EPP0813

Concomitant CNVs in healthy carriers with 7q31.1 microdeletions may suppress intellectual disability and autism spectrum disorders phenotype

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Introduction: About 66% of chromosomal microdeletions and microduplications associated with pathological conditions are inherited [Smajlagić D. et al., 2021]. The mechanisms of incomplete penetrance and variable expressivity of CNV are not fully understood. The presence of concomitant CNVs in the genome of healthy parents may have a modifying effect.
Objectives: Identification of additional CNVs in healthy carriers with 7q31.1 microdeletions.
Methods: CNVs were revealed by Agilent Technologies 60K microarray and confirmed by qPCR.
Results: We examined 3 families with inherited 7q31.1 microdeletions affecting only the *IMMP2L* gene, which is associated with intellectual disability, developmental delay and autism spectrum disorders. Family 1: Proband has intellectual disability, developmental delay, sensorimotor alalia. Microdeletion was inherited from the father, and a healthy sibling is also a carrier of rearrangement. In sibs, additional CNVs were identified: arr[hg19]: 4q31.21 (144722583_144939143)×3; 9p12p11.2(43588066_43836428)×3; 16p11.2(32066967_33773163)×1; and 17q21.31(44199517_44577208)×3. Family 2: Proband suffers from development delay, speech disorder and autism. Microdeletion was of paternal origin. The father additionally demonstrated microduplication 16p11.2p11.1(33967926-35204414)×3. Family 3: Proband was diagnosed with development delay and cerebral palsy. The mother is a carrier of a similar 7q31.1 microdeletion; two concomitant CNVs were identified in her karyotype: 9p13.1(39176840_40614884)×3; and 16p11.2p11.1(32833891_35204414)×3. Thus, healthy parents in 3 families have CNV in a common region 16p11.2, which contains the *TP53TG3* gene. It is important that *TP53TG3* expression is associated with epistatic CNV-CNV interactions [Sun, Kardia 2010].
Conclusions: Multiple CNVs in apparently healthy carriers of *IMMP2L* microdeltions may suppress disease phenotype due to the epistatic CNV-CNV interaction. This study was supported by Russian Science Foundation, grant no. 21-75-00112.

Disclosure: No significant relationships.
Keywords: intellectual disability; IMMP2L; CNV

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Identification of candidate genes of intellectual disability by single-gene deletions/amplifications mapping using chromosomal microarray analysis

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Introduction: Disease-causing deletions/amplifications may include a single gene, several exons or single/part of exon, contributing to detection of novel pathogenic genes. The localization of single-gene deletion/amplification within the gene can affect its clinical manifestation.
Objectives: Improvement of diagnosis of intellectual disability.
Methods: aCGH with 60K Agilent microarrays, qPCR.
Results: Among 1099 patients with intellectual disability potentially pathogenic single-gene deletions/amplifications were detected in 51 individuals (5%). qPCR was used to verify aberrations in 21 patients (41%). Ten mutations were of maternal origin, four - paternal, two - *de novo*, another two were confirmed without analysis of parents, and three could not be confirmed. Single-gene aberrations involving the *AGBL4* (exon 2), *ASMT* (exon 9), *CYP2C18* (whole gene), *DDX10* (promoter, exons 1-13), *GYPA* (whole gene), *LIG4* (exon 1), *LSAMP* (intron 1), *PSD3* (promoter, exons 1-11), *SNTB1* (intron 1), *SPOCK3* (exons 6-12), *STAG2* (exons 7-34), *SYT10* (promoter, exons 1-2), *TCAF2* (exon 8), *TMPRSS15* (promoter, exons 1-12), and *ZDHHC7* (promoter, exons 1-4) genes were described by us for the first time. Deletion or amplification of several exons within a gene can affect transcription as point mutation does, while the copy number change of a whole gene can lead to an abnormal amount of the protein.
Conclusions: Fifteen novel genes potentially responsible for mental health were identified. In most of them aberrations were partial deletions/duplications. Most of abnormalities were inherited from healthy parents indicating the possible presence of a point mutation on the second allele or some modifying factors. This study was supported by the Russian Science Foundation, grant 21-65-00017.

Disclosure: No significant relationships.
Keywords: intellectual disability; Single-gene deletion; Single-gene amplification

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Benefits of treadmill training for patients with Down Syndrome

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Introduction: Down syndrome (DS) is a complex condition that causes various health problems and it is accepted that treadmill training is a therapy method for some of them.
Objectives: The objective was to evaluate the effectiveness of various results of treadmill training in children and adults with DS.