Medical Xpress

Protein regulates movement of mitochondria in brain cells

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Scientists have identified a protein in the brain that plays a key role in the function of mitochondria - the part of the cell that supplies energy, supports cellular activity, and potentially wards off threats from disease. The discovery, which was reported in the *Journal of Cell Biology*, may shed new light on how the brain recovers from stroke.

"Understanding the molecular machinery that helps distribute mitochondria to different parts of the cell has only recently begun to be understood," said University of Rochester Medical Center neurologist David Rempe, M.D., Ph.D., the lead author of the study. "We know that in some disease states that mitochondria function is modified, so understanding how their activity is modulated is important to understanding how the brain responds to a pathological state."

Mitochondria are cellular power plants that generate most of the cell's supply of adenosine triphosphate (ATP), which is used as a source of chemical energy. While mitochondria are present in all of the body's cells, some cells - because of their size and purpose - need to transport mitochondria to distant sites within the cell to maintain proper function. A prominent example is neurons which have a complex cellular structure that consist of a main cell body and dendrites and axons that project out from the cell core and transmit signals to adjoining cells via synapses at their terminus.

"Neurons are at a disadvantage in terms of their anatomy," said Rempe. "They put out enormous arms of axons and dendrites and they have to

keep supplying nutrients and everything down these arms. The supply line is very long."

The supply line includes mitochondria which the cell must also push down the axons and dendrites to provide these parts of the cell with energy, help with the transmission of signals, and generally maintain cellular health. Mitochondria are constantly cycling throughout the neuron. Some are stationary while others are moving down the arms of the cell to assume their proper position. Additionally, for reasons not completely understood, at any given time about half of the mobile mitochondria in the neuron are in the process of returning to the cell body - perhaps to be recycled or replenished in some form.

Rempe and his colleagues have discovered a protein that plays a critical role in regulating the movement - or transport - of mitochondria in neuron cells. The protein, which they dubbed hypoxia upregulated mitochondrial movement regulator (HUMMR), is produced in a state of low oxygen called hypoxia. HUMMR is induced by another protein called hypoxic inducible factor 1 alpha (HIF-1) which is responsible for triggering several processes in the cell that help it function in a low oxygen environment.

The primary role of HUMMR is to regulate the proper transport and distribution of mitochondria throughout the cell, essentially ensuring that they are in the correct position. One of the ways that the University of Rochester team was able to determine this is that when HUMMR was expressed at lower than normal levels, they observed that a greater number of the mitochondria began to abandon their posts along the cell's dendrites and axon and return to the cell body proper.

Understanding the mechanisms that regulate the movement of mitochondria may help scientists identify how the brain's cells ward off and potentially repair damage. An example is the role that mitochondria

play as a calcium buffer. One of the mitochondria's functions is to help control the concentration of calcium in the cell, which the organelles can rapidly absorb and store. This capacity is important, particularly in instances when calcium levels in the cell spike during a stroke, a condition which contributes a cascading series of events that ultimately lead to a state called excitotoxicity and cell death.

One of the keys to identifying the function of HUMMR has been the appreciation in that the body operates at a relatively low oxygen level. While the air we breath consists of approximately 20% oxygen, the cells in the brain sit at somewhere between 2-5% oxygen. This creates a "normal" state of hypoxia in the brain.

However, the concentration of oxygen in the brain can drop even further in instances such as a stroke, when blood flow to a portion of the brain is cut off. This decrease in oxygen promotes the expression of HUMMR which, in turn, mobilizes mitochondria. More mitochondria in the correct position may mean the cell has a greater capacity to filter out toxic levels of calcium. Rempe and his colleagues are now investigating the role that HUMMR may play in stroke models, particularly whether or not this activity helps protect vulnerable cells that lie just outside the core areas of the brain that are damaged by stroke.

"Ultimately, these advances in our understanding of the molecular and cell biology of mitochondria have the potential to lead to novel approaches for the prevention and treatment of neurological disorders," said Rempe.

Source: University of Rochester Medical Center (news : web)