Research Article
Volume 7:6, 2020
DOI: 10.37421/ijn.2020.7.377

International Journal of Neurorehabilitation

ISSN: 2376-0281 Open Access

Analysis of the Associated Mutations of DJ-1 Gene to Parkinson's Patients in Vietnam

Nguyen Minh Duc[1], Nguyen Duc Hieu[1], Ho Truong Giang[2], Le Vo Hoang Long[2], Nghiem Ngoc Minh[1], Vo Thi Bich Thuy*[1]

[1]*Institute of Genome Research, Vietnam Academy of Science and Technology, Hoang Quoc Viet, Cau Giay, Hanoi, Vietnam*

[2]*Military Medical University, Phung Hung, Ha Dong, Hanoi, Vietnam*

Abstract

The exact causes of Parkinson's disease (PD) are currently unknown, but studies have shown that the environment and genetics are the two factors that play the biggest role in Parkinson's disease. DJ-1 gene (belong to the PARK genes) is known as the main cause of Parkinson's disease in populations. In Vietnam, the evaluation of DJ-1 gene mutation frequency in patients is necessary to clarify the pathogenesis and genetic mechanisms of this disease. In this research, we identified the frequency mutations of the DJ-1 gene in Vietnamese PD patients. The results showed that we detected some DJ-1 mutations at exon 5 and exon 7. Interestingly, Ala86Gly and Gln95Leu mutations of exon 5 and His138Pro of exon 7 are found, which leads to a change in amino acid sequence and possibly a change in a functional protein. In addition, out of more than 20 heterozygous or homozygous mutations occurring in the intron regions 4 and 5, we found that 3 homozygous mutations occurred frequently in both patient and control. The data of mutation analysis has shown the ambiguous and unforeseeable meanings; however, they possibly associated with the mutation of PD. Therefore, the study of our next will focus on the relationship between these mutations with some clinical symptoms in patients.

Keywords: Difficulty map • DJ-1 gene • PARK7 loci • Vietnamese parkinson's disease • Sequencin

Introduction

Parkinson's disease is a degenerative disorder of the central nervous system that affects a patient's movement, balance, and muscle control such as sluggish movement, and the appearance of advanced cognitive dysfunction and subtle language problems may occur [1]. Today, after Alzheimer's disease, PD is the second most common neurodegenerative disorder in the world [2]. The incidence of this disease depends on old age such as PD affects 1-2% of the population over the age of 60, but this rate increases to 4-5% at 85 years of age [3]. In Vietnam, the incidence of PD compared to other neurological diseases is about 1.6%.

The causes of PD are currently unknown, but researchers believe that the environment and genetics are the two factors that play the biggest role in PD. To date, scientists have found a link between genetic modification and a small percentage of Parkinson's onset patients under the age of 50. However, the role of genes is less commonly found in cases of late-onset disease. Genetics, in particular, mutant genes play a more important role in the early onset of Parkinson's disease [4]. At least 13 loci and 9 genes studied have been linked to PD, but only 6 genes have been found to be associated with Mendelian genetics [5]. Recent studies have focused on the transformation of these six genes, the functions of the proteins that encoded by them, the mutated proteins, and the pathways they are involved in. The genes related to PD are present inside the brain including the genes PARK1, PARK2, PINK1, LRRK2, PARK - 6 located on chromosome 1, and the Cytochrome P450 gene (CYP2D6) [6].

In the DJ-1 gene, mutations directly associated with PD mainly rare mutations only <1% of cases have an early onset [4]. With eight exons, exon 1 and exon 8 are non-coding and spliced, from exon 2 to 7 encoding for a protein 189 amino acid, which are highly conservation and expression. It was originally described as a carcinogen (oncogene), and later involved in male fertility [7,8]. The distribution of DJ-1 is naturally in the nucleus or cytoplasm, while the mutant DJ-1 shows a decrease in the nucleus position and move to the mitochondrial position [9]. DJ-1 has been shown to act as a redox-sensitive chaperone, preventing the association of synuclein and the NFL neuron subunit [10]. Furthermore, studies have demonstrated that in knocked-out DJ-1, cells are often sensitive to oxidative stress for H_2O_2 production [11,12].

