MedicalXpress

Team publishes findings on TAF1 syndrome

November 21 2019

An international, multidisciplinary research team from more than 50 institutions, led by geneticist and psychiatrist Gholson Lyon, MD, Ph.D., of the New York State Office for People With Developmental Disabilities' (OPWDD) Institute for Basic Research in Developmental Disabilities (IBR), today announced publication of findings from its study of the rare disease TAF1 syndrome.

The findings were published in the article "Missense variants in TAF1 and developmental phenotypes: challenges of determining pathogenicity," in *Human Mutation*, the official journal of the Human Genome Variation Society, published by John Wiley Press.

People with TAF1 syndrome present early in life with hypotonia, facial dysmorphia, and developmental delay that evolves into intellectual disability and/or autism spectrum disorder.

Dr. Lyon and his research team previously described a new neurodevelopmental syndrome, TAF1/MRXS33 intellectual disability syndrome, which is caused by pathogenic variants involving the X-linked gene TAF1. In the earlier study, the group identified 11 families from around the world with the syndrome.

In this recent study, sponsored by OPWDD, the researchers identified an additional 27 families with the syndrome by using a 'genotype first approach', which clusters families based on mutations in the same gene, followed by detailed clinical analysis of those families. The study integrates results from many disciplines and presents a novel phenotypic

clustering in which the phenotypes, or observable physical characteristics, of affected individuals were classified by using 51 standardized clinical descriptions, referred to as Human Phenotype Ontology (HPO) terms. Phenotypes associated with TAF1 variants show considerable clinical variability, but prominent among the previously unreported effects were brain morphological abnormalities, seizures, hearing loss, and heart malformations. These findings broaden the phenotypic spectrum of TAF1/MRXS33 intellectual disability syndrome and the range of TAF1 molecular defects in humans.

More information: Hanyin Cheng et al, Missense variants in TAF1 and developmental phenotypes: challenges of determining pathogenicity, *Human Mutation* (2019). DOI: 10.1002/humu.23936

Provided by NYS Institute for Basic Research in Developmental Disabilities