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# ASSOCIATION BETWEEN SCHIZOPHRENIA AND *DRD3 RECEPTOR* GENE VARIANTS OF IRAQI POPULATION

**Najwa Sh. Ahmed[1], Hayba Q. Younan[2], Mushtaq Talib Hashim[3] and Haneen M. Ismaeel[2]**

[1]Biotechnology Research Center, Al-Nahrain University, Baghdad, Iraq.
[2]University of Baghdad, College of Science, Biotechnology dept., Baghdad, Iraq.
[3]University of Baghdad, college of Medicine, Psychiatry. Baghdad, Iraq.

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## ABSTRACT

This study aimed to detect mutations in *DRD3 receptor* genes for schizophrenia patients in Iraq. To achieve this goal, blood samples were collected from 50 patients with schizophrenia (25 samples of male and 25 samples of female) and 10 samples of healthy, DNA was isolated and the *DRD3 receptor gene* (4147C-T and 712G-C) were amplified by using specific primers for exon1 of this gene, and then found the sequence of this region. The DNA sequencing results of flank sense of *DRD3* (4147C-T) *receptor* gene from 25 cases schizophrenia patients and healthy was found to be compatible 100% with DNA sequence of gene bank, while 98% compatibility were found for that gene in the flank sense from 10 cases schizophrenia patients and the differences may be attributed to two transversion mutations (C/G) and one transition mutation (G/A), however, 99% compatibility was found for that gene in the flank sense of another 10 cases schizophrenia patients and difference may be attributed to one transversion mutation (G/T), and 99% compatibility was found for that gene in the flank sense of another 5 cases schizophrenia patients and differences may be attributed to two transversion mutations (G/T and T/G) and one transition mutation (C/T). However, 100% compatibility was found flank sequences DNA sense of *DRD3* (712G-C) *receptor* gene from healthy and 50 cases patients with DNA sequence of gene bank. There is a significant correlation ship between schizophrenia disease and incidence of mutations (C/G; G/A; and G/T) position in exon 1 of *DRD3 receptor* gene with value ($X^2$=3.662, P>0.05), however, there is lower significant correlation ship between schizophrenia and incidence of mutations (G/T and T/G) with value ($X^2$=1.089, P>0.05). The conclusion is that there is enough evidence to support the claim that there is a relationship between the appearance of mutations and the occurrence of schizophrenia disease in Iraqi population.

**Key word:** *DRD3 receptor* gene, Schizophrenia, transition and transversion mutation**.**

## INTRODUCTION

Schizophrenia is a syndrome embrace advance range of disturbances of perception thought emotion and motor activity its an illness in which episodes of florid disturbance are usually set against a background of sustained disability, the level of chronic disability ranges

from a mild decrease in the ability to cope with stress to a profound difficulty in initiating and organizing activity that can render patients unable to care for themselves [9]. A wide range of genetic studies strongly suggests a genetic component to the inheritance of schizophrenia showed that a person is likely to have schizophrenia when other members of the family have the disorder and that the likelihood of the persons having schizophrenia is correlated with the closeness of the relationship [3]. Many associations between chromosomal sites and schizophrenia have been reported since the application of the techniques of molecular biology became widespread. In molecular genetics that of association studies takes a gene that is suspected of involvement in pathogenesis of the disorder a gene involved in dopamine metabolism and then compares the frequency of its various alleles in a series of individuals with schizophrenia as apposed to a control group, some candidate gene studies imply a weak effect of the *D3 dopamine receptor* gene [4]. The distribution of schizophrenia in families and populations is consistent with a substantial genetic basis for the disorder [8]. Several lines of evidence suggest that the dopamine D3 receptor is involved in the pathophysiology of schizophrenia. The D3 receptor has a restricted pattern of expression in brain limbic areas associated with cognitive function and motivated behavior [11]. The *D3 dopamine receptor* gene has been implicated by association studies as a possible candidate for a number of neuropsychiatric disorders and phenotypes including schizophrenia, bipolar disorder, tourette syndrome, and substance abuse [9]. The phenotype most intensively investigated in connection with DRD3 is schizophrenia, and since the original report of association [4] , there have been more than 24 independent follow-up studies of a non-synonymous A/G polymorphism (Ser9Gly) in exon 1. The present study aimed to investigate correlation between polymorphism in exon 1 of *DRD3 receptor* gene and increasing schizophrenia in Iraqi population.

