REVEIW ARTICLE

The tRNA^{leu} Gene Variation in Systemic Lupus Erythematosus Patients

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ABSTRACT

The systematic lupus erythematosus (SLE) is an autoimmune disease characterized by the immune molecules attach its own tissue, the present resarch implemented to detection tRNA^{leu} gene variation in SLE by case control study. polymerase chain reaction (PCR)-sequencing used to detection mutation, results show strong association between tRNA^{leu} encoded gene and SLE disease and this represented by the high percentage of variation in patient than control group, deletion mutation were 80 nucleotides in patients and 50 nucleotides in the control group, and substitution mutations were 103 nucleotides in patients and 81 nucleotides in the control group, the different types of substitution mutations included (G>A, G>T, G>C, A>G, A>T, A>C, C>A, C>G, C>T, T>G, T>A and T>C) in significant differences ($p = 0.007$), the present study concludes that the variations in tRNA^{leu} gene may be effect in the tRNA folding that lead to effect in amino acid transfer during protein synthesis.

Keywords: Gene variation, Systematic lupus erythematosus, The tRNA^{leu}.

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INTRODUCTION

The SLE disease is a chronic relapsing autoimmune disorder that primarily affects women. The disease coincides with the production of autoantibodies to molecules of nucleic acids and other cellular antigens, which leads to the formation of immune complexes and their deposition in the systemic organs, which causes inflammation and damage in that organ (Rai *et al.,* 2006).[1]

The disease is also a chronic disease, in which the immune system of the sick person plays a reverse role. The antibodies produced by the immune system attack healthy cells and tissues instead of the infected ones, and these complexes are deposited and attack the various internal organs of the body e.g., the lung, heart, joints, blood, kidneys and the brain and the skin (Kozora *et al*., 2012).[2]

The SLE is a Rheumatic disorder that causes aches, pain and stiffness in the joints, muscles and bones, the virulence of the disease increases when some people have a genetic predisposition to the disease as well as factors that help in the progression of the disease such as environmental factors such as ultraviolet radiation, silica, and infectious agents that induced oxidative stress.[3,4]

The mitochondrial tRNA^{leu} gene encoded to RNA molecule called a transfer RNA (tRNA), which transfer amino acid Lucien during protein synthesis.[5] Evidence found the numerous Pathological mutations in tRNA genes and tRNA processing enzymes with very complicated clinical phenotypes, The mt-tRNA genes considered as hotspots of pathological mutations, more than 200 mt-tRNA mutations have been associated with various disease states.[6] The present investigate was suggested to detect some mutation in tRNA of Lucien gene in SLE patients

METHODOLOGY

A case control study including A 40 SLE patients attended a chronic disease clinic in the Marjan hospital city and 30 healthy individuals for the control group were enrolled in the present study. Their blood samples were collected after written consents. Some criteria were excluded like cancer, Hyperthyroidism, diabetes mellitus and hypertension patients.

DNA Extraction

The deoxyribonucleic acid (DNA) was extracted from frozen blood by favorgene extraction kit, then tRNA^{leu} was amplified using site specific primer to produce 200 bp, then PCR products were sequenced by genetic analyzer (3600 thermo-fisher), sequence data analysis using MAFFT version 7, https://mafft.cbrc.jp/alignment/software.

RESULT AND DISCUSSION

The Current study aims to determination of variation in mtDNA tRNA^{leu} gene and associated with SLE. DNA extracted from frozen blood showed in Figure 1. The result of the

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Polymerase chain reaction (PCR) showed tRNA^{leu} gene product has one band about 200 bp included the tRNA^{leu} sequences that has 75n for both SLE patients and the control group as shown in Figure 2.

The results of current study show high percentage of variations in patient than control group, deletion mutation was 80 n in patients and 50 in control group, while substitution mutations were 105 in patients and 81 in control group, these mutations included (G>A, G>T, G>C, A>G, A>T, A>C, C>A, C>G, C>T, T>G, T>A and T>C) in significant differences if frequency (P 0.007) (table1), and these mutations effect on the severity of disease, our results agree with a study conducted by Karicheva *et al*.,2011[7] who described the human mtDNA mutation which associated

NCBI Sequences

With incurable human autoimmune diseases, an important number among these mutations have been detected within the tRNA genes, like 29 mutations in the *MT-TL1* gene encoding to the tRNA^{Leu,} which were reported to lower tRNA^{Leu} aminoacylation and alteration in its anti-codon in wobble position that led to defective in mitochondrial protein synthesis and decrease in the respiratory chain complexes activities.[8,9]

Numerous studies referred to the mitochondrial dysfunction have a key role in the SLE pathogenesis, including damage in mitochondrial DNA, mitochondrial dynamics alteration, abnormal mitochondrial biogenesis and energy metabolism, oxidative stress induction, mitophagy inflammatory reactions, programed cell death, specific lupus-induced organ damage also exhibits characteristic mitochondrial changes.[10] However current study agrees with Liu and Chen, (2020)[11] that Mutation in mtDNA (tRNA gen) changes the structure of tRNA, that led to metabolic disorders and affected in the protein synthesis, defects in the oxidative phosphorylation, lowering adenosine triphosphate (ATP) synthesis, and increase production of reactive oxygen species.

