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CLINICAL GENOMICS

Generation of Whole-Genome Sequencing Data for Comparing Primary and Castration-Resistant Prostate Cancer

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Because castration-resistant prostate cancer (CRPC) does not respond to androgen deprivation therapy and has a very poor prognosis, it is critical to identify a prognostic indicator for predicting high-risk patients who will develop CRPC. Here, we report a dataset of whole genomes from four pairs of primary prostate cancer (PC) and CRPC samples. The analysis of the paired PC and CRPC samples in the whole-genome data showed that the average number of somatic mutations per patients was 7,927 in CRPC tissues compared with primary PC tissues (range, 1,691 to 21,705). Our whole-genome sequencing data of primary PC and CRPC may be useful for understanding the genomic changes and molecular mechanisms that occur during the progression from PC to CRPC.

Keywords: castration-resistant prostate cancer, DNA variants, whole-genome sequencing

Availability: The whole-genome data are available in the Korean Bioinformation Center (KOBIC) biodata (http://biodata.kr/) public database under accession numbers KBRS20180406_0000001–KBRS20180406_0000008.

Introduction

Prostate cancer (PC) is the most common malignancy in males [1]. It is known that about 20% of PC patients experience disease progression and distant metastasis [2, 3]. The therapeutic options for patients with aggressive PC include prostatectomy, radiation therapy, and androgen deprivation therapy (ADT) [4]. Although ADT therapy induces short 2–3-year remissions, unfortunately, most PCs eventually progress into castration-resistant prostate cancer (CRPC) [3], which does not respond to ADT therapy and shows poor clinical behavior. Therefore, it is crucial to understand the molecular characteristics and identify robust biomarkers that are associated with the development of CRPC from primary PC.

High-throughput next-generation sequencing technologies have gradually uncovered the molecular characteristics of PC, along with CRPC [5-8]. However, many genomic studies on CRPC have been conducted on metastasized CRPC that has been discovered at distant organs. These studies of metastatic sites do not reflect the precise molecular characteristics of CRPC, because these sites are not the primary PC site and because metastatic sites have completely different microenvironments from the primary site [9]. Here, we generated a dataset of whole genomes from four pairs of primary PC and CRPC samples from the same patient (i.e., a total of eight paired samples from four PC patients). In this report, the genomic status of samples with primary PC and CRPC was explored, and different

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variants between these two distinct phenotypes were identified by comparing the genomes of primary PC and its paired CRPC.

Methods

Tissues samples

Four pairs of primary PC and CRPC tissues were obtained from Chungbuk National University Hospital (Korea) with informed consent and approval of the Internal Review Board at Chungbuk National University. To obtain a consistent variant profile that was associated with the development of CRPC, primary CRPCs were obtained from homogenous biopsy sites, and none of our PC samples was from distant metastatic sites. Detailed clinical characteristics of the four pairs of primary PC and CRPC tissues are described in Supplementary Table 1.

Whole-genome sequencing library construction and sequencing

Genomic DNA was isolated using the DNeasy Blood and Tissue kit (Qiagen, Carlsbad, CA, USA), and the sequencing library was constructed using the Illumina TruSeq DNA Library Prep Kit (San Diego, CA, USA). Next, paired-end sequencing was performed on an Illumina HiSeq X Ten sequencing instrument, yielding ~150-bp short sequencing reads.

Data analysis

The sequenced reads were aligned to human reference genome 19 using Burrows Wheelers Aligner [10], and duplicate reads were removed using Picard (Broad Institute). Then, the remaining reads were calibrated and realigned using the Genome Analysis Toolkit [11]. The realigned Binary Alignment Map files were analyzed using Strelka [12] to detect somatic single-nucleotide variants and insertions/deletions. For all programs, the default parameter settings were applied.

Results and Discussion

Quality and quantity of the sequencing data

The whole-genome sequencing (WGS) data, including the mapping rate, genome coverage, scores of the mapping quality, and duplicate reads, are summarized in Table 1. Briefly, the mapping rate and scores of the mapping quality in the four pairs of primary PC and CRPC samples were higher than 95% and 53%, respectively. In addition, the average genome coverage of our samples was over 30× (between 31.81× and 53.54×). Although coverage of several hundred times is required for detecting low-level mutations in next-generation sequence data [13], WGS with 30× sequence coverage is appropriate for comprehensive identification of tumor-specific somatic mutations [14]. These results suggest that the quality and quantity of our sequencing data are adequate for mutational analysis during the progression from PC to CRPC.

Mutation patterns identified from CRPC compared with PC

The average number of somatic mutations per patients was 7,927 in CRPC tissues compared with primary PC tissues (range, 1691 to 21,705). In particular, patient P2 had hypermutations (n = 21,705), whereas patient P1 had a low mutation frequency (n = 1,691) (Fig. 1A). To observe the mutation signatures in the development of CRPC from primary PC, we examined the spectrum of base substitutions. This analysis revealed an unusually high proportion of C:G>T:A and A:T>G:C transversions (Fig. 1B), similar to a previous study [15]. Next, the mutated sites were annotated as non-synonymous, synonymous, stop, and gain mutations. The number of mutations affecting protein-coding genes was 9, 321, 22, and 10 for the four patients (Table 2), and we observed recurrent mutations in the *ANKRD20A4, ANDRK38B, AQP7, GGT1*, and *TAS2R31* genes. Detailed information for the non-synonymous and recurrent mutations is summarized in Supplementary Table 2. Further study will

Table 1. Quality and quantity of the sequencing data

Sample ID	Total No. of reads	Mapped reads, n/%	Duplicate reads, n/%	Genome coverage (mean)	Mapping quality
P1_PC	848,047,506	808,804,115/95.37	68,671,081/8.10	37.89	54.01
P1_CRPC	948,133,472	906,103,176/95.57	261,605,851/27.59	42.86	54.05
P2_PC	850,014,794	812,799,767/95.62	132,111,659/15.54	38.24	54.10
P2_CRPC	1,119,621,752	1,074,841,222/96.00	178,460,836/15.94	50.85	54.32
P3_PC	873,087,626	831,226,978/95.21	219,433,437/25.13	39.29	54.05
P3_CRPC	1,217,525,626	1,164,525,389/95.65	182,382,654/14.98	53.54	53.79
P4_PC	740,468,590	703,382,210/94.99	138,235,516/18.67	31.81	53.21
P4_CRPC	915,523,140	875,358,078/95.40	215,503,940/23.49	41.39	54.03

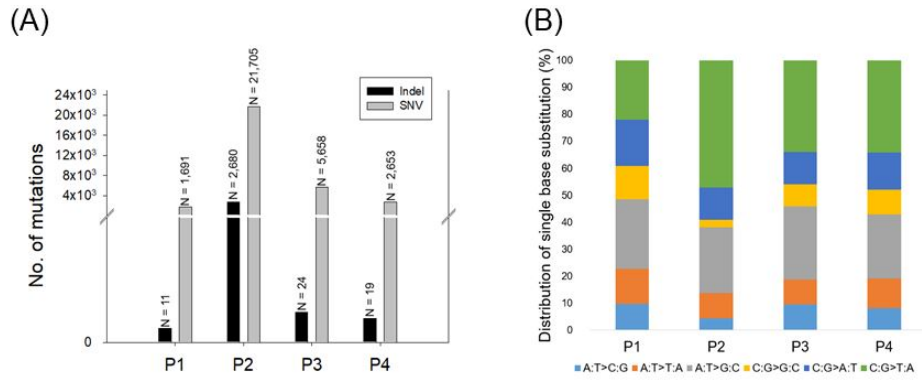

Fig. 1. Number of mutations and distribution of mutation type. (A) Somatic mutations were detected using the Strelka package with default parameter settings. (B) Relative distribution of single-base substitutions by type in each of the four paired castration-resistant prostate cancer patients. SNV, single nucleotide variant.

Table 2. Summary of mutation in exonic regions

Sample ID	Synonymous mutations	Non-synonymous mutations	Stop or gain	Mutated genes
P1	3	6	0	9
P2	104	226	10	321
P3	11	13	0	22
P4	3	8	1	10

be needed to examine whether the mutated genes are associated with the development of CRPC from primary PC.

