The impact of Copy Number Variants: from schizophrenia to forensic routine

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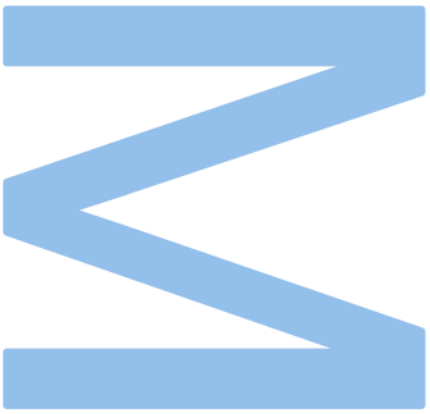

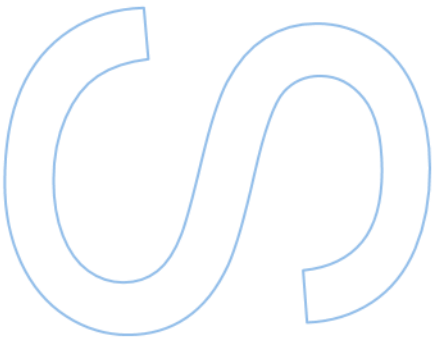

«It was the time you devoted to your rose that made it so important».

Saint-Exupéry

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Resumo

Os Variantes do Número de Cópias (CNVs) caracterizam-se pela variação no número de cópias de regiões específicas do genoma humano. Os CNVs pertencem à ampla classe das Variações Estruturais. A deteção e análise de CNVs pode fornecer uma grande variedade de informações valiosas que irão permitir dar resposta a múltiplas questões biomédicas. Os CNVs têm-se destacado como um importante fator de risco para várias doenças. Um exemplo dessas doenças é a esquizofrenia. Apesar da componente genética associada à esquizofrenia ainda não estar completamente estabelecida, os CNVs têm-se destacado como importantes fatores de risco. Tendo em conta que o estudo de CNVs fornece uma nova via promissora para a compreensão da base genética de doenças comuns, este trabalho debruçou-se no estudo de CNVs já documentados na literatura como associados à esquizofrenia. O nosso estudo mostra que, de facto, existem numerosos CNVs que afetam genes/*loci* previamente reportados para a esquizofrenia, enfatizando a ligação entre esta doença e a ocorrência de CNVs, que em muitos casos estão fora de *hotspots* de CNVs, reforçando o seu papel na suscetibilidade a esta doença. Para além da sua extrema relevância no contexto clínico, os CNVs têm ganho um destaque crescente no campo forense, essencialmente nos casos em que estes ocorrem em regiões genómicas que contenham STRs, frequentemente usados em rotina e investigações forenses. Nesta pesquisa, revisitamos a literatura para compilar os casos de *loci* utilizados na genética forense que estão em regiões genómicas impactadas por CNVs.

Palavras-chave: Variantes Estruturais, Variantes do Número de Cópias, Doenças do Neurodesenvolvimento, Esquizofrenia, *Short Tandem Repeats*, Rotina Forense.

Abstract

Copy Number Variants (CNVs) are characterized by variation in the number of copies of specific regions of the human genome. CNVs belong to the broad class of Structural Variations. Detecting and analyzing CNVs can provide a wide range of valuable information that will allow us to answer multiple biomedical questions. CNVs have been highlighted as an important risk factor for various diseases, such is schizophrenia. Although the genetic component associated with schizophrenia has not yet been fully established, CNVs have been highlighted as important risk factors. Considering that the study of CNVs provides a promising new avenue for understanding the genetic basis of common diseases, this work focused on the study of CNVs already documented in the literature as being associated with schizophrenia. Our study shows that there are indeed numerous CNVs affecting genes/*loci* previously reported for schizophrenia, emphasizing the link between this disease and the occurrence of CNVs. In some cases, these CNVs are outside CNV hotspots, reinforcing their role in susceptibility to this disease. In addition to their extreme relevance in the clinical context, CNVs have gained increasing prominence in the forensic field, essentially in cases where they occur in genomic regions containing STRs, which are often used in routine and forensic investigations. In this research, we revisited the literature to compile the cases of *loci* used in forensic genetics that are in genomic regions impacted by CNVs.

Keywords: Structural Variants, Copy Number Variants, Neurodevelopmental Disorders, Schizophrenia, Short Tandem Repeats, Forensic Routine.

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List of Abbreviations

22q11.2DS	22q11.2 Deletion Syndrome
ASD	Autism Spectrum Disorder
bp	Base Pairs
cffDNA	Cell-free Fetal DNA
CHD	Congenital Heart Disease
CNVs	Copy Number Variants
DNA	Deoxyribonucleic Acid
HIV-1	Human Immunodeficiency Virus 1
HSP	Hereditary Spastic Paraplegia
Kb	Kilobase
Mb	Megabase
Mg^{2+}	Magnesium
NIPT	Non-invasive Prenatal Testing
PANTHER	Protein Analysis Through Evolutionary Relationships
STRs	Short Tandem Repeats

1. Introduction

1.1. Structural Variation

In recent years, the discovery of a vast amount of the human genetic variation has been made possible due to the accessibility of numerous genomes [1, 2]. The impact of genetic variation on the human genome encompasses both large microscopically visible chromosomal abnormalities and small gene lesions [3, 4]. Genetic variants that modify chromosome structure are known as Structural Variants, and include inversions, translocations, duplications, and deletions [4, 5]. These structural variants can span millions of bases in the human genome and have a profound impact on cellular phenotypes, disease, and human evolution [4]. Despite their important role in medicine and molecular biology [6], and their ability to cause phenotypic differences between individuals with implications for evolutionary and ecological adaptation, structural variants are often overlooked and under-studied as a source of human genetic variation [5, 7, 8].

1.2. What are CNVs?

Copy Number Variants (CNVs) are identified by the variation in the number of copies of specific regions in the human genome, as compared to a reference genome [3, 8, 9], and are part of the larger category of structural variants [4, 5]. Since the dawn of molecular genetics and the first characterizations of gene duplications and deletions in the early 1900s, CNVs have been increasingly valued [9-12]. CNVs are deletions and duplications of segments of genomic DNA [1, 13]. These segments can range in size from a few to over a million nucleotides [13, 14]. The current minimum length for a CNV is considered to be 50 bp [13]. However, with the continuous improvement in methods for studying CNVs, the detection of smaller fragment lengths is becoming increasingly feasible [13]. Yet, the task of identifying and characterizing the functional impact of these structural variants on both cellular and whole-body physiology remain a challenge [9, 13].

1.3. Clinical implications of CNVs

CNVs have gained special relevance in the sphere of human health and clinical diagnostics due to their association with various pathologies [13, 15, 16]. As previously mentioned, CNVs are an important source of genomic variability, therefore, the analysis of these variants can provide valuable information, especially when trying to answer multiple biomedical questions for which the detection of CNVs may become crucial [13].

The duplication and deletion of DNA segments can result in the alteration of gene dosage or the interruption of the function of a number of genes, originating alternative gene products and distinct patterns of gene expression [3, 17-23]. Thus, in addition to their role in population genetic diversity, CNVs can impact gene expression and phenotype [24], particularly in cases where CNVs disrupt both regulatory and coding regions of the genome [1, 9, 17, 25].

An example of how CNVs can impact genomic regions is related to the Crohn's disease [25]. A CNV has been identified in the upstream regulatory region of the *IRGM* gene. This CNV is thought to influence gene expression, thereby playing a contributory role in the onset of the disease [25].

Moreover, CNVs have also been important in prenatal testing, either by performing direct tests on the fetus or indirectly using maternal blood, enabling the diagnosis of both rare and common diseases or predispositions [13]. Thus, the detection of CNVs is part of non-invasive prenatal testing (NIPT), which is based on the analysis of cell-free fetal DNA (cffDNA) obtained from maternal plasma [26, 27], allowing the discovery of chromosomal aneuploidies and microdeletion syndromes, such are DiGeorge syndrome and Prader-Willi syndrome [13, 28].

The human microbiome, through its interacting with the host, holds a pivotal role in the host biological processes [13, 29]. Conversely, host genomic variations can influence the composition of the microbiome, which in turn can have significant implications for the individual's health [13]. One of the examples concerning the usefulness of CNV detection in assessing microbiome balance is the association between variations in the gut microbiome and variations in the copy number of certain genomic regions [13, 30]. A study by Poole and collaborators correlated the composition and function of the human oral and intestinal microbiome to the occurrence of CNV (duplication) affecting the *AMY1 locus* [30]. The *AMY1* gene encodes the salivary amylase enzyme which is necessary for starch digestion [30-32]. The study demonstrated the association between *AMY1*

gene duplication and high numbers of salivary *Porphyromonas* which in turn is related to periodontitis. In addition, changes have been found in the gut microbiota of these individuals, namely an increased abundance of microbes resistant to starch degradation and elevated production of short-chain fatty acids [30].

Taking into consideration that CNVs may have a substantial contribution to the genetic mechanisms underlying disease susceptibility, further study of these variants may allow for a greater understanding of the etiology of many diseases as well as the variability of associated phenotypes, namely when it comes to complex diseases and traits [13, 16, 17, 33], and the susceptibility to pathogens such is the HIV-1 virus [30, 34].

1.4. CNVs and Neurodevelopmental Diseases

The data accumulated to date allow us to highlight CNVs as an important risk factor of both Mendelian and common inherited diseases [13, 15, 17, 33, 35]. Among the polygenic diseases that have been associated with CNVs are neurodevelopmental disorders [14, 36]. These disorders are characterized by the inability to reach milestones of cognitive, emotional, and motor development [14, 37]. These disorders include Autism Spectrum Disorder (ASD), schizophrenia, and intellectual disability [14, 36, 38].

In addition to predisposing individuals to these neurological phenotypes, CNVs can also be at the origin of medical syndromes of another nature, depending on the deleted or duplicated genes [39, 40]. One such example is the 22q11.2 Deletion Syndrome (22q11.2DS), whose affected individuals manifest an increased risk of neurodevelopmental/cognitive, behavioral, and social-emotional difficulties and can also have cardiac dysfunction, craniofacial phenotypes, cleft palate, and increased risk of infections [40, 41]. Furthermore, complementary studies have reported this deletion occurring at the 22q11.2 *locus*, associated with 22q11.2 Deletion Syndrome (22q11.2DS) and the risk for various congenital anomalies, as one of the strongest risk factors for schizophrenia [42, 43].

Other examples of CNVs related to neurological phenotypes are the duplication at 7q36.3 affecting the *VIPR2* gene and the deletion at 2p16.3 affecting the *NRXN1* gene, which have been documented in autism, schizophrenia and bipolar disorder [14, 39, 44]. It is important to note that, unlike the examples given above, there are many cases that report CNVs have been associated to specific diseases [14]. For instance, the deletion in 3p14.1, which involves the *FOXP1* gene, has been identified in autism [14, 45].

1.4.1. Schizophrenia

Schizophrenia is defined as a severe and complex behavioral and cognitive syndrome [14] and is characterized by diverse symptoms such as delusions and hallucinations, social withdrawal, and cognitive impairment [46]. The origins of this psychiatric disorder appear to involve both genetic and environmental components that, in turn, affect brain development [7, 46]. Schizophrenia is a highly polygenic disorder [40], for which hundreds and probably thousands of different genetic *loci* have already been implicated at the population level [46, 47]. With a heritability of about 80% [48, 49], the genetic elements that contribute to the risk of schizophrenia are both rare and common variants and CNVs [46, 48, 50].

Particularly, an association between schizophrenia and a high burden of CNVs has been identified [14, 46]. A few years ago, a comprehensive analysis of CNVs among schizophrenia patients revealed eight *loci* (1q21.1, 2p16.3, 3q29, 7q11.2, 15q13.3, distal 16p11.2, proximal 16p11.2 and 22q11.2) with genome-wide significant evidence for association with the disorder [51]. Another example illustrating this link between CNVs and schizophrenia is the 15q11.2 deletion, which affects the *TUBGCP5, CYFIP1, NIPA2,* and *NIPA1* genes and is enriched among schizophrenia patients [52-54].

There are encouraging signs of convergence of genetic factors to a set of biological processes plausible to trigger developmental disorders, although much of the risk for schizophrenia remains unexplained at the genetic level [46].

1.5. Implications of CNVs in Forensics

CNVs are also growing in relevance in the forensic field, where they may have significant implications both in determining biological kinship and in human identification. Short Tandem Repeats (STRs) are the most frequently used *loci* in forensic genetics, namely at the investigation of biological parentage or human identification cases [55, 56]. The occurrence of CNVs at the genomic region of these STRs can make their genotyping difficult and raise challenges in interpreting the results [55]. Because of the diploidy of the human genome, two alleles per individual are expected at each autosomal STR [56, 57]. In rare cases, following routine genotyping of autosomal STRs for forensic purposes,

a three-peaked profile can be detected [56]. Such atypical profiles are classified as tri-allelic patterns and may represent a category of genotyping irregularity [56, 58].

In kinship tests based on STR typing, the detection of a tri-allelic pattern at a *locus* usually raises as a first explanation the existence of CNVs, since CNVs correspond to relatively large regions of the chromosome, in which STR markers may be included [58]. Currently, there are few studies about CNVs included in genomic regions containing STR markers commonly used in kinship testing or human identification [55].

2. Objectives

Detecting CNVs in individuals and populations is crucial for understanding their potential contribution to diseases or phenotypes, as well as for gaining a deeper understanding of the human genetic variability.

Given the extreme relevance of CNVs in both forensic and clinical contexts, this work is based on two main aims:

1. To investigate the distribution and genomic locations of CNVs in genes/*loci* previously documented to be associated with schizophrenia, and compare it with genomic hotspots for CNVs.
2. Analysis of CNV hotspots regions that overlap with genomic regions containing STR markers commonly used in routine and forensic investigations.

