

Genetic associations study of rs12745968 and rs4822752 between rheumatoid arthritis and schizophrenia patients

Nur Shafawati Ab Rajab¹, Mohd Razali Salleh², Mohd Azhar Mohd Yasin³, Wan Syamimee Wan Ghazali⁴, Norlelawati Abdul Talib⁵, Wan Rohani Wan Taib⁶ and Sarina Sulong^{1*}

¹Human Genome Center, School of Medical Sciences, Universiti Sains Malaysia

²Health and Wellbeing, Faculty of Medicine, Universiti Teknologi MARA

³Psychiatry Department, School of Medical Sciences, Universiti Sains Malaysia

⁴Medical Department, School of Medical Sciences, Universiti Sains Malaysia

⁵Faculty of Medicine, International Islamic University Malaysia

⁶Faculty of Medical and Health Sciences, Universiti Sultan Zainal Abidin

ssarina@usm.my

Abstract

The association between rheumatoid arthritis (RA) and schizophrenia (SZ) is not a new issue. Since 1936, studies of the relationship between these two diseases have been received in many fields including genetics. SZ is a psychiatric disorder and RA is an autoimmune disease of the joints that occurs when the body's immune system attacks its own cells. Both diseases are thought to be influenced by multiple genetic risk factors which were modified by the environment. We postulated that individual genetic variant may have either opposing effects or same effects on the risk of schizophrenia and rheumatoid arthritis. In this study, two significant SNPs were selected from an analysis of two large databases; rs12745968 and rs4822752 represent FAM69A and CRYBB1 genes, respectively. The SNPs were genotyped using Taqman SNP Genotyping as it was high throughput and highly accurate, precise, time-efficient, and cost-effective. A total of 270 (90 RAs, 82 SZs and 98 controls) blood samples from consented subjects were extracted for DNA and genotyped for both markers. The genotyped data was validated using sequencing for selected samples. In addition to assessing allele and genotype frequencies, the results were also calculated for association and odds ratio test using SPSS software (version 22) based on chi-square calculation with 95% confidence interval (CI) and p -value <0.05 . AA genotype of rs12745968 was significantly found in SZ ($p=0.023$) and RA ($p=0.001$) patients, and CC genotype of rs4822752 was also statistically significant in SZ ($p=0.002$) and RA ($p=0.00006$) compared to controls. Likewise, susceptibility risk of AG was significantly shown in rs12745968 in RA (OR=3.0175, CI=1.059-8.598, $p=0.032$) and SZ groups (OR=6.0208, CI=1.6997-21.338, $p=0.0019$). Moreover, the heterozygous genotype, CT of rs4822752 revealed the significant risk to both diseases, RA (OR=7.8245, CI=2.8177-21.7276, $p=0.000016$) and SZ (OR=5.6676, CI=2.288-14.0395, $p=0.00007$). As a conclusion, this preliminary results provided evidences for the engagement of rs12745968 and rs4822752 as susceptibility risk to RA and SZ. However, further correlation analysis is warranted to genetically explore the risk alleles among RA/SZ which lead to important insights of pathogenesis of the disease.

Keywords: Rheumatoid arthritis; schizophrenia; SNP genotyping

*Author for Correspondence