The mutation in mtDNA may be because of high levels of oxidative damage, high mutation number were found with the elevation of ROS in the inner membrane of mitochondria. Notably the mutation in mtDNA were found to be more than mutations in nuclear DNA and this belongs to limited of DNA

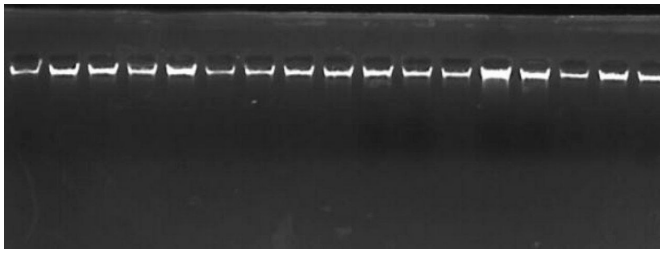

Figure 1: Electrophoreses pattern of DNA extracted from SLE patients and control, 1% Agarose, 75 v, 20 mA for 1 hour

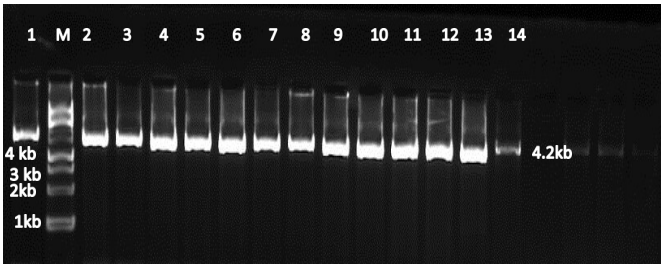

Figure 2: Electrophoreses pattern of PCR of tRNAleu gene of SLE patient and control, 1% Agarose, 75 v, 20 m for 50 min.

Table 1: The mutation frequency of tRNA^{leu} in SLE patient and control group

Type of mutations	*SLE patients*	*Control*	X^2	*Sig*
Deletion mutation	80	50	27.033	0.0076
G>A	16	3		
G>T	3	0		
G>C	2	0		
T>A	8	3		
T>G	9	3		
T>C	9	8		
A>G	13	6		
A>C	7	13		
A>T	6	7		
C>A	10	9		
C>G	6	2		
C>T	16	27		
Total	185	131		

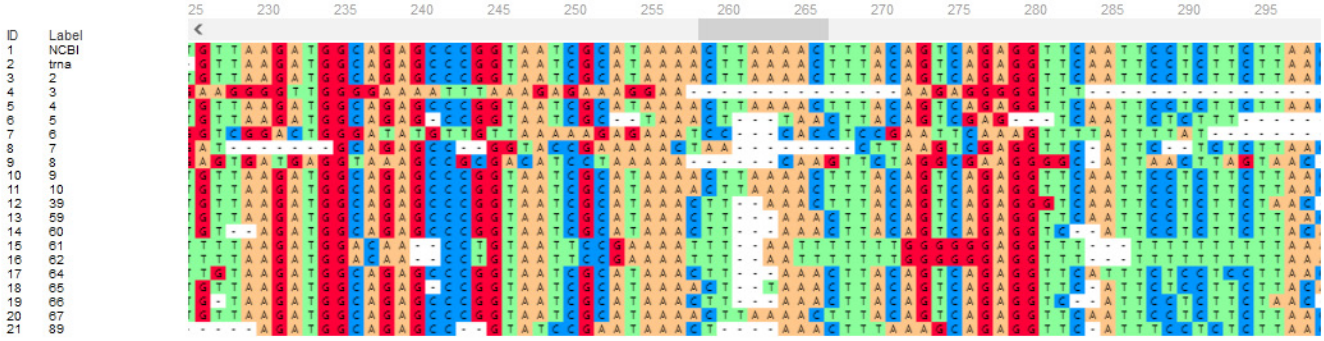

Figure 3: Multiple comparisons of study subjects mtDNA sequences of tRNA^{leu}

repair system, lack histone proteins.[12,13] The mutations were observed in current investigate may be affected in the tRNA folding and amino acid transfer during protein synthesis in SLE patents and this may be contributed in the disease severity.

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