

Newly discovered role for enzyme in neurodegenerative diseases

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Neurodegenerative diseases like Alzheimer's and Parkinson's are partly attributable to brain inflammation. Researchers at Karolinska Institutet now demonstrate in a paper published in *Nature* that a well-known family of enzymes can prevent the inflammation and thus constitute a potential target for drugs.

Research suggests that microglial cells - the nerve system's primary [immune cells](#) - play a critical part in [neurodegenerative diseases](#), such as Alzheimer's and Parkinson's. The over-activation of these cells in the brain can cause inflammation, resulting in neuronal death.

Scientists at Karolinska Institutet and Seville University, working in collaboration with colleagues at Lund University, have now found a way to prevent the activation of the microglia and consequently the inflammation they cause. The key is the blocking of enzymes called caspases, which the team has shown control microglial activation.

"The caspases are a group of enzymes known for causing cell death," says Associate Professor Bertrand Joseph, who headed the study. "That they also serve as signal molecules that govern that activity of other cells was an unexpected discovery that gives them an entirely new physiological role."

By studying [cell cultures](#) and mice, the researchers show that certain caspases (3, 7 and 8) activate rather than kill microglial cells, which triggers an inflammatory reaction. Mice given caspase inhibitors

displayed fewer activated microglia and less inflammation and [cell death](#) in the surrounding neurons.

They also examined samples from deceased Alzheimer's and Parkinson's patients and discovered a higher incidence of activated caspases in their microglial cells.

"We'll now be examining whether the substances that inhibit the caspases can be candidates for useful drugs in the treatment of certain [neurological diseases](#)," says Dr Joseph.

More information: Miguel A. Burguillos, Tomas Deierborg, Edel Kavanagh, Annette Persson, Nabil Hajji, Albert Garcia-Quintanilla, Josefina Cano, Patrik Brundin, Elisabet Englund, Jose L. Venero & Bertrand Joseph, Caspase signaling controls microglia activation and neurotoxicity, *Nature*, AOP 9 March 2011, [doi:10.1038/nature09788](https://doi.org/10.1038/nature09788)

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