

JOINT EVENT

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London, UK**Environmental Toxicology and Biological Systems****MMP9 in lung disorders: Identification and analysis of gene-environment interaction between the MMP9 C-1562T variant and cigarette smoke in the occurrence and severity of COPD****Marija M Stankovic**

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MMP9 is an elastolytic enzyme, the expression and activity of which are tightly regulated. In healthy lungs, MMP9 is not expressed, but in response to inflammatory cytokines, pulmonary and immune cells may secrete MMP9. The deregulation of MMP9 is implicated in various lung disorders, e.g. chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, cystic fibrosis (CF), carcinoma, etc. Accordingly, understanding the effect of environmental factors on MMP9 expression in lungs is of great importance. Cigarette smoke, infections, LPS and chemical agents increase the production of MMP9. Besides, genetic factors such as MMP9 C-1562T (rs3918242) functional variant, has been recognized as a risk in several disorders, but its role in COPD is controversial. Herein, results about the identification and functional assessment of gene-environment interaction between the MMP9 C-1562T variant and cigarette smoke in the pathogenesis of COPD are presented. Interaction between the C-1562T variant and cigarette smoking was analyzed using a case-control model. The effect of CSC on MMP9 expression and activity was determined by real-time PCR and gelatin zymography. The response of the C-1562T promoter variant to CSC was examined using a dual luciferase reporter assay. The frequency of T allele carriers was higher in COPD group than in smoker controls ($P=0.027$). Interaction between the T allele and cigarette smoking was identified in COPD occurrence ($P=0.005$) and severity ($P=0.001$). Expression of MMP9 mRNA and pro-MMP9 gelatinolytic activity were dose-dependent ($p<0.01$, $p<0.05$). A functional analysis of the C-1562T variant demonstrated a dose-dependent and allele specific response ($P<0.01$) to CSC. Significantly higher MMP9 promoter activity following CSC exposure was found for the promoter harbouring the T allele compared to the promoter harbouring the C allele ($P<0.05$). Our study is the first to reveal an interaction between the MMP9-1562T allele and cigarette smoke in COPD, emphasising gene-environment interactions in complex lung disorders, such as COPD.

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