Tight Junction Protein 1 Gene in Neurodegenerative Disease, New Frontier

Introduction

The older adults are a consequence of the aging process and may be susceptible to the development of metabolic diseases related to atherosclerosis such as vascular dementia, cerebrovascular disease, or neurodegenerative diseases such as essential tremor, Parkinson plus syndromes, Parkinson’s disease. Prevention, diagnosis and biomonitoring require the search for new genetic markers that are predictive of their clinical evolution or response to treatment. One of the candidate genes for these purposes is the Tight Junction Protein 1 (TJP1) gene, which codes for the Zona occludens 1 (ZO-1). It has stayed than tight junctions that constitute the blood-brain barrier which controls the intracellular diffusion and maintains the functional structural of endothelial cells. Structure or function of tight junctions can lead to the blood-brain barrier dysfunction that consequently may contribute to the development of neurodegenerative diseases. Blood-brain barrier disruption, associated with alterations of tight junctions, has been implicated in the pathogenesis of neurodegenerative disorders including multiple sclerosis, stroke, Alzheimer’s and Parkinson’s disease. In this sense, genetic marker of the gene that leads to amino acid changes, such as polymorphism rs229166 leads to a conformational change in the ZO-1 structure. Some of those polymorphisms that lead to amino acid changes in critical domains of the protein are rs1038306187 leading to the change of amino acid p.Gln791Glu in the domain guanylate kinase (Location residue 682-861). The domain ZU5 (Location residue 1701-1799) has 33 polymorphisms leading to conformational changes (Table 1). Polymorphisms that affect gene expression, by nucleotide changes at the cryptic sites of the alternative splicing, such as rs781148827, rs5478300017, rs78014403 and rs1020739943 in acceptor region, and rs1029122894 in the donor region. None of these polymorphisms have been explored for their pathogenic effect, which is why they are a new frontier of research in neurodegenerative disease related to aging, due to their effect on ZO-1 expression.

Table 1: Polymorphisms in the TJP1 en region encoding by the ZU5 domain.

<table>
<thead>
<tr>
<th>Number SNP</th>
<th>Reference</th>
<th>Nucleotide Change</th>
<th>Protein Change</th>
<th>Protein Residue</th>
<th>Number SNP</th>
<th>Reference</th>
<th>Nucleotide Change</th>
<th>Protein Change</th>
<th>Protein Residue</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs756391449</td>
<td>missense</td>
<td>T</td>
<td>Val [V]</td>
<td>1786</td>
<td>rs200636289</td>
<td>missense</td>
<td>A</td>
<td>Lys [K]</td>
<td>1732</td>
</tr>
<tr>
<td>rs778206679</td>
<td>missense</td>
<td>T</td>
<td>Cys [C]</td>
<td>1781</td>
<td>rs780493261</td>
<td>missense</td>
<td>G</td>
<td>Glu [E]</td>
<td>1732</td>
</tr>
<tr>
<td>rs769840007</td>
<td>missense</td>
<td>T</td>
<td>Ser [S]</td>
<td>1777</td>
<td>rs747547138</td>
<td>missense</td>
<td>A</td>
<td>Arg [R]</td>
<td>1728</td>
</tr>
<tr>
<td>rs771212279</td>
<td>missense</td>
<td>T</td>
<td>Asn [N]</td>
<td>1773</td>
<td>rs777243709</td>
<td>missense</td>
<td>G</td>
<td>Met [M]</td>
<td>1723</td>
</tr>
<tr>
<td>rs779424333</td>
<td>missense</td>
<td>G</td>
<td>Val [V]</td>
<td>1772</td>
<td>rs748887539</td>
<td>missense</td>
<td>G</td>
<td>Val [V]</td>
<td>1723</td>
</tr>
<tr>
<td>rs918494224</td>
<td>missense</td>
<td>A</td>
<td>Asp [D]</td>
<td>1771</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Commentary

Maria E Aguilar Aldrete1, Perla M MadrigalRuiz2, Luis Javier FloresAlvarado3, Rosalba Ruiz Mejia4, Felipe Parada Luna3 and Sergio Alberto Ramirez-Garcia**

1Department of Public Health and Psychogeriatric College, University Center of Health Sciences, Mexico
2Laboratory of Biochemistry, Department of Molecular Biology and Genomics, University Center of Health Sciences, Mexico
3Program of Public Health Master, University of the Sierra Sur, Mexico
4Institute of Public Health Research, University of the Sierra Sur, Mexico

*Corresponding author: Sergio Alberto Ramirez Garcia, Masters program in public health, Universidad Col & Ciudad Universitaria, Miahuatlán de Porfirio Díaz, México, Tel: 01(376) 76 5-23-25; email: sergio7genetica@fctmail.com

Received: August 24, 2017 | Published: January 25, 2018

Volume 3 Issue 3 - 2018

Introduction

The older adults are a consequence of the aging process and may be susceptible to the development of metabolic diseases related to atherosclerosis such as vascular dementia, cerebrovascular disease, or neurodegenerative diseases such as essential tremor, Parkinson plus syndromes, Parkinson’s disease. Prevention, diagnosis and biomonitoring require the search for new genetic markers that are predictive of their clinical evolution or response to treatment. One of the candidate genes for these purposes is the Tight Junction Protein 1 (TJP1) gene, which codes for the Zonna occludens 1 (ZO-1). It has stayed than tight junctions that constitute the blood-brain barrier which controls the intracellular diffusion and maintains the functional structural of endothelial cells. Structure or function of tight junctions can lead to the blood-brain barrier dysfunction that consequently may contribute to the development of neurodegenerative diseases. Blood-brain barrier disruption, associated with alterations of tight junctions, has been implicated in the pathogenesis of neurodegenerative disorders including multiple sclerosis, stroke, Alzheimer’s and Parkinson’s disease. In this sense, genetic marker of the gene that leads to amino acid changes, such as polymorphism rs229166 leads to a conformational change in the ZO-1 structure. Some of those polymorphisms that lead to amino acid changes in critical domains of the protein are rs1038306187 leading to the change of amino acid p.Gln791Glu in the domain guanylate kinase (Location residue 682-861). The domain ZU5 (Location residue 1701-1799) has 33 polymorphisms leading to conformational changes (Table 1). Polymorphisms that affect gene expression, by nucleotide changes at the cryptic sites of the alternative splicing, such as rs781148827, rs5478300017, rs78014403 and rs1020739943 in acceptor region, and rs1029122894 in the donor region. None of these polymorphisms have been explored for their pathogenic effect, which is why they are a new frontier of research in neurodegenerative disease related to aging, due to their effect on ZO-1 expression.

Table 1: Polymorphisms in the TJP1 en region encoding by the ZU5 domain.
There are few polymorphism studies of the ZO-1 gene in the world. It has been studied in Mexican Americans with a pathogenic effect on albuminuria such as rs2291166 [3]. Or also in the Mexican population with Mestiza and Zapoteca ancestry has been determined its allelic frequencies [2,4]. The SNP rs260526 related with inflammatory bowel disease or the SNP [5]. Or SNP rs711355, rs785423, rs813676 associated with global impression severity during risperidone treatment [6]. So its effect on the development of neurodegenerative diseases in the older adult is another of the research frontiers.

Finally it would be important to analyze the interaction of the SNP commented on TJP1 with the SNP rs767649 of miR-155 [7] which regulates the expression of TJP1, a field not well known in the development of neurodegenerative diseases related to aging, one of the most important borders at the level epigenetic and epistasia.

Acknowledgement
None.

Conflict of Interest
Authors declare that there are no conflicts of interest.

References