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# **Supplemental Data**

# **Biallelic Mutations in Citron Kinase**

## Link Mitotic Cytokinesis to Human

## **Primary Microcephaly**

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#### Supplemental Data

Supplemental Data include 3 figures and 2 tables.



#### Figure S1. Mutations in the kinase domain of CIT-K cause primary microcephaly

(A) Sequencing chromatograms illustrating *CIT* mutations in the affected children. (B) Evolutionary conservation of the residues with patient mutations across the animal kingdom. (C) Kinase domain conservation among CIT-K and other AGC kinases. The residues with patient mutations are marked with black boxes. The sequence alignment was performed using Vector NTI (Invitrogen). (D) The crystal structure of the kinase domain of ROCK1, with residues with patient mutations labeled. Hydroxyfasudil, a competitive inhibitor of ATP, is marked with arrowhead showing the ATP binding pocket. The kinase domain and residues of ROCK1 were viewed by PyMol (https://www.pymol.org).



### Figure S2. Expression level and localization of CIT-N in patient-derived NPCs

(A) Representative immunocytochemistry images of PAX6+ NPCs differentiated from iPSCs. Scale bar =  $10\mu$ m. (B) Relative mRNA level of *CIT* in affected and control NPCs. (n=3 cultures for each group). Student's t test. Bar graph: mean ± s.e.m (C) Representative immunocytochemistry images for CIT-K (white arrowhead) and midbody marker Aurora kinase B (AURKB) (yellow arrowhead) during cytokinesis in NPCs with absent, heterozygous or homozygous *CIT* mutations. The localization of CIT-K and AURKB was indistinguishable among all conditions. Scale bar =  $10\mu$ m.

### Figure S2



#### Figure S3. Identification of correctly-targeted iPSC clones in genome editing

(A) Forward primer F1 outside the 5' recombination arm, reverse primer R1 inside the puromycin cassette. This PCR allowed identification of iPSC clones with homologous targeting vector recombination. (B) Forward (F2) and reverse (R2) primers outside of Exon4 and the puromycin cassette. A ~2500 bp band represented the recombined allele, and a ~1500bp band represented the unmodified allele. Clone #35 and #36 were homozygous for homologous recombination, and were chosen for downstream studies. (C) Sanger sequencing confirmed c.317G>T mutation corrected in clone #36. (D) PCR identification of clones with LoxP-Puro-LoxP cassette removal. A ~2500 bp band represented the corrected allele, and a ~1500bp band represented removal of the LoxP-Puro-LoxP cassette. Clone #36-2 and #36-3, with LoxP-Puro-LoxP cassette removal on both alleles, were used for downstream studies.

