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Review

# Role of apoptosis in common variable immunodeficiency and selective immunoglobulin A deficiency

Reza Yazdani[a,b], Maryam Fatholahi[c], Mazdak Ganjalikhani-Hakemi[a], Hassan Abolhassani[b,d], Gholamreza Azizi[e], Kabir Magaji Hamid[f,g], Nima Rezaei[h], Asghar Aghamohammadi[b,*]

[a] Department of Immunology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Research Center for Immunodeficiencies, Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Science, Tehran, Iran
[c] Department of Biology, Faculty of Science, University of Isfahan, Isfahan, Iran
[d] Division of Clinical Immunology, Department of Laboratory Medicine, Karolinska Institutet at the Karolinska University Hospital Huddinge, Stockholm, Sweden
[e] Imam Hassan Mojtaba Hospital, Alborz University of Medical Sciences, Karaj, Iran
[f] Immunology Department, School of Public Health, Tehran University of Medical Sciences-International Campus (TUMS-IC), Tehran, Iran
[g] Immunology Department, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria
[h] Department of Immunology, School of Medicine, Tehran University of Medical Science, Tehran, Iran

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ABSTRACT

Common variable immunodeficiency (CVID) and selective IgA deficiency (SIgAD) are the most common primary immunodeficiencies in human. Both diseases share clinical manifestation and molecular defects. Increased apoptosis may be one of the mechanisms involved in the pathogenesis of CVID and SIgAD. Elevated apoptosis in this disorder leads to defective long-term survival of B-cells, reduced antibody production, decreased lymphocyte proliferation and defective cytokine secretion. For the first time, we reviewed the role of apoptosis in CVID and SIgAD.



## 1. Introduction

Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency characterized by defective antibody production and an increased incidence of recurrent bacterial infections, inflammatory and autoimmune disorders, malignancies and granuloma (Cunningham-Rundles and Bodian, 1999; Aghamohammadi et al., 2005; Chapel and Cunningham-Rundles, 2009; Aghamohammadi et al., 2010). CVID has prevalence rate of about 1:50,000 to 1:25,000 (Cunningham-Rundles, 2010; Jolles, 2013). The diagnostic criteria for CVID includes marked reduction of serum IgG, IgA, and/or IgM levels, defective specific antibody responses to protein and polysaccharide antigens and also increased susceptibility to recurrent bacterial infections as well as no evidence of profound T-cell deficiency in patients older than 4 years (Aghamohammadi et al., 2005; Chapel et al., 2008). CVID has a complex genetic basis and may arise from a number of different gene defects involved in B-cell activation and differentiation, for instance *inducible T-cell costimulator* (*ICOS*) (Grimbacher et al., 2003), *transmembrane activator and CALM interactor* (*TACI*) (Salzer et al., 2005), *B-cell activating factor-receptor* (*BAFF-R*) (Warnatz et al., 2009), *CD19, CD21, CD81* (van Zelm et al., 2006; van Zelm et al., 2010; Thiel et al., 2012; Yazdani et al., 2014), *CD20* (Kuijpers et al., 2010), *Lipopolysaccharide-responsive and beige-like anchor protein* (*LRBA*) (Lopez-Herrera et al., 2012) and *Phospholipase Cγ2* (*PLCγ2*) (Ombrello et al., 2012) genes. In spite of the results obtained from recent years, many underlying defects are not yet known (Eibel et al., 2010).

Selective IgA deficiency (SIgAD) is the most common primary antibody deficiencydescribed as serum IgA level of less than 7 mg/dl, in the presence of normal IgG subclasses and IgM as well as normal specific antibody response in individuals older than 4 years and exclusion of other causes of hypogammaglobulinaemia (Aghamohammadi et al., 2009; Wang and Hammarström, 2012). Prevalence of SIgAD differs among racial groups, ranging from lowest frequency in Asian and oriental populations to the highest frequency in Caucasians and western countries (Yel, 2010; Modell et al., 2014; Yazdani et al., 2015). Individuals with SIgAD usually are asymptomatic, however abnormality of immunoglob-

* Corresponding author at: Children's Medical Center Hospital, 62 Qarib St., Keshavarz Blvd., Tehran 14194, Iran. Fax: +98 21 6692 3054.
*E-mail address:* aghamohammadi@sina.tums.ac.ir (A. Aghamohammadi).

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