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ORIGINAL ARTICLE

Genetic polymorphisms of interleukin-22 in patients with ulcerative colitis☆

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KEYWORDS
Genetic susceptibility;
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Abstract
Background: Ulcerative colitis (UC) is a multifactorial and polygenic disease. Interleukin-22 (IL-22) is an immunomodulatory cytokine that belongs to the IL-10 family. Currently, some IL-22 polymorphisms have been associated with inflammatory processes such as rheumatoid arthritis and psoriasis vulgaris, but there are no studies on UC.
Aim: The aim of this work was to study the frequency of polymorphisms of IL-22 in Mexican patients with UC.
Methods: We studied a total of 199 Mexican patients with confirmed UC and 697 healthy controls. All individuals were born in Mexico, at least three family generations earlier. A blood sample was obtained from the UC patients and healthy controls in order to perform DNA extraction and then to determine the frequency of IL-22 polymorphisms (rs2227485, rs2272478, rs2227491).
Results: No statistical significance was found in the gene and genotype frequencies of three SNPs of IL-22 (rs2227485, rs2272478, rs2227491) between the UC patients and healthy controls. No association was found between those IL-22 SNPs and clinical features of UC.
Conclusions: There was no association between IL-22 SNPs (rs2227485, rs2272478, rs2227491) and the development of UC in a Mexican population.

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PALABRAS CLAVE
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Colitis ulcerosa

Polimorfismos genéticos de interleucina-22 en pacientes con colitis ulcerosa

Resumen
Antecedentes: La colitis ulcerosa (CU) es una enfermedad multifactorial y poligénica. La interleucina (IL) 22 es una citocina inmunomoduladora que pertenece a la familia de IL-10. Actualmente, algunos polimorfismos de la IL-22 han sido asociados con procesos inflamatorios, como artritis reumatoide y psoriasis vulgar, sin embargo, no hay estudios en pacientes con CU.
Objetivo: El objetivo del presente trabajo es estudiar la frecuencia de polimorfismos de la IL-22 en pacientes con CU.
Métodos: Se estudió a 199 pacientes mexicanos con diagnóstico confirmado de CU y 697 controles sanos. Todos los individuos de estudio nacieron en México, al igual que sus últimas 3 generaciones. Se obtuvieron muestras de sangre de cada individuo y se extrajo ADN; finalmente, se determinó la frecuencia de polimorfismos en la IL-22 (rs2227485, rs2272478, rs2227491).
Resultados: No se encontró diferencia significativa en la frecuencia del gen y genotipo de los SNP en la IL-22 (rs2227485, rs2272478, rs2227491) entre pacientes con CU y controles sanos. No se encontró asociación entre los SNP de la IL-22 y las características clínicas de la CU.
Conclusiones: Ausencia de asociación entre los SNP de la IL-22 (rs2227485, rs2272478, rs2227491) y el desarrollo de CU en población mexicana.

Introduction

Ulcerative colitis (UC) is a multifactorial disease of unknown etiology. It is considered a polygenic disorder that interacts with immunologic and environmental factors, leading to a chronic and relapsing colonic inflammation characterized by an aberrant immune response.[1] The Genome-Wide Association Studies (GWAS) of UC have identified more than 25,000 possible single nucleotide polymorphisms (SNP) for inflammatory bowel disease (IBD) in susceptible regions on several chromosomes such as 1, 3, 4, 5, 6, 7, 10, 12, 14, 16, 19, and X.[2,3] It is established that mucosal inflammation is triggered by various cytokines produced by different pathways, such as the Th1, Th2, and recently the Th17 immunological response.[4]

IL-22 is a 16.7 KDa immunomodulatory cytokine primarily produced by activated T cells and natural killer cells. It belongs to the IL-10 family, which also includes IL-19, IL-20, IL-24, IL-26, IL-28, and IL-29.[5] This cytokine acts as an effector of the Th17 pathway in response to IL-23 with pro-inflammatory and anti-inflammatory properties that may be implicated in the pathogenesis of IBD. A previous study reported an increased gene expression of IL-22 in the mucosa from rectal biopsies of patients with active UC.[6] The IL-22 gene is a 5.3 Kb region located in the 12q15 loci of the chromosome 12, close to the genes encoding IFN-γ and IL-26.[7]

Currently, some IL-22 polymorphisms have been associated with inflammatory processes, such as rheumatoid arthritis,[8] psoriasis vulgaris,[9] multiple sclerosis,[10] asthma,[11] fungal-bacterial infections, and mice models of IBD infected with Citrobacter rodentium.[12] There are no previous studies that evaluate the role of IL-22 SNPs in patients with UC. Thus, the aim of this study was to determine the frequency of IL-22 SNPs (rs2227485, rs2272478, rs2227491) in Mexican patients with UC.

Material and methods

Patients and controls

Patients: One hundred ninety-nine Mexican patients with diagnosis of UC confirmed by histology were studied. These patients were recruited from the Inflammatory Bowel Disease Clinic at the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran* in Mexico City. None of the participants had a family history of IBD.

Both demographic and clinical information were obtained via interview and from medical records. The demographic and clinical variables considered in the analysis were: current age, UC duration, extension of disease (pancolitis, left colitis, or distal colitis), presence of extraintestinal manifestations (EIMs), clinical course of disease, response to medical treatment, and the presence of procto-colectomy. The clinical course of disease was defined as: active then inactive (first episode followed by a long-term remission for more than 5 years), intermittent (fewer than 2 relapses per year), and chronic activity (persistent activity despite medical treatment). Response to medical treatment was categorized as follows: favorable, steroid-dependent (relapse when prednisone was tapered below 15 mg/day or 3 months after suspending the steroid); steroid-resistant (persistent activity with prednisone of at least 0.5 mg/kg/day); immune modulator-resistant (lack of steroid sparing with azathioprine dose of at least 2 mg/kg/day for more than 3 months).