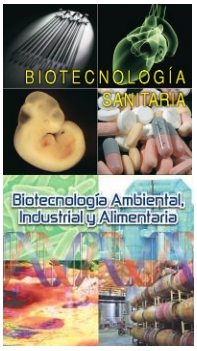
Poster

Funcional characterization of a heterozygous mutation in LRBA



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ABSTRACT

Common variable immunodeficiency (CVID) is an exclusion diagnosis that presents a highly variable clinical picture, mainly characterized by persistent hypogammaglobulinemia and recurrent bacterial infections, accompanied in 20-30% of cases by autoimmune, lymphoproliferative or granulomatous manifestations [1]. CVID is associated with alterations in a group of genes involved in the stimulation, survival and development of B lymphocytes [2], among which is included LRBA (lipopolysaccharide Responsive and Beige-Like Anchor Protein); a gene that encodes a large protein with diverse anchoring domains that is expressed in multiple tissues and intracellular structures [3]. LRBA has multiple functions; acting as a regulatory scaffold between the compartments of the endomembrane system, modulating the trafficking and activity of vesicles and proteins, including the secretion of cytokines and immunoglobulins and acting as a key factor in cell proliferation, autophagy and apoptosis; essential functions for the proper functioning of the immune system [2]. On the other hand, the protein structure of LRBA also contains characteristic domains and properties that predict its AKAP (A-kinase anchoring proteins) function; important signaling for the development and proliferation of T lymphocytes [2]. LRBA deficiency has been associated with alterations in the development, activation and autophagy of B lymphocytes, increased susceptibility to apoptosis, hypogammaglobulinemia and decreased proliferative response, findings that may be accompanied by a T lymphocyte deficiency [1].The phenotypic spectrum is very broad and most patients with biallelic deleterious mutations in LRBA develop CVID, whereas individuals with a single affected allele have a higher probability of developing this immunodeficiency or diverse autoimmune disorders [1]. In this work, we aim to study two siblings who are carriers of a heterozygous mutation in the LRBA gene (C127G>A, Gly43Ser) and display inflammatory and autoimmune manifestations. To this end, lymphoblastoid cell lines will be generated from their blood samples by EBV infection and different biochemical and immunological techniques will be performed to characterize the functional alterations of the LRBA mutation and its effect on the immune cells of the patients.

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