EVIDENCE OF "SNP" EFFECT ON THE RISK OF RHEUMATOID ARTHRITIS: EFFECTS OF COVARIATE ADJUSTMENT UPON ASSOCIATION RESULTS

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- *ABSTRACT: In this paper, an association analysis approach through covariate adjustment is proposed to classify Single Nucleotide Polymorfism (SNP) effects associated with the risk of rheumatoid arthritis (RA). Initially, the marginal effect of each SNP is evaluated by considering a single locus logistic regression. This effect is then evaluated adjusted by a covariate of known biological effect (HLA-DRB alleles) on the RA risk. To take into account possible influences of population stratification, the first ten axes of variation, resulting from a principal components analysis of the SNPs, are incorporated into the analysis as covariates. For comparison purposes, analysis without these axes is also performed. SNPs from all autosomal chromosomes of the RA data from the Genetic Analysis Workshop 16 are used in the analysis. From comparisons carried out with regard to the SNP effects obtained without and with adjustment by a covariate of known biological effect, classification of these effects is suggested in terms of direct and indirect influence, as well as influence through epistatic mechanisms. The proposed analytical procedure was shown to be useful overall, not only to disclose potentially important higher-order effects, but also to provide a classification of the SNPs.*

- *KEYWORDS: Association studies; human genetics; logistic regression; molecular markers; population-stratification.*

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