization, as opposed to hypertrophy, may be due to the fact that T cells engage in a very focused attack and the astrocytes respond in a directed, polarized manner. We know that the astrocytes respond in this polarized manner but we are continuing to investigate precisely why," said Maria G. Castro, Ph.D., co-director of the Board of Governors Gene Therapeutics Research Institute.

"We believe this is part of a defensive astrocyte response that may serve to destroy the attacking T cells," Lowenstein said. "When a T cell recognizes an astrocyte infected with a virus or identified as a foreign cell, it launches an attack. In response, the astrocyte polarizes toward the T cell and may actually end up engulfing the aggressor. If so, this could be a novel (unique) mechanism of defense by brain cells against immune cells."

Understanding the cellular and molecular mechanisms underlying this response could lead to improvements in gene therapy to the brain, as well as improvements for brain tumors, brain infections, autoimmune diseases of the brain and brain neurodegenerative diseases.

Additional research in this area may lead to new insights into how the immune system clears viral infections, transplants or tumors from the

brain. The authors suggest this could have implications in the treatment of HIV/AIDS, West Nile virus and other viral infections, brain cancer, autoimmune diseases, and the use of transplantation for the treatment of Parkinson's disease.

Source: Cedars-Sinai Medical Center

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