## Table S1 Genetic variants identified in each family from exome sequencing

Family 718

3   9620028   G   A   DCRLD2   missmes   H3   PROLEU   0.18   0.5   20.6   MM.090027     3   11337756   C   A   KAA2016   missmes   389   VALLEU   0.05   0.05   12.29   MM.015106     3   12379726   T   C   FAAP   missmes   231   ARG/UV   Ad4   1MM.03146     10   2339192   A   G   MSRB2   missmes   2540   LETTR   0.051   0.63   1.151   MM.02486     10   2339192   A   G   MSRB2   missmes   56   ARGLEU   0.031   0.63   1.131   MM.02486     10   2339192   C   A   A   C   MM.02486   missmes   57   CARGLEU   0.003   0.63   1.32   MM.02486     12   20205624   C   A   ACT   MM.02246   MM.02246     12   2046646   A   G   T   ARSHD   <	chrom	pos	dbSNP	ref	mut	gene	functionGVS	cDNA Position	AA_Change	PolyPhen Val	SIFTval	CADD PHRED	accession
3   11222916   roll 15971253   C   T   C   A   KAAAD   B   VALUE   0.185   0.085   23   NM 0101069     3   12274792   T   C   A KAAD   S30   VALUE   0.05   0.05   23   NM 0101069     3   121414562   T   C   A KARD   missense   231   A KARD   0.051   1.04   NM 01222     10   25313055   rs11020099   G   T   T   NM 014115   NM 014151     10   23307561   C   G   A AMCRDIT   missense   1220   0.03   0.03   1.04   NM 014151     11   23048124   C   A   ACCRDIT   NS 020   0.02   0.03   0.024   NM 020107     12   A   ACCRDIT   MARCRDIT   missense   1220   0.03   0.024   NM 020107     12   221455600   G   A   TARDPT   missense   230   NALATHR   0.032   0.024 <td>3</td> <td>98620028</td> <td></td> <td>G</td> <td>A</td> <td>DCBLD2</td> <td>missense</td> <td>143</td> <td>PRO/LEU</td> <td>0.118</td> <td>0.5</td> <td>20.6</td> <td>NM 080927.3</td>	3	98620028		G	A	DCBLD2	missense	143	PRO/LEU	0.118	0.5	20.6	NM 080927.3
3   113277150   C   A KAA2018   missense   3380   VAULEU   0.05   0.05   23   MM.01098     3   124141662   T   C   PAAPP   missense   2540   ILE/THR   0.051<	3	112729916	rs115971253	С	Т	C3orf17	missense	889	VAL/ILE	0.165	0.08	12.29	NM 015412.3
3   122/14782   T   C   PARPP   missense   311   ARGKLY   0.47   0.01   24   NM 031465     10   23399162   A   G   MSRB2   missense   2440   LETHR   0.396   0.02   26.4   MM 01222     10   2339305   sa116200922   G   T   T THVSL1   missense   947   ALASER   0.196   0.463   11.131   MM 02483     10   23397820   C   A   AVKR026   missense   55   ARGLEU   0.030   0.72   10.13   MM 02483     12   122748141   st14221540   T   G   V/VAL   1   0   32   NM 00717     12   3204646   A   G   AG   T massense   5140   ALA/THR   0.002   0.03   2.2.7   NM 000254     1   2304646   G   G   T   T GSER   missense   282   SER/HE   0.756   0.04   2.3.7   NM 000173	3	113377150		С	A	KIAA2018	missense	3380	VAL/LEU	0.05	0.05	23	NM 001009899.2
3   124141662   T   C   KANN   Mod 03941     10   2399192   A   G   MISSE   Mod 03941     10   2513059   rs11620092   G   T   T   T   T   NM 02341     10   27395200   C   A   ANARD26   missense   907   ALAVSER   0.169   0.49   11.04   MM 02483     10   27395200   C   A   AAARD26   missense   917   ALAVSER   0.12   2.13   NM 02491     12<12025424	3	122274792		т	С	PARP9	missense	331	ARG/GLY	0.467	0.01	24	NM 031458.2
10   23399192   A   G   MSR02   missense   241   ASIVASP   0.031   0.05   11.51   NML 012221     10   2338200   C   A   AVRC025   missense   907   ALA/DER   0.049   0.049   11.04   NML 02044     10   30317561   C   G   KVAAL462   missense   56   ARGUEU   0.003   0.072   10.01   21.8   NML 02047     12   12024424   H420150   T   G   VPS3A   missense   214   LLE/LEU   0.053   0.039   10.02   21.5   NML 00274     11   23046446   A   G   A   G   Tmissense   2540   ALA/THR   0.002   0.01   21.7   NML 00564     12   23046446   A   G   G   TTM< missense	3	124141662		Т	С	KALRN	missense	2540	ILE/THR	0.596	0.02	26.4	NM 003947.4
10   2531309   cst120092   G   A   AVR02E   Number of the sense   11.04   Number of the sense   Number of the sense   11.04   Number of the sense   11.04   Number of the sense   Number of the sense   11.04   Number of the sense   10.000   Number of the	10	23399192		A	G	MSRB2	missense	241	ASN/ASP	0.051	0.65	11.51	NM 012228.3
10   27383200   C   A   ANRCR26   missense   56   ARGLEU   0.003   0.72   10.13   NIL 014911     10   23295424   C   G   G   VARG   0.971   0.01   23.8   NIM_020441     12   1229295424   C   A   OC   NIM_011   missense   214   UELLEU   0.058   0.89   15.87   NIM_020247     16   932952060   C   T AINKRD11   missense   5340   ALATHR   0.002   0.95   0.014   23.7   NIM_000027     1   23466446   A   G   AG   AT   Timissense   282   SER/PHE   0.76   0.04   23.7   NIM_000027     1   23466496   G   A   ARBPI   missense   2822   SER/PHE   0.76   0.04   23.8   NIM_000023     2   173024102   T   C   G/G/SEP   missense   2431   ALA/VLA   NA   NA   44.63   NIM_0001033	10	25313059	rs116200992	G	Т	THNSL1	missense	907	ALA/SER	0.169	0.49	11.04	NM 024838.4
10   30317861   C   G   KMAUAR2   missense   120   GLYARG   0.971   0.01   23.8   NM_007147     12   1222954141   rs114821540   T   G   VPS3A   missense   274   ILELEU   0.058   0.89   1.5.7   NM_022316     Family 1379   C   T   ALATHR   0.002   0.95   0.024   NM_02317     Family 1379   C   T   ALATHR   0.002   0.95   0.024   NM_02317     Chrom pos   dbSNP   ref   mit   gen   functionGVS cDNA Position AA_Change Polyphen Val   SIFVal   PHRED   accession     12   2365600   G   A   AG   FSIP2   missense   1132   0.023   0.02   18.14   Mid.3733     2   17666498   rs6 (73308)   G   A   SSIP10   missense   254   ARG/LY   1   1   0.002   18.14   Mid.373   Mid.010131   33244   935448   A   G   AG	10	27389200		С	A	ANKRD26	missense	56	ARG/LEU	0.003	0.72	10.13	NM 014915.2
12   12025424   C   A   OT   missense   317   GLV/AL   1   0   32   NM_00717     12   122714111   rs114821540   C   G   VPS33A   missense   274   ILE/LEU   0.058   0.89   10.57   NM_001327     Ehrom   pos   dbSNP   ref   mud   gene   functionGVS   CDNA Position   AACTHR   0.024   NM_001327     1   234656060   G   A   TARBP1   missense   151   C/S/ARG   0.997   0.01   22.7   NM_000027     2   179457661   rs16592778   A   G   TTN   missense   714   ALA/VAL   0.997   0.01   23.2   NM_014337     2   179457661   rs16592778   A   G   TTN   missense   714   ALA/VAL   0.020   0.021   ALA/VAL   0.023   0.021   ALA   ALA/VAL   0.021   ALA/VAL   0.021   ALA/VAL   0.023   0.021   ALA	10	30317861		С	G	KIAA1462	missense	1220	GLY/ARG	0.971	0.01	23.8	NM 020848.2