3. Methods

3.1. Literature Search

3.1.1. CNVs and Schizophrenia

To find CNVs affecting genes associated with schizophrenia, a manual search of the existing literature was conducted. This research was carried out in the period from November 2022 to March 2023. Using the PubMed database (https://pubmed.ncbi.nlm.nih.gov/), this search was based on the following keywords: "CNVs and schizophrenia", "Copy Number Variants and schizophrenia", and "CNVs and schizophrenia and genes". The final list included 34 scientific articles. All the papers were manually analysed to ensure they met the criteria of simultaneously referring to schizophrenia-associated genes and they include information of the *locus* or genomic coordinates of the CNVs affecting those genes.

3.1.2. CNVs and Population Hotspots

A search of the existing literature was also conducted to make a data collection of genomic hotspots where CNVs occur. Seven scientific articles were selected and further analysed. This survey was conducted in the period February to March 2023. With the help of the PubMed database, this search was based on the following keywords: "genomic hotspots and CNVs", "genomic hotspots and Copy Number Variants" and "hotspots and CNVs".

3.1.3. CNVs in Forensics

In order to survey genes and their *loci* associated with routine forensics that are affected by CNVs, a search was conducted in the existing literature. Eight scientific articles were analysed. This survey was conducted in the period March-April 2023. Furthermore, with the help of the PubMed database, this search was based on the following keywords: "CNVs and STR *locus*", "Copy Number Variants and STR *locus*" and "CNVs and STRs and forensic".

3.2. Conversion of Genomic Coordinates

All the genomic coordinate data of the CNVs under study were converted to the same version of the reference human genome, so that it would be possible to compare the data and perform further analysis. All genomic coordinate data of the CNVs under study were converted to the NCBI36 (hg18) version of the reference human genome using the UCSC Genome Browser and the LiftOver tool [59]. This tool allowed us to load the genomic coordinate data of the CNVs under study and obtain their conversion to the new version of the human genome chosen.

3.3. Gene Ontology analysis

The study genes associated with schizophrenia and affected by CNVs were clustered and Gene Ontology analysis was performed. Using the PANTHER Classification System and the Gene List Analysis tool [60], the list of genes under study was loaded, "ID list" was selected for the list type, the organism in question "*Homo sapiens*" was selected, the analysis "Functional classification viewed in graphic charts" and the chart type "bar chart" was chosen. Two parameters were analysed for the ontology of the genes under study: Biological Process and Molecular Function. To obtain the graphs for each parameter under analysis, the genes with the category "Unclassified" were filtered. For both parameters, the most prevalent categories were analysed, where genes with the category "Unclassified" were also filtered out.

4. Results and Discussion

4.1. List of CNVs affecting schizophrenia-associated genes

This work started by collecting documented CNVs affecting genes/*loci* associated with schizophrenia. For this, a search was conducted in the existing literature. Thirty-four scientific articles were analysed [7, 40, 43, 51, 61-90] and data related to schizophrenia-associated genes in which CNVs occur, the type of event (deletion or duplication), the *locus* and genomic coordinate of the CNVs, and the version of the reference human genome used in each publication was extracted. Table S1 (Supplementary Data) presents a list of genes and *loci* associated with schizophrenia that have been found included in 712 CNVs. This set of CNVs includes variants in all chromosomes except the Y chromosome, emphasizing that CNVs associated with schizophrenia are not found in any specific region of the genome.

4.2. Representation of size distribution of CNVs under study

In order to investigate the size distribution of the CNVs under study, an analysis of the genomic coordinate data of the CNVs was performed and a plot of this distribution is shown in Figure 1. Only CNVs that were referenced to the genomic coordinate were included in this analysis. Overall, we noticed a trend of decreasing numbers of CNVs as the size of the interval increased. As a result, the size class where most of the CNVs are included is the smallest in terms of genome size (0 to 100 Kb), with 118 CNVs observed. According to the existing literature, the available technology allows the detection of CNVs with sizes above 50 Kb, while it is more difficult to detect smaller CNVs, below 50 Kb [16]. However, with methodological advances, it is expected that many CNVs with a size of less than 50 Kb will be discovered [16].

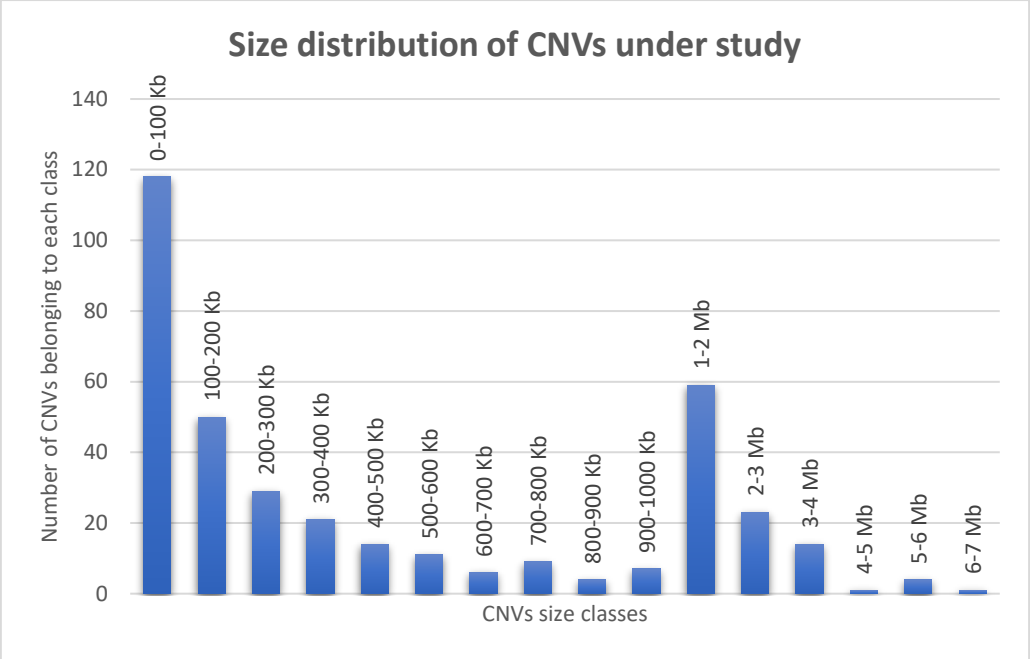

Figure 1 - Size distribution of the CNVs under study.

A noticeable trend of decreasing CNV numbers with increasing size is observed. A clear exception to this trend is shown by the class of 1-2 Mb. The reason for the high frequency of CNVs in this class remains uncertain, but it could be related to specific genome regions that are more susceptible to structural variation. However, upon analyzing the 59 CNVs in this class, it was found that they are distributed over various chromosomes (chromosome 1-4, 6-8, 11, 13, 15-18, 22, X) and are not confined to a particular region of the genome.

4.3. Comparison with mutational hotspots of CNVs

Next, a literature search was carried out to gather data on genomic hotspots where CNVs are known to occur in the human genome. Seven scientific articles were analysed [45, 91-96]. Information from these articles was compiled into a table (Table S2, Supplementary Data), allowing for the identification of 404 CNVs occurring in distinct genomic hotspots.

The initial data of CNVs affecting schizophrenia-associated genes were compared with the CNVs occurring in genomic hotspots. Only CNVs with reference to the genomic coordinate were compared with the hotspots, corresponding to 430 CNVs affecting

schizophrenia-associated genes. To perform this cross-comparison, all CNV data with genomic coordinates were converted to the same version of the reference human genome. None of the CNVs identified in schizophrenia match the exact breakpoints of the genomic hotspots for structural variation.

Therefore, our analysis focused on the *loci* rather than the precise coordinates of the breakpoints (Table 1). In 54 instances, the identified *locus* matched the one found in patients with schizophrenia. This finding is significant because cases that are reported to be prevalent in schizophrenia patients (like the 15q11.2 and 22q11.2 deletion) [42, 43, 52, 53] are part of recognized genomic hotspots.

Table 1 – Overlap of *loci* associated with schizophrenia and genomic hotspots, where CNVs are prevalent.

Chromosome	***Locus***
chr1	1p13.3, 1q21.1, 1q32.2, 1p36.13
chr2	2q11.2, 2q13, 2q21.2
chr3	3q26.1, 3q29
chr5	5p15.2, 5p15.33
chr6	6p11.2, 6p21.33, 6p25.3, 6q25.3, 6q26
chr7	7q11.22, 7q11.23, 7p13, 7q31.33, 7q36.1, 7q36.2
chr8	8p22, 8p23.1, 8p23.3
chr9	9p11.2, 9p24.3
chr10	10q11.23
chr11	11p15.1, 11q25
chr15	15q11.2, 15q11.2-q13.1, 15q13.1, 15q13.3, 15q26.3
chr16	16p11.2, 16p12.1, 16p13.11
chr17	17p11.2, 17q12, 17p12, 17q21.31
chr18	18q22.1
chr19	19p13.2, 19p13.3
chr20	20p12.1, 20q13.33
chr21	21q11.2, 21q21.1, 21q22.3
chr22	22q11.2, 22q11.21, 22q11.22, 22q11.23

In addition to its association with schizophrenia, the 15q11.2 region is also associated with other health issues. These include congenital heart disease (CHD), epilepsy, developmental delay, learning difficulties and neurobehavioral disorders [52, 97-103]. This region, which covers approximately 500 Kb, involves 4 genes expressed in the central nervous system: *NIPA1*, *NIPA2*, *CYFIP1* and *TUBGCP5* [52, 104]. The *NIPA1* gene is highly expressed in the brain, and seems to play a role in the development and maintenance of the nervous system [105]. In turn, mutations in this gene cause postural disturbance as well as autosomal dominant hereditary spastic paraplegia (HSP) [105]. Furthermore, given that the *NIPA1* gene operates as a magnesium (Mg^{2+}) transporter, changes in the concentration of Mg^{2+} imply a redistribution of the protein 1, encoded by *NIPA1* gene [105, 106].

Similarly to *NIPA1*, the *NIPA2* gene also encodes a selective Mg^{2+} transporter [105-107]. Magnesium, through its involvement in the regulation and activation of channels and receptors, holds the potential to play a pivotal role in the occurrence of seizures [105, 108]. Given the role of the *NIPA2* gene in both magnesium metabolism and the regulation of renal conservation [105-107], it is important to note that mutations in this gene can lead to a decrease in the intracellular concentration of Mg^{2+} levels and cause childhood absence epilepsy [105, 108]. Furthermore, a study by Picinelli et al. suggested that urinary Mg^{2+} levels could serve as potential informative biomarkers for quick screening of duplications or deletions in 15q11.2, given the involvement of the *NIPA1* and *NIPA2* genes in magnesium homeostasis [105, 109].

Using the Structural Variations tool available at the gnomAD database (Genome Aggregation Database), we gathered information on structural variations associated with the *NIPA1* and *NIPA2* genes (Table 2). A total of 11 structural variations (9 deletions and 2 duplications) have been recorded for the *NIPA1* gene and 7 structural variations (3 deletions, 3 duplications and 1 insertion) for the *NIPA2* gene.

Table 2 – List of CNVs obtained using gnomAD for the *NIPA1* and *NIPA2* genes.

Gene	Class	Genomic Coordinate (hg19)
NIPA1	Deletion	chr15:22748999-23268000
	Deletion	chr15:23055126-23055191
	Deletion	chr15:23064523-23064583
	Deletion	chr15:23065450-23106100
	Deletion	chr15:23066401-23066528
	Deletion	chr15:23070080-23075898
	Deletion	chr15:23072327-23076035
	Deletion	chr15:23072663-23073168
	Deletion	chr15:23076185-23076242
	Duplication	chr15:22964999-23126500
	Duplication	chr15:23035808-23054354
NIPA2	Deletion	chr15:22748999-23268000
	Deletion	chr15:23026200-23026301
	Deletion	chr15:23029789-23030537
	Duplication	chr15:22964999-23126500
	Duplication	chr15:23001000-23009000
	Duplication	chr15:23020000-23025000
	Insertion	chr15:23027948

In reference to the study conducted by Marshall and colleagues, which explores the association between CNVs and schizophrenia [51], a comparison with our data reveals that among the *loci* reported to have genome-wide association with the disorder, only the 2p16.3 is not included in a genome hotspot. The other seven *loci* (1q21.1, 3q29, 7q11.2, 15q13.3, distal 16p11.2, proximal 16p11.2 and 22q11.2) cited in Marshall's work [51] are also associated with schizophrenia (Table 1).

Based on our analysis, we can conclude that the 54 CNV *loci* identified in the overlap between schizophrenia-associated *loci* and genomic hotspot *loci* are not exclusive to schizophrenia. These *loci* are found in genomic hotspots, which are regions of the genome prone to CNVs. On the other hand, the 430 CNVs that we identified with reference to the genomic coordinate that did not overlap with the genomic hotspots

appear to be specific to schizophrenia. These CNVs occur outside of the commonly recognized genomic hotspots and may represent unique genetic variations associated with this complex mental disorder.

4.4. Gene Ontology analysis

Gene Ontology analysis was performed for the study genes associated with schizophrenia, using the PANTHER Classification System. The following parameters were analysed: Biological Process and Molecular Function. The resulting information was compiled into graphs shown in Figures 2 and 3.