***Address for Correspondence:** Vo Thi Bich Thuy, Institute of Genome Research, Vietnam Academy of Science and Technology, No. 18, Hoang Quoc Viet, Cau Giay, Hanoi 100000, Vietnam, Tel: + 84964520846; E-mail: thuytbvo.igr@gmail.com*

Received 31 August, 2020; **Accepted** 16 September, 2020; **Published** 23 September, 2020

Methods

Patient selection

Blood samples of thirty-two Parkinson patients were collected from Vietnam hospital (Table 1). The standard neurological clinical test was carried out before this study. The diagnosis based on published document [13,14]. The Medical Ethics Committee of the Institute of Genome Research (Vietnam) approved this research. All of Parkinson's patients already provided related documents.

Genomic DNA analysis

The blood samples were collected from peripheral vein patients by using venipuncture. The DNA purification kit of Thermo Science (USA) was used for extracting genomic. Polymerase chain reaction (PCR) was carried out using Taq DNA polymerase and the following primer sequences (Table 2), with conditions: 35 cycles were run at 95˚C for 45 s, 63˚C for 40 s and 72˚C for 1 min followed by 7 min terminal elongation at 72˚C. The PCR products were 392 bp (exon 2), 388 bp (exon 3), 297 bp (exon 4), 258 bp (exon 5), 297 bp (exon 6) and 378 bp (exon 7) of the DJ-1 gene. PCR was carried out in a final volume of 50µl including 2.5 mM MgCl2, 0.2 mM deoxynucleotide triphosphate, 0.5 µM forward and reverse primers, 1 U Taq polymerase (Promega- M8305, USA), and 10 ng of DNA. The quality of the PCR products was analyzed by electrophoresis agarose gel with the design size.

Purification of the amplified fragment was performed by using GeneJET PCR purification kit (Thermo Science, USA). The isolated DNA fragments were sequenced according to the manufacturers' instructions. The ABI 3500 Genetic Analyzer machine was used to read electrophoreses products.

Bioinformatic analysis

We used a sequence of DJ-1 genes on Genebank (with code NC_000001.11) as a reference sequence. The Ensemble database software supported all of the exon and protein sequences. These sequences used to determine the location of 6 exons in our research. Multiple sequence alignments

Table 1: The general information of Parkinson's disease patients (n=32).

Information	Parkinson patients
Age in research time,	66.4±6.3
Age of male patients	63.9±7.11
The number of male patients	24 (75%)
Age of female patients	63.5±7.45
The number of male patients	8 (25%)

Table 2: Primers used in the study.

Primer	Sequences (5' – 3')	Exon	Reference
E2-F	CTCTGCTTGAAAATGCTCC	Exon 2 (392bp)	[14]
E2-R	GGCAAGACATTAACAAGCG		
E3-F	TTAAAGACAGTGTTACTCTGAATT	Exon 3 (388bp)	[14]
E3-R	CATCCAGCCACCCACTTAC		
E4-F	GGCTATCTCCTGTACTTCCC	Exon 4 (297bp)	[14]
E4-R	TCACAGCCTCCTCCCGAA		
E5-F	AAATAGGTCAGAGAGCTTGTGG	Exon 5 (258bp)	[14]
E5-R	TCAAACCATCGAATGAAAGG		
E6-F	CTCAAGCAATTTTTCTACCT	Exon 6 (297bp)	[14]
E6-R	GAGGCTGAGAGAGAAGAATCG		
E7-F	ACAGTGTTGGGTTTATATGCTG	Exon 7 (378bp)	[14]
E7-R	GGACAGCGACTTCTGAACAC		

were performed by Clustal-W tools, and this result was used to determine the nucleotide and amino acid mutation. The BioEdit bioinformatics tool was used for the nucleic acid sequences of two groups (patient and control) to translate and get protein sequences.

