

# The *RAD-18 Arg302Gln (rs373572)* and *OGG1 Ser326Cys (rs1052133)* Genes Polymorphisms in Systemic Lupus Erythematosus Disease

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## Abstract

The Systemic Lupus Erythematosus (SLE) disease is an autoimmune disease incidence by different genetic and environment factors, the present research study two DNA repair genes polymorphisms in SLE disease included *RAD-18 Arg302Gln (rs373572)* and *OGG1 Ser326Cys (rs1052133)* genes, the polymorphisms were detection using allele specific PCR and PCR-SSCP, patients were diagnostic by specialist physician then DNA was isolated from whole blood, the results show that The *RAD-18* gene variation show non-significant differences between patients and control, tow genotyping (AA and AG) were observed and GG didn't observed, the distribution of AA and AG were 95.29% of patients have AA while 92.85% in control GG appeared in 4.76% of patients and 7.14% in control (OR 0.6667, P value 0.6936). The *OGG1 Ser326Cys (rs1052133)* genes polymorphisms shows there haplotypes A, B, and C represented by four pattern ABC, AC, A and C. AC (47.5%), C (30%) and A (12.5%) were more frequent in patients than control in significant level for AC (OR 8.1429, P 0.0006) and non-significant level for C (OR 5.029, P 0.0574) and A (OR 0.1196, P 0.167). the present finding concluded that SLE association with *OGG1*, and don't related with *RAD-18*.

**Keywords:** Chronic autoimmune diseases • Systemic Lupus Erythematosus • DNA • Genotyping

## Introduction

The Systemic Lupus Erythematosus also called as lupus or (SLE) is one of the chronic autoimmune diseases its recorded in a high incidence rate at the last decades its about 5 million cases in the world, The diagnosis of SLE dependent on the 11 diagnostic clinical criteria dependent by the college of rheumatology including native DNA antibodies [1]. The incidence percentages were recorded in female at nine fold higher than male and 2-3 fold higher in Asian African and native American ancestry than other population [2,3], the genome wide association found more than 50 risk alleles contributed in the SLE pathogenicity and major of them associated with immune system response in addition to the other genetic predisposition factors [4-6].

The association between SLE and DNA repair system come from the unability of cells to repair DNA lesions, different types of DNA repair systems genes polymorphisms have been reported to be associated with SLE such as DNA glycosylase for repair Sp and Gh encoded by NEIL3 [7]. Scaffold protein encoded by XRCC1 [8], DNA glycosylase encoded by OGG1 [9]. In addition to POLB that DNA gaps filled through BER; work in SHM and VDJ recombination [10-12], all these genes encoded to proteins involved in base excision repair, any mutation in genes that encoded to proteins contributed in repair activity may be associated with SLE development. Mutations in any one of these genes may be associated with increased risk for lupus development because of the abnormal in DNA repair led to generation antibody diversification, apoptosis, elevation the abnormal in DNA processing which resulted to autoantibodies generation [13].

## Research Methodology

A case control study conducted in DNA lab/university of Babylon included 45 SLE patients were attended to the chronic disease clinic in Marjan hospital city, all patients were detected by Dr. Ali Al-kazaz, and samples were collected according to ethical approval of environment and health ministry of Iraq. DNA was extracted from frozen blood, and then its concentration and purity were detected. Electrophoresis samples were implemented using agarose gel and PCR for RAD18 and OGG1 were detected via the following primers, RAD18 by allele specific PCR F1- ATA CCC ATC ACC CAT CTT C, R1- GTC TTC TCT ATA TTT TCG ATT TCT T, F2- TTA ACA GCT GCT GAA ATA GTT CG, R2- CTG AAA TAG CCC ATT AAC ATA CA. 3'for the A allele producing a 146 bp band, 106 bp of G allele, 206 bp was amplified using the F1 and the R2, at the annealing TM 58°C. *OGG1 Ser326Cys* F- GGTGGCCCTAAAGGACTCTC, R-AAGGTGCTTGGGGAATTTCT, the PCR product was 295 bp, then haplotypes were implemented by SSCP technique according to [14,15]. The data analysis using Odd ratio at CI 95% p value less than 0.05.

## Results and Discussion

The present study aims to investigated the *RAD-18 Arg302Gln (rs373572)* and *OGG1 Ser326Cys (rs1052133)* genes polymorphism in SLE patients, results show that the patients age mean was (31.34 ± 9.25) and disease duration was (9.20 ± 5.99) while the control age mean was (33.10 ± 11.38), all clinical features of SLE diagnosis criteria were detected in

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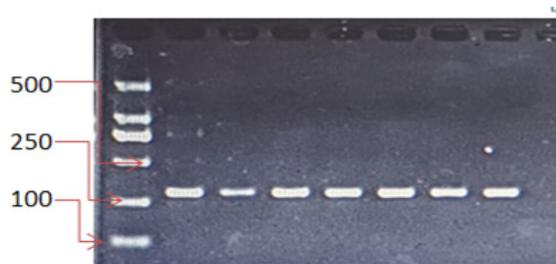
the hospital center of chronic diseases. The incidences of SLE have been increased in last years and the relation of DNA repair systems with SLE development still under investigations.

The *RAD-18* gene variation show non-significant differences between patients and control, tow genotyping (AA and AG) were observed and GG didn't appeared in present study, the distribution of AA and AG explained in Table 1.