In conclusion, PC is a heterogeneous disease and has various steps in its disease progression, including CRPC, the poorest prognostic status during the progression of PC. Understanding the molecular characteristics of the development of CRPC will help identify high-risk PC patients and develop novel therapeutic strategies to block the progression of CRPC. We generated a set of WGS data, consisting of eight PC samples containing four pairs of primary PC and CRPC samples from the same patient, because genetic mutations have the greatest potential to play a role in the progression of PC and CRPC and the therapeutic management of CRPC [16, 17]. By comparing primary PC and its paired CRPC, many somatic mutations that were significantly associated with the development of CRPC were identified, including TP53 and KMT2C, which are known to be involved in the progression of PC [16, 17]. We hope that our whole-genome sequence data of the four paired PC and CRPC tissues will be utilized by many researchers to understand the progression of PC and the resistance to androgen deprivation therapy.

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Authors' contribution

Conceptualization: SYK
Sample and data curation: SJY, WJK, WTK, PJ, HWK
WGS data generation: JHK, PJ
Data analysis: JLP, SKK
Writing – original draft: JLP, SKK
Writing – review & editing: SYK

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Supplementary materials

Supplementary data including two tables can be found with this article online at https://doi.org/10.5808/GI.2018.16.3.71.

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SUPPLEMENTARY INFORMATION

Generation of Whole-Genome Sequencing Data for Comparing Primary and Castration-Resistant Prostate Cancer

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Supplementary Table 1. Clinical characteristics of the four patients who had a primary PC biopsy followed by a CRPC biopsy

Characteristic	Patient 1 (P1)	Patient 2 (P2)	Patient 3 (P3)	Patient 4 (P4)
1st operation				
Age (y)	69	74	78	69
Type of surgery	RRP	TUR-P	TUR-P	TUR-P
PSA at operation (μg/L)	90.8	379	200	89
Gleason score	7 (3+4)	7 (4+3)	9 (4+5)	9 (4+5)
TNM stage	T3N1M0	T3N1M1	T3N1M0	T4N1M0
2nd operation				
Age (y)	81	78	79	70
Type of surgery	TUR-P	TUR-P	TUR-P	TUR-P
PSA at operation (μg/L)	133.1	166	40.2	117.3
Gleason score	7 (4+3)	7 (4+3)	9 (5+4)	9 (4+5)
TNM stage	T4N1M1	T3N1M1	T3N1M0	T4N1M0

PC, prostate cancer; CRPC, castration-refractory prostate cancer; PSA, prostate-specific antigen; RRP, radical retropubic prostatectomy; TUR-P, transurethral resection of the prostate.

Supplementary Table 2. Detailed information on the non-synonymous and recurrent mutations of all samples

Sample ID	Chrom	Start	End	Ref_allele	Var_allele	Types	Symbol	Refseq_id	Exon_num	Cdna_change	AA_change
P2	chr7	121717913	121717913	C	T	nonsynonymous SNV	AASS	NM_005763	exon23	c.G2641A	p.A881T
P2	chr17	67297370	67297370	G	A	nonsynonymous SNV	ABCA5	NM_018672	exon8	c.C1177T	p.P393S
P2	chr13	95673843	95673843	C	T	nonsynonymous SNV	ABCC4	NM_005845	exon31	c.G3964A	p.E1322K
P3	chr16	67691668	67691668	A	G	nonsynonymous SNV	ACD	NM_001082487	exon11	c.T1505C	p.V502A
P2	chr1	236914784	236914784	G	A	synonymous SNV	ACTN2	NM_001278343	exon15	c.G1671A	p.A557A
P2	chr7	149981855	149981855	C	T	nonsynonymous SNV	ACTR3C	NM_001164459	exon6	c.G551A	p.R184H
P2	chr12	52307405	52307405	G	A	nonsynonymous SNV	ACVRL1	NM_000020	exon4	c.G376A	p.V126M
P2	chr5	156916167	156916167	G	A	synonymous SNV	ADAM19	NM_033274	exon20	c.C2268T	p.S756S
P2	chr9	136303408	136303408	G	T	nonsynonymous SNV	ADAMTS13	NM_139025	exon14	c.G1627T	p.D543Y
P2	chr16	77359829	77359829	C	T	nonsynonymous SNV	ADAMTS18	NM_199355	exon13	c.G1966A	p.A656T
P2	chr12	43763134	43763134	C	T	nonsynonymous SNV	ADAMTS20	NM_025003	exon37	c.G5497A	p.A1833T
P2	chr9	18776871	18776871	G	A	nonsynonymous SNV	ADAMTSL1	NM_001040272	exon19	c.G2644A	p.V882M
P2	chr8	131964160	131964160	G	A	stopgain	ADCY8	NM_001115	exon3	c.C1195T	p.Q399X
P2	chrX	1718302	1718302	G	A	nonsynonymous SNV	AKAP17A	NM_005088	exon4	c.G1129A	p.A377T
P2	chr1	165648811	165648811	C	T	synonymous SNV	ALDH9A1	NM_000696	exon6	c.G798A	p.E266E
P2	chr18	56204909	56204909	G	T	nonsynonymous SNV	ALPK2	NM_052947	exon5	c.C2510A	p.S837Y
P2	chr16	2577913	2577913	G	A	synonymous SNV	AMDHD2	NM_001145815	exon5	c.G555A	p.T185T
P2	chr3	134090157	134090157	C	A	nonsynonymous SNV	AMOTL2	NM_001278685	exon2	c.G119T	p.R40M
P2	chr10	61833289	61833289	G	A	synonymous SNV	ANK3	NM_020987	exon37	c.C7350T	p.D2450D
P2	chr7	16650267	16650267	A	G	nonsynonymous SNV	ANKMY2	NM_020319	exon6	c.T653C	p.L218S
P2	chr9	69423721	69423721	G	A	nonsynonymous SNV	ANKRD20A4	NM_001098805	exon15	c.G2017A	p.A673T
P2	chr9	69423983	69423983	T	C	nonsynonymous SNV	ANKRD20A4	NM_001098805	exon15	c.T2279C	p.I760T
P3	chr9	69391171	69391171	G	A	nonsynonymous SNV	ANKRD20A4	NM_001098805	exon5	c.G679A	p.A227T
P1	chr2	98128234	98128234	T	C	synonymous SNV	ANKRD36B	NM_025190	exon39	c.A3087G	p.R1029R
