

Table 1: Number of de novo variants identified for each parent-child trio

Patient	Chr	StartPosition	VariantType	RefgeneGeneName	RefgeneExonFunction
1	2	152473977	Snv	NEB	nonsynonymous SNV
1	2	203417544	Indel	BMP2	frameshift deletion
1	3	49049511	Snv	WDR6	nonsynonymous SNV
1	6	30954393	Snv	MUC21	nonframeshift substitution
1	6	32485852	Indel	HLA-DRB5	frameshift insertion
1	6	32487401	Snv	HLA-DRB5	nonsynonymous SNV
1	7	100482040	Indel	SRRT	nonframeshift deletion
1	8	10467673	Snv	RP1L1	nonsynonymous SNV
1	11	1264328	Snv	MUC5B	nonsynonymous SNV
1	11	1264336	Snv	MUC5B	nonsynonymous SNV
1	11	1265144	Snv	MUC5B	nonsynonymous SNV
1	11	1265339	Snv	MUC5B	nonsynonymous SNV
1	11	1265687	Snv	MUC5B	nonsynonymous SNV
1	11	1265691	Indel	MUC5B	nonframeshift deletion
1	11	1265713	Indel	MUC5B	nonframeshift deletion
1	11	1269110	Snv	MUC5B	nonsynonymous SNV
1	11	1269856	Snv	MUC5B	nonsynonymous SNV
1	11	1269860	Snv	MUC5B	nonsynonymous SNV
1	11	66335541	Snv	CTSF	nonsynonymous SNV
1	15	41853508	Indel	TYRO3	nonframeshift insertion
1	18	34261459	Indel	FHOD3	frameshift deletion
1	19	3633460	Indel	PIP5K1C	frameshift deletion
1	19	15271953	Indel	NOTCH3	frameshift deletion
1	19	47615762	Indel	ZC3H4	nonframeshift deletion
7	3	52833908	Snv	ITIH3	nonsynonymous SNV
7	4	1388508	Snv	CRIPAK	nonframeshift substitution
7	5	115148957	Indel	CDO1	splicing
7	6	17605166	Snv	FAM8A1	nonsynonymous SNV
7	6	30954694	Snv	MUC21	nonsynonymous SNV
7	6	32489854	Snv	HLA-DRB5	nonframeshift substitution
7	6	168377178	Snv	HGC6.3	nonsynonymous SNV
7	6	168377232	Snv	HGC6.3	nonsynonymous SNV
7	12	133160024	Snv	FBRSL1	nonsynonymous SNV
7	13	21742539	Indel	SKA3	splicing
7	16	54319092	Snv	IRX3	nonsynonymous SNV
7	18	30913142	Indel	C18orf34	frameshift insertion
7	19	14561855	Snv	PKN1	nonsynonymous SNV
7	19	15271746	Indel	NOTCH3	frameshift insertion
7	19	58907572	Indel	LOC646862	nonframeshift deletion
7	1	248617054	Indel	OR2T2	frameshift insertion
7	21	46117285	Snv	KRTAP10-12	nonsynonymous SNV
7	21	46117286	Snv	KRTAP10-12	nonsynonymous SNV
20	1	152187195	Snv	HRNR	stopgain SNV
20	2	25387526	Snv	POMC	nonsynonymous SNV
20	2	189943835	Indel	COL5A2	splicing
20	3	50323926	Snv	C3orf45	nonsynonymous SNV
20	4	1388508	Snv	CRIPAK	nonframeshift substitution
20	4	84391410	Snv	FAM175A	nonsynonymous SNV
20	4	147561265	Indel	POU4F2	nonframeshift deletion

