Title: Association analysis of β2-adrenergic receptor gene polymorphisms (Arg16Gly and Gln27Glu) with asthma in the Volga-Ural region of Russia

Body: The β2-adrenergic agonists are the most potent bronchodilators for the treatment of asthma. Genetic variation in the ADRB2 gene has been hypothesized to have a role in differential response to beta-agonist (BA) therapy in asthma. Two polymorphic variants rs1042713 (Gly16Arg) and rs1042714 (Gln27Glu) were genotyped in 618 patients with physician-diagnosed asthma, aged 2-60 years (192 Russians, 139 Tatars, 82 Bashkirs and 205 mixed origins), and 366 nonasthmatic individuals (123 Russians, 91 Tatars, 51 Bashkirs and 101 mixed origins) from the Volga-Ural region of Russia. Genotypes were determined by the PCR-RFLP method. Data were analyzed using the chi-square test with Haploview software. We found significant association of Gln27Glu polymorphism with mild decrease FEV1 (60-80% of the predicted value) in Russian patients. The frequencies of genotype ADRB2*27Gln/27Gln and allele ADRB2*27Gln were increased in asthmatics of this group compared to controls (p=0.03, OR=2.25 (95%CI 1.05-4.82) and p=0.02, OR=1.97 (95%CI 1.11-3.50), accordingly). The analysis of Arg16Gly polymorphism showed significant association with moderate asthma in Tatars. The higher frequency of the ADRB2*16Gly/16Arg heterozygotes was revealed in the patients compared with controls (p=0.02, OR=2.25 (95%CI 1.15-4.03)). In summary, these results suggest an important role for polymorphisms of gene ADRB2 in the development of asthma in the Volga-Ural region of Russia.