**Table 1.** The *RAD-18 Arg302Gln* polymorphism (rs373572) in SLE patients and control groups. able 1. The *RAD-18 Arg302Gln* polymorphism (rs373572) in SLE patients and control groups.

Genotyping	Patients	Control	Odd ratio	P value
AA	-95.29%	-92.85%	0.6667	0.6936
AG	-4.76%	-7.14%	0.0887 to 5.0130	
G	0.522	0.533	1.0452	0.6221
A	0.477	0.466	0.8768 to 1.2459	

95.29% of patients have AA while in control 92.85% GG appeared in 4.76% of patients and 7.14% in control (OR 0.6667, P value 0.6936) (Figure 1).



**Figure 1.** Electrophoresis pattern of allele specific PCR for *RAD-18 Arg302Gln* (rs373572) polymorphism.

Electrophoresis pattern of allele specific PCR for *RAD-18 Arg302Gln* (rs373572) polymorphism and convention PCR for *OGG1* gene. *OGG1* gene have 295 bp for SLE patients and control SSCP electrophoresis pattern of *OGG1* the allele specific PCR, 146 bp for G allele and 106 bp for A allele for SLE patients and control (Figures 2 and 3). The values are (agaros gel electrophoresis via 70 V, 20 mA, 0.5 × of TBE for 40 min), (40% polyacrylamide gel, 1 × sscp loading stain, 100 V, 50 min and 0.5 × TBE), three haplotypes A, B and C were detection.



**Figure 2.** Convention PCR for *OGG1* gene.



**Figure 3.** SSCP electrophoresis pattern of *OGG1* the allele specific PCR.

The *RAD-18* is gene located at 3p25.3 and encoded to an E3 ubiquitin-protein ligase, it's had an important role in the repair of DNA lesions in DNA post replication, the mutation in this gene lead to accumulation of UV DNA damage and more sensitive to mutagens factors [16,17], the *RAD-18* gene polymorphism have been found that it has associated with different disease like cancer and diabetes mellitus [18]. But, the literature review about SLE association with *RAD-18* gene polymorphism were didn't recorded, this study proved that there was no association between Arg302Gln (rs373572) of *RAD-18* gene and SLE disease.

The *OGG1 Ser326Cys* (rs1052133) genes polymorphisms was studied in present study via SSCP technique, there haplotypes were observed A, B, and C represented by four pattern ABC, AC, A and C. the present results show that AC (47.5%), C (30%) and A (12.5%) were more frequent in patients than control in significant level for AC (OR 8.1429, P 0.0006) and non- significant level for C (OR 5.029, P 0.0574) and A (OR 0.1196, P 0.167). The present study shows association between *OGG1* Haplotypes and SLE disease (Table 2).

**Table 2.** The haplotype polymorphisms of *OGG1 Ser326Cys* (rs1052133) genes polymorphisms gene in study groups.

Genotyping	Patients	Control	Odd ratio	P value
ABC	-10%	-63.33%	8.1429	0.0006
AC	-47.50%	-6.66%	2.4401 to 27.1731	
C	-30%	-30.00%	5.0294 0.9505 to 26.6125	0.0574
A	-12.5	0	0.1196 0.0059 to 2.4402	0.1675

The *OGG1* is gene encoded to DNA glycosylase, bi-functional enzyme excises 8-oxoguanine induced by ROS [19], the mutations in *OGG1* have been reported and several SNPs were associated with different disease as well as rs1052133 which found associated with SLE nephritis development and with elevation 8-oxoguanine in patients plasma which deal with present study findings, the polymorphism in *OGG1* gene was suggested by elevation or lowering in enzyme activity like in homozygous of 1245 CC genotype which has higher enzyme activity [20]. Then the 1245 CG genotype and the homozygous 1245 GG genotype show lower activity than previous genotyping [21]. The activity of *OGG1* enzyme was detected by the level of 8-OHDG and this may be elevation in SLE patients which was affected by different factors like lifestyle, psychological health and types of therapies [22], the *OGG1* gene polymorphism were associated with some disease like diabetes mellitus [23], Huntington's disease and some types of cancer [24,25]. However the *OGG1* role in SLE pathogenesis didn't fully understand, on the other hand Lee concluded that the *OGG1* genotyping is one factors of SLE nephritis via C1245G polymorphism [26]. The level of DNA damage should be detected in individuals as a prognostic preliminary for avoid the prospective harmful effects which may be contributed in the development disease like SLE.

## Conclusion

The present study concluded that the *RAD-18 Arg302Gln* (rs373572) didn't associated with SLE while *OGG1 Ser326Cys* (rs1052133) associated with disease in significant differences. The incidence percentages were recorded in female at nine fold higher than male and 2-3 fold higher in Asian African and Native American Ancestry than other population, the genome wide association found more than 50 risk alleles contributed in the SLE pathogenicity and major of them associated with immune system response in addition to the other genetic predisposition factors. The Systemic Lupus Erythematosus (SLE) disease is an autoimmune disease incidence by different genetic and environment factors, the present research study two DNA repair genes polymorphisms in SLE disease included *RAD-18 Arg302Gln* (rs373572) and *OGG1 Ser326Cys* (rs1052133) genes, the

polymorphisms were detected using allele specific PCR and PCR-SSCP, patients were diagnosed by a specialist physician then DNA was isolated from whole blood, the results show that the *RAD-18* gene variation shows no significant differences between patients and control. The *RAD-18* gene is located at 3p25.3 and encoded for an E3 ubiquitin-protein ligase, it has an important role in the repair of DNA lesions in DNA post replication.

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