20 5	138661353	Indel	MATR3	splicing
20 6	30954302	Snv	MUC21	nonsynonymous SNV
20 6	30954374	Indel	MUC21	frameshift substitution
20 6	30954378	Indel	MUC21	frameshift insertion
20 6	30954393	Snv	MUC21	nonframeshift substitution
20 6	30954694	Snv	MUC21	nonsynonymous SNV
20 9	101558679	Snv	ANKS6	nonsynonymous SNV
20 10	3187897	Snv	PITRM1	nonsynonymous SNV
20 10	98273394	Indel	TLL2	nonframeshift deletion
20 11	61537824	Indel	C11orf9	frameshift deletion
20 11	64119081	Snv	CCDC88B	nonsynonymous SNV
20 12	11546675	Snv	PRB2	nonsynonymous SNV
20 12	14943486	Snv	WBP11	nonsynonymous SNV
20 12	53491528	Indel	IGFBP6	nonframeshift deletion
20 19	15271707	Snv	NOTCH3	stopgain SNV
20 19	23836725	Snv	ZNF675	nonsynonymous SNV
20 22	41650469	Indel	RANGAP1	nonframeshift deletion
26 3	42251578	Indel	TRAK1	nonframeshift deletion
26 3	46751077	Indel	TMIE	nonframeshift deletion
26 3	128292319	Indel	C3orf27	frameshift deletion
26 3	195506555	Snv	MUC4	nonsynonymous SNV
26 3	195506558	Snv	MUC4	nonsynonymous SNV
26 4	1388438	Indel	CRIPAK	frameshift deletion
26 4	54319248	Indel	FIP1L1	frameshift deletion
26 6	1390289	Indel	FOXF2	nonframeshift deletion
26 6	1611811	Indel	FOXC1	nonframeshift insertion
26 6	30954694	Snv	MUC21	nonsynonymous SNV
26 6	30955120	Indel	MUC21	nonframeshift deletion
26 6	30994035	Indel	MUC22	nonframeshift deletion
26 6	30996691	Indel	MUC22	nonframeshift deletion
26 6	30996791	Indel	MUC22	nonframeshift deletion
26 6	30996811	Indel	MUC22	nonframeshift deletion
26 6	114181210	Indel	MARCKS	frameshift insertion
26 6	161519357	Indel	MAP3K4	nonframeshift deletion
26 6	170871046	Snv	TBP	nonframeshift substitution
26 7	6820986	Snv	RSPH10B,RSPH10B2	nonsynonymous SNV
26 8	101724994	Indel	PABPC1	frameshift insertion
26 9	100616704	Indel	FOXE1	nonframeshift deletion
26 9	131452286	Indel	SET	nonframeshift deletion
26 10	26856216	Indel	APBB1IP	nonframeshift insertion
26 11	6578614	Indel	DNHD1	nonframeshift deletion
26 11	104878041	Indel	CASP5	frameshift deletion
26 12	9085328	Indel	PHC1	nonframeshift deletion
26 12	11420392	Indel	PRB3	frameshift deletion
26 12	19592757	Indel	AEBP2	nonframeshift deletion
26 12	132313145	Snv	MMP17	nonsynonymous SNV
26 12	132628617	Indel	DDX51	nonframeshift deletion
26 13	72440705	Indel	DACH1	nonframeshift deletion
26 17	17039574	Indel	MPRIIP	nonframeshift deletion
26 17	32956192	Snv	TMEM132E	nonsynonymous SNV
26 17	71205865	Indel	FAM104A	nonframeshift deletion

26 18	9887389	Indel	TXNDC2	nonframeshift deletion
26 19	3762705	Snv	MRPL54	nonsynonymous SNV
26 19	15272192	Snv	NOTCH3	stopgain SNV
26 19	52888012	Indel	ZNF880	frameshift deletion
26 20	61444633	Indel	OGFR	frameshift deletion
26 20	61444635	Indel	OGFR	frameshift deletion
26 20	61444650	Indel	OGFR	nonframeshift deletion
26 22	35661544	Indel	HMGXB4	frameshift insertion
26 X	21627678	Indel	CNKS2	nonframeshift deletion
26 X	66765170	Indel	AR	nonframeshift insertion
26 X	140993885	Indel	MAGEC1	nonframeshift deletion

