Genetic predictors of a new form of bronchopulmonary dysplasia

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Objective. Bronchopulmonary dysplasia (BPD) is a multifactorial disease with a significant genetic component. Novel genes and associated pathways may play an important role in susceptibility for the development of bronchopulmonary dysplasia in preterm infants. Our aim was to identify rare genetic variants contributing to the new form of BPD phenotype by full exome sequencing.

Methods. Full exome sequencing was performed on 39 DNA samples from patients with moderate and severe new BPD and 30 DNA samples from control group without clinical signs of BPD. After mapping and annotation, each sample showed an average of 40,000 genetic variants with a reading depth of at least 70x.

Results. All autosomal variants were filtered for allelic frequency < 1% according to the gnomAD database (version 2.1). Among them, 821 variants were found the most common (≥10%) in both the control and experimental group. Wherein 280 variants were presented with an alternative allele frequency of more than 10% in the experimental group but were found with a lower frequency in the control. Interestingly, 10 of these 280 variants were in the *ZNF717* gene. This gene encodes a Kruppel-associated box (KRAB) zinc-finger protein, which belongs to a large group of transcriptional regulators in mammals and play important roles in various cellular functions, including cell proliferation, differentiation and apoptosis. Extended bioinformatics analysis showed that 34 unique variants were found in the experimental group and were absent in the control group, which may indicate both the characteristics of Russian children with BPD and the insufficient representativeness of the control group and, in turn, requires a more in-depth analysis.

Conclusion. For the first time in Russia, large-scale studies have been carried out to identify the molecular genetic characteristics of Russian children with BPD using full exome sequencing. Our study indicates *ZNF717* gene may be relevant in BPD pathogenesis, but further research is required. These preliminary results may contribute to improving knowledge of the pathogenesis of bronchopulmonary dysplasia and targeting therapeutic interventions.