Abstract

The work was focused on detailed analysis of patients with rare genomic and gene variants. We studied the impact of these variants on the phenotype of the patients. As the majority of our patients, both syndromic and non-syndromic, were reffered to the detailed analysis due to intellectual disability and/or autism spectrum disorder, the work was focused on these two clinical diagnoses.

At the beginning we analyzed patients with aberrations detected using cytogenetic analysis, and the extent, gene content and mechanism of origin of the aberrations were refined using molecular genetic methods, most often high-resolution array CGH. Later we analyzed patients with rare or unique submicroscopic aberrations detected using aCGH or SNP array. Using these methodes we analysed in the project patients with deletions of Xp22.1-p22.3, 6q11-q13, 6q14-q16, Xq25, 1q21.1, Xp21.2-p21.3, 2p14-p15, 17q21.31, 9q21.3 a 2p15-p16.1, and a patient with an Xp21.2-p21.3 duplication.

In the last years we proceeded to the analysis of syndromic cases using next generation sequencing. This led to the identification of point mutations in the *HCFC1*, *KAT6B*, *SOS2* and *KMT2D* genes, which were further studied.

The work contributed to the knowledge about the impact of the genome and gene variants identified on the phenotype of the patients, about the mechanisms of origin of the genome variants, about the role of individual affected genes in the phenotypes and also about the utility and limitations of the genome-wide methods.

Key words: array CGH, SNP array, next generation sequencing, rare diseases, intellectual disability, autism spectrum disorders, bioinformatic analysis, genotype-phenotype correlation