12   127141   1514821540   T   G   VPS33A   missense   274   ILEALU   0.08   0.89   15.87   NM (022914     16   89347612   rs75362060   C   T   ANKRD11   missense   5340   ALA/THR   0.002   0.95   0.024   NM (01375     2nade5600   G   A   TARPH   missense   121   CYSARG   0.997   0.01   2.37   NM (00644     2   17320574   C   G   A   TARPH   Transense   2046440   A.4   A.4   0.999   0.13   2.2.2   NM (40737     2   17394571   C   C   T   OSBPL6   missense   2131   ALA/THR   NA   NA   4.463   NM (40737     2   23330146   rs675865   T   C   SCRU12   missense   2341   ALA/THR   NA   A.463   NM (401695     3   7559656   T   C   SCRU12   missense   535   ARG(VS	12	120295424		С	A	CIT	missense	317	GLY/VAL	1	0	32	NM 007174.2
16   B9347612   rs/5362060   C   T   ANKRD11   missense   5340   ALA/THR   0.002   0.95   0.024   NM_013275     Chrom   pps   dbSNP   ref   mut   gene   functionGVS   CDNA Position   AA   Change   PolyPhen Val   SIFTval   PHRED   eccession     1   230646446   A   G   AGT   missense   151   CYS/ARG   0.987   0.01   23.7   NM_000624     2   174567681   rel15552778   A   G   TTN   missense   2346   VALA/LAL   NA   NA   3.8.3   NM_003112     2   21350146   rs61733089   G   A   SP120   missense   1243   PHELEU   0.01   1   0.002   18.14     2   231380146   rs61733089   G   A   SP120   missense   1243   PHELEU   0.0111   1   7.7.3   NM_00101423     3   73024182   r   C   T <t< td=""><td>12</td><td>122748141</td><td>rs114821540</td><td>т</td><td>G</td><td>VPS33A</td><td>missense</td><td>274</td><td>ILE/LEU</td><td>0.058</td><td>0.89</td><td>15.87</td><td>NM 022916.4</td></t<>	12	122748141	rs114821540	т	G	VPS33A	missense	274	ILE/LEU	0.058	0.89	15.87	NM 022916.4
Family 1379   ps   disNP   ref   mut   gene   functionGVS cDNA Position AA_Change   PolyPhen Val   SIFTval   PHRED   accession     1   23044646   A   G   AGT   missense   151   CYS/ARG   0.987   0.01   23.7   NM.000025     1   234466060   G   A   TAREP11   missense   282   SER/PHE   0.756   0.01   23.3   NM.000564     2   173457681   r511652778   A   G   TTN   missense   2343   ALA/THR   NA   NA   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.3   1.4.4   1.3.3   1.0.002   1.4.0.01473   1.5.3 <td< td=""><td>16</td><td>89347612</td><td>rs75362060</td><td>С</td><td>Т</td><td>ANKRD11</td><td>missense</td><td>5340</td><td>ALA/THR</td><td>0.002</td><td>0.95</td><td>0.024</td><td>NM 013275.4</td></td<>	16	89347612	rs75362060	С	Т	ANKRD11	missense	5340	ALA/THR	0.002	0.95	0.024	NM 013275.4
chrom   pos   dbSNP   ref   mut   gene   functionGVS   cDNA Position   AA_Change   PolyPhen Val   SIFTval   PHRED   accession     1   23084646   A   G   ACT   missense   151   CVS/ARG   0.937   0.01   23.7   NM_000564     2   17345061   G   A   TARDPIT   missense   2338   0.04   23.3   0.04   23.3   0.04   23.3   0.04   23.3   0.023   0.02   13.4     2   21330146   ref1733089   G   A   SFIP2   missense   12.4   0.023   0.02   13.4   NM_0010013     3   7302412   T   C   SV1V12   missense   154   ARG/CY   0   1   0.002   NM_0012423     5   75695655   T   C   SV2C   missense   154   TVFHIS   0.32   2.3.4   NM_0113610     5   13930940   G   A   G   BFED16 <td< td=""><td>Famil</td><td>v 1379</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>	Famil	v 1379											
1 23846446 A G AGT missense 151 CYS/ARG 0.987 0.01 23.7 NM.000023   1 23456060 G A TARBPH missense 282 SER/PHE 0.736 0.04 28.3 NM.006544   2 179457681 rel16592778 A G TTM missense 32546 VAL/ALA NA NA NA 14.63 NM.113437   2 186664993 A G FSIP2 missense 1241 ALA/THR NA NA 4.16.3 NM.001103   3 73024182 T C GYYLT missense 1204 PHE/LEU 0.411 1 1.6.73 NM.001103   4 9336408 A G C/C72377 missense 1648 TYRHIS 0.827 0.5 24.2 NM.0114375   5 75596565 T C SV2C missense 1649 YRHIS 0.827 0.5 24.2 NM.014697   5 135513083 A AT SMA025 fmessnit	chrom	pos	dbSNP	ref	mut	gene	functionGVS	cDNA Position	AA Change	PolyPhen Val	SIFTval	PHRED	accession
1   2335560   G   A   TRARPH   Imissense   262   SERVPH   0.004   2.3.1   NM_005644     2   179203724   C   T   OSBPL6   missense   734   ALAVAL   0.099   0.13   28.2   NM_114733     2   179547681   r6115522778   A   G   FSIP2   missense   23464   VAL/ALA   NA   NA   1A.63   NM_000513     2   196664898   A   G   FSIP2   missense   2141   ALATHR   NA   NA   1A.6   NM_0010133     3   730324182   T   C   GVYLTZ   missense   1244   PHE/LEU   0.411   1   16.73   NM_0101033     4   9336408   A   G   OC773375   missense   1648   TYRNIS   0.827   0.5   24.2   NM_0114975     5   7902541   C   T   CMYAS   missense   1648   TYRNIS   0.83   23.1   NM_013976   1.013   <	1	230846446	uporti	Δ	G	AGT	missoneo	151	CYS/ARG	0.987	0.01	23.7	NM 000029 3
Lossons   D   H   House   Loss   Humber   Loss   Humber   Loss   Humber     2   179457681   r116592778   A   G   TTN   missense   32546   VAL/ALA   NA   NA   NA   14.63   NM114733     2   18666498   A   G   FSIP2   missense   2131   ALAVALA   NA   NA   44.63   NM1013343     2   231380146   r.G   G   SPIP2   missense   2431   ALAVALA   NA   NA   44.63   NM1001232     4   933648   A   G   CO72837   missense   1244   PHE/LEU   0.411   1   10.73   NM101232     5   75956665   T   C   SVZ   missense   1648   TYR/HIS   0.227   0.5   24.2   NM1014975     5   79925441   C   T   CMYA5   missense   1649   VALMCF   0.033   0.03   2.31   NM1030174     <	1	234565060		G	Δ	TARBP1	missonso	2882	SER/PHE	0.736	0.04	28.3	NM 005646 3
1   1   1   0   1   0   1   0	2	179203724		C	T	OSBPI 6	missonso	734		0.999	0.13	20.3	NM 145739 2
1   1030100   A   G   FSIP2   Insense   12210   VEX.PLX   I/W   UW   I/W   I/W </td <td>2</td> <td>179457681</td> <td>re116592778</td> <td>Δ</td> <td>G</td> <td>TTN</td> <td>micconco</td> <td>32546</td> <td></td> <td>NA</td> <td>NA</td> <td>14.63</td> <td>NM 133437.3</td>	2	179457681	re116592778	Δ	G	TTN	micconco	32546		NA	NA	14.63	NM 133437.3
1   1   0   A   0   A   0   1   1   1   0   0   1   0	2	186664898	13110332110	Δ	G	ESIP2	micconco	11132	VADADA	0.022	0.02	19.14	14141_133437.5