Results and Discussion

The results showed that 24 known pathogenic mutations among 32 PD patients (75 %) were identified (Table 3). There were 3 mutation positions (included: intron 4, intron 5 and exon 5 or 7) which were detected in two male patients. Parallel mutations in intron 4 and intron 5 were 12 cases (37.5 %) and mutation occurred at intron 4 with exon 7 were 4 cases (12.5 %). In addition, 6 PD patients showed a single mutation in intron 4 (18.75%). Our research has been identified as a large number of disease-causing mutations related to Parkinson. In particular, all of mutations of DJ-1 gene to be considered frequent in Vietnam showed a strong genetic or environmental factor influence. Researches have also shown a relationship between smoking and alcohol overuse in Parkinson's patients [15,16]. To evaluate possible links between DJ-1 promoter polymorphisms, the DJ-1 promoter region of Chinese smoking patients was sequenced with three single nucleotide polymorphisms (SNPs) (rs17523802, rs226249, and rs35675666) and one 18 bp deletion (rs200968609) [17]. Patient information with Parkinson's disease for the DJ-1 mutation (Table 3).

To identify mutations lead to PD and clearly understand the role of DJ-1 gene, we carried out sequencing full-length DJ-1 gene of all 32 patients. The results were shown in Table 4.

Patients (1E; 22E; 24E and 32E) have mutations at exon 7 and intron 4. Patients 6E and 7E showed that 3 mutations were discovered in intron 4; intron 5 and exon 5 or exon 7, respectively. The sequencing results also gave us a clearer view of the two mutations at exon 7, only one nucleotide mutation led to a change in amino acid at position 138, Histidine was changed by Proline (c.413A>C p.H138P). At the other mutation, there was no amino acid alteration phenomenon while Glycine remained unchanged (c.411A>T p.G138G). Differences in the gene sequence occurring at exon 5 were expressed only in 6E PD patient with 2 mutations in regions intron 4 and 5. In particular, 2 mutations of exon 5 show the change of amino acid sequence (c.284A>T p.Q95L and c.257C>G p.A86G).

The result showed that a mutation was found in the intron border of exons, 22 mutations appeared in intron 4, intron 5 (Table 4) (Figure 1). There are 5 heterozygous mutations (included, IVS5+33A>T, IVS5+41G>T, IVS6-17T>G, IVS6-18T>G, and IVS6-28A>C) and 1 homozygous mutation in intron 5 (included, IVS5+30G>A). In addition, we found 11 heterozygous mutations in intron 4 (IVS5-11C>T, IVS5-49T>C, IVS5-12T>C, IVS5-13T>C, IVS5-4C>G, IVS5-5A>G, IVS5-14T>C, IVS5-15T>C, IVS5-16G>T, IVS5-24T>G, and IVS5-38A>C). Surprisingly, three mutations among five homozygous mutations in intron 4 were found in all of PD patients, included IVS4+30T>G, IVS4+45G>A and IVS4+46G>A. This result is completely consistent with the previous researches, Tarantino have found many polymorphic variants with similar frequency both in patients and in controls (IVS1-53G>A, IVS1-15T>C, IVS3-109C>T, IVS4+30T>G, IVS4+45G>A, IVS4+46G>A, IVS6-216G>A, g.168_185del and R98Q) [18-21].

Our research team has found two heterozygous mutations of exon 5 that change amino acid (Ala86Gly, Gln95Leu) in one patient comparing with the control sequence. Compare with previous researches, mutations in this gene were first-time described in two European families, in which a mutation that removed the 14 kb segment covering a large part of the coding region, including exons 1 to 5 in a Dutch family [22]; deleted exon 5 in Iranian patients [23]; or and highly conserved amino acid (leucine) was mutated to proline (L166P) in an Italian family [22], Isoleucine to Phenylalanine (Ile105Phe) homozygous in Indian patients [24]. Furthermore, the Ala167Ala mutation was determined in a United Kingdom patient (homozygote) and a North American patient (heterozygote) [24,25].

