

## Editorial comment

# Suggestive evidence on the genetic link between mitochondria dysfunction and autism

An editorial comment to Marui T, Funatogawa I, Koishi S et al. "The NADH-ubiquinone oxidoreductase 1 alpha subcomplex 5 (NDUFA5) gene variants are associated with autism" (1)

Among the psychiatric disorders with a strong genetic component, autism is at the top of the list. Genetics accounts for 90% of the vulnerability for Autism. As for any complex trait, a number of genetic variants either from one or several genes contribute to the disease each with a small size effect. Thus, no one single gene will explain all of the susceptibility to Autism. In this issue of the *Acta Psychiatrica Scandinavica*, Marui et al. (1) reported association of genetic variants known as single-nucleotide polymorphism (SNP) in a mitochondrial gene the NADH-ubiquinone oxidoreductase 1  $\alpha$  subcomplex 5 (*NDUFA5*) with Autism. They conducted the study in two independent samples, a case-control and a replication sample of families mainly to account for the small sample size of the first cohort. Individual SNP analyses showed association with two SNPs in the case-control study but not in the family sample. When these two SNPs were combined in haplotypes, the A allele for SNP rs12666974 and the T allele for SNP rs3779262 are less frequently present among patients and not transmitted to the affected children in the family sample. The authors did not report the Odds ratio or the size effect of this genetic contribution that most likely are low. Although mitochondrial dysfunction has been reported in autism spectrum (8%) (2), it is not clear whether this dysfunction contributes directly or indirectly to the susceptibility of Autism.

Similarly, this association study is the first to establish a relationship between a mitochondrial gene and Autism. This study is based on a candidate gene for Autism and conducted in two independent samples, a conventional approach in molecular genetics. Whether the results that emerge from this study are false positive may depend on future studies. As the authors indicated in the manuscript, future studies will be necessary to further understand or confirm the role of *NDUFA5* in Autism. These studies may include larger sample sizes, presence of mitochondrial dysfunction, and different ethnic background. Ultimately, the validity of any genetic finding relies on biological interpretation and experimental evidence.

Sandra Villafuerte  
Molecular & Behavioral Neuroscience Institute,  
University of Michigan,  
Ann Arbor, MI, USA  
E-mail: svillafu@umich.edu

## References

1. MARUI T, FUNATOGAWA I, KOISHI S et al. The NADH-ubiquinone oxidoreductase 1 alpha subcomplex 5 (*NDUFA5*) gene variants are associated with autism. *Acta Psychiatr Scand* 2011;**123**:118–124.
2. HASS R. Autism and mitochondrial disease. *Dev Disabil Res Rev* 2010;**16**:144–153.