The Identification Of The Genetic Cause Of The Cerebellar Hypoplasia Disorder

M.S. Protasova [1,2], A.P. Grigorenko [1,2,3], T.V. Tyazhelova [2], T.V. Andreeva [1,2], D.A. Reshetov [1,2], F.E. Gusev [1,2], I.L. Kuznetsova [2], A.Y.Goltsov [2], S.A. Klyushnikov [4], S.N. Illarioshkin [4], E.I. Rogaev [1,2,3,5*]*

[1] Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk 630090, Russia
[2] Department of Genomics and Human Genetics, Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow 119991, Russia
[3] Department of Psychiatry, Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, Massachusetts 01604, USA
[4] Department of Neurogenetics, Research Center of Neurology, Russian Academy of Medical Sciences, Moscow 125367, Russia
[5] Faculty of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow 119234, Russia
* Corresponding e-mail: rogaev@vigg.ru, protasova@rogaevlab.ru

Summary. To identified genetic cause of congenital hypoplasia cerebellum in two families with different syndromes high- throughput sequencing analysis was performed. X-linked non-progressive ataxia in first family from Mongolian ancestry was caused by genetic defects in *ABCB7* gene and modifying by *ATP7A* gene.
Key words. Cerebellar hypoplasia/atrophy, congenital ataxia, disequilibrium syndrome, *ABCB7*, *ATPA7A*

INTRODUCTION

Hypoplasia and atrophy of cerebellum form a group of rare development disorders characterized by early childhood onset, gross motor development delay, truncal and limb ataxia, dysarthria, nystagmus and ophthalmoplegia, with or without cognitive decline. Here we present the case of the family from the Republic of Buryatia in Russia that includes the three generations of male patients with non-progressive form of ataxia (Illarioshkin et al., 1996). The characteristic features of this syndrome are the delay in developmental milestones, inability to sit up to 15 months old and walk without support up to 7 years old. Although motor function was impaired, neither muscle weakness, nor cognitive impairment or memory disorders were revealed and no ionic imbalance was detected.

CONCLUSIONS

Whole-genome sequencing of the patients with non-progressive cerebellar ataxia in large Buryat family revealed the missense mutation in ABC-cassette transporter subfamily B member 7 (*ABCB7*) and the 41,4 kb deletion in copper transporter gene (*ATP7A*) with complete loss of phosphoglycerate mutase retrogene (*PGAM4*) (Protasova et al., 2015). The identified mutation in *ABCB7* gene leads to the substitution of high conserved glycine to serine in intra mitochondrial ATPase substrate binding domain (ATM). In addition we found the deletion in *ATP7A* gene, that truncates first of the six metal binding domain in copper transporter and most likely does not distract the function of protein, however exerts possible modifying effect. The work was supported by the Government of the Russian Federation (№ 14.B25.31.0033).

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