Association of *tbc1d1* gene variants with sporadic amyotrophic lateral sclerosis in Greek patients

K. Mitropoulos[1], E. Merkouri-Papadima[2], C. Mizzi[2], R. Drmanac[3], T. Katsila[2], G. P. Patrinos[2]
[1]*School of Medicine, University of Athens, Greece*
[2]*Department of Pharmacy, University of Patras School of Health Sciences, Greece*
[3]*Research and Development, Complete Genomics Inc, USA*

Amyotrophic lateral sclerosis (ALS) is one of the most common forms of motor neuron disease. ALS is a neurodegenerative disorder that affects the upper and lower motor neurons in the motor cortex, brain stem, and spinal cord and leads to death within 3-5 years. Approximately 90% of the ALS patients suffer from sporadic ALS, having both an environmental etiology and a strong genetic component. Today, there is no effective treatment or diagnostic means for ALS patients. We have previously identified novel genomic loci to be associated with sporadic ALS in sporadic ALS patients of Greek origin. Here, we have performed whole-genome sequencing of 10 ALS patients and 7 healthy (non-ALS) individuals of Hellenic origin, using the DNA nanoballs proprietary approach of Complete Genomics Inc (110x sequencing depth). Following extensive data analysis, we identified 174 genomic variants that were present in all 10 ALS patients but none of the 7 non-ALS ethnically matched controls. Replication of genotyping in 27 sporadic ALS patients and 50 ethnically matched control individuals showed that *TBC1D1* genomic variants are positively associated with the disease phenotype (p0.017). TBC1D1 has been identified as a regulator of insulin-dependent glucose transport and variants in the *TBC1D1* gene were linked to obesity. This is the first study that reveals an association between the *TBC1D1* gene and ALS pathobiology. Nevertheless, due to the small sample size, this should only be considered a pilot study and replication in a larger population cohort is needed to confirm this finding.