## MATERIALS AND METHODS

### Subjects & DNA extraction

Whole blood samples was obtained from 50 Iraqi patients affected by schizophrenia (25 male and 25 female, age ranged 18-62 years) and also obtained from healthy men used as a control group, the disease were diagnosed by the consultant medical staff at Rasheed Teaching Hospital . Whole blood was collected (4ml) into an EDTA- tube; the samples were stored at -20°C until further processing. DNA was extracted from the samples by wizard genomic (DNA purification kit, Promega, USA) according to the isolating genomic DNA from whole blood protocol. DNA extracted from 300 µl whole blood in each case. The volume of the extracted DNA solution was usually 100 µl were stored at -20°C.

### Detection of Gene *DRD3* by Using PCR

A 281 bp fragment containing exon 1 of *DRD3* (4147C-T) was amplified using a forward primer (DRD3 4147C-T: 5′-CGTCAACTTCCATGCTGCTAT-3′) and a reverse primer (DRD3 4147C-T: 5′-TAAAAAGGCAGGGGAACAGA-3′) and 262bp fragment containing exon 1 of *DRD3* (712G-C) was amplified using a forward primer (DRD3 712G-C:5′-TTGGGCCTCAGCCTGCCTTAAAAGTCG-3′) and a reverse primer (DRD3 712 G-C: 5′-GGAAAGGGTGACAAACTTGG-3′) (Primers set supplied by alpha DNA Company, Canada). The PCR amplification was performed in a total volume of 25µl containing 2µl DNA (conc. 100 ng/µl), 12.5 µl Go Taq green master mix 2X (green maschuiter mix is a premixed ready to use solution containing Taq DNA polymerase, dNTPs, $MgCl_2$ and reaction buffers at optimal

concentrations for efficient amplification of DNA template by PCR supplied by promega (Promega corporation, USA), 1µl of each primer (10 pmol/µL) and up to 25µl with nucleases free water. The thermal cycling was as follows: Denaturation at 94 °C for 7 min, followed by 33 cycles of 94 °C for 1min, 58°C for 1 min, and 72 °C for 1min, with final incubation at 72 °C for 7 min [1] using a thermal Cycler (Multigene TM Gradient Thermal Cycler, Labnet International, Korea). The PCR products were separated by 1.5% agarose gel electrophoresis and visualized by exposure to ultraviolet light (302nm) after ethidium bromide staining.

**Sequencing**

Sequencing of exon 1 of *DRD3* gene was done by Macro gen company/USA for sequencing of products through used individual up and downstream primer was used in each sequencing reactions.

**Sequence Alignment**

Homology searches were conducted between the sequence of standard gene BLAST program which is available at the national center biotechnology information (NCBI) online at (http:// www.ncbi.nlm.nih.gov) and using BioEdit program and ExPASY program for amino acid sequence.

**Statistical analysis**

The statistical analysis is a very important final step in the research to analyse and evaluate the obtained results. Medical statistics of this study was conducted via computer based statistical program which was: $\mathbf{X^2}$ for Windows computer package. The statistical analysis tests which used in this were as follows: P value <0.05 is considered a significant correlation.

## RESULTS AND DISCUSSION

The genomic DNA from 50 patient were extracted using wizard genomic DNA promega, *DRD3* (4147C-T and 712G-C) gene from genomic DNA were amplified by using specific PCR primers for exon 1, results shown in figure (1) indicated that a yield of single band of the desired product with a molecular weight about 281 bp for exon 1 *DRD3* (4147C-T) gene and 262 bp for exon 1 *DRD3* (712G-C) gene was obtained.

