

Lack of Association between *Interleukin-12* Gene Polymorphisms and Recurrent Aphthous Stomatitis

Isaac Firouze Moqadam¹, Shamsolmoulouk Najafi², Mahsa Mohammadzadeh³, Alireza Zare Bidoki⁴, Hila Yousefi^{5,6,7}, Elham Farhadi⁸, Arghavan Tonekaboni², Ghasem Meighani⁹, Mohsen Mohammadzadeh¹⁰, Ali Akbar Amirzargar⁴, and Nima Rezaei^{7,11*}

1. Molecular Medicine Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Dental Research Center, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
3. Orthodontic Department, Dental Branch, Islamic Azad University, Tehran, Iran
4. Molecular Immunology Research Center, Tehran University of Medical Sciences, Tehran, Iran
5. Nature of Gene Mutation Group (NGMG), Universal Scientific Education and Research Network (USERN), Tehran, Iran
6. Department of Endodontics, Dental Branch, Islamic Azad University, Tehran, Iran
7. Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran
8. Department of Hematology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
9. Department of Pediatrics, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
10. Department of Ophthalmology, Khatam Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
11. Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Boston, MA, USA

Recurrent Aphthous Stomatitis (RAS) is the most common oral inflammatory disease, which is a painful, ulcerative condition of the oral cavity¹ and is characterized by episodic, small, round ulcers with erythematous halos². Although several factors such as systemic diseases, nutritional factors, psychological stress, local trauma, allergies, smoking and hormonal alterations could be associated with RAS, genetic factors seem to have an important role in predisposition to this condition whereas the exact pathogenesis of the disease has not clearly been understood³.

Interleukin (IL)-12 which is secreted by macrophages and dendritic cells has a key role in differentiation of Th0 cells into Th1 cells⁴, and therefore it could theoretically have a role in RAS pathogenesis. Considering the fact that SNP could affect the cytokine secretion, an attempt was made to evaluate the alleles and genotypes frequencies of *IL12* gene in a group of patients with RAS.

In this investigation, 5 ml blood from sixty four Iranian patients with confirmed diagnosis of RAS⁵ was collected in the EDTA tubes. DNA was extracted using a phenol-chloroform method. This project was approved by Ethics Committee of Tehran University of Medical Sciences. Written informed consent was obtained from all subjects before sampling. *IL12* gene typing was performed by Polymerase Chain Reaction with Sequence-Specific Primers (PCR-SSP) assay (PCR-SSP kit, Heidelberg University, Heidelberg, Germany), similar to what explained before⁶. The allele and genotype frequencies of *IL12* (A -1188 C) were investigated. Allele frequencies were estimated by direct gene counting. The results were compared to the number of alleles and genotypes in 140 healthy controls from the same re-

gion. Chi-square test was used to compare frequencies of alleles, genotypes and haplotypes between patients and control groups. The odds ratio (OR) and 95% Confidence Intervals (95%CI) were calculated. P-value (*p*) of less than 0.05 was considered significant.

The results showed that A allele was the most frequent allele among patients and controls. It was detected in 77.1% of patients and was detected in 72.9% of healthy controls. This has been reflected in AA genotype, which was the most common genotype among all enrolled individuals. AA genotype was detected in 57.9% of the patients, which was insignificantly higher than 51.4% in the controls. No significant difference was found on *IL12* alleles and genotype frequencies between the patients and the controls (Table 1).

In several studies, association of number of cytokine gene polymorphisms in pathogenesis of RAS has been investigated^{7,8}. In this study, the possible role of *IL12* SNP with RAS was investigated and no association was found which is similar to previous studies⁹. It has been documented that an A to C exchange in the 3'-UTR of *IL12* gene at position -1188 correlates with low cytokine secretion¹⁰. In the present study, *IL12* SNP was evaluated at that position which is located in the promoter region of the gene. However, no significant difference on *IL12* (A -1188 C) alleles and genotypes between the patients and the controls was found.

Lack of association between *IL12* (A -1188 C) polymorphisms and RAS could indicate that IL-12 has no significant role in pathophysiology of RAS.

Keywords: Interleukin 12, Recurrent aphthous stomatitis, Single nucleotide polymorphisms

Table 1. Comparison of alleles, genotype frequencies of *IL12* between patients with RAS and the control group

Position	Alleles/ Genotypes/Haplotypes	RAS (n=60), n(%)	Controls (n=140), n(%)	p-value	Odds Ratio (95% Confidence Interval)
-1188	A	91(77.1)	204(72.9)	0.446	1.26(0.74-2.15)
	C	27(22.9)	76(27.1)	0.446	0.80(0.47-1.36)
	AA	34(57.6)	72(51.4)	0.519	1.28(0.67-2.48)
	CA	23(39)	60(42.9)	0.727	0.85(0.44-1.66)
	CC	2(3.4)	8(5.7)	0.387	0.58(0.08-3.08)

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*Corresponding author: Nima Rezaei, M.D., Ph.D., Children's Medical Center Hospital, Dr Gharib St, Keshavarz Blvd, Tehran, Iran
Tel: +98 21 66929234
Fax: +98 21 66929235
E-mail: rezaei_nima@tums.ac.ir

Received: 25 Dec 2015
Accepted: 13 Feb 2016