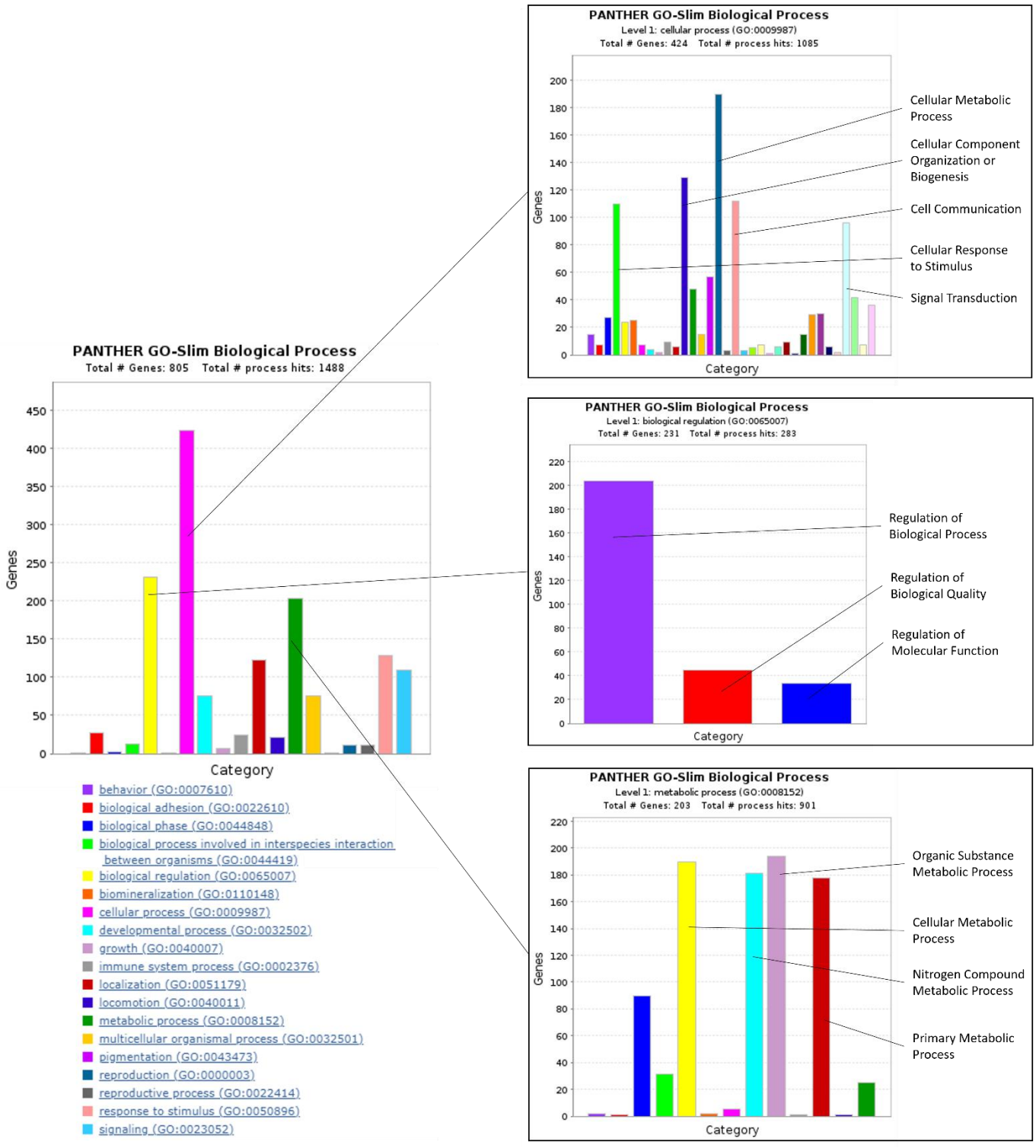

Figure 2 – Gene ontology analysis: biological process.

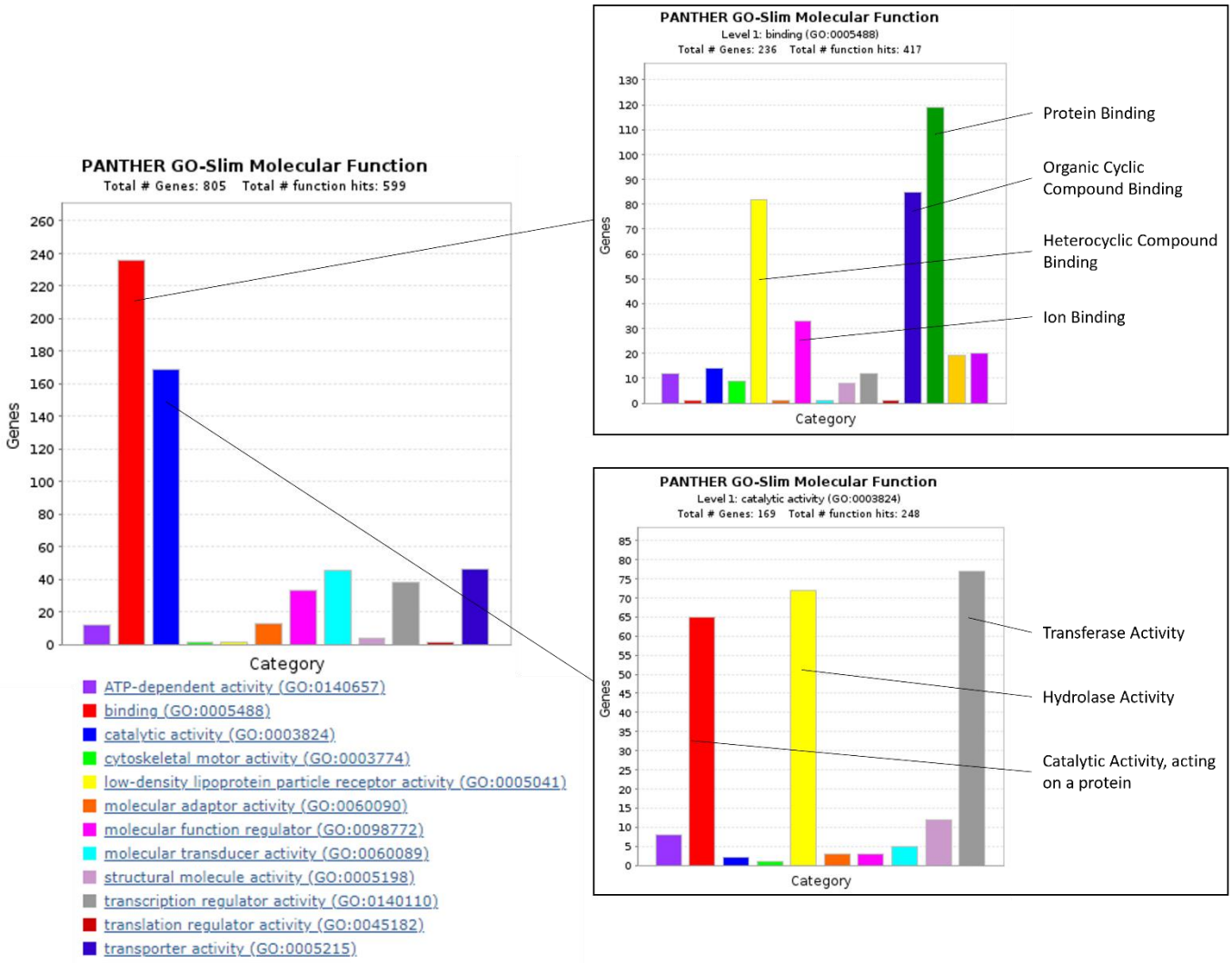

Figure 3 – Gene ontology analysis: molecular function.

For the Biological Process parameter, the prominent categories include cellular process, biological regulation, and metabolic process. As for the Molecular Function parameter, binding and catalytic activity are the standout categories.

In the Biological Process category, we have three main subcategories:

Cellular Process: This includes cellular metabolic process, cellular component organization or biogenesis, and cell communication.

Biological Regulation: This involves regulation of biological process, regulation of biological quality, and regulation of molecular function.

Metabolic Process: This covers organic substance metabolic process, cellular metabolic process, and nitrogen compound metabolic process.

In the Molecular Function category, we have two main subcategories:

Binding: This includes protein binding, organic cyclic compound binding, and heterocyclic compound binding.

Catalytic Activity: This involves transferase activity, hydrolase activity, and catalytic activity acting on a protein.

Related to the cellular process subcategory, in which most of the schizophrenia-related genes are associated, are linked to cellular metabolic processes, such as *DMRT1*, *GSTT2*, *PRKCA, FBXO45*, *SENP5* and *PAK2* genes. A study by Kumperscak et al. revealed a patient with schizophrenia carrying the 3q29 deletion, encompassing the partial deletion of the *PAK2* and *SENP5* genes [62]. This deletion has been shown to be a major risk factor for schizophrenia [62, 110]. The *PAK2* gene encodes the serine/threonine kinase enzyme PAK2, which is a critical regulator of cytoskeleton dynamics [62].

The *SENP5* gene is highly expressed in cerebellum [111]. The cerebellum is traditionally known for its role in gathering information from various cortical areas and subsequently transmitting this information to the primary motor cortex [112-115]. This process enables the control of motor functions such as coordination, balance, and posture [115]. However, emerging evidence suggests that the cerebellum also plays a pivotal role in non-motor functions such as cognition and emotion [112, 115, 116].

Individuals diagnosed with schizophrenia often display a range of symptoms, including various cognitive impairments, suggesting a potential deficiency in a key cerebral regulatory component [117]. Considering the cerebellum's involvement in multiple cortical activities, any dysfunction in the cerebellum could result in a variety of cortical malfunctions [117-120]. This, in turn, could manifest as the diverse symptoms and cognitive dysfunctions observed in schizophrenia [117-120].

Neuropathology studies have provided relevant evidence of cerebellar abnormalities in schizophrenia [117, 121]. Some studies have reported that patients with schizophrenia express decreased blood flow in the cerebellum in a wide range of tasks that affect brain functional systems, such as memory, attention, social cognition, and emotion [117, 122-127].

Next, the genes under study were also analyzed for molecular function, and it was found that most of these genes are associated with binding. More specifically, most of these genes that are affected by CNVs and are linked to schizophrenia are associated with

protein binding, such as the *NRCAM*, *CNTN6*, *CDH13*, *DOCK8*, *NDE1* and *RB1CC1* genes. A study by Ayalew et al. reported the association of the *NRCAM* gene with cell connectivity and adhesion, and its relevance in schizophrenia [128]. The *NRCAM* gene is responsible for encoding a protein that functions as a neuronal cell adhesion molecule [128]. This molecule is an ankyrin-binding protein that plays a crucial role in neuron-neuron adhesion [128]. It promotes directional signaling during the growth of axonal cones, a process integral to neuronal development and function [128].

4.5. CNVs in Forensics

In the concluding stage of this study, which is grounded in a master's degree in forensic genetics, the goal was to identify the genes and *loci* affected by CNVs that are relevant to the forensic field. Eight scientific articles were analysed [57, 58, 129-134] (Table 3). The number of *loci* affected by CNVs is nine, although it shall be noted that the information available in the STRBase database [135] include 401 patterns reported for which the tri-allelic pattern was observed. The influence of CNVs in the tri-allelic pattern obtained in forensic investigations can be demonstrated by the work of Lukka et al. [131]. This study reported that routine paternity tests revealed the existence of tri-allelic patterns in multiple STR *loci*, namely the case of the TPOX *locus* (2p25.3). These tri-allelic patterns, which are characterized as three-band observed at a single STR *locus*, are an example of genotyping challenges found in forensic genetics [131].

Table 3 - List of *loci* affected by CNVs, and which are associated with forensic routine.

Locus		**Genomic Hotspot with occurrence of CNVs**	**Reference**
AMELY	Yp11.2	Yes	[129]
AMELX	Xp22.1-Xp22.3	-	[129]
DYS458, MSY1, AMEL-Y	Yp11.2	Yes	[130]
TPOX	2p25.3	-	[57, 131, 132]
Penta D	21q22.3	Yes	[58]
D21S11	21q21.1	Yes	[58]
D3S1358	3p21.31	-	[133, 134]

In a routine paternity test involving a family trio, an example was observed (as shown in Figure 4) where a tri-allelic pattern was present in the TPOX *locus.* Additionally, a chromosome duplication larger than 1.59 Mb was found surrounding the TPOX *locus* on chromosome 2 in both the mother and child [131].

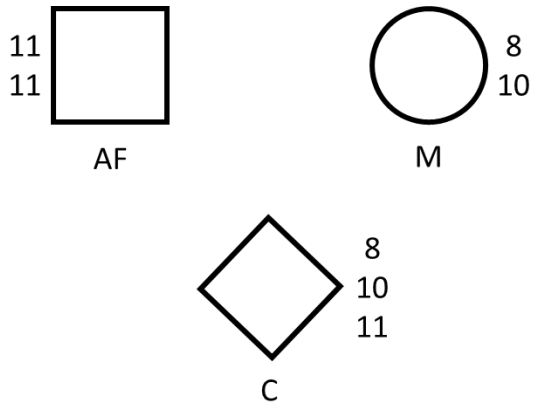

Figure 4 – Analysis of tri-allelic patterns for the *TPOX* marker observed in a trio of paternity tests (AF - alleged father, M - mother, C - child).

The alleged father's genotype at the TPOX *locus* is 11,11, the mother's is 8,10 and the child's is 8,10,11 [131]. The child seems to have inherited one allele from the father and two alleles from the mother [131]. This study highlights the possibility that this tri-allelic pattern, which causes challenges in forensic investigation, is based on the duplication found in the 2p25.3 region, which probably belongs to a copy number polymorphism [131, 136, 137].

5. Conclusion

A comprehensive analysis of CNVs allows for a deeper exploration and comprehension of the human genome and also aids in understanding their potential role in diseases.

One of the objectives of this study was to investigate the association between CNVs and schizophrenia, by studying and analyzing the distribution and genomic location of these variants in genomic regions previously documented as associated with schizophrenia. Our research indeed confirmed that numerous CNVs impacting genes/*loci* linked to this disease were discovered.

Another objective was to compare our data on CNVs associated with genes/*loci* documented in schizophrenia with previously documented genomic hotspots where CNVs occur, in order to verify if there was an overlap between both data. On one side, we observed that there was no overlap between the genomic coordinates of the studied. We identified several cases where CNVs are present, which are both genomic hotspots and *loci* associated with schizophrenia. This implies that these *loci* might not be only linked to schizophrenia, as they were discovered in genomic hotspots that are more prone to the presence of CNVs. Conversely, we found hundreds of genomic coordinates of CNVs that correspond to the exact breakpoints that did not align with the hotspots. These are likely to be schizophrenia-specific, contributing to increase the risk of this neurodevelopmental disorder.

In addition, we found instances that are routinely used in forensic investigations that overlap with our dataset of genomic hotspots for CNVs, indicating that these CNVs occurring in a region containing STR markers used in forensic genetics can challenge the investigation of biological parentage and human identification.

6. References

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Supplementary Data

Table S1 - List of genes previously reported in schizophrenia-affected families.

