Cirugía y Cirujanos. 2016;84(1):28–36

CIRUGÍA y CIRUJANOS
Órgano de difusión científica de la Academia Mexicana de Cirugía
Fundada en 1933
www.amc.org.mx www.elsevier.es/circir

ORIGINAL ARTICLE

High frequency of ancestral allele of the *TJP1* polymorphism rs2291166 in Mexican population, conformational effect and applications in surgery and medicine☆

Sergio Alberto Ramirez-Garcia[a], Luis Javier Flores-Alvarado[b], Luz Rosalba Topete-González[c], Claudia Charles-Niño[d], Manuel Mazariegos-Rubi[e], Nory Omayra Dávalos-Rodríguez[e,*], Grupo Multidisciplinario para el Estudio Integral de las Enfermedades Metabólicas e Infecciosas en población Mexicana

[a] *Universidad de la Sierra Sur, Instituto de Investigaciones sobre la Salud Pública, Sistema de Universidades Estatales de Oaxaca (SUNEO), Miahuatlán de Porfirio Díaz, Oaxaca, Mexico*
[b] *Programa de Doctorado en Genética Humana, Benemérita Universidad de Guadalajara, Mexico*
[c] *Laboratorio de Patología Clínica, Hospital Regional Valentín Gómez Farías, Instituto de Seguridad y Servicios Sociales de los trabajadores del Estado, Guadalajara, Jalisco, Mexico*
[d] *Departamento de Microbiología y Patología, Centro Universitario de Ciencias de la Salud, Benemérita Universidad de Guadalajara, Guadalajara, Jalisco, Mexico*
[e] *Laboratorio de Variación Genética y Enfermedad del Instituto de Genética Humana, Departamento de Biología Molecular y Genómica, Centro Universitario de Ciencias de la Salud (CUCS), Benemérita Universidad de Guadalajara, Jalisco, Mexico*

Received 18 November 2014; accepted 2 June 2015

KEYWORDS
Gen TJP1;
Tight junctions;
Cell polarity;
Cell traffic

Abstract
Background: *TJP1* gene encodes a ZO-1 protein that is required for the recruitment of occludins and claudins in tight junction, and is involved in cell polarisation. It has different variations, the frequency of which has been studied in different populations. In Mexico there are no studies of this gene. These are required because their polymorphisms can be used in studies associated with medicine and surgery. Therefore, the aim of this study was to estimate the frequency of alleles and genotypes of rs2291166 gene polymorphism *TJP1* in Mexico Mestizos population, and to estimate the conformational effect of an amino acid change.

☆ Please cite this article as: Ramirez-Garcia SA, Flores-Alvarado LJ, Topete-González LR, Charles-Niño C, Mazariegos-Rubi M, Dávalos-Rodríguez NO, et al. Alta frecuencia del alelo ancestral del polimorfismo rs2291166 de *TJP1* en población mexicana, efecto conformacional así como las aplicaciones en cirugía y medicina. Cirugía y Cirujanos. 2016;84:28–36.

* Corresponding author at: Instituto de Genética Humana, Dr. Enrique Corona Rivera, Programa de Doctorado en Genética Humana, Centro Universitario de Ciencias de la Salud, Benemérita Universidad de Guadalajara, Sierra Mojada 950, edificio Q, Segundo nivel, Col.: Lomas de Independencia, Apartado Postal 72340, Guadalajara, Jalisco, Mexico. Tel.: +52 33 1058 5200 ext. 3646.
E-mail address: sergio7genetica@Hotmail.com (N.O. Dávalos-Rodríguez).

Material and methods: A total of 473 individuals were included. The rs2291166 polymorphism was identified PASA PCR-7% PAGE, and stained with silver nitrate. The conformational effect of amino acid change was performed *in silico*, and was carried out with servers ProtPraram Tool and Search Database with Fasta.
Results: The most frequent allele in the two populations is the ancestral allele (T). A genotype distribution similar to other populations was found. The polymorphism is in Hardy–Weinberg, $p > 0.05$. Changing aspartate to alanine produced a conformational change.
Conclusions: The study reveals a high frequency of the ancestral allele at rs2291166 polymorphism in the Mexican population.