P2	chr2	98128473	98128473	G	A	nonsynonymous SNV	ANKRD36B	NM_025190	exon39	c.C2848T	p.R950C
P2	chr17	34050697	34050697	C	T	synonymous SNV	AP2B1	NM_001030006	exon22	c.C2835T	p.Y945Y
P2	chr8	42025184	42025184	A	G	nonsynonymous SNV	AP3M2	NM_001134296	exon9	c.A1012G	p.M338V
P2	chr1	10493990	10493990	C	T	nonsynonymous SNV	APITD1-CORT	NM_001270517	exon2	c.C143T	p.A48V
P2	chr9	33385733	33385733	C	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G657A	p.M219I
P2	chr9	33385740	33385740	A	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.T650A	p.L217H
P2	chr9	33385750	33385750	C	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G640A	p.G214R
P2	chr9	33385771	33385771	C	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G619A	p.G207S
P2	chr9	33385784	33385784	C	G	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G606C	p.E202D
P2	chr9	33385786	33385786	C	G	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G604C	p.E202Q
P2	chr9	33385828	33385828	C	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G562A	p.A188T
P2	chr9	33385852	33385852	C	T	nonsynonymous SNV	AQP7	NM_001170	exon7	c.G538A	p.G180R
P3	chr9	33386146	33386146	C	A	nonsynonymous SNV	AQP7	NM_001170	exon6	c.G454T	p.V152F
P2	chr11	72437998	72437998	C	T	nonsynonymous SNV	ARAP1	NM_001040118	exon3	c.G176A	p.R59H
P2	chr4	153809416	153809416	G	A	nonsynonymous SNV	ARFIP1	NM_001287431	exon8	c.G923A	p.R308H
P3	chr5	149008403	149008403	A	G	synonymous SNV	ARHGEF37	NM_001001669	exon12	c.A1692G	p.L564L
P2	chr5	90669632	90669632	C	T	nonsynonymous SNV	ARRDC3	NM_020801	exon7	c.G1057A	p.V353I
P2	chr1	23765719	23765719	G	A	stopgain	ASAP3	NM_001143778	exon10	c.C922T	p.R308X
P2	chr8	62559359	62559359	G	A	nonsynonymous SNV	ASPH	NM_032466	exon6	c.C569T	p.T190I
P2	chr1	63329766	63329766	T	C	nonsynonymous SNV	ATG4C	NM_178221	exon11	c.T1313C	p.L438P
P2	chr3	130650924	130650924	G	A	nonsynonymous SNV	ATP2C1	NM_001001486	exon3	c.G176A	p.G59D
P2	chr13	31835161	31835161	G	A	nonsynonymous SNV	B3GALTL	NM_194318	exon7	c.G538A	p.V180I
P2	chr15	40758297	40758297	C	T	nonsynonymous SNV	BAHD1	NM_001301132	exon7	c.C2308T	p.R770C
P2	chr1	32201471	32201471	C	T	nonsynonymous SNV	BAI2	NM_001294335	exon23	c.G3224A	p.G1075D
P2	chr11	118772429	118772429	G	A	nonsynonymous SNV	BCL9L	NM_182557	exon6	c.C2023T	p.R675C
P3	chr2	32716525	32716525	G	C	nonsynonymous SNV	BIRC6	NM_016252	exon44	c.G8240C	p.S2747T
P2	chr3	9781124	9781124	C	A	synonymous SNV	BRPF1	NM_004634	exon3	c.C1041A	p.R347R
P2	chr10	93753543	93753543	G	A	synonymous SNV	BTAF1	NM_003972	exon22	c.G3138A	p.L1046L
P2	chr5	180486728	180486728	G	A	nonsynonymous SNV	BTNL9	NM_152547	exon11	c.G1474A	p.D492N
P2	chr15	45250696	45250696	C	T	nonsynonymous SNV	C15orf43	NM_152448	exon3	c.C272T	p.A91V
P2	chr16	4626235	4626235	C	T	nonsynonymous SNV	C16orf96	NM_001145011	exon5	c.C1754T	p.A585V
P2	chr7	7278034	7278034	A	G	synonymous SNV	C1GALT1	NM_020156	exon3	c.A369G	p.S123S
P2	chr2	24255780	24255780	C	T	nonsynonymous SNV	C2orf44	NM_025203	exon3	c.G1855A	p.A619T
P2	chr19	6692959	6692959	C	T	synonymous SNV	C3	NM_000064	exon26	c.G3366A	p.A1122A
P3	chr19	48722180	48722180	C	T	synonymous SNV	CARD8	NM_014959	exon10	c.G1101A	p.E367E
P2	chr19	5772833	5772833	G	A	nonsynonymous SNV	CATSPERD	NM_152784	exon20	c.G1798A	p.A600T
P2	chr12	123265872	123265872	C	A	nonsynonymous SNV	CCDC62	NM_201435	exon3	c.C391A	p.L131I
P1	chr2	135711846	135711846	T	G	nonsynonymous SNV	CCNT2	NM_001241	exon9	c.T1821G	p.S607R
P2	chr4	91229728	91229728	G	A	nonsynonymous SNV	CCSER1	NM_001145065	exon2	c.G293A	p.S98N
P2	chr12	7550954	7550954	G	A	synonymous SNV	CD163L1	NM_174941	exon7	c.C1635T	p.C545C
P2	chr9	5457379	5457379	A	G	nonsynonymous SNV	CD274	NM_014143	exon3	c.A353G	p.Y118C
P2	chr3	45153778	45153778	G	A	nonsynonymous SNV	CDCP1	NM_022842	exon3	c.C452T	p.P151L
P2	chr10	73501571	73501571	C	T	nonsynonymous SNV	CDH23	NM_022124	exon36	c.C4738T	p.R1580C
P2	chr16	62055291	62055291	G	A	nonsynonymous SNV	CDH8	NM_001796	exon2	c.C17T	p.A6V
P2	chr22	46776797	46776797	C	T	nonsynonymous SNV	CELSR1	NM_014246	exon22	c.G7144A	p.E2382K
P2	chr3	424296	424296	C	A	nonsynonymous SNV	CHL1	NM_006614	exon18	c.C2118A	p.N706K
P2	chr3	424298	424298	A	G	nonsynonymous SNV	CHL1	NM_006614	exon18	c.A2120G	p.E707G
P3	chr19	59063292	59063292	G	A	synonymous SNV	CHMP2A	NM_198426	exon5	c.C522T	p.S174S
P2	chr7	2473499	2473499	G	A	nonsynonymous SNV	CHST12	NM_018641	exon2	c.G1225A	p.E409K
P4	chr7	73790318	73790318	G	C	synonymous SNV	CLIP2	NM_003388	exon10	c.G1587C	p.S529S
P2	chr1	26507365	26507365	G	A	nonsynonymous SNV	CNKSR1	NM_001297647	exon3	c.G370A	p.A124T
P2	chr1	103431078	103431078	C	T	nonsynonymous SNV	COL11A1	NM_001854	exon38	c.G2881A	p.G961S
P2	chr6	75855148	75855148	A	G	synonymous SNV	COL12A1	NM_004370	exon25	c.T4584C	p.N1528N
P2	chr20	61938843	61938843	C	A	synonymous SNV	COL20A1	NM_020882	exon6	c.C498A	p.A166A
P2	chr9	117051232	117051232	C	T	synonymous SNV	COL27A1	NM_032888	exon44	c.C4137T	p.G1379G
P2	chr9	137582889	137582889	G	A	nonsynonymous SNV	COL5A1	NM_001278074	exon2	c.G241A	p.A81T

