

P014 Genetic variants of Matrix Metalloproteinases 1, 9 and 12 in Chronic Obstructive Pulmonary Disease

I. Haq^{1,2}, SR Johnson², EU COPD Gene Scan Project and N.Kalsheker¹.

¹Divisions of Clinical Chemistry and ²Therapeutics and Molecular Medicine, Queens Medical Centre, University of Nottingham

The genetic factors that play a role in Chronic Obstructive Pulmonary Disease (COPD) are poorly understood. Candidates based on pathogeneses include the Matrix Metalloproteinases (MMPs) genes which play a role in tissue remodelling and fit in with the protease – antiprotease imbalance theory of COPD causation. Previous MMP genetic studies in COPD have reported conflicting associations mainly due to under – powered studies or inadequate coverage of the genes.

To address these issues we genotyped 26 single nucleotide polymorphisms (SNPs) in MMPs – 1, 9 and 12 samples in 977 COPD patients and 876 non COPD smokers of European descent closely matched for age, sex and smoking history.

No significant associations of SNPs with disease were observed. However, severity of disease analysis identified haplotypes related to two unlinked SNPs in MMP-12 (rs652438 and rs2276109) that showed an association with severe COPD, corresponding to GOLD Stages III and IV (n=635). The odds ratio was 0.72 for haplotypes GA/GG/AG compared to AA (95% c.i. 0.59-0.88, p=0.0039). MMPs-1 and 9 showed no such associations. These data suggest that haplotypes of MMP-12 are acting as modifiers of disease severity.