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# Scientists identify new protein in the neurological disorder dystonia

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A collaborative discovery involving Kansas State University researchers may lead to the first universal treatment for dystonia, a neurological disorder that affects nearly half a million Americans.

Michal Zolkiewski, associate professor of biochemistry and molecular biophysics at Kansas State University, and Jeffrey Brodsky at the University at Pittsburgh co-led a study that focused on a mutated protein associated with early onset torsion dystonia, or EOTD, the most severe type of dystonia that typically affects adolescents before the age of 20. Dystonia causes involuntary and sustained muscle contractions that can lead to paralysis and abnormal postures.

"It's a painful and debilitating disease for which there is no cure or treatment that would be effective for all patients," Zolkiewski said. "There are some treatments that are being tested, but nothing is really available to those patients that would cure the symptoms completely."

In addition to Zolkiewski and Brodsky, researchers involved in the study included Hui-Chuan Wu, Kansas State University doctoral student in biochemistry and molecular biophysics, Taiwan, and colleagues at the University of Texas Southwestern Medical Center and the University of Adelaide in Australia.

The *Journal of Biological Chemistry* recently published the team's study, "The BiP molecular chaperone plays multiple roles during the biogenesis of TorsinA, a AAA+ ATPase associated with the neurological disease

Early-Onset Torsion Dystonia." The study was funded by the Dystonia Medical Research Foundation.

Researchers built the study on a decade-old discovery that patients with early onset torsion dystonia typically have a mutated gene that encodes the protein TorsionA.

"TorsinA is a protein that all people have in their bodies," Zolkiewski said. "It appears to perform an important role in the nervous system, but currently nobody knows what that role is. There also is no understanding of the link between the mutation and dystonia."

In order to study protein expression in a living organism, researchers used yeast—one of the simplest living systems. The yeast was engineered to produce the human protein TorsionA.

Observations revealed that a second protein named BiP—pronounced "dip"—helps process the TorsinA protein and maintain its active form. Additionally, researchers found that BiP also guides TorsinA to being destroyed by cells if the protein is defective. Humans carry the BiP protein as well as the TorsinA protein.

"BiP is a molecular chaperone that assists other proteins in maintaining their function," Zolkiewski said. "In this study we found that BiP really has a dual role. On one hand it's helping TorsinA and on the other it's leading to its degradation."

Future studies may focus on BiP as a target for treating dystonia, as modulating BiP in human cells would affect TorsinA, Zolkiewski said.

"Because we don't know what exactly the function of TorsinA is, we may not be able to design a treatment based on that protein," Zolkiewski said. "We know what BiP does, however. It is a pretty well-studied

chaperone, which makes it much easier to work with."

**More information:** www.jbc.org/content/289/18/12727.full

Provided by Kansas State University