For sequence-based mutation data analysis in exon 7, we have found 2 heterozygous mutations (a.411T>C và c.413A>C) in this exon, however, only c.413A>C change amino acid Histidine to Proline (His138Pro). Same as exon 5 case, 7E patient had both mutations with sequence difference at intron 4 and 5. This data contributed new mutations to the list of mutations on exon 7 of the known DJ-1 gene; such as Thr154Lys mutation homozygous [26], Pro158del mutation homozygous [27], Glu163Lys mutation homozygous [28], Leu166Pro mutation homozygous [22], and Leu172Gln mutation homozygous [29].

The results of heterozygous mutations can affect the efficiency of the intron-splicing process, and lead to the accumulation of undecoded pre-RNA in the nucleus. It will degenerate rapidly or may lead to activation of the alternative unknown splice site that affects the gene coding region. In some cases, this variant is predicted to become an aberrant transcript of the DJ-1 gene [19-21]. In addition, homozygous mutations predicted to lead in a loss function of the protein while another sequence variation or deletion or duplication was not detected. Our report is the first research about Vietnamese

Table 3: Patient information with Parkinson's disease for the DJ-1 mutation.

No	ID code of patient	Sex*	Age of sample	Mutations
1	1E	M	67	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Exon 7 (c.411T>C; c.413A>C)
2	2E	F	50	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Intronn5 (IVS6-28A>C)
3	6E	M	67	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-4C>G) Intronn5 (IVS5+30G>A; IVS5+41G>T) Exon 5 (c.257C>G; c284A>T)
4	7E	M	50	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-49T>C) Intron 5 (IVS5+30G>A) Exon 7 (c.411T>C)
5	8E	M	60	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-12T>C; IVS5-11C>T)
6	9E	M	75	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Intronn5 (IVS5+30G>A)
7	10E	M	60	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-11C>T) Intronn5 (IVS5+41G>T)
8	12E	M	74	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS4+92T>C; IVS4+109G>T; IVS5-5A>G) Intronn5 (IVS5+30G>A)
9	14E	F	61	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-16G>T)
10	16E	M	71	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-13T>C; IVS5-11C>T)
11	17E	M	69	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-12T>C; IVS5-11C>T)
12	18E	M	78	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-12T>C; IVS5-11C>T)
13	19E	M	57	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-15T>C) Intronn5 (IVS5+30G>A)
14	21E	M	69	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A)
15	22E	M	57	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-14T>C; IVS5-13T>C) Exon 7 (c.411T>C)
16	23E	M	60	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-49T>C) Intronn5 (IVS5+30G>A; IVS5+41G>T)
17	24E	M	70	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Exon 7 (c.413A>C)
18	25E	F	69	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Intronn5 (IVS5+41G>T)
19	27E	F	74	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Intronn5 (IVS5+30G>A)
20	28E	M	69	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-49T>C; IVS5-38A>C; IVS5-24T>G) Intronn5 (IVS5+41G>T)
21	29E	M	68	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Intronn5 (IVS5+33A>T; IVS5+41G>T
22	30E	M	67	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-49T>C) Intronn5 (IVS5+41G>T)
23	31E	M	71	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A; IVS5-11C>T) Intronn5 (IVS6-18T>C; IVS6-17T>G)
24	32E	M	57	Intronn4 (IVS4+30T>G; IVS4+45G>A; IVS4+46G>A) Exon 7 (c.411T>C)

(*Male: M; Female: F)

Table 4: The sequence mutations on exons and introns of DJ-1 gene.