2   2010001   1001 3000 0   A   0.100000000000000000000000000000000000	2	231380146	re61733089	G	Δ	SP100	missense	2431		NA	NA.	4 162	NM 003113 3
J Jobertoz I C OKI22 Inspense Itols	3	73024182	1301133003	т	0	GYVI T2	micconco	1204	DHE/LEU	0.411	1	16 72	NM 001080393 1
1   0.0000   A   0   0.00000000000000000000000000000000000	4	9336408		Δ	G	0072837	micconco	25		0.411	1	0.002	NM_001242328.1
3 73020 1 C 7020 Integense 1040 111011 0.027 0.03 2.4.2 Nm_01374   5 79025441 C T CMYAS missense 853 ARG/CVS 0.046 0.027 13.24 Nm_032115   5 135613083 A AT SMAD5 frameshift 0 0.069 0.12 12.56   10 10300766 rs17655877 C G PRCI missense 2501 PRO/ARG 0.787 0.04 23.2 NM_015062   10 12300766 rs17655877 C G PRCI missense 1121 ASP/GLY 0.997 0.02 33 NM_144567   10 12521435 rs112981683 T C CPMM2 missense 1131 ARS6221 0.02 34 NM_01010968   11 11228529 rs35664667 T C CT Missense 181 THR/ALA 0.012 0.46 6.234 NM_0010768   12 122853964 G A RIF34 ing-syno		75596565		T	C	SV/2C	micconco	1648		0 927	0.5	24.2	NM 014979 1
3   1922411   0   1   NIRU   missense   1033   VAL/MET   0.038   0.03   23.1   NM_002115     5   135613083   A   AT   SMAD5   frameshit   0   0.069   0.12   12.56     10   103900766   rs17855877   C   G   PPRC1   missense   2501   PR0/ARG   0.787   0.04   23.2   NM_016067     10   125521435   rs11291683   T   C   CPXM2   missense   1121   ASP/GLV   0.997   0.02   33   NM_118146     11   125521435   rs1121   ASP/GLV   0.997   0.066   23   NM_198146     11   11228529   rs3664667   T   C   PDU2AF1   missense   8132   ARG/GLN   0.013   0.28   23.1   NM_0010747     12   121853964   G   A   RNF34   ting-synonym   12   NA   NA   16.6   NM_1913427     14   105417500   C <td>5</td> <td>79025441</td> <td></td> <td>C</td> <td>т</td> <td>CMYA5</td> <td>micconco</td> <td>853</td> <td>ARGICYS</td> <td>0.046</td> <td>0.02</td> <td>12.24</td> <td>NM 153610 3</td>	5	79025441		C	т	CMYA5	micconco	853	ARGICYS	0.046	0.02	12.24	NM 153610 3
3   035000   6   A   Cricka   missense   10-0   04-0	5	80030040		G	1	CDD09	missense	1849	VAL/MET	0.040	0.02	22.1	NM 032110 3
J   Josh Joso   K   A   G   Johne J	5	1355130340		0	AT	SMADE	framochift	1045	VAL/IVIL I	0.058	0.03	12.56	14141_032113.3
10 124091985 A G BTBC16 missense 1211 ASP/GLY 0.997 0.02 33 NM_144551   10 125521435 rs112981683 T C CPXM2 missense 1130 LYS/ARG 1 0.066 23 NM_198146   11 73369281 C T OD24 missense 8132 ARG/GLN 0.013 0.28 23.1 NM_010988   11 1112285291 rs35664667 T C POU2AF1 missense 181 THR/ALA 0.012 0.46 6.244 NM_0006235   12 120295365 T G CT missense 181 THR/ALA 0.012 0.46 6.244 NM_001747   12 121853964 G A RNF34 fing-synonym 12 NA NA 16.6 NM_194271   14 105417500 C T AHNAK2 missense 231 MET/LE 0.003 0.39 10.15 NM_0101837   20 3804572 G T C20729 missens	10	103900766	re 17855877	0	G	DDDC1	missoneo	2501		0.797	0.12	22.30	NM 015062 3
In   International and the series   Internaternatise <thinternaternational and="" series<="" th="" the=""></thinternaternational>	10	12/00/085	1311033011	1	G	BTBD16	missense	1121	ASPICIV	0.997	0.04	23.2	NM 144587 2
International internatintered international international international inter	10	124031303	re112081683	т	C	CDVM2	micconco	1730		1	0.02	22	NM 198148 2
In   1000201   CO   I   OD24   Imissense   0132   ACS/SCH   OD23   0223   23.1   Imissense   0132   Incomposition     11   111226529   rs35664667   T   C   POUZAF1   missense   376   LYS/GLN   1   0   26.7   NM_00623     12   120295365   T   G   CT   missense   376   LYS/GLN   1   0   26.7   NM_00623     12   120295365   T   G   A   RNF34   ing-synonym   12   NA   NA   NA   16.6   NM_194271     14   106417500   C   T   AHNAK2   missense   4288   GLU/LYS   0.086   0.2   3.783   NM_138422     20   3804572   G   T   C200r29   missense   623   ALA/GLU   0.522   0.01   23.5   NM_0014825     21   37444851   G   C   LOC1001   missense   505   0.05   0.22	11	78360281	13112301003	C	т	0074	missense	8132		0.012	0.00	23	NM 001098816.2
11 112223 153004007 1 0 PO2247 1 101 0 26.7 NM_007174   12 12285365 T G CIT missense 376 LYS/GLN 1 0 26.7 NM_007174   14 105417500 C T AHNAK2 missense 4288 GLU/LYS 0.086 0.2 3.783 NM_138420   20 3804572 G T C20orf29 missense 231 MET/LE 0.003 0.39 10.15 NM_0118347   20 3843058 C A MAVS missense 632 ALA/GLU 0.522 0.01 23.5 NM_020746   21 33694796 C T URB1 missense 5332 ASP/ASN 0.127 0.15 22 NM_014825   21 37444851 G C LOC1001 missense 2327 PRO/LEU 0.851 0.08 19.24 NM_173568   Formily 1924   chrom pos dbSNP ref mut gene <	11	1112285201	1035554657	т	C	DOU24	missense	191		0.013	0.26	6 324	NM 006235 2
12 12023003 1 0 0 1 0 20.7 NML00717   12 121853964 G A RNF34 iing-synonym 12 NA NA 16.6 NM_194271   14 106417500 C T AHNAK2 missense 4288 GLU/LYS 0.086 0.2 3.783 NM_138420   20 3843058 C A MAVS missense 623 ALA/GLU 0.522 0.01 23.5 NM_00746   21 33694796 C T URB1 missense 5332 ASP/ASN 0.127 0.15 22 NM_014822   21 37444851 G C I URB1 missense 505 0.05 0.22 20.4 NM_01757   21 43531659 C T PRDM15 frameshift 0 NA NA 12.37 NM_133432   2 179440696 r555853138 C T TTN missense 2122 Glu688Ly 0.998 0.04 35 NM_032166   2	12	12020525	1533004007	т	G	CIT	missense	276	I VS/CLN	0.012	0.40	0.234	NM 007174 2
12 12/10/3304 13/4 INA	12	121253305		G	0	DNE24	ting ourony m	12	LT3/GLN	NA	NIA	20.7	NM 194271 1
14 1034 17300 C 1 Allivak2 Inissense 4200 GUC173 0.080 0.2 3.783 NM_113442   20 3804572 G T C200729 missense 231 MET/LE 0.003 0.39 10.15 NM_018347   20 3843058 C A MAVS missense 623 ALA/GUU 0.522 0.01 23.5 NM_018447   21 33694796 C T URB1 missense 5332 ASP/ASN 0.127 0.15 22 NM_014825   21 37444851 G C LOC1001 missense 505 0.05 0.22 20.4 NM_01757   21 43587457 TC T PRDM15 frameshit 0 NA NA 12.37    Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position AA_Change PolyPhen Val SIFT val PHRED Accessior   2 179440696 rs55853138 C T <td>14</td> <td>105417500</td> <td></td> <td>0</td> <td>T</td> <td></td> <td>missones</td> <td>12</td> <td>CLUEVE</td> <td>0.086</td> <td>0.2</td> <td>2 702</td> <td>NM 129420 2</td>	14	105417500		0	T		missones	12	CLUEVE	0.086	0.2	2 702	NM 129420 2