P2	chr6	70962003	70962003	G	A	nonsynonymous SNV	COL9A1	NM_001851	exon27	c.C1780T	p.P594S
P2	chr19	19014144	19014144	G	A	nonsynonymous SNV	COPE	NM_007263	exon7	c.C668T	p.A223V
P2	chr4	47765397	47765397	T	G	nonsynonymous SNV	CORIN	NM_001278585	exon3	c.A415C	p.S139R
P2	chr1	207697185	207697185	G	A	synonymous SNV	CR1	NM_000573	exon5	c.G717A	p.T239T
P2	chr16	84879496	84879496	C	T	synonymous SNV	CRISPLD2	NM_031476	exon3	c.C345T	p.G115G
P2	chr11	10800514	10800514	C	T	synonymous SNV	CTR9	NM_014633	exon25	c.C3384T	p.A1128A
P2	chr9	105767032	105767032	G	A	nonsynonymous SNV	CYLC2	NM_001340	exon4	c.G236A	p.R79H
P2	chr11	6647272	6647272	C	A	stopgain	DCHS1	NM_003737	exon17	c.G6610T	p.G2204X
P2	chr5	112349113	112349113	T	C	nonsynonymous SNV	DCP2	NM_152624	exon11	c.T1195C	p.F399L
P2	chr11	47236791	47236791	A	T	nonsynonymous SNV	DDB2	NM_000107	exon1	c.A104T	p.K35M
P2	chrX	23019747	23019747	G	T	nonsynonymous SNV	DDX53	NM_182699	exon1	c.G1573T	p.D525Y
P2	chr14	24766049	24766049	G	A	synonymous SNV	DHRS1	NM_001136050	exon3	c.C189T	p.C63C
P2	chr9	93375670	93375670	A	C	nonsynonymous SNV	DIRAS2	NM_017594	exon2	c.T440G	p.F147C
P2	chr5	118482607	118482607	T	C	nonsynonymous SNV	DMXL1	NM_005509	exon16	c.T2645C	p.L882S
P2	chr17	7701997	7701997	C	T	synonymous SNV	DNAH2	NM_020877	exon54	c.C8520T	p.G2840G
P2	chr20	62560854	62560854	C	T	synonymous SNV	DNAJC5	NM_025219	exon3	c.C297T	p.F99F
P2	chr19	10244950	10244950	C	A	nonsynonymous SNV	DNMT1	NM_001130823	exon40	c.G4807T	p.A1603S
P2	chr13	99574324	99574324	G	A	nonsynonymous SNV	DOCK9	NM_001130049	exon6	c.C566T	p.A189V
P2	chr19	2211180	2211180	G	A	synonymous SNV	DOT1L	NM_032482	exon15	c.G1434A	p.A478A
P2	chr6	30916772	30916772	G	A	synonymous SNV	DPCR1	NM_080870	exon2	c.G531A	p.T177T
P3	chr16	57735900	57735900	G	C	nonsynonymous SNV	DRC7	NM_001289162	exon6	c.G557C	p.C186S
P2	chr18	28993551	28993551	A	G	nonsynonymous SNV	DSG4	NM_177986	exon16	c.A3116G	p.Q1039R
P2	chr12	89744510	89744510	G	A	synonymous SNV	DUSP6	NM_001946	exon2	c.C693T	p.F231F
P2	chr17	45421607	45421607	A	G	nonsynonymous SNV	EFCAB13	NM_152347	exon7	c.A383G	p.Y128C
P2	chr11	10822143	10822143	T	C	nonsynonymous SNV	EIF4G2	NM_001172705	exon17	c.A1696G	p.N566D
P2	chr11	10825838	10825838	C	A	nonsynonymous SNV	EIF4G2	NM_001172705	exon6	c.G479T	p.S160I
P2	chr20	33868539	33868539	C	T	nonsynonymous SNV	EIF6	NM_001267810	exon4	c.G287A	p.R96Q
P3	chr5	96129512	96129512	A	G	synonymous SNV	ERAP1	NM_016442	exon6	c.T1068C	p.A356A
P2	chr3	56026099	56026099	G	A	synonymous SNV	ERC2	NM_015576	exon11	c.C2241T	p.I747I
P2	chr2	97637859	97637859	C	T	nonsynonymous SNV	FAM178B	NM_001122646	exon3	c.G343A	p.V115M
P1	chr12	50745820	50745820	G	A	synonymous SNV	FAM186A	NM_001145475	exon4	c.C4795T	p.L1599L
P2	chr9	71998620	71998620	C	A	nonsynonymous SNV	FAM189A2	NM_004816	exon7	c.C569A	p.P190H
P2	chr9	34726428	34726428	C	T	nonsynonymous SNV	FAM205A	NM_001141917	exon4	c.G809A	p.R270Q
P2	chr5	137680706	137680706	C	T	nonsynonymous SNV	FAM53C	NM_001135647	exon4	c.C329T	p.P110L
P2	chr7	128323029	128323029	C	T	nonsynonymous SNV	FAM71F2	NM_001290254	exon6	c.C461T	p.T154I
P1	chr1	143906122	143906122	C	A	nonsynonymous SNV	FAM72D	NM_207418	exon3	c.G245T	p.G82V
P2	chr19	13033565	13033565	C	T	synonymous SNV	FARSA	NM_004461	exon13	c.G1524A	p.A508A
P2	chr5	150911360	150911360	G	A	nonsynonymous SNV	FAT2	NM_001447	exon13	c.C9599T	p.T3200M
P2	chr11	92534441	92534441	C	T	synonymous SNV	FAT3	NM_001008781	exon9	c.C8262T	p.G2754G
P2	chr16	747115	747115	C	T	synonymous SNV	FBXL16	NM_153350	exon2	c.G291A	p.T97T
P2	chr7	19184962	19184962	G	A	synonymous SNV	FERD3L	NM_152898	exon1	c.C24T	p.C8C
P2	chr7	4794165	4794165	G	A	synonymous SNV	FOXK1	NM_001037165	exon3	c.G822A	p.S274S
P2	chr17	79496121	79496121	C	A	synonymous SNV	FSCN2	NM_001077182	exon1	c.C564A	p.S188S
P4	chr4	47033734	47033734	C	A	synonymous SNV	GABRB1	NM_000812	exon1	c.C66A	p.V22V
P2	chr9	35739655	35739655	G	A	nonsynonymous SNV	GBA2	NM_020944	exon9	c.C1552T	p.R518W
P2	chr9	74828816	74828816	C	T	nonsynonymous SNV	GDA	NM_001242505	exon5	c.C487T	p.R163W
P2	chr22	25024113	25024113	G	A	nonsynonymous SNV	GGT1	NM_001288833	exon14	c.G1402A	p.V468M
P3	chr22	25016939	25016939	A	G	nonsynonymous SNV	GGT1	NM_001288833	exon9	c.A635G	p.Q212R
P3	chr22	25016941	25016941	C	G	nonsynonymous SNV	GGT1	NM_001288833	exon9	c.C637G	p.L213V
P2	chr16	74499705	74499705	C	T	nonsynonymous SNV	GLG1	NM_001145667	exon19	c.G2536A	p.E846K
P2	chr16	4383406	4383406	T	C	synonymous SNV	GLIS2	NM_032575	exon2	c.T231C	p.P77P
P1	chr15	22743379	22743379	A	G	synonymous SNV	GOLGA6L1	NM_001001413	exon8	c.A1764G	p.R588R
P2	chr17	36493026	36493026	C	T	synonymous SNV	GPR179	NM_001004334	exon4	c.G1062A	p.L354L
P2	chr9	139243183	139243183	G	A	synonymous SNV	GPSM1	NM_001145638	exon10	c.G1242A	p.A414A
P2	chr11	105483053	105483053	G	A	nonsynonymous SNV	GRIA4	NM_001112812	exon2	c.G139A	p.A47T
P1	chr12	13715916	13715916	G	A	nonsynonymous SNV	GRIN2B	NM_000834	exon13	c.C4256T	p.P1419L
P3	chr19	48918157	48918157	C	T	synonymous SNV	GRIN2D	NM_000836	exon6	c.C1449T	p.C483C
P3	chr12	48723164	48723164	C	T	synonymous SNV	H1FNT	NM_181788	exon1	c.C90T	p.G30G
P2	chr12	112617039	112617039	A	T	nonsynonymous SNV	HECTD4	NM_001109662	exon63	c.T10748A	p.L3583H
P2	chr2	197298108	197298108	G	A	nonsynonymous SNV	HECW2	NM_020760	exon2	c.C40T	p.R14C
P2	chr3	124729314	124729314	C	T	synonymous SNV	HEG1	NM_020733	exon7	c.G3042A	p.P1014P
P2	chr15	28389828	28389828	G	A	nonsynonymous SNV	HERC2	NM_004667	exon72	c.C11131T	p.P3711S
P2	chr22	19379633	19379633	A	G	synonymous SNV	HIRA	NM_003325	exon9	c.T927C	p.L309L
P2	chr2	75112708	75112708	C	T	nonsynonymous SNV	HK2	NM_000189	exon13	c.C1927T	p.R643W
P2	chr1	221057764	221057764	G	T	nonsynonymous SNV	HLX	NM_021958	exon4	c.G1185T	p.E395D
P2	chr5	162902656	162902656	C	A	nonsynonymous SNV	HMMR	NM_012484	exon11	c.C1243A	p.L415I
P4	chr1	13183226	13183226	T	C	nonsynonymous SNV	HNRNPCL2	NM_001136561	exon2	c.A647G	p.K216R
P4	chr1	13183263	13183263	T	C	nonsynonymous SNV	HNRNPCL2	NM_001136561	exon2	c.A610G	p.I204V
P2	chr3	148857851	148857851	A	G	nonsynonymous SNV	HPS3	NM_032383	exon2	c.A278G	p.N93S
P2	chr4	3162014	3162014	G	A	synonymous SNV	HTT	NM_002111	exon29	c.G3759A	p.T1253T
P2	chr3	50357001	50357001	T	C	nonsynonymous SNV	HYAL2	NM_033158	exon3	c.A920G	p.E307G
P2	chr15	60747587	60747587	G	A	synonymous SNV	ICE2	NM_001276385	exon7	c.C721T	p.L241L
P2	chr1	159897253	159897253	C	T	nonsynonymous SNV	IGSF9	NM_020789	exon21	c.G3374A	p.R1125H
P2	chr8	42176889	42176889	G	A	nonsynonymous SNV	IKBKB	NM_001242778	exon13	c.G1289A	p.S430N
P2	chr10	124753476	124753476	A	G	synonymous SNV	IKZF5	NM_001271840	exon5	c.T1080C	p.P360P
P2	chr7	2629653	2629653	G	A	nonsynonymous SNV	IQCE	NM_152558	exon14	c.G1157A	p.R386H
P2	chr12	250444	250444	G	A	nonsynonymous SNV	IQSEC3	NM_001170738	exon5	c.G2146A	p.V716M
P2	chr4	185309945	185309945	C	T	synonymous SNV	IRF2	NM_002199	exon9	c.G1017A	p.S339S
P3	chr1	62713246	62713246	G	A	synonymous SNV	KANK4	NM_181712	exon9	c.C2781T	p.H927H
P2	chr12	5153884	5153884	G	A	nonsynonymous SNV	KCNA5	NM_002234	exon1	c.G571A	p.V191I
P2	chr3	19492662	19492662	C	T	nonsynonymous SNV	KCNH8	NM_144633	exon10	c.C1591T	p.P531S
P2	chr14	88652179	88652179	G	A	synonymous SNV	KCNK10	NM_021161	exon7	c.C1317T	p.S439S

