



Abstracts

Articles appearing in the December 2020 issue

Congenital immobility and stiffness related to biallelic *ATAD1* variants

Objective To delineate the phenotype associated with biallelic *ATAD1* variants.

Methods We describe 2 new patients with *ATAD1*-related disorder diagnosed by whole-exome sequencing and compare their phenotype to 6 previous patients.

Results Patients 1 and 2 had a similar distinctive phenotype comprising congenital stiffness of limbs, absent spontaneous movements, weak sucking, and hypoventilation. Both had absent brainstem evoked auditory responses (BEARs). Patient 1 carried the homozygous p.(His357Argfs*15) variant in *ATAD1*. In the light of the finding in patient 1, a second reading of exome data for patient 2 revealed the novel homozygous p.(Gly128Val) variant.

Conclusions Analysis of the phenotypes of these 2 patients and of the 6 previous cases showed that biallelic *ATAD1* mutations are responsible for a unique congenital encephalopathy likely comprising absent BEAR, different from hyperekplexia and other conditions with neonatal hypertonia.

[NPub.org/NG/9603a](https://pubmed.ncbi.nlm.nih.gov/36030303/)

Association of blood-based transcriptional risk scores with biomarkers for Alzheimer disease

Objective To determine whether transcriptional risk scores (TRSs), a summation of polarized expression levels of functional genes, reflect the risk of Alzheimer disease (AD).

Methods Blood transcriptome data were from Caucasian participants, which included AD, mild cognitive impairment, and cognitively normal controls (CN) in the Alzheimer's Disease Neuroimaging Initiative (ADNI, n = 661) and AddNeuroMed (n = 674) cohorts. To calculate TRSs, we selected functional genes that were expressed under the control of the AD risk loci and were identified as being responsible for AD by using Bayesian colocalization and mendelian randomization methods. Regression was used to investigate the association of the TRS with diagnosis (AD vs CN) and MRI biomarkers (entorhinal thickness and hippocampal volume). Regression was also used to evaluate whether expression of each functional gene was associated with AD diagnosis.

Results The TRS was significantly associated with AD diagnosis, hippocampal volume, and entorhinal cortical thickness in the ADNI. The association of the TRS with AD diagnosis and entorhinal cortical thickness was also replicated in AddNeuroMed. Among functional genes identified to calculate the TRS, *CD33* and *PILRA* were significantly upregulated, and *TRAPPC6A* was significantly downregulated in patients with AD compared with CN, all of which were identified in the ADNI and replicated in AddNeuroMed.

Conclusions The blood-based TRS is significantly associated with AD diagnosis and neuroimaging biomarkers. In blood, *CD33* and *PILRA* were known to be associated with uptake of β -amyloid and herpes simplex virus 1 infection, respectively, both of which may play a role in the pathogenesis of AD.

Classification of evidence The study is rated Class III because of the case control design and the risk of spectrum bias.

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