Sequencing of coding regions of the amplified product (Exon 1) for these samples were done seeking for detection of any mutation within these sequences related to schizophrenia development as shown in figure (1). The results were compared with data obtained from Gene Bank published BLAST program which is available at the NCBI online at www.ncbi.nlm.nih.gov and using BioEdit program. Alignment of *DRD3* (4147C-T) gene of all groups (Healthy and patient) with data published for known sequence seeking for enough homology. A homology with *DRD3* (4147C-T) gene of *Homo sapiens* from the Gene Bank was done using the BioEdit software. 100% compatibility of that gene was found with *DRD3* (4147C-T) gene from healthy and 25 cases from schizophrenia patients with standard *DRD3* (4147C-T) of Gene Bank results as shown in figure (2).

The *DRD3* (4147C-T) gene from 10 schizophrenia patients shows 98% compatibility with standard *DRD3* (4147C-T) *gene* of Gene Bank, and there are two transversion mutations (C/G) lead to change translate amino acid from Histidine to Aspartic acid; from Cystein to Tryptophan respectively and one transition mutation (G/A) lead to change translate amino acid from Valine to Isoleucine, as shown in figure (3) and table (1) shown type of mutation and predicted effect.

While there are one transversion mutation (G/T) in the flank DNA sense of *DRD3* (4147C-T) gene from 10 schizophrenia patients shows 99% compatibility with standard *DRD3* (4147C-T) gene of Gene Bank,

lead to change translate amino acid from serine to isoleucine. As shown in figure (4) and table (1).

However, there are one transversion mutation (G/T) and lead to change translate amino acid from Serine to Isoleucin , and one transition mutation (C/T) in the flank DNA sense of *DRD3* (4147C-T) gene (silent) and one transversion mutation (T/G) lead to change amino acid from Cysteine to Glisine from 5 schizophrenia patients shows 99% compatibility with standard *DRD3* (4147C-T) gene of Gene Bank as shown in figure (5) and table (1).

The results were compared with data obtained from Gene Bank published BLAST program which is available at the NCBI online at www.ncbi.nlm.nih.gov and using BioEdit program. Alignment of *DRD3* (712 G/C) gene of all groups (Healthy and patient) with data published for known sequence seeking for enough homology. A homology with *DRD3* (712G/C) gene of *Homo sapiens* from the Gene Bank was done using the BioEdit software. 100% compatibility of that gene was found with *DRD3* (712G/C) gene from healthy and all cases from schizophrenia patients with standard *DRD3* (721G/C) of Gene Bank results as shown in figure (6).

The A206G transition in the sequence of the dopamine type 3 *DRD3 receptor* gene that leads to a Ser9Gly amino-acid substitution in the N terminal extracellular domain of the receptor are genetic polymorphisms previously implicated to confer susceptibility to psychiatric disorders [2,15]. European multicentre studies indicate significant association between schizophrenia and C-102 variant of the T-102C polymorphism [12,14] as well as an increased homozygosity of either allele of the DRD3 polymorphism [6]. However, negative associations have widely been reported, especially for the DRD3 Ser9Gly transition [16,1]. *DRD3 receptor* gene polymorphisms in Greek samples, in order to investigate the distribution of the allelic variants within the population and to examine their putative correlation with schizophrenia. A common variant of a single nucleotide polymorphism (SNP) of A/G at position 25 of the DRD3 coding sequence has been identified [4] and Sivagnanasundaram, refer to association between schizophrenia and the Ser9Gly variant of the dopamine *D3 receptor* gene has been the subject of numerous studies and suggested that these SNPs and the corresponding coding changes may exerta combined or synergistic effect on susceptibility to schizophrenia [10] and Talkowski, refer to association SNP of DRD3 receptor gene with risk for schizophrenia [13]. An excess frequency of homozygotes for both alleles was originally reported in schizophrenic patients [7]. The DRD3 cDNA was believed to consist of six exons (total length 1.2 kb) and five introns (total length_45 kb). However, neither the extent of the 5_UTR nor the location of the promoter (s) were known. An additional 1724 bp of 5_ flanking sequence has been recently reported but no gene structure has been attributed to this [10]. Ishiguro *et al.*, refer to the 59 region of the DRD3 gene and found three novel polymorphisms: 712G/C, 205A/G, and Ala38Thr, case-control comparisons in 153 Japanese schizophrenia patients and 122 Japanese controls did not suggest an association between Ala38Thr and schizophrenia and Indicates unknown variant in linkage disequilibrium with the DRD3 haplotypes associated with schizophrenia [5]. There is study a significant correlation ship between schizophrenia and incidence of mutations (C/G; G/A; and G/T) position in exon 1 of *DRD3* (4147C-T) *receptor* gene ($X^2$=3.662, P>0.05), however, there is lower significant correlation ship between schizophrenia and incidence of mutations (G/T

