

TOLL-LIKE RECEPTOR 9 PROMOTER POLYMORPHISMS IN COPD AND SARCOIDOSIS

S. Pabst¹, O. Bradler¹, D. Skowasch¹, C. Grohé²

¹Medical Clinic II, University of Bonn, Germany;

² Evangelische Lungenklinik Berlin-Buch, Germany

Background: The aetiology of inflammatory diseases of the lung such as sarcoidosis and chronic obstructive pulmonary disease (COPD) is multifactorial. The main trigger for developing a COPD is inhalative tobacco smoking while exogenous factors causing sarcoidosis are unclear. In both diseases there is an underlying genetic susceptibility determining probably both the onset and the course of the diseases. Toll-like receptor (TLR-) 9 plays an important role in innate immunity by recognizing bacterial CpG-DNA motifs. It is unclear whether SNPs in TLR9 are able to alter the course of sarcoidosis or COPD or even raise the susceptibility for developing one of the disorders.

Patients and Methods: We examined two single nucleotide polymorphisms (SNPs) in the promoter region of the TLR-9 gene (T1486C and T1237C) in 175 COPD patients (59% with a stable course of the disease and 41% an instable course with more than 3 exacerbations over the last 3 years) and 166 sarcoidosis patients (19% with an acute and 81% with a chronic course of the disease lasting > 2 years) comparing each group to 233 healthy controls. Polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis was used for genotyping. Pearson's chi-square test was applied for statistical analysis (SPSS 17).

Results: The C-allele frequency of T1486C was significantly elevated in COPD patients ($p=0.014$). In woman, this finding was even more evident ($p=0.006$). There was no difference comparing the stable with the instable COPD group. For T1237C there were no significant associations comparing the COPD cohort with the controls.

In the sarcoidosis cohort we could observe a significantly higher prevalence of the C-allele for T1237C in the chronic sarcoidosis cohort in comparison to the control group ($p=0.038$). For T1486 there no statistical association was observed.

Conclusion: This is the first study showing an association between a SNP (T1486C) in the TLR-9 gene and the onset of COPD. Moreover, we could demonstrate that T1237C is able to alter the course of sarcoidosis as a disease-modifying gene. This study underlines that SNPs in TLR9 might be involved in acquiring and maintaining lung diseases such as sarcoidosis and COPD.