P2	chr9	2718329	2718329	G	A	nonsynonymous SNV	KCNV2	NM_133497	exon1	c.G590A	p.R197H
P2	chr9	2718811	2718811	G	A	nonsynonymous SNV	KCNV2	NM_133497	exon1	c.G1072A	p.E358K
P2	chr5	93731993	93731993	C	A	nonsynonymous SNV	KIAA0825	NM_001145678	exon17	c.G3109T	p.G1037C
P2	chr4	123109168	123109168	T	A	nonsynonymous SNV	KIAA1109	NM_015312	exon7	c.T746A	p.I249N
P2	chr7	86548553	86548553	C	T	synonymous SNV	KIAA1324L	NM_001291991	exon10	c.G753A	p.L251L
P2	chr8	12878748	12878748	G	C	nonsynonymous SNV	KIAA1456	NM_020844	exon5	c.G560C	p.G187A
P2	chr17	51901021	51901021	G	A	synonymous SNV	KIF2B	NM_032559	exon1	c.G627A	p.P209P
P2	chr16	57800795	57800795	G	A	nonsynonymous SNV	KIFC3	NM_001130100	exon10	c.C1321T	p.R441W
P2	chr7	151860143	151860143	G	A	stopgain	KMT2C	NM_170606	exon43	c.C10519T	p.R3507X
P2	chr20	60897810	60897810	G	A	synonymous SNV	LAMA5	NM_005560	exon46	c.C6069T	p.C2023C
P2	chr1	226127223	226127223	C	T	nonsynonymous SNV	LEFTY2	NM_001172425	exon4	c.G473A	p.R158Q
P2	chr20	62369231	62369231	G	T	nonsynonymous SNV	LIME1	NM_017806	exon3	c.G156T	p.Q52H
P2	chr7	141830756	141830756	C	T	synonymous SNV	LOC93432	NM_001293626	exon4	c.C195T	p.C65C
P2	chr7	141921015	141921015	C	T	nonsynonymous SNV	LOC93432	NM_001293626	exon48	c.C6704T	p.A2235V
P2	chr8	23198655	23198655	C	T	nonsynonymous SNV	LOXL2	NM_002318	exon4	c.G593A	p.R198H
P2	chr2	74762810	74762810	G	A	nonsynonymous SNV	LOXL3	NM_032603	exon8	c.C1321T	p.R441C
P2	chr3	188242554	188242554	C	A	synonymous SNV	LPP	NM_001167672	exon4	c.C408A	p.P136P
P2	chr3	188478021	188478021	A	G	nonsynonymous SNV	LPP	NM_001167672	exon7	c.A920G	p.Q307R
P2	chr3	197541786	197541786	G	A	synonymous SNV	LRCH3	NM_032773	exon2	c.G270A	p.S90S
P2	chr12	12284925	12284925	G	T	nonsynonymous SNV	LRP6	NM_002336	exon18	c.C3800A	p.A1267D
P2	chr1	3703590	3703590	G	A	synonymous SNV	LRRC47	NM_020710	exon2	c.C900T	p.D300D
P2	chr15	101514116	101514116	G	A	nonsynonymous SNV	LRRK1	NM_024652	exon3	c.G205A	p.G69S
P2	chr21	47642621	47642621	G	A	synonymous SNV	LSS	NM_001145437	exon3	c.C111T	p.I37I
P2	chr2	33588519	33588519	C	T	nonsynonymous SNV	LTBP1	NM_001166266	exon24	c.C3070T	p.R1024W
P2	chr10	102762419	102762419	C	G	nonsynonymous SNV	LZTS2	NM_032429	exon2	c.C124G	p.P42A
P2	chr19	12760769	12760769	C	T	nonsynonymous SNV	MAN2B1	NM_001173498	exon18	c.G2222A	p.R741H
P2	chr11	65374772	65374772	G	A	synonymous SNV	MAP3K11	NM_002419	exon5	c.C1458T	p.R486R
P2	chr6	161519381	161519381	C	T	nonsynonymous SNV	MAP3K4	NM_001301072	exon17	c.C3584T	p.A1195V
P2	chr2	32094946	32094946	C	T	nonsynonymous SNV	MEMO1	NM_001137602	exon7	c.G664A	p.G222R
P2	chr1	40431585	40431585	G	A	nonsynonymous SNV	MFSD2A	NM_001287808	exon4	c.G145A	p.V49M
P3	chr13	24453442	24453442	A	G	synonymous SNV	MIPEP	NM_005932	exon4	c.T504C	p.D168D
P2	chr21	37713754	37713754	C	T	synonymous SNV	MORC3	NM_015358	exon6	c.C666T	p.P222P
P2	chr8	16035397	16035397	G	A	nonsynonymous SNV	MSR1	NM_002445	exon2	c.C101T	p.P34L
P2	chr1	17085485	17085485	G	A	synonymous SNV	MST1L	NM_001271733	exon10	c.C1206T	p.A402A
P2	chr8	66620167	66620167	G	A	nonsynonymous SNV	MTFR1	NM_001145838	exon5	c.G755A	p.R252Q
P3	chr17	56585872	56585872	G	C	nonsynonymous SNV	MTMR4	NM_004687	exon7	c.C508G	p.L170V
P3	chr4	71347270	71347270	A	C	nonsynonymous SNV	MUC7	NM_152291	exon3	c.A809C	p.D270A
P2	chr14	23855715	23855715	G	A	nonsynonymous SNV	MYH6	NM_002471	exon33	c.C4768T	p.R1590C
P2	chr17	27442424	27442424	T	C	nonsynonymous SNV	MYO18A	NM_078471	exon13	c.A2263G	p.M755V
P2	chr20	44695742	44695742	G	A	nonsynonymous SNV	NCOA5	NM_020967	exon5	c.C581T	p.A194V
P2	chr20	33345744	33345744	C	T	synonymous SNV	NCOA6	NM_001242539	exon7	c.G807A	p.Q269Q
P2	chr5	149932868	149932868	C	T	stopgain	NDST1	NM_001301063	exon14	c.C2452T	p.R818X
P2	chr14	75558144	75558144	G	A	synonymous SNV	NEK9	NM_033116	exon19	c.C2271T	p.G757G
P2	chr4	1985200	1985200	A	T	nonsynonymous SNV	NELFA	NM_005663	exon11	c.T1466A	p.I489N
P2	chr17	46136248	46136248	G	A	nonsynonymous SNV	NFE2L1	NM_003204	exon6	c.G1564A	p.G522S
P2	chr3	52522104	52522104	C	T	nonsynonymous SNV	NISCH	NM_007184	exon16	c.C2596T	p.R866C
P2	chr6	28227287	28227287	C	T	synonymous SNV	NKAPL	NM_001007531	exon1	c.C138T	p.R46R
P2	chr19	55451566	55451566	C	T	synonymous SNV	NLRP7	NM_206828	exon4	c.G621A	p.A207A
P2	chr19	36339049	36339049	C	T	stopgain	NPHS1	NM_004646	exon11	c.G1334A	p.W445X
P2	chr7	24329150	24329150	T	C	nonsynonymous SNV	NPY	NM_000905	exon3	c.T221C	p.I74T
P2	chr9	102595040	102595040	C	T	stopgain	NR4A3	NM_173200	exon5	c.C1054T	p.R352X
P2	chr10	123720940	123720940	G	A	nonsynonymous SNV	NSMCE4A	NM_001167865	exon7	c.C937T	p.R313W
P2	chr12	96077428	96077428	C	T	nonsynonymous SNV	NTN4	NM_021229	exon6	c.G1240A	p.D414N
P2	chr12	121458570	121458570	C	T	nonsynonymous SNV	OASL	NM_001261825	exon4	c.G949A	p.A317T
P2	chr1	228494778	228494778	C	A	nonsynonymous SNV	OBSCN	NM_001271223	exon56	c.C14974A	p.L4992M
P2	chr12	123463440	123463440	C	T	synonymous SNV	OGFOD2	NM_024623	exon7	c.C492T	p.Y164Y
P2	chr9	95179704	95179704	C	T	nonsynonymous SNV	OMD	NM_005014	exon2	c.G137A	p.R46H
P2	chr3	193364934	193364934	G	A	nonsynonymous SNV	OPA1	NM_130833	exon17	c.G1673A	p.R558Q
P2	chr11	6816103	6816103	G	T	synonymous SNV	OR6A2	NM_003696	exon1	c.C837A	p.V279V
P2	chr12	122064670	122064670	C	A	nonsynonymous SNV	ORAI1	NM_032790	exon1	c.C23A	p.P8H
P2	chr11	3141665	3141665	C	T	nonsynonymous SNV	OSBPL5	NM_020896	exon6	c.G592A	p.V198I
P2	chr11	73980711	73980711	C	T	nonsynonymous SNV	P4HA3	NM_182904	exon11	c.G1453A	p.V485M
P2	chr17	79803557	79803557	C	T	synonymous SNV	P4HB	NM_000918	exon9	c.G1239A	p.T413T
P2	chr1	2453189	2453189	C	T	nonsynonymous SNV	PANK4	NM_018216	exon2	c.G175A	p.A59T
P2	chr5	140237805	140237805	G	A	synonymous SNV	PCDHA10	NM_031859	exon1	c.G2172A	p.A724A
P2	chr5	140751739	140751739	C	T	nonsynonymous SNV	PCDHGB3	NM_032097	exon1	c.C1778T	p.A593V
P2	chr5	140857873	140857873	G	A	synonymous SNV	PCDHGC3	NM_032402	exon1	c.G2190A	p.P730P
P2	chr3	33886989	33886989	G	A	nonsynonymous SNV	PDCD6IP	NM_001162429	exon12	c.G1565A	p.R522H
P2	chr15	85660946	85660946	C	T	nonsynonymous SNV	PDE8A	NM_001243137	exon17	c.C1394T	p.T465M
P2	chr5	176917897	176917897	C	T	synonymous SNV	PDLIM7	NM_203352	exon7	c.G444A	p.P148P
P2	chr19	7553881	7553881	C	A	nonsynonymous SNV	PEX11G	NM_001270539	exon1	c.G16T	p.G6C
P2	chr3	179689389	179689389	T	C	nonsynonymous SNV	PEX5L	NM_016559	exon2	c.A86G	p.Q29R
P2	chr12	48534546	48534546	G	A	synonymous SNV	PFKM	NM_001166688	exon13	c.G1233A	p.P411P
P2	chr11	3832637	3832637	A	T	nonsynonymous SNV	PGAP2	NM_001145438	exon3	c.A319T	p.T107S
P2	chr13	50087264	50087264	G	C	nonsynonymous SNV	PHF11	NM_001040444	exon4	c.G169C	p.E57Q
P2	chr11	118516526	118516526	C	T	nonsynonymous SNV	PHLDB1	NM_001144758	exon17	c.C3490T	p.R1164W
P2	chr19	43982212	43982212	C	T	nonsynonymous SNV	PHLDB3	NM_198850	exon15	c.G1775A	p.R592H
P2	chr4	527610	527610	A	G	nonsynonymous SNV	PIGG	NM_001127178	exon12	c.A2575G	p.N859D
P3	chr19	44082791	44082791	T	C	synonymous SNV	PINLYP	NM_001193621	exon3	c.T192C	p.H64H
P2	chr8	22212997	22212997	C	T	synonymous SNV	PIWIL2	NM_001135721	exon23	c.C2901T	p.C967C
P2	chr8	145024752	145024752	G	A	synonymous SNV	PLEC	NM_201380	exon1	c.C123T	p.P41P
P2	chr3	48465810	48465810	C	T	nonsynonymous SNV	PLXNB1	NM_002673	exon3	c.G211A	p.G71S