and T/G) position in exon 1 of *DRD3* (4147C-T) *receptor* gene ($X^2$=1.089, P>0.05), the conclusion is that there is enough evidence to support the claim that schizophrenia is related to these mutations.

## REFERENCE


1. Anney, R.J.; Rees, M.I.; Bryan, E.; Spurlock, G.; William, N.; Norton, N.; William, H.; Cardon, A.; Zammit, S.; Jones, S.; Hoogendoorn, B. and Smith, K. (2002). Characterization, mutation detection and association analysis of alternative promoters and 5 UTRs of the human dopamine D3 receptor gene in schizophrenia. Molecular psychiatry, 7: 493-502.
2. Baron, M. (2001). Genetics of schizophrenia and the new millennium: progress and pitfalls. Am. J. Hum. Genet., 68: 299– 312.
3. Bary, N.J. and Owen, M.J. (2001). Searching for schizophrenia genes. Trends Mol. Med., 7: 169-174.
4. Crocq, M.A.; Mant, R.; Asherson, P.; Williams, J.; Hode, Y.; Mayerova, A.; Collier, D.; Lannfelt, L.; Sokoloff, P.; Schwartz, J.C.; Gill, M.; Macher, J.P.; McGufn, P. and Owen, M.J. (1992). Association between schizophrenia and homozygosity at the dopamine D3 receptor gene. J. Med. Genet., 29: 858-860.
5. Ishiguro, H.; Okuyama, Y.; Toru, M. and Arinami, T. (2000). Mutation and association analysis of the 59 region of the dopamine D3 receptor gene in schizophrenia patients: identification of the Ala38Thr polymorphism and suggested association between DRD3 haplotypes and schizophrenia. Molecular Psychiatry, 5: 433–438.
6. Jonsson, E.; Lannfelt, L. and Sokoloff, P. (1993). Lack of association between schizophrenia and alleles in the dopamine D3 receptor gene. Acta. Psychiatr. Scand., 87: 345– 349.
7. Lannfelt, L.; Sokoloff, P.; Martes, M.; Pilon, C.; Giros, B.; Schwartz, J.; Jonsson, E. and Sedvall, G. (1992). Amino acid substitution in the D3 dopamine receptor as a useful polymorphism for investigating psychiatric disorders. Psychiat. Genet., 2: 249-256.
8. Risch, N. (1990). Genetic linkage and complex diseases, with special reference to psychiatric disorders. Genet. Epidemiol., 7: 3–16.
9. Shafer, R.A. and Levant, B. (1998). The D3 dopamine receptor in cellular and organismal function. Psychopharmacology, 135: 1–16.
10. Sivagnanasundaram, S.; Morris, A.G. and Hunt, D.M. (1999). Human dopamine D3 receptor 5_-flanking sequence. Unpublished sequence data. Accession No. AF033621. NID g5256826.
11. Sokoloff, P.; Giros, B.; Martres, M.P.; Bouthenet, M.L. and Schwartz, J.C. (1990). Molecular cloning and characterization of a novel dopamine receptor (D3) as a target for neuroleptics. Nature, 347: 146–151.
12. Spurlock, G.; Williams, J. and McGuffin, P. (1998). European Multicentre Association Study of Schizophrenia: a study of the DRD2 Ser311Cys and DRD3 Ser9Gly polymorphisms. Am. J. Med. Genet., 81: 24–28.
13. Talkowski, M.; Kirov, G.; Bamne, M.; Georgieva, L.; Torres, G.; Mansour, H.; Chowdari, K.; Milanova, V.; Wood, J.; McClain, L.; Konasale, P. and Shirts, B. (2008). A network of dopaminergic gene variations implicated as risk factors for schizophrenia. Human Molecular Genetics, 17(5): 747–758.
14. Williams, J.; Owen, M.J. and Spurlock, G. (1995). Searching for susceptibility genes for schizophrenia: the European Multicentre Association Study. New Trends Exp. Clin. Psychiatry., 11: 7– 12.
15. Williams, J.; Spurlock, G. and McGuffin, P. (1996). Association between schizophrenia and T102C polymorphism of the 5-hydroxytryptamine type 2a-receptor gene. European Multicentre Association Study of Schizophrenia (EMASS) Group. Lancet, 347: 1294– 1296.
16. Yang, L.; Li, T. and Wiese, C. (1993). No association between schizophrenia and homozygosity at the D3 dopamine receptor gene. Am. J. Med. Genet.; 48: 83– 86.

