Polymorphism of Foxp3 gene affects the frequency of regulatory T cells and disease activity in patients with rheumatoid arthritis in Iranian population


*Department of Basic Science, Faculty of Medicine, Maragheh University of Medical Sciences, Maragheh, Iran
**Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
**Department of Oncology-Pathology, Immune and Gene therapy Lab, Cancer Center Karolinska (CCK), Karolinska University Hospital Solna and Karolinska Institute, Stockholm, Sweden

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disease that mainly affects joints and characterized by chronic joint inflammation and infiltration of various immune cells in the synovium. Forkhead box P3 (Foxp3)-expressing regulatory T cells (Tregs) play a crucial role in preventing autoimmunity and undesirable T cell responses. However, there are controversial reports regarding the defective function or frequency of these cells in various studies, which may be in part related to different polymorphisms of Foxp3 and influence of ethnicity on these differences. Therefore, the main subject of this study was to evaluate the association of Foxp3 gene polymorphism and Treg frequency in Iranian patients with RA. Accordingly, 240 RA patients diagnosed according to American college of rheumatology 2010 criteria and 240 normal subjects were recruited for this study. Genomic DNA was genotyped for -3279 C/A Foxp3 gene SNP using the PCR-RFLP. The frequency of Tregs and serum levels of interleukin (IL)-10, transforming growth factor (TGF)-β, anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) were determined by flow cytometry and ELISA methods, respectively. The results showed a significant association of Foxp3 –3279 A allele with augmented risk of RA in Iranian patients compared to wild-type allele. While the frequencies of CA and AA genotypes were significantly higher in patients, RA patients with AA genotype had a significant lower frequency of Tregs compared to patients with CC and CA genotypes. Consistently, TGF-β and IL-10 significantly diminished in patients with AA genotype compared to patients with CA and CC genotypes. Our findings indicated that the AA genotype of Foxp3 in RA patients is associated with downregulation of Tregs and susceptibility to RA in the Iranian population.

1. Introduction

Rheumatoid arthritis (RA) is one of the most common chronic inflammatory autoimmune diseases characterized by destruction of the joint cartilage and bone. RA is associated with inflammation and pathological infiltration of lymphocytes in the synovium [1]. This condition might be resulted from both humoral and cell mediated immune responses. T cells are the main synovial membrane-infiltrated immune cells in RA patients [2]. Failure of self-antigens tolerance is one of the main triggers of the RA, which is characterized by constitutive stimulation of immune system leading to tissue damage [3]. Although the immunopathogenesis of RA remains elusive, the main reason seems

* Corresponding author at: Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
** Corresponding author at: Department of Immunology, School of Medicine, Semnan University of Medical Sciences, Semnan, 35198-99951, Iran.
E-mail addresses: A.salek@semums.ac.ir (A.S. Farrokhi), jadidi@themed.ac.ir (F. Jadidi-Niaragh).

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