

Neurons with good housekeeping are protected from Alzheimer's

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Some neurons in the brain protect themselves from Alzheimer's with a cellular cleaning system that sweeps away toxic proteins associated with the disease, according to a new study from Columbia University and the

University of Cambridge.

The study, led by neuroscientist Karen Duff, Ph.D., of Columbia University Vagelos College of Physicians and Surgeons; Harry Fu, Ph.D., now at Ohio State University; and Michele Vendruscolo, Ph.D., of the University of Cambridge, was published online today in *Nature Neuroscience*.

Cells that Resist Alzheimer's Clear Themselves of Toxic Tau Proteins

Early in the course of Alzheimer's disease, neurons in the brain become clogged with toxic tau proteins that impair and eventually kill the neurons.

The new study found that more tau accumulates in certain types of neurons, because [cellular systems](#) that clear the proteins from the cells are predicted to be less effective in these neurons.

Researchers have long known that neurodegenerative diseases like Alzheimer's affect some neurons but not others, even leaving neighboring neurons unharmed. But the reasons for this selectivity have been difficult to identify.

New Techniques Probed Inner Workings of Single Cells

The new study was only possible because of new techniques that allow researchers to probe individual cells in the [brain](#).

When Duff and her colleagues examined data from single neurons in the [human brain](#), they detected signs that the components of a cellular

cleaning system were less abundant in the neurons that accumulate tau proteins.

To confirm the connection between the cleaning system and tau buildup, the researchers manipulated one of the components—a [protein](#) called BAG3—in mouse neurons. When the researchers decreased BAG3 levels in mouse neurons, tau piled up. But when BAG3 expression was enhanced, the neurons were able to rid themselves of excess tau.

The researchers have tantalizing, still unpublished data that the same housekeeping deficiencies found in vulnerable [neurons](#) occur with aging, which might explain the link between advanced age and Alzheimer's disease.

"If we can develop therapies to support these natural defense mechanisms and stop tau from accumulating," Duff says, "we might be able to prevent, or at least slow, the development of Alzheimer's and other tau-related [neurodegenerative diseases](#)."

More information: Hongjun Fu et al, A tau homeostasis signature is linked with the cellular and regional vulnerability of excitatory neurons to tau pathology, *Nature Neuroscience* (2018). [DOI: 10.1038/s41593-018-0298-7](#)

Provided by Columbia University Irving Medical Center

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