Gene	Event	Citoband/*locus*	CNV region	Reference Human Genome	Reference
ASTN2	Deletion	9q33.1	chr9:116683530-116876208	GRCh38 (hg38)	[64]
			chr9:116634744-116742416		
			chr9:116683530-116733612		
BIRC6	Deletion	2p22.3	chr2:32528746-32559427		
CACNA1C	Deletion	12p13.33	chr12:2687956-2741851		
CACNA2D1	Deletion	7q21.11	chr7:81478831-84097791		
CNTN6	Deletion	3p26.3	chr3:1264992-1295956		
CSMD1	Deletion	8p23.2	chr8:3877806-3959547		
			chr8:3873130-3959547		
			chr8:3876145-3961401		
			chr8:3876145-3967152		
			chr8:2724493-4921893		
CTNND2	Deletion	5p15.2	chr5:11567352-11629138		
DLG2	Deletion	11q14.1	chr11:84809995-84986152		
			chr11:84877230-84963429		
			chr11:84114371-84650078		
			chr11:84405313-84547789		
DLGAP2	Deletion	8p23.3	chr8:1050516-1327901		
DMD	Deletion	Xp21.1	chrX:31774439-31859356		
			chrX:32070396-32212245		
DOCK8	Deletion	9p24.3	chr9:10000-400952		
DPP10	Deletion	2q14.1	chr2:115503140-115527426		
DPP6	Deletion	7q36.2	chr7:153822158-153968005		
ELP4	Deletion	11p13	chr11:31405793-31548667		
FAM92B	Deletion	16q24.1	chr16:84593050-85516675		
FHIT	Deletion	3p14.2	chr3:60408194-60672864		
			chr3:60389119-60571624		
			chr3:60438915-60817364		
GRID2	Deletion	4q22.1	chr4:92590068-92732357		
			chr4:92930845-93092974		
HECW2	Deletion	2q33.1	chr2:196588283-196600831		
KATNAL2	Deletion	18q21.1	chr18:47026162-47075742		
KIAA1586	Deletion	6p12.1	chr6:57046622-57092420		
			chr6:57046622-57088889		
LPP	Deletion	3q28	chr3:188420063-188540464		
			chr3:188343948-188435451		
MACROD2	Deletion	20p12.1	chr20:14656734-14876708		
			chr20:14631584-14707775		
MBD5	Deletion	2q23.1	chr2:148157591-148226058		
			chr2:148211972-148423169		
			chr2:148139385-148242336		
			chr2:147990605-148350066		
			chr2:148158424-148226279		

MSRA	Deletion	8p23.1	chr8:10252025-10336231	GRCh38 (hg38)	[64]
NPAS3	Deletion	14q13.1	chr14:33318664-33378429		
NRXN1	Deletion	2p16.3	chr2:50721552-50944617		
			chr2:50836961-51084060		
			chr2:50975328-51121693		
P4HA2	Deletion	5q31.1	chr5:131428263-132208822		
PARD3B	Deletion	2q33.3	chr2:205264941-205497509		
			chr2:205102232-205198713		
PCDH15	Deletion	10q21.1	chr10:54690788-54898513		
PDE11A	Deletion	2q31.2	chr2:177895779-177946731		
PRKN	Deletion	6q26	chr6:162267721-162302278		
			chr6:162145541-162226576		
			chr6:162308970-162630627		
			chr6:162609404-162813090		
			chr6:161933685-162059574		
			chr6:162166123-162288233		
			chr6:161966350-162292493		
			chr6:162194743-162324250		
			chr6:162290852-162564693		
			chr6:162332720-162499424		
			chr6:162265361-162429333		
			chr6:162411708-162476625		
			chr6:161816395-162018868		
			chr6:162200873-162544554		
			chr6:162222675-162297617		
			chr6:162144053-162229459		
			chr6:162151583-162270607		
			chr6:162349019-162495982		
			chr6:162088360-162527858		
			chr6:162229459-162495982		
			chr6:161982200-162323320		
PTPRM	Deletion	18p11.23	chr18:7773472-8250054		
PTPRT	Deletion	20q12	chr20:42472130-42562200		
			chr20:42232174-42274201		
RB1CC1	Duplication	8q11.23	chr8:52714195-52957953		
			chr8:52425901-52662180		
			chr8:52426168-52664096		
			chr8:52698006-53562665		
			chr8:52541254-52713461		
			chr8:52541981-52850712		
RBFOX1	Deletion	16p13.2	chr16:7029167-7099643		
			chr16:6631947-7029167		
			chr16:6622570-6720408		
			chr16:6773909-6978067		
			chr16:6355716-6937802		
			chr16:6360351-6582207		
RELN	Deletion	7q22.1	chr7:103491380-103507508		
SHOX	Deletion	Xp22.33	chrX:621471-636910		

SLITRK5	Deletion	13q31.2	chr13:87545067-87934031	GRCh38 (hg38)	[64]
TAF13	Deletion	1p13.3	chr1:109048899-109079629		
TMLHE	Deletion	Xq28	chrX:155531678-155556173		
			chrX:155530103-155550495		
TOP3B	Deletion	22q11.22	chr22:21956007-22224188		
TRAPPC9	Deletion	8q24.3	chr8:140417391-140444832		
ULK4	Deletion	3p22.1	chr3:41609544-41811095		
			chr3:41760954-41858293		
			chr3:41803875-41849829		
VIPR2	Duplication	7q36.3	chr7:158726427-159193469		
			chr7:159061689-159335973		
VPS13B	Deletion	8q22.2	chr8:99047163-99227439		
			chr8:99118484-99159135		
WWOX	Deletion	16q23.1	chr16:79103200-79402155		
ZNF804A	Deletion	2q32.1	chr2:184830819-184884225		
HFE2	Duplication	1q21.1	chr1:145601945-148889374		
			chr1:145601945-146049618		
			chr1:145601945-146041785		
	Deletion	1q21.1	chr1:145601945-146048346		
GJA5	Deletion	1q21.1	chr1:145430995-148427734		
			chr1:145430995-148257619		
			chr1:145580669-149095000		
LMAN2L, ARID5A	Deletion	2q11.2	chr2:96063558-97079140		
ST6GAL2	Deletion	2q12.2-q12.3	chr2:106445028-107839483		
ARHGEF4	Deletion	2q21.1	chr2:130725519-131168548		
DLG1, PAK2	Deletion	3q29	chr3:195990063-197617301		
			chr3:196154147-197376501		
ELN, GTF2I	Duplication	7q11.23	chr7:73312644-74726596		
CHAT, SLC18A3	Duplication	10q11.22-q11.23	chr10:46157933-50098267		
SACS	Deletion	13q12.12	chr13:22968338-24323208		
NIPA1	Deletion	15q11.2	chr15:22681827-23226874		
			chr15:22444190-23226874		
			chr15:22673143-23226874		
			chr15:22770232-23126124		
			chr15:22751662-23126124		
			chr15:22673675-23126124		
UBE3A	Duplication	15q11.2-q13.1	chr15:23157975-28774125		
			chr15:23319712-28684313		
APBA2	Deletion	15q13.1-q13.2	chr15:28821222-30470957		
	Duplication	15q13.1-q13.2	chr15:28917240-30379798		
CHRNA7, FAN1	Deletion	15q13.2-q13.3	chr15:30325774-32194551		
	Duplication	15q13.2-q13.3	chr15:30506022-32161746		
			chr15:30568981-32151126		
SEMA7A, ARID3B	Duplication	15q24.1-q24.2	chr15:72640623-75277317		
			chr15:74071509-77878298		

NDE1, MYH11	Deletion	16p13.11	chr16:14780667-16415941	GRCh38 (hg38)	[64]
			chr16:15328439-16443962		
	Duplication	16p13.11	chr16:15029830-16415941		
			chr16:15030738-16517711		
			chr16:15318125-16294378		
		16p13.11-p12.3	chr16:15085515-18775195		
			chr16:15279737-18291544		
EEF2K, CDR2	Deletion	16p12.1	chr16:21928119-22428075		
	Duplication	16p12.1	chr16:21928119-22435412		
SH2B1, ATP2A1	Deletion	16p11.2	chr16:28351819-29325073		
KCTD13, TBX6	Duplication	16p11.2	chr16:29480853-30254620		
			chr16:29614026-30184960		
			chr16:29640511-30184960		
	Deletion	16p11.2	chr16:29627836-30184960		
PMP22	Deletion	17p12	chr17:14178908-15518547		
HNF1B	Deletion	17q12	chr17:36357256-37995300		
COMT, TBX1	Deletion	22q11.21	chr22:18159879-21387988		
			chr22:18159879-21362822		
			chr22:18163926-21277123		
			chr22:18802709-21343709		
			chr22:18832909-21123588		
			chr22:18846939-21221413		
			chr22:18880919-21123588		
			chr22:18880919-20346734		
CRKL, SNAP29	Deletion	22q11.21	chr22:20346735-21149007		
			chr22:20346735-21277123		
			chr22:20358985-21123588		
ADORA2A	Duplication	22q11.22-q11.23	chr22:22624794-24654160		
		22q11.23	chr22:23317839-24597843		
			chr22:23317839-24654160		
BCR, RAB36	Deletion	22q11.22-q11.23	chr22:22638171-23320336		
STS	Deletion	Xp22.31	chrX:6526750-8172018		
			chrX:6536927-8156323		
			chrX:6776477-7923774		
PAK2, SENP5	Deletion	3q29		GRCh37 (hg19)	[65]
TM6SF1, ADMTS3, SH3GL3, BNC1, BDTB1, FAM103A1, HOMER2, WHAMM, AP3B2, CPEB1, RPS17L	Duplication	15q25.2			
MAP3K3, DDX42	Deletion		chr17:61737993-61887860	GRCh37 (hg19)	[66]
DNAJA2, NETO2	Duplication		chr16:47004235-47124878		
PLEKHD1, SLC39A9	Duplication		chr14:69921835-69979453		
MATK, ZFR2	Duplication		chr19:3800538-3847280		
NRXN1	Deletion		chr2:50,15-51,26	GRCh37 (hg19)	[67]
VIPR2	Duplication		chr7:158,82-158,94		

GNB1, CALML6, TMEM52, KIAA1751, GABRD	Duplication	1p36.33	chr1:1.85–2.11	GRCh37 (hg19)	[68]
ELOVL6	Duplication		chr4:110.97–111.12		
AQP12A, KIF1A	Duplication		chr2:241.63–241.75		
FAM149A, FLJ38576, CYP4V2	Duplication		chr4:187.05–187.14		
TRIML1, TRIML2	Deletion		chr4:189.01–189.07		
IRGM, ZNF300, SMIM3	Deletion		chr5:150.16–150.30		
PHACTR2	Duplication		chr6:144–144.15		
GLIS3	Deletion		chr9:3.82–4.3		
SLC1A1	Deletion		chr9:4.49–4.59		
CGNL1	Duplication		chr15:57.67–57.84		
GALR1	Duplication		chr18:74.96–74.98		
PRKCZ	Duplication		chr1		
SRSF11	Duplication		chr1		
NCKAP5	Deletion		chr2		
UTS2D	Duplication		chr3		
CCDC50	Duplication		chr3		
KLKB1	Duplication		chr4		
F11	Duplication		chr4		
OR2Y1	Duplication		chr5		
FAM49B	Duplication		chr8		
MIR5194	Duplication		chr8		
ZNF252P	Duplication		chr8		
TMED10P1	Duplication		chr8		
HIPK3	Duplication		chr11		
PTPRJ	Duplication		chr11		
OR4B1	Duplication		chr11		
MAPKAPK5	Duplication		chr12		
GCOM1	Deletion		chr15		
MYZAP	Deletion		chr15		
LOC283693	Duplication		chr15		
SCARNA15	Duplication		chr15		
FSD2	Duplication		chr15		
LYSMD4	Deletion		chr15		
UQCRC2	Deletion		chr16		
PDZD9	Deletion		chr16		
C16orf52	Deletion		chr16		
VWA3A	Deletion		chr16		
EEF2K	Deletion		chr16		
POLR3E	Deletion		chr16		
CDR2	Deletion		chr16		
ANKRD26P1	Duplication		chr16		
SHCBP1	Duplication		chr16		
ALOX12P2	Deletion		chr17		
RNF135	Duplication		chr17		
DPRXP4	Duplication		chr17		

PTPRM	Duplication		chr18	GRCh37 (hg19)	[68]
VRK3	Duplication		chr19		
ZNF473	Duplication		chr19		
FLJ26850	Duplication		chr19		
LILRB5	Duplication		chr19		
PTPRT	Deletion		chr20		
COL18A1	Duplication		chr21		
ALG10B	Duplication	12q12		NCBI36 (hg18)	[69]
WBSCR17	Duplication	7q11.22			
DLG2	Deletion	11q14.1			
B3GAT1	Duplication	11q25			
PABPC4L	Deletion	4q28.3			
BARD1	Deletion	2q35			
DPP6	Duplication	7q36.2			
FHIT	Deletion	3p14.2		NCBI36 (hg18), GRCh37 (hg19)	[69], [46]
NAP5	Deletion	2q21.2		NCBI36 (hg18)	[69]
LRP1B	Duplication	2q22.2			
ABCC4	Duplication	13q32.1			
ST6GALNAC1	Duplication	17q25.1			
FAM155A	Deletion	13q33.3			
CGNL1	Deletion	15q21.3			
PRKCA	Deletion	17q24.2			
POLR3C	Deletion	1q21.1			
ZNF364	Deletion	1q21.1			
CD160	Deletion	1q21.1			
PDZK1	Deletion	1q21.1			
GPR89A	Deletion	1q21.1			
FAM82A	Duplication	2q22.2			
GALNT13	Duplication	2q24.1			
KCNJ3	Duplication	2q24.1			
SMARCC1	Duplication	3p21.31			
DHX30	Duplication	3p21.31			
MAP4	Duplication	3p21.31			
FRAS1	Duplication	4q21.21			
ANXA3	Duplication	4q21.21			
RGS12	Duplication	4p16.2			
HGFAC	Duplication	4p16.2			
DOK7	Duplication	4p16.2			
LRPAP1	Duplication	4p16.2			
ADRA2C	Duplication	4p16.2			
ELL2	Duplication	5q15			
PCSK1	Duplication	5q15			
PMS2	Deletion	7p22.1			
JTV1	Deletion	7p22.1			
EIF2AK1	Deletion	7p22.1			
JAK2	Duplication	9p24.1			
INSL6	Duplication	9p24.1			
INSL4	Duplication	9p24.1			