P2	chrX	153037428	153037428	G	A	nonsynonymous SNV	PLXNB3	NM_001163257	exon16	c.G2696A	p.R899Q
P2	chr9	140357909	140357909	C	T	nonsynonymous SNV	PNPLA7	NM_152286	exon28	c.G3226A	p.G1076R
P2	chr9	140409916	140409916	G	A	synonymous SNV	PNPLA7	NM_152286	exon11	c.C1065T	p.S355S
P2	chr10	79769417	79769417	G	A	nonsynonymous SNV	POLR3A	NM_007055	exon14	c.C1787T	p.T596M
P2	chr19	621497	621497	G	A	nonsynonymous SNV	POLRMT	NM_005035	exon10	c.C2201T	p.P734L
P2	chr8	128429072	128429072	A	G	nonsynonymous SNV	POU5F1B	NM_001159542	exon1	c.A961G	p.T321A
P2	chr3	20043420	20043420	T	C	synonymous SNV	PP2D1	NM_001252657	exon2	c.A192G	p.L64L
P2	chr5	149206366	149206366	C	T	nonsynonymous SNV	PPARGC1B	NM_001172698	exon3	c.C383T	p.S128L
P2	chr11	70224300	70224300	C	T	synonymous SNV	PPFIA1	NM_177423	exon26	c.C3549T	p.D1183D
P2	chr12	81653435	81653435	G	A	synonymous SNV	PPFIA2	NM_001220473	exon31	c.C3720T	p.G1240G
P4	chr19	49643309	49643309	C	T	stopgain	PPFIA3	NM_003660	exon18	c.C2332T	p.R778X
P2	chr12	27820121	27820121	G	T	nonsynonymous SNV	PPFIBP1	NM_003622	exon13	c.G1014T	p.E338D
P2	chr1	12853385	12853385	C	T	synonymous SNV	PRAMEF1	NM_023013	exon2	c.C9T	p.I3I
P2	chr1	12921367	12921367	C	A	nonsynonymous SNV	PRAMEF2	NM_023014	exon4	c.C1158A	p.S386R
P2	chr1	12921387	12921387	C	T	nonsynonymous SNV	PRAMEF2	NM_023014	exon4	c.C1178T	p.A393V
P2	chr1	12921451	12921451	C	T	synonymous SNV	PRAMEF2	NM_023014	exon4	c.C1242T	p.A414A
P2	chr6	57185336	57185336	G	A	nonsynonymous SNV	PRIM2	NM_001282488	exon3	c.G236A	p.R79Q
P2	chr4	16026930	16026930	C	T	nonsynonymous SNV	PROM1	NM_001145850	exon5	c.G515A	p.G172D
P2	chr2	95954292	95954292	C	T	nonsynonymous SNV	PROM2	NM_144707	exon22	c.C2396T	p.A799V
P2	chr2	95954294	95954294	G	A	nonsynonymous SNV	PROM2	NM_144707	exon22	c.G2398A	p.V800I
P2	chr16	30666043	30666043	G	A	nonsynonymous SNV	PRR14	NM_024031	exon8	c.G752A	p.R251H
P2	chr12	72176363	72176363	G	A	nonsynonymous SNV	RAB21	NM_014999	exon6	c.G460A	p.V154M
P3	chr7	102232889	102232889	T	C	nonsynonymous SNV	RASA4B	NM_001277335	exon16	c.A1673G	p.Q558R
P3	chr7	102246378	102246378	C	T	nonsynonymous SNV	RASA4B	NM_001277335	exon5	c.G355A	p.E119K
P2	chr11	66411150	66411150	G	A	synonymous SNV	RBM14-RBM4	NM_001198845	exon2	c.G567A	p.A189A
P2	chr13	49085916	49085916	C	T	nonsynonymous SNV	RCBTB2	NM_001286832	exon5	c.G94A	p.V32M
P2	chr5	98128962	98128962	C	T	synonymous SNV	RGMB	NM_001012761	exon5	c.C942T	p.A314A
P2	chr1	26881684	26881684	C	T	nonsynonymous SNV	RPS6KA1	NM_002953	exon10	c.C799T	p.R267W
P2	chr1	218504376	218504376	G	T	nonsynonymous SNV	RRP15	NM_016052	exon5	c.G792T	p.K264N
P4	chr21	45108081	45108081	A	G	nonsynonymous SNV	RRP1B	NM_015056	exon13	c.A1826G	p.N609S
P4	chr11	63487376	63487376	G	A	nonsynonymous SNV	RTN3	NM_001265589	exon3	c.G1402A	p.V468M
P2	chr3	187088638	187088638	C	T	nonsynonymous SNV	RTP4	NM_022147	exon2	c.C218T	p.T73M
P2	chr18	76753731	76753731	C	T	synonymous SNV	SALL3	NM_171999	exon2	c.C1740T	p.T580T
P2	chr11	10014581	10014581	G	A	stopgain	SBF2	NM_030962	exon11	c.C1123T	p.Q375X
P2	chr17	71361403	71361403	C	T	nonsynonymous SNV	SDK2	NM_001144952	exon38	c.G5299A	p.V1767M
P2	chr17	71382626	71382626	C	T	nonsynonymous SNV	SDK2	NM_001144952	exon31	c.G4456A	p.E1486K
P2	chr1	156142697	156142697	G	A	synonymous SNV	SEMA4A	NM_001193300	exon11	c.G1215A	p.T405T
P2	chr3	47164963	47164963	C	T	nonsynonymous SNV	SETD2	NM_014159	exon3	c.G1163A	p.R388Q
P2	chr3	20225420	20225420	C	A	nonsynonymous SNV	SGOL1	NM_001199257	exon2	c.G100T	p.G34C
P2	chr17	7534963	7534963	C	T	synonymous SNV	SHBG	NM_001146280	exon5	c.C612T	p.A204A
P2	chr19	55944952	55944952	C	T	synonymous SNV	SHISA7	NM_001145176	exon4	c.G1188A	p.S396S