20 304302 G 1 COURDS missense 231 Michicle 0.003 0.39 10.15 NM_010347   20 3843058 C A MAVS missense 623 ALA/GLU 0.522 0.01 23.5 NM_020746   21 33694796 C T URB1 missense 5332 ASP/ASN 0.127 0.15 22 NM_014825   21 37444851 G C LOC1001 missense 505 0.05 0.22 20.4 NM_01757   21 43531659 C T T PRDN15 frameshift 0 NA NA 12.37   Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position A_Change PolyPhen Val SIFT val PHRED Accession   2 179440696 rs55853138 C T TTN missense 2122 Glu688Lys 0.998 0.04 35 NM_032168   2 190338924 G A	14	2004572		C	T	C20od20	missense	4200	MET/ILE	0.000	0.2	10.15	NM 019247.2
20 33693056 C A MAVS missense 623 ALAGLO 0.522 0.01 23.5 NM_020744   21 33694796 C T URB1 missense 5332 ASP/ASN 0.127 0.15 22 NM_014825   21 37444851 G C LOC1001 missense 505 0.05 0.22 20.4 NM_001757   21 43287457 TC T PRDM15 frameshift 0 NA NA 12.37   21 43531659 C T UMODL1 missense 2327 PRO/LEU 0.851 0.08 19.24 NM_173566   Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position AA_Change PolyPhen Val SIFT val PHRED Accession   2 179440696 rs55853138 C T TTN missense 2126 Ser689Asn 0.966 0.313 21.8 NM_032168   2 190338924 G A GRM2	20	3004572		G	1	CZUOIIZ9	missense	231		0.003	0.39	10.15	NNI_010347.2
21 3399/39 C T ORBT Inissense 5332 ASP/ASN 0.127 0.13 22 NM_014825   21 37444851 G C LOC1001 missense 505 0.05 0.22 20.4 NM_01757   21 43287457 TC T PRDM15 frameshift 0 NA NA NA 12.37   21 43531659 C T UMODL1 missense 2327 PRO/LEU 0.851 0.08 19.24 NM_173568   Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position AA_Change PolyPhen Val SIFT val PHRED Accession   2 179440696 rs55853138 C T TTN missense 2126 Ser689Asn 0.966 0.313 21.8 NM_032168   2 190338928 G A WDR75 missense 2126 Ser689Asn 0.966 0.313 21.8 NM_003268   3 51749962 rs151188856	20	22604706		C	T	UDD4	missense	623	ACDIACN	0.322	0.01	23.5	NM 014925.2
21 3744451 G G 1.00101, fillssense 305 0.03 0.22 20.4 NM_001737   21 43287457 TC T PRDM15 frameshift 0 NA NA NA 12.37   21 43531659 C T UMODL1 missense 2327 PRO/LEU 0.851 0.08 19.24 NM_173566   Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position AA_Change PolyPhen Val SIFT val PHRED Accession   2 179440696 rs55853138 C T TTN missense 43568 Arg14448GIn 1 0.006 23.6 NM_133432   2 190338924 G A WDR75 missense 2126 Ser689Asn 0.966 0.313 21.8 NM_032168   3 51749962 rs151188856 G A GRM2 missense 2412 Asp725Asn 1 0.017 33 NM_003335   12 123444667 C<	21	27444054		C	C	LOCIONI	missense	5332	ASF/ASN	0.127	0.15	22	NM 001757 2
21 4328/437 1C 1 PROMIS infinitestinit 0 NA NA 12.37   21 43531659 C T UMODL1 missense 2327 PRO/LEU 0.851 0.08 19.24 NM_173568   Family 1924   chrom pos dbSNP ref mut gene functionGVS cDNA Position AA_Change PolyPhen Val SIFT val PHRED Accession   2 179440696 rs55853138 C T TTN missense 43568 Arg14448GIn 1 0.006 23.6 NM_133432   2 190338924 G A WDR75 missense 2122 Glu688Lys 0.998 0.04 35 NM_032168   3 51749962 rs151188856 G A GRM2 missense 2212 Sli688Lys 0.999 0 25.4 NM_003335   3 49849583 C T UBA7 missense 922 Gly251Arg 0.999 0 25.4 NM_003335   12 120276639 <td>21</td> <td>12207457</td> <td></td> <td>TC</td> <td>T</td> <td>DDDM46</td> <td>framesahit</td> <td>505</td> <td></td> <td>0.05</td> <td>0.22</td> <td>20.4</td> <td>NIVI_001757.2</td>	21	12207457		TC	T	DDDM46	framesahit	505		0.05	0.22	20.4	NIVI_001757.2
Z1   43331833   C   T   OMODELT   Inissense   Z327   PROLED   0.831   0.08   13.24   NM_17386     Family 1924     chrom   ps   dbSNP   ref   mut   gene   functionGVS   cDNA Position   AA_Change   PolyPhen Val   SIFT val   PHRED   Accession     2   179440696   rs55853138   C   T   TTN   missense   43568   Arg14448GIn   1   0.006   23.6   NM_133432     2   190338924   G   A   WDR75   missense   2122   Glu688Lys   0.998   0.04   35   NM_032168     3   190338928   G   A   WDR75   missense   2126   Ser689Asn   0.966   0.313   21.8   NM_0032168     3   49849583   C   T   UBA7   missense   2412   Asp725Asn   1   0.017   33   NM_003335     12   123444667   C   T   ABCB9   missense	21	43201431		0	T		iramesniit	0207	DDO/LEU	0.051	NA 0.00	12.37	NIM 472569 2
Chrom   pos   dbSNP   ref   mut   gene   functionGVS   cDNA Position   AA_Change   PolyPhen Val   SIFT val   PHRED   Accession     2   179440696   rs55853138   C   T   TTN   missense   43568   Arg14448Gln   1   0.006   23.6   NM_13343;     2   190338924   G   A   WDR75   missense   2122   Glu688Lys   0.998   0.04   35   NM_032168     2   190338928   G   A   WDR75   missense   2126   Ser689Asn   0.966   0.313   21.8   NM_032168     3   51749962   rs151188856   G   A   GRM2   missense   2412   Asp725Asn   1   0.017   33   NM_003335     3   49849583   C   T   UBA7   missense   922   Gly251Arg   0.999   0   25.4   NM_003335     12   120276639   T   A   CIT   missense   745   Asp230Val </td <td>Lomil</td> <td>43531653</td> <td></td> <td>U</td> <td></td> <td>ONIODET</td> <td>missense</td> <td>2321</td> <td>FRUILLU</td> <td>0.001</td> <td>0.06</td> <td>15.24</td> <td>14141_17.5500.5</td>	Lomil	43531653		U		ONIODET	missense	2321	FRUILLU	0.001	0.06	15.24	14141_17.5500.5
chrom   pos   dbSNP   ref   mut   gene   functionGVS   cDNA Position   AA_Change   PolyPhen Val   SIFT val   PHRED   Accession     2   179440696   rs55853138   C   T   TTN   missense   43568   Arg14448Gln   1   0.006   23.6   NM_13343:     2   190338924   G   A   WDR75   missense   2122   Glu688Lys   0.998   0.04   35   NM_032168     2   190338928   G   A   WDR75   missense   2126   Ser689Asn   0.966   0.313   21.8   NM_032168     3   51749962   rs151188856   G   A   GRM2   missense   2412   Asp725Asn   1   0.017   33   NM_003335     12   123444667   C   T   B&A7   missense   426   Arg39His   0.968   0.138   29.9   NM_0196255     12   120276639   T   A   CIT   missense   158   His39	Famil	y 1924		12	1 52								0.20
2 179440696 rs55853138 C T TTN missense 43568 Arg14448Gln 1 0.006 23.6 NM_133432   2 190338924 G A WDR75 missense 2122 Glu688Lys 0.998 0.04 35 NM_032168   2 190338928 G A WDR75 missense 2122 Glu688Lys 0.998 0.04 35 NM_032168   3 51749962 rs151188856 G A GRM2 missense 2412 Asp725Asn 1 0.017 33 NM_003235   3 49849583 C T UBA7 missense 922 Gly251Arg 0.999 0 25.4 NM_003355   12 123444667 C T ABC89 missense 426 Arg39His 0.968 0.138 29.9 NM_012625   12 120270639 T A CIT missense 745 Asp230Val 0.98 0 35 NM_0012069   12 120884493 rs149168717 C T <td>chrom</td> <td>pos</td> <td>dbSNP</td> <td>ref</td> <td>mut</td> <td>gene</td> <td>functionGVS</td> <td>cDNA Position</td> <td>AA_Change</td> <td>PolyPhen Val</td> <td>SIFT val</td> <td>PHRED</td> <td>Accession</td>	chrom	pos	dbSNP	ref	mut	gene	functionGVS	cDNA Position	AA_Change	PolyPhen Val	SIFT val	PHRED	Accession