**Figures and Tables:**

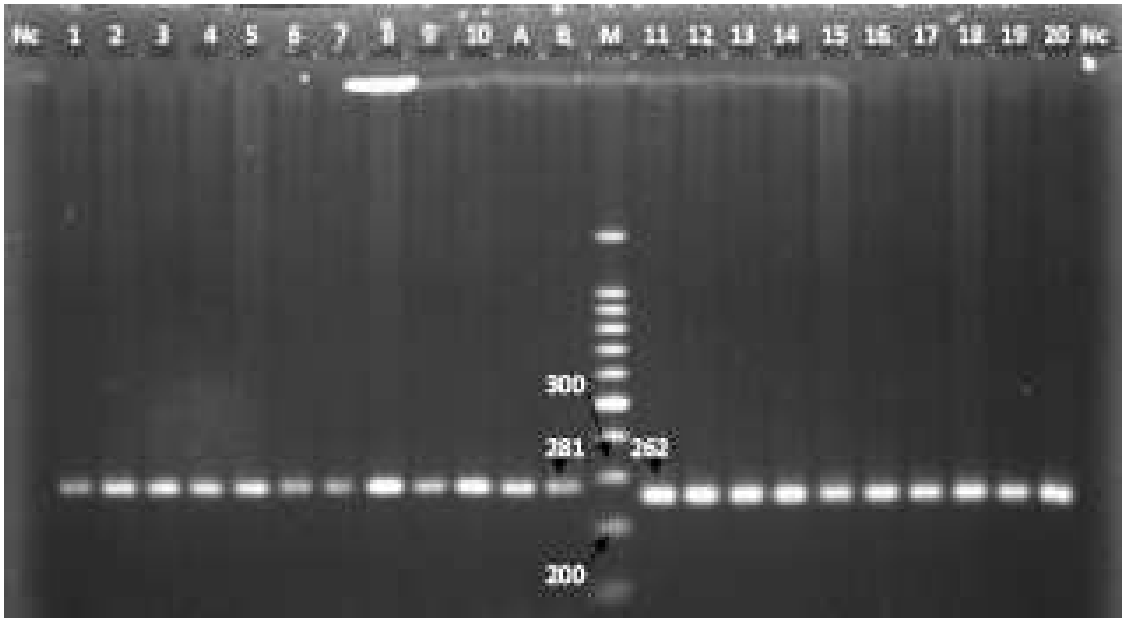


**Figure 1:** Agarose gel electrophoresis for amplified *DRD3* gene of schizophrenia patients and healthy. Bands were fractionated by electrophoresis on a 1.5 % agarose gel (2 h., 5V/cm, 0.5X TBE buffer) and visualized under U.V. light after staining with ethidium bromide staining. Lane: 12 (M:100bp ladder); Lane: N (negative control); Lane: 1,2,3,4,5,6,7,8,9,10 product for exon 1 *DRD3* (4147C-T) gene; and Lane: 11,12,13,14,15,16,17,18,19,20 product for exon 1 *DRD3* (712G-C) gene, Lane A, B: Healthy.

**Homo sapiens chromosome 3 genomic contig, Features flanking this part of subject sequence: D (3) dopamine receptor isoform a**
**Score = 374 bits (202), Expect = 4e-101, Identities = 202/202 (100%), Gaps = 0/202 (0%) Strand=Plus/Minus**

```
Query 1          CAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAACAAATAATTAAAA  60
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390225  CAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAACAAATAATTAAAA  20390166

Query  61        CTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTTCAGGAAGACTGTT  120
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390165  CTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTTCAGGAAGACTGTT  20390106

Query  121       ATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCATAACTGATGGGGAC  180
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390105  ATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCATAACTGATGGGGAC  20390046

Query  181       CTGACAACTCTCTGTTCCCCTG  202
                 ||||||||||||||||||||||
Sbjct  20390045  CTGACAACTCTCTGTTCCCCTG  20390024
```

**Figure (2):** Sequencing of sense flanking the partial *DRD3* (4147C-T) gene for healthy as compared with standard *DRD3* (4147C-T) obtained from Gene Bank.

```
Homo sapiens chromosome 3 genomic contig, Features flanking this part of subject
sequence:  D(3) dopamine receptor isoform a
Score = 316 bits (171), Expect = 4e-84,Identities = 177/180 (98%), Gaps = 0/180 (0%)
Strand=Plus/Minus

Query  19        ACTGATACTTGGCACACAGTAATAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTC  78