PALABRAS CLAVE
Gen *TJP1*;
Uniones estrechas;
Polaridad celular;
Tráfico celular

Alta frecuencia del alelo ancestral del polimorfismo rs2291166 de *TJP1* en población mexicana, efecto conformacional así como las aplicaciones en cirugía y medicina

Resumen
Antecedentes: El gen *TJP1* codifica para una proteína ZO-1, necesaria para el reclutamiento de las ocludinas y claudinas en las uniones estrechas y participa en la polarización celular. Tiene diferentes variaciones cuya frecuencia ha sido estudiada en numerosas poblaciones; sin embargo en México no hay estudios de este gen, siendo necesarios ya que sus polimorfismos pueden ser usados en estudios de asociación en medicina y en cirugía. Por tal motivo el objetivo de este estudio fue estimar la frecuencia de alelos y genotipos del polimorfismo rs2291166 del gen *TJP1* en población mestiza de México; así como estimar el efecto conformacional del cambio de un aminoácido.
Material y métodos: Se incluyeron 473 individuos. El polimorfismo rs2291166 se identificó por PCR-PASA y PAGE al 7% teñida con nitrato de plata. El efecto conformacional de cambio de aminoácido se realizó *in silico* con los servidores ProtPraram Tool y Search Database with Fasta.
Resultados: El alelo más frecuente en las dos poblaciones es el alelo ancestral (T). Se encontró una distribución similar a otras poblaciones respecto a los genotipos. El polimorfismo está en equilibrio de Hardy-Weinberg, $p > 0.05$. El cambio de aspartato por alanina produce un cambio conformacional.
Conclusiones: El estudio revela alta frecuencia del alelo ancestral en población mexicana del polimorfismo rs2291166 y produce un cambio en la estructura de ZO-1.

Background

In the postgenomic era there are three paradigms of interest in general surgery: the carrying out of customised surgical procedures, prediction and the prevention of pre-inter- and post-surgical complications.[1–3] Few studies on genes have been carried out on the Mexican population, and the ones that have focused on the process of fibrogenesis, on polymorphisms in genes *TGF-β*, *PAI-1*, *AT*, which are associated with post-mammoplasty capsular contracture or response to treatment with pirfenidone.[4–6] In clinical practice the polymorphism rs1345365 of *ELMO1*[7] has recently been proposed as a marker.

Apart from these genes, new markers must be sought to be used in everyday diseases of the oncology, urology, gynaecological, internal medicine and gastroenterological surgeon. These would be, for example: acute pancreatitis, chronic pancreatitis, hydatiform mole; several types of cancer (thyroid, pancreas, biliary ducts, liver and colon). Variants of the *TJP1* (Tight Junction Protein-1) gene are proposed as markers in customised practice. This is for two reasons: *first*, that the *TJP1* gene encodes ZO-1 (Zona Occludens-1) protein, which forms part of the narrow or contact cell-to-cell bonds because it participates in cellular differentiation, cytokinesis and chemotaxis.[8–12] *Second*, because alteration in the architecture of ZO-1 was reported in animal models, in *in vivo* studies and tissue cultures, in two groups: either through reduction of the protein expression, or its increase; for the first case this corresponds to partial molar pregnancies, complete hydatiform moles, intrahepatic cholangiocarcinomas and extra hepatics such as extraheptatic tumours, tumours of the gallbladder, and stage 4TLM breast tumours.[12–16] The second group includes pancreatic ductal adenocarcinoma, stage I-II de cancer of the colon and cancer of the colon with liver metástasis.[17–22] The increase of TJP1 has been recently reported in 71% of gastrointestinal neoplasia cases, where expression is proportional to tumour diameter, histological staging and the