RefgeneExonLocation

NEB:NM_001164507:exon75:c.A11082T:p.L3694F,NEB:NM_001164508:exon75:c.A11082T:p.L3694F,NEB:NM_C
BMPR2:NM_001204:exon11:c.1519delA:p.I507fs,
WDR6:NM_018031:exon2:c.A634C:p.N212H,
MUC21:NM_001010909:exon2:c.441_486CAGCACAGCCACCAACTCTGACTCCAGCACAACTCCAGTGAGGC
HLA-DRB5:NM_002125:exon5:c.765_766insA:p.H256fs,
HLA-DRB5:NM_002125:exon3:c.C398T:p.A133V,
SRRT:NM_001128852:exon7:c.809_811del:p.270_271del,SRRT:NM_001128854:exon7:c.809_811del:p.270_271c
RP1L1:NM_178857:exon4:c.G3935A:p.G1312E,
MUC5B:NM_002458:exon31:c.C6218T:p.P2073L,
MUC5B:NM_002458:exon31:c.T6226C:p.W2076R,
MUC5B:NM_002458:exon31:c.G7034A:p.R2345H,
MUC5B:NM_002458:exon31:c.A7229G:p.N2410S,
MUC5B:NM_002458:exon31:c.G7577T:p.R2526I,
MUC5B:NM_002458:exon31:c.7581_7595del:p.2527_2532del,
MUC5B:NM_002458:exon31:c.7603_7665del:p.2535_2555del,
MUC5B:NM_002458:exon31:c.A11000G:p.N3667S,
MUC5B:NM_002458:exon31:c.C11746G:p.P3916A,
MUC5B:NM_002458:exon31:c.C11750G:p.T3917R,
CTSF:NM_003793:exon2:c.T226G:p.S76A,
TYRO3:NM_006293:exon2:c.308_309insCCTGAA:p.S103delinsSLN,
FHOD3:NM_025135:exon12:c.1371_1372del:p.457_458del,
PIP5K1C:NM_012398:exon17:c.1979delC:p.P660fs,
NOTCH3:NM_000435:exon33:c.6461_6486del:p.2154_2162del,
ZC3H4:NM_015168:exon2:c.57_80del:p.19_27del,
ITIH3:NM_002217:exon9:c.C1046T:p.T349M,
CRIPAK:NM_175918:exon1:c.209_238CCCATGTGGAGTGCCACCTGCTCATGTGC,
CDO1:NM_001801:exon3:c.171-2->T
FAM8A1:NM_016255:exon3:c.T863C:p.I288T,
MUC21:NM_001010909:exon2:c.C742G:p.P248A,
HLA-DRB5:NM_002125:exon2:c.196_198GAG,
HGC6.3:NM_001129895:exon1:c.A155T:p.Q52L,
HGC6.3:NM_001129895:exon1:c.T101C:p.V34A,
FBRSL1:NM_001142641:exon17:c.C2798T:p.P933L,
SKA3:NM_145061:exon5:c.332-1->TGGATATAGTCCACGTGTCAAGAAAAATTCA,NM_001166017:exon5:c.332-
IRX3:NM_024336:exon2:c.G701C:p.G234A,
C18orf34:NM_198995:exon10:c.874dupA:p.M292fs,C18orf34:NM_001105528:exon9:c.874dupA:p.M292fs,
PKN1:NM_213560:exon6:c.A922C:p.T308P,PKN1:NM_002741:exon6:c.A904C:p.T302P,
NOTCH3:NM_000435:exon33:c.6692dupC:p.P2231fs,
LOC646862:NM_001195135:exon1:c.116_118del:p.39_40del,
OR2T2:NM_001004136:exon1:c.956_957insTG:p.T319fs,
KRTAP10-12:NM_198699:exon1:c.C169T:p.R57C,
KRTAP10-12:NM_198699:exon1:c.G170A:p.R57H,
HRNR:NM_001009931:exon3:c.C6910T:p.R2304X,
POMC:NM_001035256:exon3:c.C116T:p.T39M,POMC:NM_000939:exon2:c.C116T:p.T39M,
COL5A2:NM_000393:exon16:c.961-2->T
C3orf45:NM_153215:exon2:c.G83A:p.S28N,
CRIPAK:NM_175918:exon1:c.209_238CCCATGTGGAGTGCCACCTGCTCATGTGC,
FAM175A:NM_139076:exon5:c.C422T:p.T141I,
POU4F2:NM_004575:exon2:c.535_537del:p.179_179del,

