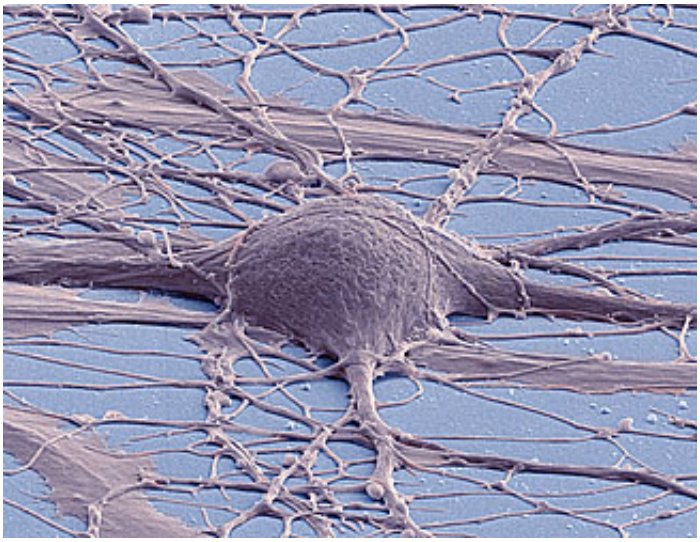
MedicalXpress

Cell biologists discover crucial 'traffic regulator' in neurons

April 19 2017



This is a scanning electron micrograph (false color) of a human induced pluripotent stem cell-derived neuron. Credit: Thomas Deerinck, UC San Diego

Cell biologists from Utrecht University have discovered the protein that may be the crucial traffic regulator for the transport of vital molecules inside nerve cells. When this traffic regulator is removed, the flow of traffic comes to a halt. 'Traffic jams' are reported to play a key role in neurodegenerative diseases such as Alzheimer's and Parkinson's disease. The results of their research will be published in the scientific journal *Neuron* on April 19.

Neurons are the main cells in the nervous system. They process

information by sending, receiving, and combining signals from around the brain and the body. All neurons have a cell body where molecules vital for its functioning and maintenance are produced. The axon, a long and slender extension that can reach one metre in length in humans, sends information from the nerve cell to other nerve cells. Neuronal survival is highly dependent on the transport of vital molecules within this axon. Research has shown that defects in the transport function in the axons play a key role in degenerative brain diseases such as Alzheimer.

First comprehensive map

"Previous research examined transport processes in small areas of the axon, such as the very beginning or the very end. This left it unclear how the movement of molecules through the axon was regulated over long distances. In our study, we provide the first comprehensive map of transport in mammalian axons", says Casper Hoogenraad, Professor of Cell Biology at Utrecht University, explaining the relevance of this study.

Stumped

In most neurons, an area between the cell body and the axon called the 'axon initial segment' serves as a checkpoint: only some molecules can pass through it. This area has stumped scientists for more than a decade. Why should one type of molecule be able to pass through this area, while others cannot? The answer is to be found in the traffic regulator, a protein called MAP2. "With this discovery, we have answered a fundamental question about the unique functioning of nerve cells that has occupied scientists for a long time", lead author of the study Dr Laura Gumy says.

Driving force

The cell biologists from Utrecht first discovered that larger quantities of MAP2 accumulate between the cell body and the axon. When they removed MAP2 from the neuron, the normal pattern of molecule movement changed. Certain molecules suddenly ceased to enter the axon, whereas others accumulated in the axon instead of passing through to the cell body. This abnormal transport indicates that MAP2 is the driving force behind transport within the axon.

Car key

The cell biologists from Utrecht University went on to make another very important discovery. Since axons are so long, transport in the neurons is carried out by sets of proteins - known as 'motor proteins' - that carry packages of other proteins on their back. As it turns out, MAP2 is able to switch a specific 'motor protein' on or off, like a car key. This means that MAP2 actually controls which packages of molecules may enter the axon and which may not. Targeting the activity of the transport engine allowed the researchers to make another interesting discovery: MAP2 is also able to control the delivery of molecules at specific points along the axon.

New targets for therapies

"Transport within axons has been shown to fail in Alzheimer, Parkinson's disease and Huntington's disease, as well as in many other diseases. When the neuron is no longer able to control where molecules go, or is unable to get molecules to where they need to be, it cannot do its job. By understanding how transport works, we have laid the foundation for considering new targets and potential therapies for various neurodegenerative disorders", Casper Hoogenraad concludes.

More information: *Neuron* (2017). DOI: 10.1016/j.neuron.2017.03.046