RLN2	Duplication	9p24.1		NCBI36 (hg18)	[69]
RLN1	Duplication	9p24.1			
C9orf46	Duplication	9p24.1			
CD274	Duplication	9p24.1			
PDCD1LG2	Duplication	9p24.1			
KIAA1432	Duplication	9p24.1			
ERMP1	Duplication	9p24.1			
MLANA	Duplication	9p24.1			
KIAA2026	Duplication	9p24.1			
RANBP6	Duplication	9p24.1			
GYS2	Deletion	12p12.1			
MPHOSPH9	Duplication	12q24.31			
C12orf65	Duplication	12q24.3			
CDK2AP1	Duplication	12q24.31			
SBNO1	Duplication	12q24.31			
SPECC1	Duplication	17p11.2			
SPECC1L	Duplication	22q11.23			
ADORA2A	Duplication	22q11.23			
NRXN1	Deletion	p16.3	chr2	NCBI36 (hg18)	[70]
PLGLA, RGPD3, ST6GAL2, RPGD4	Deletion	q12.2–q12.3	chr2		
TFRC, ZDHHC19, OSTalpha, PCYT1A, TCTEX1D2, TM4SF19, UBXN7, RNF168, C3orf43, WDR53, FBXO45, LRRC33, C3orf34, PIGX, PAK2, SENP5, NCBP2, LOC152217, PIGZ, MFI2, DLG1, BDH1, LOC220729	Deletion	q29	chr3		
FSTL5	Deletion	q32.1–q32.2	chr4		
EDIL3	Deletion	q14.3	chr5		
CSMD3	Deletion	q23.3	chr8		
JAM3, NCAPD3, VPS26B, THYN1, ACAD8, GLB1L3, GLB1L2, B3GAT1	Deletion	q25	chr11		
GOLGA6L6, GOLGA8C, BCL8, LOC646214, CXADRP2, POTEB, NF1P1, LOC727924, OR4M2, OR4N4, OR4N3P, GOLGA8DP, GOLGA6L1, TUBGCP5, CYFIP1, NIPA2, NIPA1, WHAMML1, GOLGA9P, HERC2P2	Deletion	q11.2	chr15		
DKFZP434L187, CHRFAM7A, FAM7A1, FAM7A2, ARHGAP11B, MTMR15, MTMR10, TRPM1, MIR211, KLF13, OTUD7A, CHRNA7, ARHGAP11A	Duplication	q13.2-q13.3	chr15		
C16orf45, KIAA0430, NDE1, MIR484, MYH11, C16orf63, ABCC1, ABCC6	Duplication	p13.11	chr16		
COX10, CDRT15, HS3ST3B1, MGC12916, CDRT7, PMP22, TEKT3, CDRT4, FAM18B2	Deletion	p12	chr17		
ACCN1, CCL genes, MCP3, TMEM132E	Duplication	q12	chr17		
UPB1	Duplication	22q11.23		GRCh37 (hg19)	[71]
MBD5	Duplication	2q23.1			
ZNF92		7q11.21		NCBI36 (hg18)	[54]

ZMYM5	Duplication	13q12.11		NCBI36 (hg18)	[54]
MAGEA11	Duplication	Xq28			
DMRT1		9p24.3			
VPS13B	Deletion	8q22.2			
BCL9, PRKAB2	Duplication	1q21.1		NCBI36 (hg18)	[72]
ANAPC1, BCL2L11, MERTK	Deletion	2q13			
DRD3, LSAMP, ZBTB20	Deletion	3q13.31			
IRX1, IRX2, IRX4, NDUFS6	Deletion	5p15.33-p15.32			
CHAT, ERCC6, GDF2, MAPK8, SLC18A3	Duplication	10q11.22-q11.23			
MAGEL2, NDN, UBE3A	Duplication	15q11-q13			
DOC2A, MAPK3, QPRT, SEZ6L2, TBX6	Duplication	16p11.2			
FOXC1, GMDS, NRN1, TUBB2B	Deletion	6p25.3-p25.1			
COG5, DOCK4, FOXP2, GPR85, IMMP2L, LAMB1, NRCAM, PNPLA8	Deletion	7q22.2-q31.1			
DLGAP2	Deletion	8p23.3-p23.1			
DNMT1	Duplication	19p13.3-p13.2			
MYT1L	Duplication	2p25.3			[73], [78]
NRXN1	Deletion	2p16.3			[54], [73], [78], [87]
	Duplication	2p16.3			[73], 78]
CTNND2	Duplication	5p15.2			
ASTN2	Deletion	9q33.1			[73]
	Duplication	9q33.1			[73], [78]
		2p16.3			[73]
JPH3, BANP	Duplication		chr16		
L3MBTL4	Duplication		chr18		
NDNL2, KIAA0527	Duplication	15q13.1		NCBI36 (hg18)	[7]
WWOX	Duplication	16q23.1			
ZNHIT3, MYOHD1	Duplication	17q12			
PRKRIP1	Duplication	7q22.1			
MYOM2	Duplication	8p23.3			
SSTR5	Duplication	16p13.3			
PRKAG2		7q36.1			[74]
CEBPD		8q11.21			
KLF4		9q31.2			
RXRA		9q34.2			
UBADC1		9q34.2			
LCN6		9q34.2			
LCN8		9q34.3			
C9orf37		9q34.3			
COL13A1		10q22.1			
LHX5		12q24.13			
RHCG		15q26.1			
SEPT9		17q25.2			
STK11		19p13.3			
PVR		19q13.31			
BU678720		21q21.1			
C21orf57		21q22.3			

CNTN6	Duplication	3p26.3	chr3	NCBI36 (hg18)	[75]
PARK2	Deletion	6q26	chr6	NCBI36 (hg18), GRCh37 (hg19)	[75], [46]
SLC7A13	Duplication	8q21.3	chr8	NCBI36 (hg18)	[75]
NRG3	Duplication	10q23.1	chr10		
LRFN5	Deletion	14q21.1	chr14		
MACROD2	Deletion	20p12.1	chr20	NCBI36 (hg18), GRCh37 (hg19)	[75], [46]
ADARB1	Duplication	21q22.3	chr21	NCBI36 (hg18)	[75]
ANKRD35	Duplication	1q21.1	chr1		
CD160	Duplication	1q21.1	chr1		
ITGA10	Duplication	1q21.1	chr1		
LIX1L	Duplication	1q21.1	chr1		
NUDT17	Duplication	1q21.1	chr1		
PEX11B	Duplication	1q21.1	chr1		
PIAS3	Duplication	1q21.1	chr1		
POLR3C	Duplication	1q21.1	chr1		
RBM8A	Duplication	1q21.1	chr1		
ZNF364	Duplication	1q21.1	chr1		
S100A10	Duplication	1q21.3	chr1		
THEM4	Duplication	1q21.3	chr1		
SEC16B	Duplication	1q25.2	chr1		
OR14C36	Deletion	1q44	chr1		
OR2M2	Deletion	1q44	chr1		
OR2M3	Deletion	1q44	chr1		
OR2M4	Deletion	1q44	chr1		
OR2M7	Deletion	1q44	chr1		
OR2T1	Deletion	1q44	chr1		
OR2T12	Deletion	1q44	chr1		
OR2T2	Deletion	1q44	chr1		
OR2T33	Deletion	1q44	chr1		
OR2T4	Deletion	1q44	chr1		
OR2T6	Deletion	1q44	chr1		
AHSA2	Duplication	2p15	chr2		
KIAA1841	Duplication	2p15	chr2		
PEX13	Duplication	2p15	chr2		
USP34	Duplication	2p15	chr2		
CNTN4	Duplication	3p26.3	chr3	NCBI36 (hg18), GRCh37 (hg19)	[75], [46]
ATG3	Deletion	3q13.2	chr3	NCBI36 (hg18)	[75]
BTLA	Deletion	3q13.2	chr3		
CD200	Deletion	3q13.2	chr3		
SLC35A5	Deletion	3q13.2	chr3		
C4orf45	Duplication	4q32.1	chr4		
RAPGEF2	Duplication	4q32.1	chr4		
LOC729920	Deletion	7p21.1	chr7		
CCDC146	Duplication	7q11.23	chr7		
LOC100132832	Deletion	7q11.23	chr7		
PMS2L11	Duplication	7q11.23	chr7		
POMZP3	Duplication	7q11.23	chr7		
UPK3B	Duplication	7q11.23	chr7		
PTPRN2	Deletion	7q36.3	chr7		

CSMD1	Duplication	8p23.2	chr8	NCBI36 (hg18)	[75]
PRKG1	Duplication	10q21.1	chr10		
RXFP2	Deletion	13q13.1	chr13		
A26B3	Deletion	21q11.2	chr21		
LOC441956	Deletion	21q11.2	chr21		
PDPR	Deletion		chr16:68743639–68770545	NCBI36 (hg18)	[76]
QPRT, DOC2A, TBX6	Duplication		chr16:29425212–30134444		
COMT	Deletion		chr22:17404806–19941349		
CACNA1B	Deletion		chr9:140145139–140152969		
RET	Deletion		chr10:42932615–42934354		
WDR1	Deletion		chr4:9881886–9884092		
RIT2, PIK3C3	Deletion		chr18:38310567–38311765		
SUMF1	Deletion		chr3:4063809–4074877		
PDE1C	Duplication		chr7:32177451–32392975		
PTPRG	Deletion		chr3:61803641–61811383		
FSTL5, RAPGEF2	Deletion		chr4:162417655–162424561		
IRX4	Deletion		chr5:2097129–2111366		
PRIM2A, RAB23	Deletion		chr6:57268143–57272458		
FAM19A2	Deletion		chr12:60558836–60563972		
SHC2	Duplication		chr19:426716–434473		
FST	Deletion		chr5:52702915–52718131		
TM2D3, TARSL2	Duplication		chr15:99980078–100033288		
ATXN1	Duplication		chr6:16499554–16508717		
PARK2	Deletion		chr6:162740476–162741040		
GJD2	Deletion		chr15:32717247–32765105		
AL833583	Deletion		chr7:142941348–142963649		
CAMK2D	Deletion		chr4:114573691–114581335		
TGFBR3	Deletion		chr1:92014319–92021028		
PTPRB, KCNMB4	Deletion		chr12:69158942–69164294		
ASTN2	Deletion		chr9:118485630-118678308	NCBI36 (hg18)	[77]
			chr9:118436844-118544516		
			chr9:118485630-118535712		
BIRC6	Deletion		chr2:32607317-32637998		
CACNA1C	Deletion		chr12:2667383-2721278		
CACNA1H	Deletion		chr16:1128687-1264608		
			chr16:1128687-1315831		
CACNA2D1	Deletion		chr7:80946083-83565043		
CCDC91	Deletion		chr12:28287457-28307416		
CDH11	Deletion		chr16:62987568-63825440		
CNKSR2	Deletion		chrX:21244407-21353706		
CNTN6	Deletion		chr3:1281676-1312640		
			chr3:1221211-1320244		
CNTNAP4	Duplication		chr16:74898416-74928638		
CNTNND2	Deletion		chr5:11620464-11682250		
DIP2C	Duplication		chr10:504831-528621		
			chr10:504831-520701		
			chr10:500636-528238		
DLG2	Deletion		chr11:84198686-84374844		
			chr11:84265922-84352121		
			chr11:83503062-84038769		
			chr11:83794004-83936480		
	Duplication		chr11:83238235-83275937		
			chr11:83235818-83275056		
			chr11:83548723-83583891		

DLGAP2	Deletion		chr8:987923-1263474	NCBI36 (hg18)	[77]
	Duplication		chr8:707778-1204805		
DMD	Deletion		chrX:31702477-31787394		
			chrX:31998434-32140283		
			chrX:31597646-31916389		
	Duplication		chrX:32694309-32749535		
DOCK8	Deletion		chr9:0-390952		
DPP6	Deletion		chr7:153150176-153296023		
DPYD	Deletion		chr1:97639975-97985452		
DSCAM	Duplication		chr21:40547618-40571598		
DST	Duplication		chr6:56484145-56556545		
FHIT	Deletion		chr3:60368967-60633637		
			chr3:60399688-60778108		
			chr3:60349892-60532397		
			chr3:60687927-60923656		
FOXP2	Deletion		chr7:113430288-113588694		
GRID2	Deletion		chr4:93730242-93872531		
			chr4:94071019-94233148		
IL1RAPL1	Duplication		chrX:29730890-29869444		
KANSL1	Duplication		chr17:41495554-41569975		
KAT2B	Deletion		chr3:20075527-20089245		
KATNAL2	Deletion		chr18:42806531-42856111		
MACROD2	Deletion		chr20:14585380-14805354		
			chr20:14560230-14636421		
			chr20:14542548-14658649		
			chr20:14575178-14761411		
MARK1	Deletion		chr1:214987824-219319335		
MBD5	Deletion		chr2:148631630-148700097		
			chr2:148613424-148716375		
			chr2:148686011-148897208		
			chr2:148700097-148775840		
			chr2:148464644-148824105		
			chr2:148632463-148700318		
			chr2:148579652-148819841		
MCPH1	Deletion		chr8:5931207-6692666		
			chr8:6439335-6475187		
MSRA	Deletion		chr8:10146945-10231151		
			chr8:9980078-10093754		
MYT1L	Duplication		chr2:2119472-2281835		
NLGN4X	Duplication		chrX:5976237-6083329		
NPAS3	Deletion		chr14:32857621-32917386		
NR3C2	Deletion		chr4:149392377-149420863		
NRXN1	Deletion		chr2:50802194-51025259		
			chr2:50917603-51164702		
			chr2:51055970-51202335		
			chr2:50993493-51062626		
OPHN1	Deletion		chrX:67333345-67371129		
PARD3B	Deletion		chr2:205837910-206070478		
			chr2:205675201-205771682		
PCDH15	Deletion		chr10:56120554-56328279		
PCM1	Deletion		chr8:17830740-17893480		
			chr8:17672304-17862467		
PHF12	Deletion		chr17:24253562-24283413		
PHIP	Duplication		chr6:79780934-79842010		