Number of mutation	Ref Seq	Allele 1	Allele 2	Amino acid 1	Amino acid 2	Position in cDNA	Amino acid position	Intron position	Change	Heterozygous or Homozygous (*)
1	C	C	G	A	G	257	86	-	c.257C>G p.A86G	+
1	A	A	T	Q	L	284	95	-	c.284A>T p.Q95L	+
1	A	A	C	H	P	413	138	-	c.413A>C p.H138P	+
4	T	T	C	G	G	411	137	-	c.411T>C p.G137G	+
24	T	T	G					30	IVS4+30T>G	-
24	G	G	A					45	IVS4+45G>A	-
24	G	G	A					46	IVS4+46G>A	-
1	T	T	C					92	IVS4+92T>C	-
1	G	G	T					109	IVS4+109G>T	-
1	C	C	G					-4	IVS5-4C>G	-
1	A	A	G					-5	IVS5-5A>G	-
6	C	C	T					-11	IVS5-11C>T	+
3	T	T	C					-12	IVS5-12T>C	+
2	T	T	C					-13	IVS5-13T>C	+
1	T	T	C					-14	IVS5-14T>C	+
1	T	T	C					-15	IVS5-15T>C	+
1	G	G	T					-16	IVS5-16G>T	+
1	T	T	G					-24	IVS5-24T>G	+
1	A	A	C					-38	IVS5-38A>C	+
4	T	T	C					-49	IVS5-49T>C	+
7	G	A	A					30	IVS5+30G>A	-
1	A	A	T					33	IVS5+33A>T	+
7	G	G	T					41	IVS5+41G>T	+
1	T	T	G					-17	IVS6-17T>G	+
1	T	T	G					-18	IVS6-18T>G	+
1	A	A	C					-28	IVS6-28A>C	+

(*Heterozygous: +; Homozygous: -)

Figure 1. Position sequences of 22 mutations in Intron 4 (A) and Intron 5 (B). (+): Homozygous mutation; (-): Heterozygous mutations.

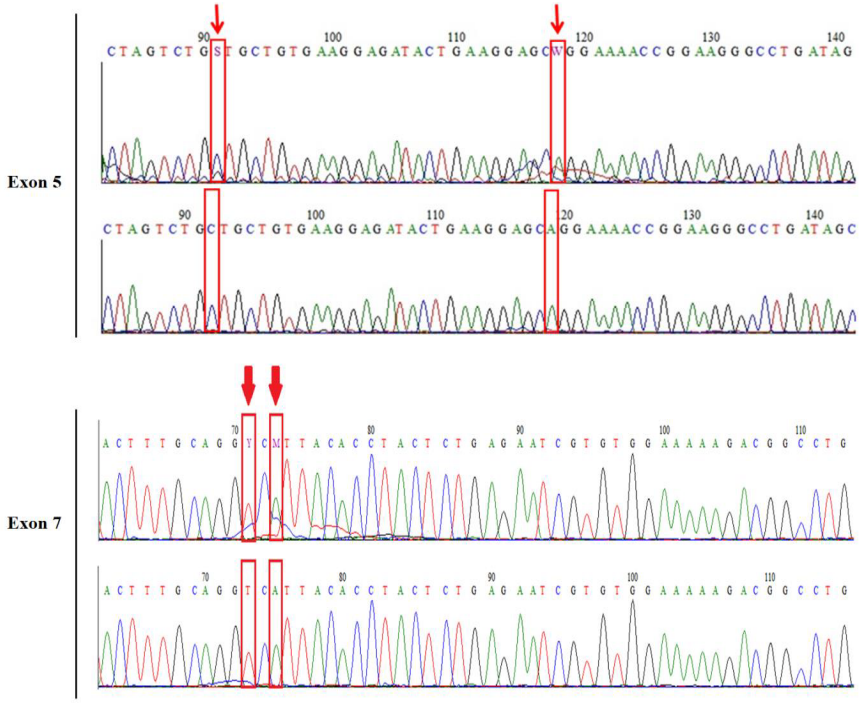

Figure 2. The automated capillary sequencing of exon 5 and exon 7 in DJ-1, included: Ala86Gly (c.257C>G; p.A86G), Gln95Leu (c.284A>T; p.Q95L), Gly137Gly (c.411T>C; p.G137G), and His138Pro (c.413A>C; p.H138P). A heterozygous mutation carrier compare with a homozygous control type carrier.