MATR3:NM_199189:exon16:c.2371+2->ATA,NM_001194954:exon15:c.2371+2->ATA,NM_018834:exon13:c.2371
MUC21:NM_001010909:exon2:c.C350T:p.A117V,
MUC21:NM_001010909:exon2:c.422_428GAC,
MUC21:NM_001010909:exon2:c.426_427insTGTG:p.T142fs,
MUC21:NM_001010909:exon2:c.441_486CAGCACAGCCACCAACTCTGACTCCAGCACAACTCCAGTGAGGC
MUC21:NM_001010909:exon2:c.C742G:p.P248A,
ANKS6:NM_173551:exon1:c.G95T:p.G32V,
PITRM1:NM_001242307:exon21:c.A2351G:p.N784S,PITRM1:NM_014889:exon21:c.A2348G:p.N783S,PITRM1:N
TLL2:NM_012465:exon1:c.47_49del:p.16_17del,
C11orf9:NM_001127392:exon5:c.567_570del:p.189_190del,C11orf9:NM_013279:exon5:c.540_543del:p.180_181
CCDC88B:NM_032251:exon18:c.G3092A:p.R1031H,
PRB2:NM_006248:exon3:c.T337A:p.S113T,
WBP11:NM_016312:exon10:c.C1213T:p.P405S,
IGFBP6:NM_002178:exon1:c.27_29del:p.9_10del,
NOTCH3:NM_000435:exon33:c.C6732A:p.Y2244X,
ZNF675:NM_138330:exon4:c.A1010G:p.E337G,
RANGAP1:NM_002883:exon11:c.1101_1103del:p.367_368del,
TRAK1:NM_014965:exon13:c.1890_1895del:p.630_632del,
TMIE:NM_147196:exon4:c.370_375del:p.124_125del,
C3orf27:NM_007354:exon3:c.253_254del:p.85_85del,
MUC4:NM_018406:exon2:c.G11896A:p.A3966T,
MUC4:NM_018406:exon2:c.C11893G:p.H3965D,
CRIPAK:NM_175918:exon1:c.139_161del:p.47_54del,
FIP1L1:NM_001134937:exon16:c.1429_1430del:p.477_477del,FIP1L1:NM_030917:exon16:c.1447_1448del:p.48
FOXF2:NM_001452:exon1:c.107_109del:p.36_37del,
FOXC1:NM_001453:exon1:c.1131_1132insGGC:p.G377delinsGG,
MUC21:NM_001010909:exon2:c.C742G:p.P248A,
MUC21:NM_001010909:exon2:c.1168_1257del:p.390_419del,
MUC22:NM_001198815:exon3:c.827_847del:p.276_283del,
MUC22:NM_001198815:exon3:c.3483_3512del:p.1161_1171del,
MUC22:NM_001198815:exon3:c.3583_3597del:p.1195_1199del,
MUC22:NM_001198815:exon3:c.3603_3617del:p.1201_1206del,
MARCKS:NM_002356:exon2:c.454dupA:p.K152fs,
MAP3K4:NM_005922:exon17:c.3572_3577del:p.1191_1193del,
TBP:NM_003194:exon3:c.222_249GCAGCAGCAGCAGCAGCAGCAGCAGCAG,TBP:NM_001172085:exon2:c.16
RSPH10B2:NM_001099697:exon15:c.C1637T:p.T546M,RSPH10B:NM_173565:exon15:c.C1637T:p.T546M,
PABPC1:NM_002568:exon6:c.761_762insT:p.K254fs,
FOXE1:NM_004473:exon1:c.508_519del:p.170_173del,
SET:NM_001248001:exon1:c.21_23del:p.7_8del,
APBB1IP:NM_019043:exon15:c.1800_1801insCCG:p.P600delinsPP,
DNHD1:NM_144666:exon25:c.8089_8091del:p.2697_2697del,
CASP5:NM_001136112:exon3:c.241delA:p.T81fs,CASP5:NM_004347:exon3:c.202delA:p.T68fs,CASP5:NM_0011
PHC1:NM_004426:exon8:c.1275_1277del:p.425_426del,
PRB3:NM_006249:exon3:c.666_724del:p.222_242del,
AEBP2:NM_153207:exon1:c.124_126del:p.42_42del,AEBP2:NM_001114176:exon1:c.124_126del:p.42_42del,
MMP17:NM_016155:exon1:c.G106A:p.G36S,
DDX51:NM_175066:exon1:c.223_225del:p.75_75del,
DACH1:NM_004392:exon1:c.201_203del:p.67_68del,DACH1:NM_080760:exon1:c.201_203del:p.67_68del,DACH
MPRIP:NM_201274:exon6:c.546_551del:p.182_184del,MPRIP:NM_015134:exon6:c.546_551del:p.182_184del,
TMEM132E:NM_207313:exon5:c.G1037A:p.R346Q,
FAM104A:NM_001098832:exon4:c.425_427del:p.142_143del,FAM104A:NM_032837:exon3:c.362_364del:p.121_