RBFOX1	Deletion		chr16:7019169-7089645	NCBI36 (hg18)	[77]
			chr16:6621949-7019169		
			chr16:6612572-6710410		
			chr16:6763911-6968069		
			chr16:6345718-6927804		
			chr16:6350353-6572209		
			chr16:6936804-7168750		
RELN	Deletion		chr7:102919063-102935191		
	Duplication		chr7:103053127-103356383		
SHANK3	Deletion		chr22:49475041-49491535		
SLCO1B3	Deletion		chr12:20758254-21204096		
			chr12:20901419-20921755		
SMURF1	Duplication		chr7:98479220-98574460		
TAF13	Deletion		chr1:109393044-109423774		
TOP3B	Deletion		chr22:20640379-20908581		
VIPR2	Duplication		chr7:158211879-158678920		
VPS13B	Deletion		chr8:100128567-100308843		
			chr8:100199888-100240539		
ZNF804A	Deletion		chr2:185403791-185457197		
CHAT, SLC18A3	Duplication	10q11.21-q11.23	chr10:46389894-51528033		
SACS	Deletion	13q12.12	chr13:22440477-23795346		
NIPA1	Deletion	15q11.2	chr15:20133413-20742709		
			chr15:20194004-20987146		
			chr15:20194004-20751393		
			chr15:20295570-20654444		
			chr15:20295570-20672888		
			chr15:20295570-20750861		
UBE3A	Duplication	15q11.2-q13.1	chr15:20133413-26728500		
			chr15:20987146-26818312		
APBA2	Deletion	15q13.1-q13.2	chr15:26865409-28550452		
	Duplication	15q13.1-q13.2	chr15:26937064-28459293		
CHRNA7, FAN1	Deletion	15q13.3	chr15:28405269-30274044		
	Duplication	15q13.3	chr15:28585517-30241239		
			chr15:28648476-30230619		
SEMA7A, ARID3B	Duplication	15q24.1-q24.2	chr15:70720018-73356711		
			chr15:72150903-75957695		
KCTD13, TBX6	Deletion	16p11.2	chr16:29546658-30103782		
	Duplication	16p11.2	chr16:29399675-30173442		
			chr16:29532848-30103782		
			chr16:29559333-30103782		
SH2B1, ATP2A1	Deletion	16p11.2	chr16:28270641-29243895		
EEF2K, CDR2	Deletion	16p11.2	chr16:21753133-22445650		
			chr16:21846941-22346897		
	Duplication	16p11.2	chr16:21846941-22354234		
NDE1, MYH11	Deletion	16p13.11	chr16:14782025-16417299		
			chr16:15329797-16445320		
	Duplication	16p13.11	chr16:14958777-16417299		
			chr16:15031188-16417299		
			chr16:15032096-16519069		
			chr16:15086873-18694018		
			chr16:15281095-18292902		
			chr16:15319483-16295736		
HNF1B	Deletion	17q12	chr17:31695581-33492318		

GJA5	Deletion	1q21.1	chr1:143633473-146748995	NCBI36 (hg18)	[77]
			chr1:144096740-146196514		
			chr1:144459685-146366506		
			chr1:144470366-146366506		
			chr1:144494342-146196514		
			chr1:144752226-146748995		
HFE2	Deletion	1q21.1	chr1:144098013-144644461		
			chr1:144098013-144607294		
	Duplication	1q21.1	chr1:143706467-144752226		
			chr1:144048423-144982989		
			chr1:144096740-144752226		
			chr1:144104567-144723013		
CRKL, SNAP29	Deletion	22q11.21	chr22:18869378-19833296		
			chr22:18870550-19961412		
			chr22:19043275-19807877		
COMT, TBX1	Deletion	22q11.21	chr22:17022646-20047111		
			chr22:17022646-20072277		
			chr22:17026693-19961412		
			chr22:17170222-20027998		
			chr22:17200422-19807877		
			chr22:17214452-19905702		
			chr22:17248432-19807877		
			chr22:17248432-19379822		
			chr22:17271966-18870550		
BCR, RAB36	Deletion	22q11.22-q11.23	chr22:21310642-21992523		
ADORA2A	Duplication	22q11.23	chr22:21297264-23380127		
			chr22:21990026-23380127		
			chr22:21990026-23323810		
LMAN2L, ARID5A	Deletion	2q11.2	chr2:96093033-97108604		
ST6GAL2	Deletion	2q12.2-q12.3	chr2:106421996-107857512		
			chr2:106427916-107822371		
ARHGEF4	Deletion	2q21.1	chr2:131199562-131642591		
	Duplication	2q21.1	chr2:130707779-131473335		
DLG1, PAK2	Deletion	3q29	chr3:196828801-198872788		
			chr3:197201331-198828569		
			chr3:197365415-198587769		
ELN, GTF2I	Duplication	7q11.23	chr7:72364576-73778866		
STS	Deletion	Xp22.31	chrX:6454791-8100059		
			chrX:6464968-8084364		
			chrX:6472965-7851815		
A2BP1	Deletion	16p13.2		NCBI36 (hg18)	[78]
	Duplication				
CHRNA7	Deletion	15q13.3			
	Duplication				
CNTNAP2	Deletion	7q35-q36.1			
COMT	Deletion	22q11.21		NCBI36 (hg18)	[78], [87]
CYFIP1	Deletion	15q11.2		NCBI36 (hg18)	[78]
	Duplication				
EFCAB2	Duplication	1q44			
ERBB4	Deletion	2q34			
GSTT2	Duplication	22q11.23			
KIF26B	Deletion	1q44			
	Duplication				
NDE1	Duplication	16p13.1			

NTAN1	Duplication	16p13.1		NCBI36 (hg18)	[78]
PI4KCA	Deletion	22q11.21			
	Duplication				
PRODH	Deletion	22q11.21			
	Duplication				
NBPF1, NBPF10	Duplication	1p36.13		NCBI36 (hg18)	[79]
FAM27A	Duplication	9p11.2			
SLC7A13	Duplication		chr8	GRCh37 (hg19)	[80]
SGCZ	Duplication		chr8		
WWP2	Duplication		chr16		
RYR2	Deletion	1q43	chr1:235475280–235639644	NCBI36 (hg18)	[43]
NAP5	Deletion	2q21.2	chr2:133504420–133879778		
HTN1, HTN3	Deletion	4q13.3	chr4:70935504–70969553		
BMP2K, PAQR3	Deletion	4q21.21	chr4:79944612–80081979		
CSMD1	Deletion	8p23.2	chr8:4121968–4299810		
MSRA	Deletion	8p23.1	chr8:10066862–10155414		
EHMT1	Duplication	9q34.3	chr9:139762152–139797423		
	Deletion		chr9:139769564–139792102		
DLG2	Deletion	11q14.1	chr11:83472750–83842973		
			chr11:84006106–84226064		
RPH3A	Deletion	12q24.13	chr12:111723795–111776045		
DLGAP1, FLJ35776	Deletion	18p11.31	chr18:3515935–4332609		
MACROD2	Deletion	20p12.1	chr20:14694326–14863051		
CNTNAP2	Deletion		chr7	GRCh37 (hg19)	[81]
MAGI1	Duplication		chr3		
ZIC1	Duplication		chr6		
TSPAN7	Duplication		chr7		
LOC102724434, CAV2, CAV1, LINC01510, MET, CAPZA2, ST7AS1, ST7, ST7-OT4	Deletion		chr11		
KDM4B, PTPRS, ZNRF4, TINCR, SAFB2, SAFB, C19orf70, HSD11B1L, RPL36, LONP1, CATSPERD, PRR22, DUS3L, NRTN, FUT6, FUT3, LOC101928844, FUTS, NDUFA11, VMAC, CAPS, RANBP3	Duplication		chr18		
PYY	Deletion	17q21.31	chr17	NCBI36 (hg18)	[82]
EPHA3	Deletion	3p11.2-3p11.1	chr3		
LOC441242, INTS4L2, CCT6P1, SNORA22	Deletion	7q11.21	chr7		
OR52N2	Deletion	11p15.4	chr11		
LOC283914, LOC146481, LOC100130700	Duplication	16p11.1	chr16		
KIAA1211L	Deletion	2q11.2	chr2		
GPR139	Deletion	16p12.3	chr16		
BCR	Deletion	22q11.2	chr22:19786712-19795854	NCBI36 (hg18)	[83]
VIPR2	Duplication	7q36.3	chr7:158731401-158810016		
OTUD7A	Deletion	15q13.3	chr15:29694064-29705665		
VIPR2, BC042556	Duplication	7q36.3	chr7:158448321-158605936		
MTMR15	Deletion	15q13.3	chr15:28881608-28991107		
CR597873, SDHALP2	Duplication	3q29	chr3:196826549-196872080		
PARK2	Duplication	6q26	chr6:162835583-162997592		

CACNA1C	Deletion	11q14.1		NCBI36 (hg18)	[84]
HS6ST1	Deletion	11q14.1			
PYCR1	Deletion	11q14.1			
DRD2	Deletion	11q14.1			
MeCP2	Deletion	11q14.1			
CPLX1	Duplication	Xp22.33-p11.1			
		Xp22.31			
G6PC	Duplication	10p15.3			
GRIN2B	Duplication	10p15.3			
MDGA1	Duplication	10p15.3			
GSR	Deletion	19p13.11			
FXN	Deletion	19p13.11			
ATCAY	Deletion	19p13.11			
SHANK2	Deletion	8p23.1-p22			
PCDHB14	Deletion	8p23.1-p22			
PAX6	Deletion	8p23.1-p22			
TXNL1	Duplication	18p11.21-q11.1			
SNAP29	Duplication	18p11.21-q11.1			
CACNA1B	Deletion		chr9	GRCh37 (hg19)	[85]
CACNA2D4	Deletion		chr12		
CACNG2	Deletion		chr22		
IGLL5	Duplication	22q11.22		GRCh37 (hg19)	[86]
MSR1	Duplication	8p22			
DLG2	Duplication	11q14.1			
CTDSPL	Duplication	3p22.2			
SKAP2	Duplication	7p15.2			
HECW1	Duplication	7p13			
MRGPRX1	Deletion	11p15.1			
MLIP	Deletion	6p12.1			
SKI, MORN1	Duplication	1p36.33			
PEX11B	Deletion	1q21.1		GRCh37 (hg19)	[87]
GJA8	Deletion	1q21.1-q21.2			
NSD1	Deletion	5q35.3			
ALDOA, TBX6	Deletion	16p11.2			
TSC2	Deletion	16p13.3			
ABCC6	Deletion	16p13.11-p12.3			
		16p13.11			
	Duplication	16p13.11-p12.3			
PMP22	Deletion	17p12			
CNKSR2	Duplication	Xp22.12			
LMAN2L	Deletion	2q11.2			
HLA-B, MICB	Deletion	6p21.33			
HCN1	Deletion	5p12			
PDSS1	Deletion	10p12.1	chr10	GRCh37 (hg19)	[88]
LOC642131	Duplication	15q11.2	chr15		
CES1	Duplication	16q12.2	chr16		
DISC1	Duplication	1q42.2		NCBI36 (hg18)	[78], [89]
	Deletion			NCBI36 (hg18)	[89]
NDE1, MYH11	Duplication	16p13.11			
	Deletion				
CIT	Duplication	12q24.23			

NRXN1	Deletion		chr2:50000000–51100000	NCBI36 (hg18)	[90]
WBS	Duplication		chr7:72400000–73800000		
VIPR2	Duplication		chr7:158500000–158600000		
SATB2	Duplication		chr2:198874627–199903114		
CHL1, CNTN6	Duplication		chr3:57010–1054024		
CNTN6, CNTN4	Duplication		chr3:1134787–2375967		
PCDH7	Duplication		chr4:31014644–32191478		
AREG, BTC	Duplication		chr4:75528333–76702535		
ZFP42	Duplication		chr4:188342786–189950157		
			chr4:188698113–189920157		
TIAM2	Deletion		chr6:154918196–155991693		
PENK	Deletion		chr8:57437447–59006759		
ODZ4, DLG2	Duplication		chr11:79782071–81358036		
LRIG3	Deletion		chr12:56820511–59741054		
RB1, HTR2A	Duplication		chr13:46505958–47784283		
NDE1, ABCC1	Deletion		chr16:15550310–18070334		
LHX1	Duplication		chr17:32227936–33270047		
FAM32B, GNAL	Duplication		chr18:10587874–11910658		
FBXO42	Duplication	1p36.13	chr1	GRCh37 (hg19)	[46]
OR6Y1, OR6P1	Duplication	1q23.1	chr1		
PLEK	Duplication	2p14,2p13.3	chr2		
CHL1	Duplication	3p26.3	chr3		
	Deletion				
BCHE	Duplication	3q26.1	chr3		
SCD5	Deletion	4q21.22	chr4		
PDE4D	Deletion	5q12.1	chr5		
F2RL2, IQGAP2	Deletion	5q13.3	chr5		
REEP5	Deletion	5q22.2	chr5		
RASGEF1C	Deletion	5q35.3	chr5		
MTRNR2L9, KHDRBS2	Duplication	6q11.1	chr6		
IMMP2L	Deletion	7q31.1	chr7		
	Duplication				
GRM8	Deletion	7q31.33	chr7		
BLK	Duplication	8p23.1	chr8		
SYK	Duplication	9q22.2	chr9		
BTRC	Duplication	10q24.32	chr10		
OPCML	Duplication	11q25	chr11		
WNK1	Deletion	12p13.33	chr12		
LECT1, SUGT1, HNRNPA1L2	Duplication	13q14.3	chr13		
KLF13, OTUD7A, MTMR10, FAN1, CHRNA7, LOC283710, ARHGAP11B, TRPM1, CHRFAM7A	Duplication	15q13.2, 15q13.3	chr15		
KLF13, OTUD7A, MTMR10, FAN1, GOLGA8O, CHRNA7, LOC283710, ARHGAP11B, TRPM1	Duplication	15q13.2, 15q13.3	chr15		
RBFOX1	Deletion	16p13.3	chr16		
EEF2K, OTOA, POLR3E, CDR2, C16orf52, UQCRC2, PDZD9, VWA3A	Deletion	16p12.2	chr16		
VPS53	Deletion	17p13.3	chr17		
ZNHIT3, LHX1, DUSP14, MRM1, ACACA, DDX52, DHRS11, SYNRG, C17orf78, HNF1B, AATF, MYO19, PIGW, TADA2A, GGNBP2	Duplication	17q12	chr17		
ARL4D	Duplication	17q21.31	chr17		

