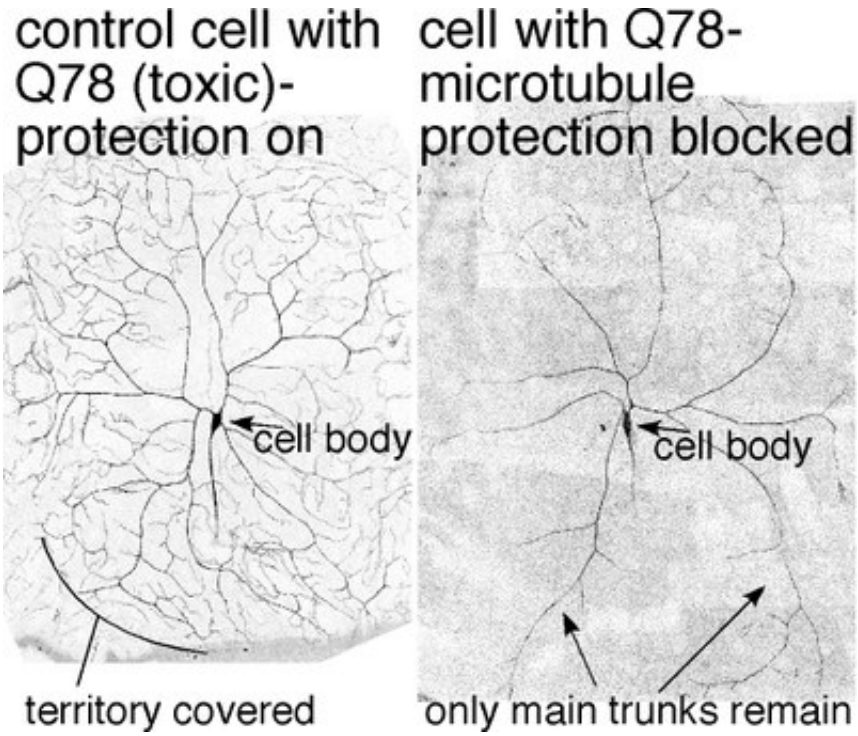
Nerve pathway for combating axon injury and stress may hold benefits for individuals with neurodegenerative disorders

June 27 2012



Neurons expressing a toxic form of spinocerebellar ataxia type 3 (SCA3) with protective pathway enabled (left) and blocked (right). Credit: Melissa Rolls.

(Medical Xpress) -- Researchers from the Huck Institutes' Center for Cellular Dynamics — led by Center director Melissa Rolls — have found that a neuroprotective pathway initiated in response to injured or stressed neural axons serves to stabilize and protect the nerve cell against

further degeneration.

Neurons, or nerve cells, typically have a single axon that transmits signals to other neurons or to output cells such as muscle tissue, and as these axons extend for long distances within the cell, they are thus at risk for injury.

Furthermore — if an axon is damaged, its parent neuron can no longer function; and since many animals develop only one set of neurons, those neurons will mount major responses to axon injury.

"Neurons are quite remarkable cells," says Dr. Rolls. "Most of them need to survive and function for your entire lifetime. Maybe then it shouldn't be a surprise that they do not give up easily when damaged or stressed, but it is amazing to be able to watch them fight back and stabilize themselves."

Dissecting Drosophila

Dr. Rolls and her team set out to understand these cellular responses to axon injury by observing the effects of severing fruit fly axons with a laser.

What they found was that the neurons responded to the injury by increasing production of microtubules — cytoskeletal components responsible for maintaining cell structure and providing platforms for intracellular transport — in order to stabilize the neural dendrites, which are the branched structures responsible for transmitting signals to the nerve cell body.

In addition to acute injury response, the team also investigated neurons' response to long-term axon stress — and found similar results.

Accumulation of misfolded proteins or protein aggregates — responsible for neurodegenerative diseases such as Huntington's disease and spinocerebellar ataxia — induced the same type of cytoskeletal changes as acute axon injury.

Dr. Rolls elaborates: "The assays that we use are all in vivo, so we can literally watch what the neurons do in different scenarios, including cutting of their axon. Being able to observe the cellular responses gave us some ideas we would not have come up with otherwise. For example, it is not intuitive that expressing a protein that causes degeneration would trigger the cell to turn on a pathway that delays degeneration."

Conclusions and implications

Based on their observations, the authors suggest that this pathway represents an endogenous neuroprotective response to axon stress — and could potentially be developed into a diagnostic tool for the detection of early stages of neurodegenerative disease, or even utilized in novel therapies for such illnesses.

"We don't yet know if all types of neurodegenerative disease trigger this type of stabilization pathway; but if there are some diseases in which it is off, then it may be beneficial to try to turn it on to help the neurons resist degeneration," says Dr. Rolls.

The results of the study have been published in *Proceedings of the National Academy of Sciences.*

Provided by Pennsylvania State University