A new syndrome caused by mutations in AHDC1

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A team of researchers led by Baylor College of Medicine have identified the gene underlying a newly recognized genetic syndrome that has symptoms of sleep apnea, delayed speech and hyptonia, or generalized upper body weakness.

The study published online today in the *American Journal of Human Genetics*.

The Baylor researchers first studied a patient from Australia with these symptoms who had been seen by many doctors and had multiple diagnostic tests, without any diagnosis.

Although there was no family history of the disease, the researchers performed DNA sequence analysis on the patient and her parents to determine if there was an underlying genetic cause for her symptoms.

The results showed damaging mutations had newly arisen in five genes in the patient when compared with the parents DNA sequence.

One gene was a candidate for causing the disease because similar mutations were never seen in healthy control individuals.

"This led us to ask if there were any other undiagnosed disease cases that had similar mutations in this gene," said Dr. Fan Xia, assistant professor of molecular and human genetics and in the Whole Genome Laboratory at Baylor and the first author on the report.

An examination of data from unsolved cases at Baylor's Whole Genome Laboratory revealed three such possibilities, Xia said.

The team then performed DNA sequencing on these patients and their parents.

"We found that these patients also had damaging mutations that had newly arisen in the same gene AHDC1," said Xia. "The independent occurrence of new mutations in each of these families is extremely strong evidence that this gene is the cause of this syndrome."

The mutations are in the 'AT-Hook binding DNA motif Containing' gene, AHDC1.

"Little is known about this gene and the discovery of its link to this syndrome is an important advance towards analyzing its function," said Dr. Richard Gibbs, director of the Human Genome Sequencing Center at Baylor and the corresponding author on the report.

Checking the clinical records of the four patients showed an unrealized similarity between the symptoms of each patient. The DNA discovery had therefore brought together patients from Australia, Pennsylvania and two different cities in Texas.

"This study illustrates a remarkable confluence of advanced technical development, data sharing and detailed clinical studies," said Gibbs. "We have simultaneously provided answers for the affected families and advanced an important basic research question."

The researchers noted that the frequency of this syndrome is not yet known, but extrapolating from the Baylor Whole Genome Laboratory suggests that there could be hundreds of affected individuals worldwide.

Provided by Baylor College of Medicine