European Respiratory Society
Annual Congress 2013

Abstract Number: 5287
Publication Number: P1046

Abstract Group: 6.3. Tobacco, Smoking Control and Health Education
Keyword 1: Smoking **Keyword 2:** Genetics **Keyword 3:** Public health

Title: Polimorphism in the site rs12914008 of the CHRNB4 subunit gene may be associated with the fast transition from initial smoking to nicotine dependence (ND)

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Body: Genetic factors substantially determine tobacco smoking. Recently genes encoding nicotine receptor CHRNA5, CHRNA3 and CHRNB4 subunits have been considered potentially involved in the pathogenesis of ND. We aimed to investigate whether the CHRNA5-CHRNA3-CHRNB4 nicotinic receptor subunit gene cluster affects risk for ND in the Kashubian population, North Poland. The study sample consisted of 790 current smokers of the Kashubian origin. Genotyping for polymorphisms in the sites rs16969968, rs578776, rs7743870 and rs12914008 of the CHRNA5, CHRNA3 and CHRNB4 subunits genes was performed in blood samples, and genotypes were correlated with CPD (cigarettes per day) and with Fagerstrom Test for Nicotine Dependence (FTND) score with the use of multivariate logistic regression analysis. We found that A allele carriers of rs16969968 polymorphism had higher risk of heavier smoking, i.e. >=10 CPD than G allele carriers (OR = 1.45; 95% CI: 1.03-2.05). In turn, no association was found between studied polymorphisms and the FTND score in the entire study group. However, in the separate investigation for allelic association in the group of subjects with the history of smoking shorter than 5 years a higher risk of strong ND (>=4 in the FTND score) in A allele carriers than G allele carriers of rs12914008 polymorphism was found (OR = 26.86; 95% CI: 2.63-273.6). In conclusion, polymorphism in the sites rs16969968 and rs12914008 of CHRNA5 and CHRNB4 subunits genes may influence the severity of ND and the fast transition from initial smoking to ND, respectively. This work was carried out with the aid of a grant from the NCN (Grant N N404 270839).