CCDC102B, TMX3	Duplication	18q22.1	chr18	GRCh37 (hg19)	[46]
FHAD1, KAZN, C1orf195, TMEM51	Duplication	1p36.21	chr1		
RNF115, GPR89A, RBM8A, LOC100288142, PIAS3, CD160, HFE2, ANKRD34A, LIX1L, POLR3GL, ANKRD35, ITGA10, PEX11B, NUDT17, NBPF10, TXNIP, PDZK1, POLR3C	Deletion	1q21.1	chr1		
CAMKMT, PREPL, SLC3A1	Deletion	2p21	chr2		
TACR1	Deletion	2p12	chr2		
APOD, MUC4, MUC20, PPP1R2	Duplication	3q29	chr3		
TLR3	Duplication	4q35.1	chr4		
EXOC3, C5orf55, SLC9A3, AHRR	Duplication	5p15.33	chr5		
DEFA6, DEFB1, DEFA4	Duplication	8p23.1	chr8		
SGK223	Deletion	8p23.1	chr8		
T2	Duplication	8p22	chr8		
TTC39B	Deletion	9p22.3	chr9		
IZUMO3	Duplication	9p21.3	chr9		
AVPI1, PI4K2A	Duplication	10q24.2	chr10		
DJC15, EPSTI1	Duplication	13q14.11	chr13		
C14orf132	Deletion	14q32.2	chr14		
PKD1L2, BCMO1	Duplication	16q23.2	chr16		
CDH13	Deleção	16q23.3	chr16		
C18orf42	Duplication	18p11.31	chr18		
SMARCB1, MMP11, C22orf43, DDTL, RGL4, SLC2A11, MIF, CHCHD10, DERL3, C22orf15, IGLL1, GSTT2B, ZNF70, DDT, VPREB3, GSTT2, ADORA2A, SNRPD3, FAM211B, CABIN1, SPECC1L, GUCD1, SUSD2, GGT5, UPB1, GGT1	Duplication	22q11.23	chr22		
ALPP, ALPPL2	Duplication	2q37.1	chr2		
CRBN, TRNT1	Duplication	3p26.2	chr3		
VGLL4	Deletion	3p25.3	chr3		
GIMD1	Duplication	4q24	chr4		
GSTA5, GSTA1, GSTA2	Deletion	6p12.2	chr6		
PRIM2	Duplication	6p11.2	chr6		
EYS	Deletion	6q12	chr6		
CACNA2D1	Duplication	7q21.11	chr7		
CYLC2	Deletion	9q31.1	chr9		
CUL2	Duplication	10p11.21	chr10		
B4GALNT3	Deletion	12p13.33	chr12		
TM2D3, TARSL2	Duplication	15q26.3	chr15		
PRDM7	Duplication	16q24.3	chr16		
UTP6, OMG, CRLF3, RAB11FIP4, ATAD5, COPRS, TEFM, ADAP2, RNF135, NF1, SUZ12, EVI2A, EVI2B	Deletion	17q11.2	chr17		
KATL2	Duplication	18q21.1	chr18		
PAK7	Duplication	20p12.2	chr20		
CDH4	Deletion	20q13.33	chr20		
OR4F5	Duplication	1p36.33	chr1		
TYW3	Duplication	1p31.1	chr1		
ABCA4	Duplication	1p22.1	chr1		
CTTNBP2NL	Duplication	1p13.2	chr1		

PDE4DIP, NBPF9, LOC100288142	Duplication	1q21.1	chr1	GRCh37 (hg19)	[46]
HSD11B1	Duplication	1q32.2	chr1		
SPATA17	Deletion	1q41	chr1		
RYR2	Duplication	1q43	chr1		
C1orf229, ZNF669, ZNF124, ZNF670	Deletion	1q44	chr1		
C2orf70, CIB4	Duplication	2p23.3	chr2		
THADA	Duplication	2p21	chr2		
T8B, T8	Deletion	2p13.1	chr2		
LRRTM4	Deletion	2p12	chr2		
TMEM169, MARCH4, PECR, XRCC5, MREG	Duplication	2q35	chr2		
SLC19A3	Deletion	2q36.3	chr2		
SETMAR	Deletion	3p26.1	chr3		
GRM7	Duplication	3p26.1	chr3		
FGD5, NR2C2	Duplication	3p25.1	chr3		
WDR48, SCN11A, SCN5A, SCN10A	Duplication	3p22.2	chr3		
DOK7	Duplication	4p16.3	chr4		
RBPJ, CCKAR	Duplication	4p15.2	chr4		
FGF5, C4orf22	Duplication	4q21.21	chr4		
STPG2	Duplication	4q23, 4q22.3	chr4		
RANBP9	Duplication	6p23	chr6		
DEFB114, DEFB113	Deletion	6p12.3	chr6		
FAM83B	Duplication	6p12.1	chr6		
C6orf163	Duplication	6q15	chr6		
LPA	Duplication	6q26, 6q25.3	chr6		
AGPAT4, PARK2	Duplication	6q26	chr6		
MLLT4, HGC6.3	Duplication	6q27	chr6		
SDK1	Deletion	7p22.2	chr7		
ARL4A, SCIN	Deletion	7p21.3	chr7		
ETV1	Duplication	7p21.2	chr7		
DGKB	Deletion	7p21.2	chr7		
AGMO	Deletion	7p21.2	chr7		
TSPAN13, TSPA	Duplication	7p21.1	chr7		
ELMO1	Duplication	7p14.2	chr7		
ABCA13	Deletion	7p12.3	chr7		
GRB10	Duplication	7p12.1	chr7		
CRCP, ASL	Duplication	7q11.21	chr7		
LHFPL3	Duplication	7q22.2	chr7		
TDRP	Duplication	8p23.3	chr8		
DLC1, C8orf48	Duplication	8p22	chr8		
MTUS1, PDGFRL	Deletion	8p22	chr8		
ADAM28	Deletion	8p21.2	chr8		
RNF122, FUT10, MAK16, TTI2	Duplication	8p12	chr8		
UNC5D	Duplication	8p12	chr8		
LYN,TGS1	Duplication	8q12.1	chr8		
WWP1	Duplication	8q21.3	chr8		
CDH17	Duplication	8q22.1	chr8		
COL22A1	Deletion	8q24.23	chr8		
PTPRD	Duplication	9p23	chr9		
ADAMTSL1	Duplication	9p22.1	chr9		
FAM205A	Deletion	9p13.3	chr9		
G14	Deletion	9q21.2	chr9		
AKR1C1	Duplication	10p15.1	chr10		

PARD3	Deletion	10p11.21	chr10	GRCh37 (hg19)	[46]
PTEN	Duplication	10q23.31	chr10		
SLIT1, ARHGAP19	Duplication	10q24.1	chr10		
CCDC147, GSTO2, GSTO1	Deletion	10q25.1	chr10		
PDDC1, TALDO1	Deletion	11p15.5	chr11		
LRRC4C	Duplication	11p12	chr11		
FNBP4, MTCH2, AGBL2	Duplication	11p11.2	chr11		
PCNXL3, EHBP1L1, KCNK7, SCYL1, SSSCA1, MAP3K11, SIPA1, LTBP3, RELA, FAM89B	Deletion	11q13.1	chr11		
AGAP1	Deletion		chr2:236981798–236985995	GRCh37 (hg19)	[91]
PDHA2, STPG2-AS1	Deletion		chr4:97082599–97083209		
ZC3H7B	Deletion		chr22:41708180–41710931		
MACROD1	Deletion		chr11:63906001–63915000		
KIF26A, C14orf180	Duplication		chr14:105002123–105005283		
CLASP1	Deletion		chr2:122388452–122389350		
SLC23A2	Deletion		chr20:4941352–4943771		
ANKH, LOC101929454	Deletion		chr5:14878611–14879349		
CDK5RAP2	Deletion		chr9:123318744–123320055		
PPP1R12A	Deletion		chr12:80272063–80273569		
LOC101926897, DIAPH3	Deletion		chr13:59453830–59457813		
IMMP2L	Deletion	7q31.1	chr7:111431428–111618385	NCBI36 (hg18)	[92]
			chr7:111453103–111544709		
			chr7:111509431–111521305		
TXNDC11, ZC3H7A	Duplication	16p13.13	chr16:11729544–11754368		
PRKAB2, BCL9, ACP6, GJA5, GJA8	Duplication	1q21.1, 1q21.2	chr1	GRCh37 (hg19)	[93]
PRKAB2, BCL9, ACP6, GJA5, GJA9	Duplication	1q21.1, 1q21.2	chr1		
BCL2L11, ANAPC1, MERTK	Duplication	2q13	chr2		
TRA2B	Deletion	3q27.1, 3q27.2	chr3		
DRD3, ZBTB20, GAP43, LSAMP	Deletion	3q13.31	chr3		
SUMF1, ITPR1	Deletion	3p26.1	chr3		
NDUFS6, IRX4, IRX2, IRX1	Deletion	5p15.33, 5p15.32	chr5		
SLC12A7, SLC6A19, SLC6A18, SLC6A3, IRX1, IRX2, IRX4, NDUFS6	Deletion	5p15.33, 5p15.32, 5p15.31, 5p15.2	chr5		
EXOC2, FOXQ1, FOXF2, FOXC1, GMDS, TUBB2A, NRN1, TUBB2B	Deletion	6p25.3, 6p25.2, 6p25.1	chr6		
RNASET2, FGFR1OP, WDR27, TBP	Duplication	6q26, 6q27	chr6		
SLC26A4, SLC26A3, NRCAM, THAP5, IMMP2L, DOCK4, TMEM168, FOXP2	Deletion	7q22.3, 7q31.1, 7q31.2	chr7		
GPRIN2, MAPK8, ERCC6, GDF2, CHAT, SLC18A3	Duplication	10q11.22, 10q11.23	chr10		
LRRC63, HTR2A, SUCLA2, ITM2B, RB1, SETDB2, SETDB2-PHF11, KCNRG, KPNA3	Deletion	13q14.13, 13q14.2, 13q14.3	chr13		
TRPM1, KLF13, OTUD7A, CHRNA7	Deletion	15q13.2, 15q13.3	chr15		

MAGEL2, NDN, UBE3A, GABRB3, GABRA5, GABRG3	Duplication	15q11.2, 15q12, 15q13.1	chr15	GRCh37 (hg19)	[93]
KCTD13, DOC2A, MAPK3, PRRT2, QPRT, SEZ6L2, TBX6	Duplication	16p11.2	chr16		
ANKRD24, DAPK3, MAP2K2, KDM4B, RPL36, SLC25A41, SLC25A23, TUBB4A, MAP2K7, DNMT1, SLC44A2, DNM2, DOCK6	Duplication	19p13.3, 19p13.2	chr19		
FTSJ1, SLC38A5, SLC35A2, KCND1, WDR45, WDR13, SYP, CACNA1F, SHROOM4, NUDT10, NUDT11	Duplication	Xp11.23, Xp11.22	chrX		

Table S2 - List of previously reported CNV hotspots.

Genomic hotspots (Region)	Genomic Coordinates	Reference Human Genome	Reference
1q21.1	chr1:144825000-146075000	NCBI36 (hg18)	[94]
	chr1:144103100-144330084		
11q14.3	chr11:89070781-89514825		
12p11.23	chr12:27196123-27621264		
15q11.2-q13.1	chr15:18432358-26745127		
15q13.1	chr15:26625000-30675000		
	chr15:28656923-30232692		
	chr15:26996715-28157315		
	chr15:26996715-28160880		
15q23-q24.1	chr15:66890869-71938416		
16p13.11_12.1	chr16:15074999-16725000		
	chr16:14301502-18700753		
16p11.2	chr16:29425000-30275000		
16q22	chr16:68859156-72903506		
	chr16:68883052-69808186		
	chr16:68832773-70006429		
17q12	chr17:31355103-33660562		
2q12.1	chr2:103280257-108770547		
22q11.21	chr22:16925000-20075000		
3q29	chr3:196789663-198943245		
15q25.3	chr15:82625000-83675000		
8p22	chr8:12594361-14327206		
9p24.3	chr9:207823-1674250		
	chr9:207823-316999		
10q11.23	chr10:49086581-50679930		
2q11.2	chr2:96113899-97049810		
5p15.33	chr5:369328-725118		
7q36.2	chr7:152199145-153299935		
	chr1:31181042-31195047		
	chr13:51122056-51164168		
	chr13:66471619-66500012		
	chr15:60083019-60098128		
	chr16:87956630-87986100		
	chr17:11690163-11706471		
	chr2:213918176-213941138		
	chr3:58776011-58807951		
	chr3:58776031-58815772		
	chr3:58779367-58805501		
	chr3:58782388-58816295		
	chr3:58782526-58808613		
	chr3:162176742-162205106		
	chr4:38475250-38506096		
	chr4:54796337-54814034		
	chr11:107736766-107753751		
	chr11:107737766-107754732		
	chr11:125749831-125771417		
	chr16:68924327-68963148		