                 ||| ||||||| ||||||||| ||||||||||||||||||||||||||||||||||||
Sbjct  20390252  ACTCATACTTGCCACACAGTAGTAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTC  20390193

Query  79        TTACAGAAAGAGAACAAATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAA  138
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390192  TTACAGAAAGAGAACAAATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAA  20390133

Query  139       CCCCACGAATGTTTCAGGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGC  198
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390132  CCCCACGAATGTTTCAGGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGC  20390073
```

**Figure (3)**: Sequencing of sense flanking the partial DRD3 (4147C-T) gene for 10 cases schizophrenia as compared with standard *DRD3* (4147C-T) obtained from Gene Bank.

```
Homo sapiens chromosome 3 genomic contig, Features flanking this part of
subject sequence: D(3) dopamine receptor isoform a
Score =   399 bits (216),  Expect = 5e-109, Identities = 218/219 (99%), Gaps = 0/219 (0%)
 Strand=Plus/Minus

Query  1         AGTATTAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAACA  60
                 |||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390236  AGTAGTAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAACA  20390177

Query  61        AATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTTCA  120
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390176  AATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTTCA  20390117

Query  121       GGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCATAA  180
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390116  GGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCATAA  20390057

Query  181       CTGATGGGGACCTGACAACTCTCTGTTCCCCTGCCTTTT  219
                 |||||||||||||||||||||||||||||||||||||||
Sbjct  20390056  CTGATGGGGACCTGACAACTCTCTGTTCCCCTGCCTTTT  20390018
```

**Figure (4):** Sequencing of sense flanking the partial *DRD3* (4147C-T) gene for 10 cases schizophrenia patients as compared with standard *DRD3* (4147C-T) obtained from Gene Bank.

