— Sat-211 —

Heterozygote disadvantage of HLA-DRB1*0405 and DRB1*0901 in susceptibility of rheumatoid arthritis in the Korean population.

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This study investigated the association of susceptible and protective HLA-DRB1 alleles with rheumatoid arthritis (RA). Patients with RA (n=574) and controls with the same ethnic background (n=392) were included in this study. HLA-DRB1 typing and further subtyping of all alleles were performed by polymerase chain reaction, sequence-specific oligonucleotide probe hybridization, and direct DNA sequencing analysis. The frequency of the DRB1*0405 allele and DRB1*0901 allele was statistically significantly increased in patients with RA [P = 3.5 X 10-24, ORs 4.40 (95% CI 3.24-5.99), and P = 3.1 X 10-5, ORs 1.90 (95% CI 1.40-2.58), respectively]. Several alleles (DRB1*0403, *0406, *0701, *0802, *1101, *1202, *1301, *1302, *1403, and *1405) showed significant protective effects. Susceptible and protective alleles showed gene dosage effect, and associated with RA independently each other. The compound heterozygote DRB1*0405/*0901 genotype showed the highest risk for RA [Pc = 1.81 X 10-11, ORs 58.5 (95% CI 7.99-427.7)]. The age at disease onset was significantly lower in patients with at least one copy of DRB1*0405. Radiographic changes (stages 2-4) were more frequent in patients with at least one copy of DRB1*0405. These data suggest that the specific susceptible and protective alleles were independently associated with RA. Also heteozygote DRB1*0405/*0901 has the highest synergistic susceptible effect on RA. Only the DRB1*0405 is associated with the age at disease onset and severity of RA.

— Sat-212 —

Correlation between Methylenetetrahydrofolate Reductase (MTHFR) Gene Polymorphism and Methotrexate Toxicity in Korean Rheumatoid Arthritis Patients

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Objective: The C677T mutants in MTHFR gene polymorphism have been thought to be as a genetic risk factor for methotrexate-related adverse effects of rheumatoid arthritis patients. We tried to disclosure the relationship between the C677T mutants of MTHFR polymorphism and methotrexate toxicity of rheumatoid arthritis patients in Korea. ***Method***: We enrolled 385 (355 females, 30 males) patients with rheumatoid arthritis, who have been received oral methotrexate. Genotypic analysis of MTHFR polymorphism was determined by polymerase chain reaction. The correlation between MTHFR genotype, age, RF positivity, RA process stage, KHAQ and adverse effects was analyzed by the spearman's rank correlation test. The frequency analysis of C677T genotype and adverse effects was done by Chi-square test. ***Results***: The results of MTHFR genotypic analysis shows 132 patients with 677CC, 193 patients with 677CT, 59 patients with 677TT. The frequency of homozygosity for the TT alle is 15.5% in Koreans higher than 10% in Caucasians. 121 of the 385 patients (31.4%) had some kinds of side effects by methotrexate. The correlation of methotrexate-related toxicity and MTHFR polymorphism was identified (p value<0.05). The relative risk, which of adverse effects could be occurred by low dose methotrexate in rheumatoid arthritis patients, was 2.06 (95% confidence interval 1.27-3.35, p value<0.05). ***Conclusion***: There is positive correlation between toxicities of methotrexate and MTHFR polymorphism. Mutants of C677T gene may increase risk of adverse effects.