2   190338924   G   A   WDR75   missense   2122   Glu688Lys   0.998   0.04   35   NM_032164     2   190338928   G   A   WDR75   missense   2126   Ser689Asn   0.966   0.313   21.8   NM_032164     3   51749962   rs151188856   G   A   GRM2   missense   2412   Asp725Asn   1   0.017   33   NM_00835     3   49849583   C   T   UBA7   missense   922   Gly251Arg   0.999   0   25.4   NM_003335     12   123444667   C   T   ABC89   missense   426   Arg39His   0.968   0.138   29.9   NM_012059     12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_012059     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454	2	179440696	rs55853138	С	Т	TTN	missense	43568	Arg14448GIn	1	0.006	23.6	NM_133432.3
2   190338928   G   A   WDR75   missense   2126   Ser689Asn   0.966   0.313   21.8   NM_032164     3   51749962   rs151188856   G   A   GRM2   missense   2412   Asp725Asn   1   0.017   33   NM_00835     3   49849583   C   T   UBA7   missense   922   Gly251Arg   0.999   0   25.4   NM_00335     12   123444667   C   T   ABCB9   missense   426   Arg39His   0.968   0.138   29.9   NM_012059     12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_012059     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001	2	190338924		G	A	WDR75	missense	2122	Glu688Lys	0.998	0.04	35	NM_032168.1
3   51749962   rsi51188856   G   A   GRM2   missense   2412   Asp725Asn   1   0.017   33   NM_000835     3   49849583   C   T   UBA7   missense   922   Gly251Arg   0.999   0   25.4   NM_00335     12   123444667   C   T   ABCB9   missense   426   Arg39His   0.968   0.138   29.9   NM_012625     12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_012625     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_00525393     13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002 </td <td>2</td> <td>190338928</td> <td></td> <td>G</td> <td>A</td> <td>WDR75</td> <td>missense</td> <td>2126</td> <td>Ser689Asn</td> <td>0.966</td> <td>0.313</td> <td>21.8</td> <td>NM_032168.1</td>	2	190338928		G	A	WDR75	missense	2126	Ser689Asn	0.966	0.313	21.8	NM_032168.1
3   49849583   C   T   UBA7   missense   922   Gly251Arg   0.999   0   25.4   NM_00333     12   123444667   C   T   ABCB9   missense   426   Arg39His   0.968   0.138   29.9   NM_01625     12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_012069     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_00525393     13   95673848   A   G   ABCC4   missense   4108   Lys124Glu   0.012   23.2   NM_004066     18   580778   A   G   CETN1   missense   4100   Lys124Glu   0.017   0.108   14.51   NM_004066	3	51749962	rs151188856	G	A	GRM2	missense	2412	Asp725Asn	1	0.017	33	NM_000839.3
12   123444667   C   T   ABCB9   missense   426   Arg39His   0.968   0.138   29.9   NM_019625     12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_012069     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_00525393     13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002   23.2   NM_005845     18   580778   A   G   CETN1   missense   410   Lys124Glu   0.017   0.108   14.51   NM_004066	3	49849583		С	T	UBA7	missense	922	Gly251Arg	0.999	0	25.4	NM_003335.2
12   120270639   T   A   CIT   missense   745   Asp230Val   0.98   0   35   NM_0012069     12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_00525393     13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002   23.2   NM_00525393     18   580778   A   G   CETN1   missense   410   Lys124Glu   0.017   0.108   14.51   NM_004066	12	123444667		С	Т	ABCB9	missense	426	Arg39His	0.968	0.138	29.9	NM_019625.3
12   120884493   rs149168717   C   T   G00000257   missense   158   His39Tyr   0.085   0.454   22.8   NM_176818     12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_00525393     13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002   23.2   NM_005845     18   580778   A   G   CETN1   missense   410   Lys124Glu   0.017   0.108   14.51   NM_004066	12	120270639		Т	A	CIT	missense	745	Asp230Val	0.98	0	35	NM_001206999.1
12   120662133   G   A   PXN   missense   918   Arg19Trp   0.999   0.001   25.1   XM_0052539     13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002   23.2   NM_005845     18   580778   A   G   CETN1   missense   410   Lys124Glu   0.017   0.108   14.51   NM_004066	12	120884493	rs149168717	С	Т	G0000025	missense	158	His39Tyr	0.085	0.454	22.8	NM_176818.2
13   95673848   A   G   ABCC4   missense   4078   Ile1320Thr   0.954   0.002   23.2   NM_005845     18   580778   A   G   CETN1   missense   410   Lys124Glu   0.017   0.108   14.51   NM_004066	12	120662133		G	Α	PXN	missense	918	Arg19Trp	0.999	0.001	25.1	XM_005253915.1
18 580778 A G CETN1 missense 410 Lys124Glu 0.017 0.108 14.51 NM_004066	13	95673848		A	G	ABCC4	missense	4078	Ile1320Thr	0.954	0.002	23.2	NM_005845.3
10 1101	18	580778		Α	G	CETN1	missense	410	Lys124Glu	0.017	0.108	14.51	NM_004066.1
19 41198211 r5144343899 T C ADCK4 missense 1431 Tyr455Cys 0.998 0 22 XM_0052592	19	41198211	rs144343899	Т	С	ADCK4	missense	1431	Tyr455Cys	0.998	0	22	XM_005259272.1
19   41205970   AC   C   ADCK4   splice_donor   27.1	19	41205970	Name of States	AC	С	ADCK4	splice_donor	2020/12.4				27.1	
19 40964447 rs144111604 C T BLVRB missense 195 Glu29Lys 0.013 0.56 25.4 XM_00525913	19	40964447	rs144111604	С	T	BLVRB	missense	195	Glu29Lys	0.013	0.56	25.4	XM_005259157.1
19 47883001 rs200643374 A G DHX34 missense 3090 Asn914Ser 0.028 0.145 35 NM_014681	19	47883001	rs200643374	Α	G	DHX34	missense	3090	Asn914Ser	0.028	0.145	35	NM_014681.5
19   44536034   C   A   ZNF222   stop_gained   422   Cys109X   11.1   NM_0011299	19	44536034		С	Α	ZNF222	stop_gained	422	Cys109X			11.1	NM_001129996.1
X 79979316 A C BRWD3 missense 1844 His527Gln 0.743 0.251 22.9 NM_153252	Х	79979316		А	С	BRWD3	missense	1844	His527Gln	0.743	0.251	22.9	NM_153252.4
X   131203569   G   A   G00000134   missense   908   Asp221Asn   0.07   0.08   26.5   XM_00526243	Х	131203569		G	Α	G0000134	missense	908	Asp221Asn	0.07	0.08	26.5	XM_005262424.1