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Homo sapiens chromosome 3 genomic contig, Features flanking this part of
subject sequence:  D(3) dopamine receptor isoform a
  Score =   392 bits (212),  Expect = 8e-107,  Identities = 218/221 (99%), Gaps = 0/221
(0%), Strand=Plus/Minus

Query  1         CACAGTATTAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAA  60
                 ||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390238  CACAGTAGTAGCCCAGATGTAGTTGTCTTCATCTTCATTTGTTTTCTTACAGAAAGAGAA  20390179

Query  61        CAAATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTT  120
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390178  CAAATAATTAAAACTCTGTAAGTCTTAATGAGGTGCTAAGGAGGAACCCCACGAATGTTT  20390119

Query  121       CAGGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCAT  180
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20390118  CAGGAAGACTGTTATTCAGCACTGAGGGATTGAACATCAGCAAAGCAGGACAAATGTCAT  20390059

Query  181       AACTGATGGGGACCTGACAACTCTCTGTTCCCTGGCCTTTT  221
                 |||||||||||||||||||||||||||||||  |||||||
Sbjct  20390058  AACTGATGGGGACCTGACAACTCTCTGTTCCCCTGCCTTTT  20390018
```

**Figure (5):** Sequencing of sense flanking the partial *DRD3* (4147C-T) gene for 5 cases schizophrenia patient as compared with standard *DRD3* (4147C-T) obtained from Gene Bank.

**Table (1):** Types of mutations detected in partial *DRD3* (4147C-T) gene of schizophrenia patients.

| No. | location of gene bank | Nucleotide change | No. of sample | Amino acid change | Predicted effect | Type of mutation |
|---|---|---|---|---|---|---|
| 1 | C/G 2+ | CAT/ GAT | 10 | Histidine/ Aspartic acid | Missense | Transversion |
| 2 | C/G 4+ | TGC/ TGG | 10 | Cysteine/ Tryptophan | Missense | Transversion |
| 3 | G/A 8+ | GTA/ ATA | 10 | Valine/ Isoleucine | Missense | Transition |
| 4 | G/T 2+ | AGT/ ATT | 10 | Serine/ Isoleucin | Missense | Transversion |
| 5 | G/T 3+ | AGT/ ATT | 5 | Serine/ Isoleucin | Missense | Transversion |
| 6 | C/T 71+ | CCC/CCT | 5 | Proline/ Proline | Silent | Transition |
| 7 | T/G 72+ | TGC/GGC | 5 | Cysteine/ Glisine | Missense | Transversion |

```
Homo sapiens chromosome 3 genomic contig, Features flanking this part of subject
sequence: D(3) dopamine receptor isoform a

 Score =  292 bits (158),  Expect = 8e-77, Identities = 158/158 (100%), Gaps = 0/158
(0%) Strand=Plus/Minus

Query  1         AAAGCTCTTGGCAGCAGCGGTGCTATCTCCAGGGTAGCGGCTGCCCTCCTCTGAATAATG  60
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20388194  AAAGCTCTTGGCAGCAGCGGTGCTATCTCCAGGGTAGCGGCTGCCCTCCTCTGAATAATG  20388135

Query  61        AGAAAATTATAATTATTATCAAGAATTATTATTATGTTTTAAAATACATTGAGTGCAAAC  120
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  20388134  AGAAAATTATAATTATTATCAAGAATTATTATTATGTTTTAAAATACATTGAGTGCAAAC  20388075

Query  121       AGTGTGCCAAGATAAAGGACAATTTTTTTAAACAATTC  158
                 |||||||||||||||||||||||||||||||||||||
Sbjct  20388074  AGTGTGCCAAGATAAAGGACAATTTTTTTAAACAATTC  20388037
```

**Figure (6):** Sequencing of sense flanking the partial *DRD3* (712G/C) gene for healthy and all cases schizophrenia patient as compared with standard *DRD3* (712G/C) obtained from Gene Bank.