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Title: Polymorphisms of MDR1, ADRB2 and IL13 genes are markers of therapy-resistant bronchial asthma (BA) in Russian patients

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Body: Background. BA is multifactorial disease caused by the interaction of genes and environment. Genetic polymorphisms influence BA development, progression and severity as well as response to BA therapy. Aim. To assess severity of BA and effectiveness of BA pharmacotherapy in patients with different genetic background. Methods. Genomic DNA was extracted from peripheral leukocytes. We investigated 4 SNPs by PCR-RFLP in 122 BA patients and in 103 healthy controls.

Gene	SNP	dbSNP	Restrictase
Multidrug resistance 1 (MDR1)	C3435T	rs1045642	MboI
Beta-2-adrenergic receptor (ADRB2)	Gly16Arg	rs1042713	NcoI
Beta-2-adrenergic receptor (ADRB2)	Gln27Glu	rs1042714	BseXI
Interleukin 13 (IL13)	Arg130Gln	rs20541	AluI

Results. Distribution of genotypes was similar to other European populations, except MDR1 gene. We revealed numerous associations of genetic variants with increased risk (IR): 3435CC with IR of BA (OR=3.92, 95%CI 1.74-8.79); 3435CC with IR of GCS doses more than 20 mg of prednisolon (OR=20.89, 95%CI 5.10-85.53); 3435CC with IR of therapy-resistant BA (OR=6.12, 95%CI 2.42-15.48); 16Gly with IR of respiratory failure (OR=17.31, 95%CI 2.01-149.28); 27GluGlu with IR of therapy-resistant BA (OR=3.35, 95%CI 1.16-9.66); 130Gln with IR of therapy-resistant BA (OR=2.09, 95%CI 1.01-4.30). Conclusion. Analysis of MDR1, ADRB2 and IL13 polymorphisms is useful for both preventive care (revealing subjects with increased predisposition to BA) and pharmacotherapy optimization due to prediction of BA severity and risk of therapy-resistant BA.