TXNDC2:NM_032243:exon2:c.712_756del:p.238_252del,TXNDC2:NM_001098529:exon2:c.913_957del:p.305_31
MRPL54:NM_172251:exon1:c.A7G:p.T3A,
NOTCH3:NM_000435:exon33:c.A6247T:p.K2083X,
ZNF880:NM_001145434:exon4:c.1179_1203del:p.393_401del,
OGFR:NM_007346:exon7:c.1666delG:p.E556fs,
OGFR:NM_007346:exon7:c.1668_1678del:p.556_560del,
OGFR:NM_007346:exon7:c.1683_1730del:p.561_577del,
HMGXB4:NM_001003681:exon5:c.1163dupA:p.E388fs,
CNKSR2:NM_014927:exon20:c.2635_2637del:p.879_879del,CNKSR2:NM_001168648:exon20:c.2635_2637del:p
AR:NM_000044:exon1:c.182_183insGCAGCA:p.Q61delinsQQQ,
MAGEC1:NM_005462:exon4:c.695_799del:p.232_267del,

04543:exon71:c.A10317T:p.L3439F,

C,

del,SRRT:NM_015908:exon7:c.809_811del;p.270_271del,SRRT:NM_001128853:exon7:c.809_811del;p.2

1->TGGATATAGTCCACGTGTCAAGAAAAATTCA

|+2->ATA,NM_001194956:exon12:c.1507+2->ATA,NM_001194955:exon13:c.2371+2->ATA

C,

M_001242309:exon18:c.A2054G:p.N685S,

del,

3_483del,FIP1L1:NM_001134938:exon13:c.1225_1226del:p.409_409del,

2_189GCAGCAGCAGCAGCAGCAGCAGCAGCAG,

136109:exon2:c.28delA:p.T10fs,

1:NM_080759:exon1:c.201_203del:p.67_68del,

122del,

19del,

.879_879del,CNKSR2:NM_001168649:exon19:c.2488_2490del:p.830_830del,CNKSR2:NM_001168647:e

70_271del,

xon19:c.2545_2547del;p.849_849del,