Commentary

Tight junction protein 1 gene in neurodegenerative disease, new frontier

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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 dementias, 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 than 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 neurological diseases[1]. 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.[1] 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.[2] 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

Number SNP	Reference	Nucleotide Change	Protein Change	Protein Residue	Number SNP	Reference	Nucleotide Change	Protein Change	Protein Residue
rs756391449	missense	T	Val [V]	1786	rs200636289	missense	A	Lys [K]	1732
	contig reference	C	Ala [A]	1786		contig reference	G	Glu [E]	1732
rs778206679	missense	T	Cys [C]	1781	rs780493261	missense	A	Thr [T]	1729
	contig reference	C	Arg [R]	1781		contig reference	G	Ala [A]	1729
rs376984007	missense	T	Ser [S]	1777	rs747547138	missense	A	Arg [R]	1728
	contig reference	C	Pro [P]	1777		contig reference	G	Gly [G]	1728
rs771212279	missense	T	Asn [N]	1773	rs777243709	missense	G	Met [M]	1723
	contig reference	G	Lys [K]	1773		contig reference	A	Ile [I]	1723
rs779424333	missense	G	Val [V]	1772	rs748887539	missense	G	Val [V]	1723
	missense contig	T	Phe [F]	1772		contig reference	A	Ile [I]	1723
	contig reference	C	Leu [L]	1772	rs770484844	missense	A	Asn [N]	1722
rs918494224	missense	A	Asp [D]	1771		contig reference	G	Ser [S]	1722
	contig reference	G	Gly [G]	1771	rs748606073	missense	A	Ile [I]	1721
rs769318736	missense	G	Glu [E]	1754		contig reference	G	Val [V]	1721
	contig reference	A	Lys [K]	1754	rs745589986	missense	C	Gln [Q]	1718

Table Continued....

Number SNP	Reference	Nucleotide Change	Protein Change	Protein Residue	Number SNP	Reference	Nucleotide Change	Protein Change	Protein Residue
rs772813539	missense	C	Ser [S]	1752		contig reference	G	Glu [E]	1718
	contig reference	T	Leu [L]	1752	rs772012909	missense	C	Thr [T]	1717
rs748862082	missense	G	Val [V]	1749		contig reference	T	Ile [I]	1717
	contig reference	C	Leu [L]	1749	rs775526130	missense	A	Met [M]	1713
rs770667262	missense	A	Asn [N]	1747		contig reference	G	Val [V]	1713
	contig reference	G	Ser [S]	1747	rs776556981	missense	A	Asp[D]	1712
rs55855417	contig reference	A	Asn [N]	1745		contig reference	G	Gly [G]	1712
	missense	G	Asp [D]	1745	rs200635441	missense	G	Lys [K]	1710
rs759442574	contig reference	A	Gln[Q]	1744		contig reference	T	Asn [N]	1710
	missense	G	Arg [R]	1744	rs200271901	missense	G	Ser [S]	1710
rs578134163	contig reference	G	Arg [R]	1741		contig reference	A	Asn [N]	1710
	missense	A	Lys [K]	1741	rs750682659	missense	A	Lys [K]	1706
rs976771573	contig reference	G	Glu [E]	1741		contig reference	T	Ile [I]	1706
	missense	A	Lys [K]	1741	rs758653969	missense	A	Asp[D]	1705

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 determinate 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.

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None.

Conflict of interest

Authors declare that there are no conflicts of interest.

References

1. Bednarczyk J, Lukasiuk K. Tight junctions in neurological diseases. *Acta Neurobiol Exp*. 2011;71(4):393–408.
2. Ramirez GSA, Flores ALJ, Topete-G LR, et al. High frequency of ancestral allele of the TJP1 polymorphism rs2291166 in Mexican population, conformational effect and applications in surgery and medicine. *Cir Cir*. 2016;84(1):28–36.
3. Lehman DM, Leach RJ, JohnsonPT, et al. Evaluation of tight junction protein 1 encoding zona occludens 1 as a candidate gene for albuminuria in a Mexican American population. *Exp Clin Endocrinol Diabetes*. 2006;114(8):432–437.
4. Madrigal RP, Dávalos RNO, Ramírez GSA, et al. Polymorphism P.D1134a of the TJP1 in population with Zapotec ancestry: A marker for potential thyroid cancer and other neoplasms. *Revista Médica*. MD 2015;7(1):20–26.
5. Norén E, Almer S, Söderman J. Genetic variation and expression levels of tight junction genes identifies association between MAGI3 and inflammatory bowel disease. *BMC Gastroenterol*. 2017;17(1):68.
6. Clark SL, Souza RP, Adkins DE, et al. Genome-wide association study of patient-rated and clinician-rated global impression of severity during antipsychotic treatment. *Pharmacogenet Genomics*. 2013;23(2):69–77.
7. Xie K, Ma H, Liang C, et al. A functional variant in miR-155 regulation region contributes to lung cancer risk and survival. *Oncotarget*. 2015;15(6):42781–4292.