Parkinson patients associated mutations of DJ-1 gene, thus, there are several possibilities associated with the mechanism of these altered mutations, such as altering mRNA stability, secondary structure, transcriptional activity, or altering protein synthesis, folding, level, cyclic and / or functional. Besides, indeterminate genetic pathways and differences in environmental factors may contribute to phenotypic variation among PD patients (Figure 2).

Conclusions

Although we identified several alterations in the DJ-1 gene, the present study is the first to evaluate the mutation frequency of this gene in Vietnamese Parkinson patients. To clearly understand the pathogenic associations of the patient with the DJ-1 gene, the advanced studies focusing on large genetic cohort and epigenetic inactivation mechanisms involving these genes are required in PD patients and in their relatives with suspected symptoms. The data obtained in the present study might be useful in clinical genome wide association studies.

References

1. Moore, O, Kreitler, S, Ehrenfeld, M, and Giladi, N, et al. "Quality of life and gender identity in Parkinson's disease". *J Neural Transm Suppl* 112(2005):1511-1522.
2. Mhyre, TR, Boyd, JT, Hamill, RW, and Maguire-Zeiss, KA. Protein Aggregation and Fibrillogenesis in Cerebral and Systemic Amyloid Disease. *Subcellular Biochemistry* 65(2012):389.
3. Fahn, S. Description of Parkinson's disease as a clinical syndrome. *Ann N Y Acad Sci* 991(2003):1-14.
4. Klein, C, and Lohmann-Hedrich, K. Impact of recent genetic findings in Parkinson's disease. Curr Opin Neurol 20(2007):453-464.
5. Lesage, S, and Brice, A. Parkinson's disease: from monogenic forms to genetic susceptibility factors. *Hum Mol Genet* 18(2009):R48-R59.
6. Klein, C. and Westenberger, A. Genetics of Parkinson's disease. *Cold Spring Harb Perspect Med* 2(2012):a008888.
7. Nagakubo, D, Taira, T, Kitaura, H, and Ikedaet, M, et al. DJ-1, a novel oncogene which transforms mouse NIH3T3 cells in cooperation withras. *Biochem Biophys Res Commun* 231(1997):509-513.
8. Wagenfeld, A., Yeunget, CH, Strupat, K, and Cooper, TG, et al. Shedding of a rat epididymal sperm protein associated with infertility induced by ornidazole and α-chlorohydrin. *Biol Reprod* 58(1998):1257-1265.
9. Moore, DJ, Zhang, L, Troncoso, J, and Lee, MK, et al. Association of DJ-1 and parkin mediated by pathogenic DJ-1 mutations and oxidative stress. *Hum Mol Genet* 14(2005):71-84.
10. Shendelman, S, Jonason, A, Martinat, C, and Leete, T, et al. DJ-1 is a redox-dependent molecular chaperone that inhibits αsynuclein aggregate formation. *PLoS Biol* 2(2004):e362.
11. Yokota, T, Sugawara, K, Ito, K, and Takahashi, R, et al. Down regulation of DJ-1 enhances cell death by oxidative stress, ER stress, and proteasome inhibition. *Biochem Biophys Res Commun* 312(2003):1342-1348.
12. Mitsumoto, A, and Nakagawa, Y. DJ-1 is an indicator for endogenous reactive oxygen species elicited by endotoxin. *Free Radic Res* 35(2001):885-893.
13. Clarke, CE, Patel, S, Ives, N, and Rick, CE, et al. Clinical effectiveness and cost-effectiveness of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's disease: a large pragmatic randomised controlled trial (PD REHAB). *Health Technol Assess* 20(2016):1-96.
14. Lockhart, P, Lincoln, S, Hulihan, M, and Kachergus, J, et al. DJ-1 mutations are a rare cause of recessively inherited early onset parkinsonism mediated by loss of protein function. *J Med Genet* 41(2004):e22.
15. Noyce, AJ, Bestwick, JP, Silveira-Moriyama, L, and Hawkes, CH, et al., Metaα analysis of early nonmotor features and risk factors for Parkinson disease. *Ann Neurol* 72(2012):893-901.
16. Zhang, D, Jiang, H, and Xie, J. Alcohol intake and risk of Parkinson's disease: a meta-analysis of observational studies. *Mov Disord* 29(2014):819-822.
17. He, L, Lin, S, Pan, H, and Shen, R, et al. Lack of association between DJ-1 gene promoter polymorphism and the risk of Parkinson's disease. *Front Aging Neurosci* 11(2019):24.
18. Tarantino, P, Civitelli, D, Annesi, F, and De Marco, EV, et al. Compound heterozygosity in DJ-1 gene non-coding portion related to parkinsonism. *Parkinsonism Relat* 15(2009):324-326.
19. Berget, SM. Exon recognition in vertebrate splicing. J Biol Chem 270(1995):2411-2414.
20. La Cognata, V, D'Agata, V, Cavalcanti, F, and Cavallaro, S, et al. Splicing: is there an alternative contribution to Parkinson's disease? *Neurogenetics* 16(2015):245-263.
21. La Cognata, V, and Cavallaro, S. PARK7 (Parkinsonism associated deglycase). *Atlas genet cytogenet* 2016.

