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Differential effects of GSTM1, GSTT1 and CYP1A1 on the association between active and passive smoke exposure and rheumatoid arthritis risk

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Polymorphisms in GSTM1, GSTT1 and Cytochrome P4501A1 gene influence the rate of metabolism of polycyclic aromatic hydrocarbon (PAH) present in tobacco smoke. Because the physicochemical composition of mainstream and sidestream smoke differ, we conducted a case-control study to assess a possible differential effect of GSTM1, GSTT1, and CYP1A1 genotypes on the relationship between active/passive smoke exposure and rheumatoid arthritis risk. 88 patients diagnosed by rheumatoid arthritis and 148 sex and age- matched healthy controls were interviewed to obtain active and passive smoking history. Individuals were genotyped for GSTM1, GSTT1 and CYP1A1 using PCR techniques. Multivariate logistic regression analysis was performed to estimate rheumatoid arthritis risk in relation to smoking history by allele status and interaction effects.

The demographic characteristics of the study population were similar in sex and age distribution, smoking status, and alcohol intake ($p>0.05$). The observed allele frequencies of the GSTM1, GSTT1, CYP1A1 polymorphisms did not show the difference between the patients and controls ($p>0.05$). Compared with never regularly exposed to tobacco smoke, the adjusted odds ratios (AORs) for current smoking and ex-smoking were 8.793 [95% CI: 1.180-65.534] and 2.622 [95% CI: 0.302-22.783] in the heterozygous or homozygous variant type (W/M and M/M) of CYP1A1, and not increased in wild type (WT). Current smoking exposure was associated with GSTM1 null-genotype [AOR, 95% CI: 20.360,

1.680-246.752] but not with GSTT1 null-genotype [AORs 95% CI: 1.384, 0.134-14.291]. Among those with the CYP1A1 W/M or M/M genotypes the rheumatoid arhritis risk in relation to passive smoking was grater than those with the CYP1A1 WT genotype:[AORs 95% CI: 3.323, 1.436-7.688 for CYP1A1 W/M or M/M genotypes, 1.091, 0.341-3.491 for CYP1A1 WT genotypes]. It is suggested that the GSTM1 and CYP1A1 genetic polymorphisms have differential effects on the association of active and passive smoking with rheumatoid arthritis and the presence of the heterozyous or homozyous variant types of CYP1A1 (WM or M/M) appears to enhance the magnitude of the association between active/passive smoke exposure and rheumatoid arthritis. Larger studies will be needed to confirm these preliminary findings.

Keyword : Rheumatoid arthritis, smoking, polymorphism, GSTM1, GSTT1, CYP1A1