# Scientists learn what makes nerve cells so strong

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How do nerve cells—which can each be up to three feet long in humans—keep from rupturing or falling apart?

Axons, the long, cable-like projections on neurons, are made stronger by a unique modification of the common molecular building block of the cell skeleton. The finding, which may help guide the search for treatments for neurodegenerative diseases, was reported in the April 10 issue of *Neuron* by researchers at the University of Illinois at Chicago College of Medicine.

Microtubules are long, hollow cylinders that are a component of the cytoskeleton in all cells of the body. They also support transport of molecules within the cell and facilitate growth. They are made up of polymers of a building-block substance called tubulin.

"Except for neurons, cells' microtubules are in constant dynamic flux—being taking apart and rebuilt," says Scott Brady, professor and head of anatomy and cell biology at UIC and principal investigator on the study. But only neurons grow so long, he said, and once created they must endure throughout a person's life, as much as 80 to 100 years. The microtubules of neurons are able to withstand laboratory conditions that cause other cells' microtubules to break apart.

Brady had been able to show some time ago that the neuron's stability depended on a modification of tubulin.

"But when we tried to figure out what the modification was, we didn't have the tools," he said.

Yuyu Song, a former graduate student in Brady's lab and the first author of the study, took up the question. "It was like a detective story with many possibilities that had to be ruled out one by one," she said. Song, who is now a post-doctoral fellow at Howard Hughes Medical Institute at Yale School of Medicine, used a variety of methods to determine the nature of the modification and where it occurs.

She found that tubulin is modified by the chemical bonding of polyamines, positively charged molecules, at sites that might otherwise be chinks where tubulin could be broken down, causing the microtubules to fall apart. She was also able to show that the enzyme transglutaminase was responsible for adding the protective polyamines.

The blocking of a vulnerable site on tubulin would explain the extraordinary stability of neuron microtubules, said Brady. However, convincing others required the "thorough and elegant work" that Song brought to it, he said. "It's such a radical finding that we needed to show all the key steps along the way."

The authors also note that increased microtubule stability correlates with decreased neuronal plasticity—and both occur in the process of aging and in some neurodegenerative diseases. Continued research, they say, may help identify novel therapeutic approaches to prevent neurodegeneration or allow regeneration.

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