P2	chr4	77661881	77661881	A	G	nonsynonymous SNV	SHROOM3	NM_020859	exon5	c.A2555G	p.E852G
P2	chr20	44685925	44685925	G	A	nonsynonymous SNV	SLC12A5	NM_001134771	exon25	c.G3311A	p.R1104H
P2	chr11	793531	793531	G	A	synonymous SNV	SLC25A22	NM_024698	exon5	c.C291T	p.D97D
P2	chr6	35911729	35911729	C	T	nonsynonymous SNV	SLC26A8	NM_001193476	exon20	c.G2861A	p.R954H
P2	chr9	131118031	131118031	C	T	nonsynonymous SNV	SLC27A4	NM_005094	exon12	c.C1730T	p.A577V
P2	chr12	7967015	7967015	C	T	nonsynonymous SNV	SLC2A14	NM_001286236	exon10	c.G1133A	p.R378Q
P2	chr6	88210308	88210308	G	A	nonsynonymous SNV	SLC35A1	NM_006416	exon3	c.G277A	p.V93M
P2	chr5	150856184	150856184	C	T	nonsynonymous SNV	SLC36A1	NM_078483	exon9	c.C856T	p.R286W
P2	chr21	43999880	43999880	G	A	nonsynonymous SNV	SLC37A1	NM_018964	exon20	c.G1556A	p.C519Y
P2	chr12	56630942	56630942	G	A	nonsynonymous SNV	SLC39A5	NM_173596	exon12	c.G1297A	p.A433T
P2	chr11	57254576	57254576	G	A	nonsynonymous SNV	SLC43A1	NM_003627	exon14	c.C1525T	p.P509S
P2	chr12	48172839	48172839	G	A	synonymous SNV	SLC48A1	NM_017842	exon2	c.G165A	p.T55T
P2	chr12	101595962	101595962	G	T	nonsynonymous SNV	SLC5A8	NM_145913	exon3	c.C449A	p.P150H
P2	chr1	110737350	110737350	G	A	synonymous SNV	SLC6A17	NM_001010898	exon9	c.G1449A	p.T483T
P2	chr10	98799812	98799812	C	T	nonsynonymous SNV	SLIT1	NM_003061	exon21	c.G2230A	p.V744M
P2	chr3	164908587	164908587	C	A	nonsynonymous SNV	SLITRK3	NM_014926	exon2	c.G32T	p.R11I
P2	chr5	176056580	176056580	C	T	nonsynonymous SNV	SNCB	NM_001001502	exon3	c.G76A	p.V26I
P3	chr6	158357041	158357041	A	G	nonsynonymous SNV	SNX9	NM_016224	exon14	c.A1412G	p.Y471C
P1	chr1	109890149	109890149	G	A	nonsynonymous SNV	SORT1	NM_001205228	exon7	c.C380T	p.S127L
P2	chr4	52926593	52926593	G	A	synonymous SNV	SPATA18	NM_145263	exon2	c.G96A	p.T32T
P2	chr9	90538055	90538055	C	T	nonsynonymous SNV	SPATA31C1	NM_001145124	exon4	c.C3233T	p.A1078V
P2	chr1	32256451	32256451	C	T	nonsynonymous SNV	SPOCD1	NM_001281987	exon16	c.G3365A	p.R1122H
P2	chr12	53461960	53461960	G	A	synonymous SNV	SPRYD3	NM_032840	exon7	c.C822T	p.I274I
P2	chr19	41029363	41029363	C	G	nonsynonymous SNV	SPTBN4	NM_020971	exon17	c.C3674G	p.A1225G
P2	chr5	179260189	179260189	G	A	synonymous SNV	SQSTM1	NM_001142298	exon7	c.G660A	p.T220T
P2	chr14	35482700	35482700	C	T	nonsynonymous SNV	SRP54	NM_003136	exon9	c.C785T	p.A262V
P2	chr15	42983298	42983298	G	A	synonymous SNV	STARD9	NM_020759	exon23	c.G9522A	p.K3174K
P2	chr12	56750351	56750351	G	A	nonsynonymous SNV	STAT2	NM_005419	exon2	c.C5T	p.A2V
P2	chr2	48808621	48808621	T	C	synonymous SNV	STON1-GTF2A1L	NM_001198594	exon1	c.T849C	p.P283P
P2	chr9	130440720	130440720	G	A	nonsynonymous SNV	STXBP1	NM_001032221	exon16	c.G1370A	p.R457H
P2	chr20	46318966	46318966	C	A	nonsynonymous SNV	SULF2	NM_198596	exon5	c.G641T	p.R214M
P2	chr6	152557290	152557290	A	G	nonsynonymous SNV	SYNE1	NM_033071	exon109	c.T20135C	p.M6712T
P3	chr19	36497373	36497373	A	G	synonymous SNV	SYNE4	NM_001297735	exon3	c.T480C	p.C160C
P2	chr6	132966980	132966980	G	T	nonsynonymous SNV	TAAR1	NM_138327	exon1	c.C163A	p.H55N
P2	chr10	123843251	123843251	G	A	synonymous SNV	TACC2	NM_001291877	exon4	c.G1236A	p.P412P
P1	chr12	11183722	11183722	A	C	nonsynonymous SNV	TAS2R31	NM_176885	exon1	c.T213G	p.F71L
P4	chr12	11183421	11183421	C	T	nonsynonymous SNV	TAS2R31	NM_176885	exon1	c.G514A	p.V172M
P4	chr12	11183427	11183427	T	G	nonsynonymous SNV	TAS2R31	NM_176885	exon1	c.A508C	p.S170R
P2	chr17	59482684	59482684	C	T	synonymous SNV	TBX2	NM_005994	exon6	c.C1173T	p.T391T
P2	chr5	149755432	149755432	C	T	nonsynonymous SNV	TCOF1	NM_001135244	exon12	c.C1853T	p.A618V
P2	chr16	10729667	10729667	T	C	nonsynonymous SNV	TEKT5	NM_144674	exon6	c.A1195G	p.T399A