22. Bonifati, V, Rizzu, P, van Baren, MJ, and Schaap, O, et al. Mutations in the DJ-1 gene associated with autosomal recessive early-onset parkinsonism. *science* 299(2003):256-259.

23. Darvish, H, Movafagh, A, Omrani, MD, and Firouzabadi, SG, et al. Detection of copy number changes in genes associated with Parkinson's disease in Iranian patients. *Neurosci Lett* 551(2013):75-78.

24. Abbas, MM, Govindappa, ST, Sudhaman, S, and Thelma, BK, et al., Early onset Parkinson's disease due to DJ1 mutations: An Indian study. *Parkinsonism Relat Disord* 32(2016):20-24.

25. Abou-Sleiman, PM, Fiesel, FC, Caulfield, TR, and Hudec, R, et al. A heterozygous effect for PINK1 mutations in Parkinson's disease? *Ann Neurol* 60(2006):414-419.

26. Di Nottia, M, Masciullo, M, Verrigni, D, and Petrillo, S, et al., DJ-1 modulates mitochondrial response to oxidative stress: clues from a novel diagnosis of PARK7. *Clin Genet* 92(2017):18-25.

27. Macedo, MG, Verbaan, D, Fang, Y, and van Rooden, SM, et al. Genotypic and phenotypic characteristics of Dutch patients with early onset Parkinson's disease. *Mov Disord* 24(2009):196-203.

28. Annesi, G, Savettieri, G, Pugliese, P, and D'Amelio, M, et al., DJ-1 mutations and parkinsonism-dementia-amyotrophic lateral sclerosis complex. *Ann Neurol* 58(2005):803-807.

29. Taipa, R, Pereira, C, Reis, I, and Alonso, I, et al. DJ-1 linked parkinsonism (PARK7) is associated with Lewy body pathology. *Brain* 139(2016):1680–879.

How to cite this article: Duc NM, Hieu ND, Giang HT, and Hoang Long LV, et al. "Analysis of the Associated Mutations of DJ-1 Gene to Parkinson's Patients in Vietnam". Int J Neurorehabilitation Eng 7 (2020) doi: 10.37421/ijn.2020.7.377