Abbreviations. Chrom, chromosome; pos, position; ref, reference; mut, mutation.

#### Table S2 Additional variants identified in 1379-B1-1 from exome sequencing

We identified additional compound heterozygous variants and dominant variants in subject 1379-B1-1.

### Compound heterozygous variants

CHROM	POS	effect	gene_name	dbSNP	HGVS_c	HGVS_p	transcript_id	impact
2	201488623	missense variant	AOX1	rs369839297	c.2041G>A	p.Asp681Asn	ENST00000374700	MODERATE
2	201501730	missense_variant	AOX1	rs144419430	c.2443G>A	p.Gly815Arg	ENST00000374700	MODERATE
6	157488190	missense_variant	ARID1B	rs34786733	c.2857G>A	p.Gly953Ser	ENST00000350026	MODERATE
6	157522223	missense_variant	ARID1B	rs34870395	c.4456A>T	p.Met1486Leu	ENST00000350026	MODERATE
2	29287937	splice region variant	C2orf71		c.3669-5 3669-4insCA		ENST00000331664	LOW
2	29287938	splice_region_variant	C2orf71		c.3669-6_3669-5insA		ENST00000331664	LOW
1	17256337	splice region variant	CROCC		c.352-4G>A		ENST00000375541	LOW
1	17256531	splice_region_variant	CROCC	rs371339969	c.537+5G>A		ENST00000375541	LOW
1	156/99967	missense variant	IOGAP3	rs1/19623112	C 4334G>A	n Arg1///5His	ENIST00000361170	MODERATE
1	156520100	missense_variant	IQGAP3	rs59573847	c.1778G>T	p.Arg593Leu	ENST00000361170	MODERATE
16	471 4700		MCDNI	100760303	- 562.0050		ENET00000262270	LOW
10	4714702	splice_region_variant	MGRNI	15199709383	C.302-8C/G		ENST00000262370	LOW
10	4/3321/	splice_region_variant	MGKN1	rs200737185	C.1483-81>C		ENS10000262370	LOW
3	195512549	inframe deletion	MUC4		c.5854 5901delCCTCT	p.Pro1952 Thr1967del	ENST0000463781	MODERATE
3	195518118	frameshift_variant	MUC4		c.326_332delATGTGAT	p.Asn109fs	ENST00000463781	HIGH
5	1/122/1975	missansa variant		rc2822///9	c 3526G>A	n Glv1176Ser	ENIST00000221484	MODERATE
5	141324976	missense_variant	PCDH12	rs13188049	c.3525A>C	p.Arg1175Ser	ENST00000231484	MODERATE
10	2107021		DITOM 1		- 212003 4	- 470701-	ENICTO0000451104	MODEDATE
10	318/831	missense_variant	PITRMI	rs34837384	C.2120G>A	p.Arg/0/Gin	ENS100000451104	MODERATE
10	3214939	missense_variant	PITRMI	rs199766052	C.26G>1	p.Giy9vai	ENS10000380989	MODERATE
9	8331582	frameshift_variant&s	PTPRD	rs200157286	c.4303_4304insT	p.Ser1435fs	ENST00000397611	HIGH
9	8331584	stop_gained&splice_r	PTPRD		c.4302C>A	p.Cys1434*	ENST00000397611	HIGH
19	50037548	missense variant	RCN3		c.341T>A	p.Ile114Lys	ENST00000270645	MODERATE
19	50040307	missense_variant	RCN3	rs77227069	c.463G>A	p.Val155Met	ENST0000270645	MODERATE
15	42977810	missense variant	STARD9	rs140924205	c.4034T>G	p.IIe1345Ser	ENST00000290607	MODERATE
15	42978141	missense_variant	STARD9	rs376229251	c.4365A>C	p.Glu1455Asp	ENST00000290607	MODERATE
15	42077910	missonso voriant	STADDO	rc140004005	0.4024T>C	n llo12455 or	ENET00000280607	MODERATE
15	42577610	missense_variant	STARDS	15140324203	c.40541/G	p.nei3433ei	ENST0000230007	MODERATE
15	42982383	missense_vanant	STARDS	15115491032	0.8807021	p.Gly2936Val	EINS10000290807	MODERATE
15	42978141	missense_variant	STARD9	rs376229251	c.4365A>C	p.Glu1455Asp	ENST00000290607	MODERATE
15	42982583	missense_variant	STARD9	rs115491632	c.8807G>T	p.Gly2936Val	ENST00000290607	MODERATE
6	152623062	missense_variant	SYNE1	rs150376715	c.17270C>G	p.Thr5757Arg	ENST00000423061	MODERATE
6	152647218	missense_variant	SYNE1	rs35493783	c.15100G>A	p.Asp5034Asn	ENST00000423061	MODERATE

Abbreviations. Chrom, chromosome; pos, position; ref, reference; mut, mutation; HGVS, Human Genome Variation Society; HGVS\_c, cDNA location; HGVS\_p, protein location.