	chr2:116264115-116287283	NCBI36 (hg18)	[94]
	chr2:232722656-232752016		
	chr2:232724406-232752723		
	chr2:232725283-232753281		
	chr2:232726222-232754154		
	chr20:63848-91170		
	chr3:144248009-144287782		
	chr6:26514226-26552479		
	chr9:17248979-17277215		
	chr9:17254976-17277216		
	chr9:95891470-95916186		
	chr9:95892664-95917517		
	chr9:95895726-95920532		
	chr11:94398668-94422793		
	chr13:66213547-66248610		
	chr6:52729617-52771620		
	chr11:56075176-56113063		
	chr11:56100952-56136937		
	chr12:51130292-51152169		
	chr12:51131038-51153030		
	chr12:51131713-51153641		
	chr12:51131713-51173092		
	chr6:52758032-52797115		
	chr17:36756663-36775230		
	chr1:70146799-70164769		
	chr6:52738196-52778804		
	chr6:52739527-52780178		
	chr8:71771170-71811746		
	chr8:71772142-71812740		
	chr11:93541125-93550334		
	chr8:15459053-15479728		
	chr8:15459644-15480527		
	chr8:15460924-15481502		
	chr8:15461520-15482427		
	chr8:15462411-15483151		
	chr19:58635421-58673115		
	chr19:58637062-58674821		
	chr22:26920578-26939753		
	chr22:26922186-26940238		
	chr6:71702475-71713033		
	chr6:71703270-71713808		
	chr6:71703672-71714238		
	chr6:71704421-71715059		
	chr6:71705104-71715710		
	chr5:126254342-126268089		
	chr5:126254994-126268755		

	chr5:126255360-126269105	NCBI36 (hg18)	[94]
	chr5:126255700-126269427		
	chr5:126257139-126271113		
	chr5:126257577-126271311		
	chr9:71282100-71313721		
	chr9:71284957-71314452		
	chr9:71285631-71314852		
	chr9:71286629-71315881		
	chr9:5292794-5329656		
	chr16:74090198-74130702		
	chr16:74090525-74131014		
	chr16:74096080-74137424		
	chr1:86178391-86186818		
	chr17:36456655-36475593		
	chr17:36464664-36475593		
	chr10:100703151-100940746		
	chr11:125746831-125774417		
	chr16:74087525-74134014		
	chr19:58288427-58600264		
	chr2:178421751-178469907		
	chr2:213915176-213944138		
	chr3:162173742-162208106		
	chr4:38475453-38505894		
	chr4:54793337-54817034		
	chr4:54793337-54838343		
	chr6:26511226-26555479		
	chr8:15141259-16659481		
	chr19:58597470-58650878		
	chr19:62569652-62601491		
	chr2:232719656-232757154		
	chr20:60848-94170		
	chr6:52726617-52774620		
	chr9:17251976-17280216		
	chr11:56097952-56139937		
	chr11:56072176-56116063		
	chr12:51128713-51156641		
	chr19:58634062-58677821		
	chr6:52755032-52800115		
	chr17:36753663-36778230		
	chr8:71769142-71815740		
	chr9:5289794-5332656		
	chr17:36461664-36478593		
	chr8:48483461-48750000		
	chr1:172813690-172929227		
	chr1:31178042-31198047		
	chr11:86628362-87450467		
	chr13:51119056-51167168		
	chr13:66468619-66503012		
	chr15:97274780-97826232		
	chr16:68923105-68964107		
	chr16:68924395-68961849		

	chr17:11687163-11709471	NCBI36 (hg18)	[94]
	chr3:58773011-58810951		
	chr8:88455946-88680000		
	chr9:93399807-95962364		
	chr11:107733766-107757732		
	chr19:61398731-61435513		
	chr2:116261115-116290283		
	chr3:144245009-144290782		
	chr9:95888470-95919186		
	chr11:94395668-94425793		
	chr2:116241694-116394317		
	chr15:60080019-60101128		
	chr22:43632564-43642175		
	chr3:187109666-187192347		
	chr5:150255197-150291579		
	chr6:29150022-29251227		
	chr6:57016532-57067336		
	chr7:149750000-149955000		
	chr6:29170622-29251227		
	chr6:29649385-29664662		
	chr6:57019262-57064537		
	chr2:73679654-73757822		
	chr19:63022929-63057804		
	chr7:65735947-65777648		
	chr19:58021000-58078109		
	chr2:234158915-234230618		
15q11.2q13.3	chr15:18045749-30589746	NCBI36 (hg18)	[48]
15q13.1q13.3	chr15:26994610-30522495		
16p13.12	chr16:14936606-16426815		
	chr16:15386338-16177142		
16p13.11	chr16:15170619-18662509		
16p11.31p12.3	chr16:15367033-18321829		
16p11.2	chr16:28730254-28949347		
	chr16:29554938-30104150		
	chr16:29655898-29979351		
	chr16:29546342-30129401		
17p12	chr17:13958086-15457720		
17q12	chr17:31880822-33305362		
17q21.31	chr17:41063431-41533855		
3q29	chr3:197188186-198861094		
	chr3:197391142-199430926		
	chr3:196825112-197208742		
5q35	chr5:175479594-177400099		
7q11.23	chr7:72300576-73798218		
	chr7:72300576-72486542		
8p23.1	chr8:8085497-11899019		
	chr8:11373083-11434911		
15q11.2-q13.1	chr15:18193472-26871283		
22q11.21	chr22:17266528-19800553		
	chr22:18562002-18748556		
22q11.22	chr22:21298606-23362762		
15q11.2	chr15:20301665-20602651		
5q35.2	chr5:175479593-175584441		
	chr5:175504664-175584441		
7p15.3	chr7:31583983-31702682		

16p12.1	chr16:21645311-22520339	NCBI36 (hg18)	[48]
1q21.1	chr1:145303997-145357746		
	chr1:144106777-144451305		
16p22.3	chr16:72859686-72917454		
17p11.2	chr17:15301836-16542913		
17q12	chr17:32250000-32400000		
	chr17:34089604-34566438		
17q21.32	chr17:42115600-42437714		
2q11.1	chr2:95159338-95228560		
5p15.33	chr5:370492-1003781		
	chr5:90252-1630763		
7q36.2	chr7:152102637-153356944		
7q11.22	chr7:68820751-68904999		
	chr7:69876932-70546042		
	chr7:68713709-69068502		
5q21.1	chr5:98793016-98851760		
7p13	chr7:45180992-45274014		
9p13.1	chr9:38634661-38791196		
Yp11.2	chrY:3072083-6154525		
18q22.1	chr18:62370731-62372170	NCBI36 (hg18)	[95]
	chr18:60186868-60188223		
	chr18:61917905-61920159		
19p13.3	chr19:2860172-2861422		
19p13.2	chr19:11900599-11907030		
19q13.33	chr19:56823616-56842030		
19q13.41	chr19:58014801-58053170		
19q13.42	chr19:60168046-60169690		
20q13.12	chr20:41705581-41707310		
21q22.3	chr21:43794624-43797920		
	chr21:46434207-46435260		
	chr21:46481946-46483100		
22q11.21	chr21:16871523-16873120		
22q12.3	chr22:31257932-31258510		
	chr22:34942923-34944355		
22q13.2	chr22:41209145-41335150		
1p36.13	chr1:17548473-17551517		
	chr1:17078749-17093217		
1p36.11	chr1:25457812-25537782		
1p13.3	chr1:109988369-110060631		
	chr1:110016535-110046454		
1q32.1	chr1:204622578-204670033		
1q32.2	chr1:205763104-205821509		
2q13	chr2:112761633-112766181		
	chr2:109800216-109804879		
4q32.3	chr4:166377398-166378505		
5q33.3	chr5:159282379-159283692		
6p25.3	chr6:200650-329973		
6p21.32	chr6:32066855-32093500		
6q25.3	chr6:160431936-160432431		
7q11.21	chr7:64204377-64274741		
	chr7:64187507-64205734		
	chr7:64354006-64359878		
	chr7:64732214-64750224		

7q11.22	chr7:71682534-71684330	NCBI36 (hg18)	[95]
7q31.33	chr7:126301909-126340192		
7q34	chr7:141388076-141441024		
7q36.1	chr7:151532774-151539767		
8p23.3	chr8:584449-589454		
8p23.1	chr8:7330051-7342809		
9p12	chr9:41552631-41641509		
10p11.22	chr10:33229325-33230534		
	chr10:31483544-31485487		
10q11.23	chr10:51158267-51158937		
11p15.1	chr11:17166514-17167872		
12p13.2	chr12:11917753-11918281		
14q24.3	chr14:73064141-73121720		
15q26.3	chr15:97007643-97011339		
16p12.1-p12.2	chr16:21641198-21716960		
16q22.1	chr16:68702855-68754003		
16q22.2	chr16:69404749-69760030		
16q22.3	chr16:70646001-70669798		
16q24.2	chr16:86580132-86581743		
17p13.2	chr17:3988918-3989416		
17p11.2	chr17:20285952-20335955		
	chr17:16657468-16665371		
17q21.1	chr17:36785827-36793150		
17q22	chr17:53042845-53044836		
17q23.2	chr17:55766887-55768922		
1q21.1	chr1:142612557-142700497		
1q42.3	chr1:232978568-233024889		
2p22.2	chr2:37811582-37859388		
3q26.1	chr3:163994833-164109307		
4p16.1	chr4:9117494-9354801		
	chr4:9229907-9241989		
4q32.2	chr4:163613458-163615903		
5q23.3	chr5:130360261-130360757		
6p22.1	chr6:26878702-26883319		
6p21.31	chr6:33691917-33693857		
6p11.2	chr6:57730820-57739182		
6q16.1	chr6:95250114-95251113		
7q35	chr7:143539578-143541360		
8p11.21	chr8:42309719-42313291		
8q21.11	chr8:75525410-75529549		
9p11.2	chr9:46608158-46622405		
9q12	chr9:67147030-67191484		
10q22.3	chr10:81128690-81226767		
11q14.3	chr11:89324164-89328039		
11q22.3	chr11:103772866-103778468		
12p12.3	chr12:17336026-17337197		
13q21.31	chr13:60856422-60857183		
14q31.1	chr14:81568879-81573106		
15q11.2	chr15:19044664-19093683		
16p11.2	chr16:32364447-32569534		
	chr16:33392351-33398613		
	chr16:33494966-33540569		

17p12	chr17:15730266-15734437	NCBI36 (hg18)	[95]
17q21.2	chr17:36675163-36685731		
19p13.12	chr19:14907340-14910599		
19p12	chr19:20592635-20593903		
	chr19:21540540-21558083		
19q12	chr19:35978675-35981288		
20p13	chr20:3960496-3964421		
20p12.1	chr20:15657506-15660363		
20q11.23	chr20:35166578-35167640		
20q13.2	chr20:51908207-51917753		
	chr20:53671106-53671794		
20q13.33	chr20:61195163-61196042		
21q11.2	chr20:13738734-13739562		
21q21.1	chr21:15510264-15513034		
22q11.23	chr22:22604143-22607619		
1q21.1	chr1: 146500000–147500000	GRCh37 (hg19)	[96]
15q11.2	chr15: 22800000–23100000		
15q13.3	chr15: 31300000–32500000		
16p13.11	chr16: 15000000–16300000		
16p12	chr16:21900000–22500000		
16p11.2	chr16: 29600000–30200000		
22q11.2	chr22: 18800000–21600000		
5p15.33	chr5:801638-878490	NCBI36 (hg18)	[97]
	chr5:873107-875260		
	chr5:739174-810625		
	chr5:854901-868134		
	chr5:878048-902921		
5p14.1	chr5:29097870-29102737		
6q26	chr6:160936851-160990675		
15q11.2	chr15:22075954-22219532		
	chr15:22223136-22269801		
	chr15:22223136-22283122		
2q37.3	chr2:242154846-242156009		
	chr2:242177893-242179344		
5p15.33	chr5:801796-802806		
	chr5:731066-903941		
	chr5:865074-878564		
	chr5:878644-896918		
	chr5:1223372-1223922		
	chr5:1231138-1233723		
	chr5:1244347-1245032		
	chr5:1244697-1245362		
5p15.2	chr5:12728510-12812105		
6p21.33	chr6:31301055-31302293		
6q26	chr6:160945968-160989821		
7p14.1	chr7:38251784-38277712		

8p23.3	chr8:222152-223442	NCBI36 (hg18)	[97]
	chr8:314452-317471		
	chr8:327542-376235		
8p23.1	chr8:6998231-7003644		
	chr8:12275769-12284550		
	chr8:12277919-12282956		
10q26.3	chr10:135189858-135365034		
	chr10:135200460-135327915		
	chr10:135087012-135250713		
11q25	chr11:134414510-134418045		
15q11.2	chr15:22008036-22064226		
	chr15:22216498-22275711		
	chr15:22036906-22057667		
	chr15:21881157-21930943		
	chr15:21898042-22057470		
	chr15:22037969-22346531		
	chr15:22149509-22165215		
	chr15:22155449-22205345		
	chr15:22202279-22299076		
15q26.3	chr15:99607966-99611267		
2q21.2	chr2:132727944-132764103		
	chr2:132733351-132752848		
15q11.2	chr15:24112281-24154189	GRCh37 (hg19)	[98]
	chr15:24369643-24468460		
	chr15:24369643-24649604		
	chr15:24376622-24468460		
15q11–q13	chr15:25962058-26019039		
15q13.3	chr15:30936285-32514341		
	chr15:32922947-32971934		
16p13.11	chr16:15092778-15225383		
	chr16:15493046-16291983		
	chr16:15493046-18164698		
16p11.2	chr16:28825605-29042014		
	chr16:29652488-30192359		
17q12	chr17:33684035-33768199		
22q11.2	chr22:18115392-18633446		
	chr22:18889490-21463730		
	chr22:22314463-22362353		
	chr22:22314463-22379067		
1q21.1	chr1:144100000–144600000	NCBI36 (hg18)	[99]
	chr1:145000000–146350000		
3q29	chr3:197400000–198900000		
10q22–q23	chr10:81120000–89070000		
15q13.3	chr15:28700000–30200000		
15q24	chr15:72200000–73800000		
16p13.11	chr16:15400000–16400000		
16p11.2	chr16:29500000–30100000		
16p11.2–p12.2	chr16:22000000–28000000		
17q12	chr17:31800000–33300000		
17q21.31	chr17:41000000–41700000		
22q11.2	chr22:19800000–22000000		