P2	chr4	183601429	183601429	C	T	synonymous SNV	TENM3	NM_001080477	exon8	c.C1566T	p.C522C
P2	chr4	183675584	183675584	A	G	nonsynonymous SNV	TENM3	NM_001080477	exon21	c.A4064G	p.N1355S
P2	chr2	74328243	74328243	G	T	nonsynonymous SNV	TET3	NM_001287491	exon11	c.G4328T	p.S1443I
P2	chr8	133953708	133953708	C	T	synonymous SNV	TG	NM_003235	exon26	c.C5154T	p.T1718T
P2	chr15	90168813	90168813	A	G	nonsynonymous SNV	TICRR	NM_152259	exon20	c.A5272G	p.K1758E
P2	chr6	43466794	43466794	C	T	nonsynonymous SNV	TJAP1	NM_001146018	exon5	c.C55T	p.R19W
P2	chr4	186997978	186997978	G	A	nonsynonymous SNV	TLR3	NM_003265	exon2	c.G205A	p.A69T
P2	chr10	98287041	98287041	T	C	nonsynonymous SNV	TM9SF3	NM_020123	exon14	c.A1631G	p.Y544C
P2	chr1	9661353	9661353	C	A	nonsynonymous SNV	TMEM201	NM_001010866	exon5	c.C797A	p.P266H
P3	chr12	83251095	83251095	G	A	synonymous SNV	TMTC2	NM_152588	exon2	c.G390A	p.T130T
P2	chr9	117848307	117848307	T	C	nonsynonymous SNV	TNC	NM_002160	exon3	c.A1703G	p.H568R
P2	chr1	151131714	151131714	G	A	nonsynonymous SNV	TNFAIP8L2	NM_024575	exon2	c.G541A	p.E181K
P2	chr8	22974499	22974499	C	T	synonymous SNV	TNFRSF10C	NM_003841	exon5	c.C735T	p.I245I
P2	chr7	5415779	5415779	G	A	synonymous SNV	TNRC18	NM_001080495	exon9	c.C2685T	p.H895H
P2	chr9	140174129	140174129	G	A	nonsynonymous SNV	TOR4A	NM_017723	exon2	c.G988A	p.E330K
P4	chr17	7578406	7578406	C	T	nonsynonymous SNV	TP53	NM_001126115	exon1	c.G128A	p.R43H
P2	chr3	36898406	36898406	G	A	nonsynonymous SNV	TRANK1	NM_014831	exon12	c.C2675T	p.T892M
P2	chr6	42236388	42236388	A	T	nonsynonymous SNV	TRERF1	NM_001297574	exon5	c.T941A	p.L314Q
P4	chr22	38120429	38120429	T	C	synonymous SNV	TRIOBP	NM_001039141	exon7	c.T1866C	p.D622D
P2	chr3	101284699	101284699	T	C	synonymous SNV	TRMT10C	NM_017819	exon2	c.T1074C	p.R358R
P2	chr17	16330832	16330832	C	T	synonymous SNV	TRPV2	NM_016113	exon8	c.C1321T	p.L441L
P2	chr7	128802240	128802240	G	A	nonsynonymous SNV	TSPAN33	NM_178562	exon3	c.G166A	p.A56T
P2	chr5	112769438	112769438	G	T	nonsynonymous SNV	TSSK1B	NM_032028	exon1	c.C1099A	p.Q367K
P2	chr2	179418902	179418902	T	C	nonsynonymous SNV	TTN	NM_001256850	exon283	c.A84013G	p.T28005A
P2	chr2	220116419	220116419	G	A	synonymous SNV	TUBA4A	NM_006000	exon3	c.C243T	p.G81G
P1	chr1	162557345	162557345	T	A	nonsynonymous SNV	UAP1	NM_003115	exon6	c.T915A	p.S305R
P2	chr1	11345759	11345759	G	A	synonymous SNV	UBIAD1	NM_013319	exon2	c.G588A	p.P196P
P2	chr16	4910928	4910928	C	T	nonsynonymous SNV	UBN1	NM_001288656	exon7	c.C935T	p.T312M
P2	chr2	170936456	170936456	G	T	nonsynonymous SNV	UBR3	NM_172070	exon37	c.G5332T	p.V1778F
P2	chr2	128903396	128903396	A	G	nonsynonymous SNV	UGGT1	NM_020120	exon18	c.A1871G	p.E624G
P2	chr9	6497255	6497255	G	C	synonymous SNV	UHRF2	NM_152896	exon11	c.G1662C	p.R554R
P2	chr17	73809925	73809925	G	A	nonsynonymous SNV	UNK	NM_001080419	exon6	c.G842A	p.C281Y
P2	chr21	33706597	33706597	G	A	nonsynonymous SNV	URB1	NM_014825	exon29	c.C4732T	p.R1578W
P2	chr6	133034996	133034996	A	C	nonsynonymous SNV	VNN1	NM_004666	exon1	c.T179G	p.L60W
P2	chr3	51475690	51475690	C	T	nonsynonymous SNV	VPRBP	NM_001171904	exon7	c.G734A	p.G245D
P2	chr12	122748206	122748206	C	T	nonsynonymous SNV	VPS33A	NM_022916	exon3	c.G209A	p.R70H
P2	chr15	83478514	83478514	G	A	stopgain	WHAMM	NM_001080435	exon1	c.G36A	p.W12X
P2	chr8	10756026	10756026	A	G	synonymous SNV	XKR6	NM_173683	exon3	c.T1362C	p.A454A
P2	chr11	102100535	102100535	G	T	nonsynonymous SNV	YAP1	NM_006106	exon7	c.G1217T	p.G406V
P2	chr12	10875506	10875506	C	T	nonsynonymous SNV	YBX3	NM_003651	exon1	c.G205A	p.A69T
P2	chr1	154987895	154987895	C	T	synonymous SNV	ZBTB7B	NM_001256455	exon2	c.C759T	p.S253S
P2	chr14	75537900	75537900	G	A	synonymous SNV	ZC2HC1C	NM_024643	exon2	c.G624A	p.T208T
P3	chr5	840661	840661	A	G	nonsynonymous SNV	ZDHHC11	NM_024786	exon5	c.T733C	p.F245L
P2	chr20	50768945	50768945	C	T	nonsynonymous SNV	ZFP64	NM_199426	exon6	c.G1780A	p.E594K
P2	chr1	40928756	40928756	T	C	nonsynonymous SNV	ZFP69B	NM_023070	exon5	c.T1100C	p.V367A
P2	chr3	124952610	124952610	C	T	synonymous SNV	ZNF148	NM_021964	exon9	c.G960A	p.T320T
P2	chr19	12243837	12243837	C	T	synonymous SNV	ZNF20	NM_001203250	exon4	c.G1155A	p.T385T
P2	chr11	123596938	123596938	G	A	nonsynonymous SNV	ZNF202	NM_001301780	exon7	c.C1714T	p.R572C
P2	chr17	30696676	30696676	G	A	synonymous SNV	ZNF207	NM_003457	exon11	c.G1335A	p.P445P
P2	chr19	45575818	45575818	A	G	synonymous SNV	ZNF296	NM_145288	exon3	c.T469C	p.L157L
P2	chr19	57868510	57868510	G	C	nonsynonymous SNV	ZNF304	NM_020657	exon3	c.G1273C	p.G425R
P2	chr20	44582471	44582471	G	A	synonymous SNV	ZNF335	NM_022095	exon18	c.C2559T	p.G853G
P2	chr19	44418260	44418260	G	A	nonsynonymous SNV	ZNF45	NM_003425	exon10	c.C1328T	p.P443L
P2	chr15	64967247	64967247	A	C	nonsynonymous SNV	ZNF609	NM_015042	exon4	c.A2194C	p.K732Q
P2	chr16	31090677	31090677	T	C	nonsynonymous SNV	ZNF646	NM_014699	exon2	c.T3032C	p.I1011T
P2	chr8	37555536	37555536	C	T	stopgain	ZNF703	NM_025069	exon2	c.C1117T	p.Q373X
P4	chr3	75787576	75787576	A	G	nonsynonymous SNV	ZNF717	NM_001290208	exon5	c.T1198C	p.C400R
P2	chr7	149557821	149557821	G	A	synonymous SNV	ZNF862	NM_001099220	exon7	c.G1572A	p.A524A
P2	chr19	22940393	22940393	A	C	nonsynonymous SNV	ZNF99	NM_001080409	exon4	c.T2318G	p.F773C