## Dominant variants

CHROM	POS	effect	gene_nar	dbSNP	HGVS_c	HGVS_p	transcript_id	impact
1	1254762	stop_gained	CPSF3L		c.256A>T	p.Lys86*	ENST00000545578	HIGH
1	120277963	missense_variant	PHGDH		c.689G>A	p.Arg230His	ENST0000369409	MODERATE
1	156499967	missense_variant	IQGAP3	rs149623112	c.4334G>A	p.Arg1445His	ENST0000361170	MODERATE
1	156520100	missense_variant	IQGAP3	rs59573847	c.1778G>T	p.Arg593Leu	ENST0000361170	MODERATE
2	74274744	missense_variant	TET3	rs148646838	c.1295T>C	p.Val432Ala	ENST00000409262	MODERATE
2	110922668	missense_variant	NPHP1	rs113450177	c.503C>T	p.Ala168Val	ENST00000355301	MODERATE
2	152483510	splice_region_variant	NEB	rs141088433	c.10347+6C>T		ENST00000397345	LOW
2	171240217	splice_region_variant	MYO3B	rs146172688	c.1186-3C>T		ENST00000408978	LOW
2	201488623	missense_variant	AOX1	rs369839297	c.2041G>A	p.Asp681Asn	ENST00000374700	MODERATE
3	45049073	splice_region_variant	EXOSC7	rs145650051	c.771+6G>A		ENST00000265564	LOW
3	47452676	missense_variant	PTPN23	rs138329311	c.3388G>A	p.Gly1130Ser	ENST0000265562	MODERATE
3	52430897	missense_variant	DNAH1		c.11624C>T	p.Thr3875Met	ENST00000420323	MODERATE
3	186947662	missense_variant	MASP1		c.1327C>T	p.Arg443Trp	ENST0000337774	MODERATE
5	98115646	stop_gained	RGMB	rs201449079	c.622G>T	p.Gly208*	ENST0000308234	HIGH
5	141324975	missense variant	PCDH12	rs3833449	c.3526G>A	p.Gly1176Ser	ENST0000231484	MODERATE
5	141324976	missense variant	PCDH12	rs13188049	c.3525A>C	p.Arg1175Ser	ENST0000231484	MODERATE
6	56342136	splice region variant	DST	rs34892827	c.13806+7G>A		ENST0000244364	LOW
6	152623062	missense variant	SYNE1	rs150376715	c.17270C>G	p.Thr5757Arg	ENST00000423061	MODERATE
6	152623062	missense variant	SYNE1	rs150376715	c 17483C>G	n Thr5828Arg	ENST0000367255	MODERATE
6	152647218	missense variant	SYNE1	rs35493783	c.15100G>A	p.Asp5034Asp	ENST00000423061	MODERATE
6	157488100	missense variant	ARID1R	rs34786722	c 2896G>A	n Gly966Ser	ENST0000346095	MODERATE
6	157522222	missense_variant	ARIDID	rc3/870205	C 44564 ST	n Met1496Lou	ENST00000340003	MODERATE
7	13/322223	missense_variant	ANDID	1554670555	0.44JUA>1	p.Wellieu	ENST00000330020	MODERATE
7	12443510	missense_variant	ACRUS		C.23G/C	p.valsteu	ENST00000275558	MODERATE
-	134/19612	missense_variant	AGBL3		C.12/UC>I	p.Arg424Cys	ENS10000436302	MODERATE
/	143096736	splice_region_variant	EPHA1	rs149923216	c.835+8C>I		ENS100000275815	LOW
8	33361259	splice_region_variant	TTI2	rs199720231	c.1115+7C>G		ENST00000360742	LOW
8	52384860	missense_variant	PXDNL		c.699C>A	p.Ser233Arg	ENST0000356297	MODERATE
8	120814146	missense_variant	TAF2		c.680A>G	p.His227Arg	ENST0000378164	MODERATE
8	141034062	missense_variant	TRAPPC9		c.2671A>C	p.Thr891Pro	ENST0000438773	MODERATE
8	144995672	missense_variant	PLEC	rs200683827	c.8221G>A	p.Ala2741Thr	ENST00000398774	MODERATE
9	13158047	missense_variant	MPDZ		c.3422C>T	p.Thr1141lle	ENST00000541718	MODERATE
9	98677946	splice_region_variant	ERCC6L2	rs367808564	c.822-4A>G		ENST00000288985	LOW
9	135940049	missense_variant	CEL		c.249C>A	p.Phe83Leu	ENST00000372080	MODERATE
10	3187831	missense_variant	PITRM1	rs34837384	c.2120G>A	p.Arg707GIn	ENST00000451104	MODERATE
10	3214939	missense_variant	PITRM1	rs199766052	c.26G>T	p.Gly9Val	ENST0000380989	MODERATE
10	32856748	frameshift_variant	CCDC7		c.1351_1354delAC	p.Thr451fs	ENST00000277657	HIGH
10	37433935	missense variant	ANKRD30	A	c.1238C>T	p.Pro413Leu	ENST0000361713	MODERATE
10	60562867	missense variant	BICC1	rs77500675	c.2046A>T	p.Glu682Asp	ENST0000373886	MODERATE
11	20907067	missense variant	NELL1	rs115437355	c.584A>G	p.Gln195Arg	ENST0000357134	MODERATE
11	34129870	inframe insertion	NAT10	rs139367378	c.100 102dupAAA	p.Lvs34dup	ENST00000257829	MODERATE
11	46766098	missense variant	CKAP5		c.5554G>A	p.Val1852Met	ENST00000312055	MODERATE
11	62656158	missense variant	SIC3A2	rs201220940	c.1583C>T	n Ala528Val	ENST0000338663	MODERATE
11	65487790	inframe deletion	RNASEH2	rs1/1875736	c 268 270delAAG	n lys90del	ENST00000308418	MODERATE
12	57964521	missense variant	GUI	rc120600204	c.1624GNT	p.Lyssoder	ENST00000542426	MODERATE
12	102246725	colico rogion variant	DAL	rc62509624	c. 707, 74 ST	р.Авочдоег	ENST00000552106	LOW
12	103240733	spice_region_variant	ACACO	1502306024	C.707-7A21	- A	ENST00000335100	MODEDATE
12	103702100	missense_variant	ACACB	1514771/930	C.091/G>A	p.Arg2300GIN	ENST0000338432	MODERATE
13	254/98/8	missense_variant	LACCI	12/32218/2	C.22981>A	p.Asp/66Giu	ENST0000381884	LOW
12	44454253	splice_region_variant	LACCI	15/3403585	C3/C>A	- Userses	EINST00000325686	LOW
12	429//810	missense_variant	STARD9	15140924205	c.40341>G	p.lle1345Ser	ENS100000290607	MODERATE
15	42978141	missense_variant	STARD9	rs376229251	c.4365A>C	p.Glu1455Asp	ENST00000290607	MODERATE
15	42982583	missense_variant	STARD9	rs115491632	c.8807G>T	p.Gly2936Val	ENST0000290607	MODERATE
15	75644499	missense_variant	NEIL1		c.482T>C	p.lle161Thr	ENST00000355059	MODERATE
15	84506964	missense_variant	ADAMTSL	rs112527144	c.724A>G	p.Lys242Glu	ENST0000286744	MODERATE
16	27715275	missense_variant	KIAA0556	rs143325975	c.1345G>A	p.Gly449Ser	ENST00000261588	MODERATE
16	56875738	missense_variant	NUP93	rs147381896	c.1973G>A	p.Arg658His	ENST00000564887	MODERATE
16	67298319	missense_variant	SLC9A5		c.1907T>G	p.Val636Gly	ENST00000299798	MODERATE
16	71571175	missense_variant	CHST4	rs141141955	c.595C>T	p.His199Tyr	ENST00000338482	MODERATE
17	649703	missense_variant	GEMIN4		c.1580A>G	p.Asn527Ser	ENST00000319004	MODERATE
17	7671259	missense variant	DNAH2	rs146539788	c.3717C>A	p.Asp1239Glu	ENST00000389173	MODERATE
17	16068429	missense variant	NCOR1		c.155C>T	p.Ser52Leu	ENST0000395848	MODERATE
17	62024398	splice region variant	SCN4A	rs142270113	c.3441+7G>A		ENST00000435607	LOW
19	8161433	missense variant	FBN3	rs115948457	c.5434A>G	p.lle1812Val	ENST00000270509	MODERATE
19	9868536	frameshift variant	7NE846		c 1213 1216delAA	n Asn405fc	ENST0000397902	HIGH
19	18256549	solice region variant	MAST2	rs73925428	c 2953-505T	Pirosi 40015	ENST00000357502	LOW
19	50037549	missance variant	RCNP	.575525420	c 3/1T>A	n lle114lyc	ENST00000202011	MODEPAT
10	50040307	missense_valialit	DCND	rc77027060	0.0411/A	p.ne114Lys	ENST00000270043	MODERATE
17	00040307	missense variant	NUN3	13//22/009	C.403G2A	p.valicolviet	LINS100002/0045	INOUEKAIE