## SUPPLEMENTARY TABLES

**Table EI.** Genes included in the panel

**Table EII**. Recommendations for therapy, gene by gene

Figure E1

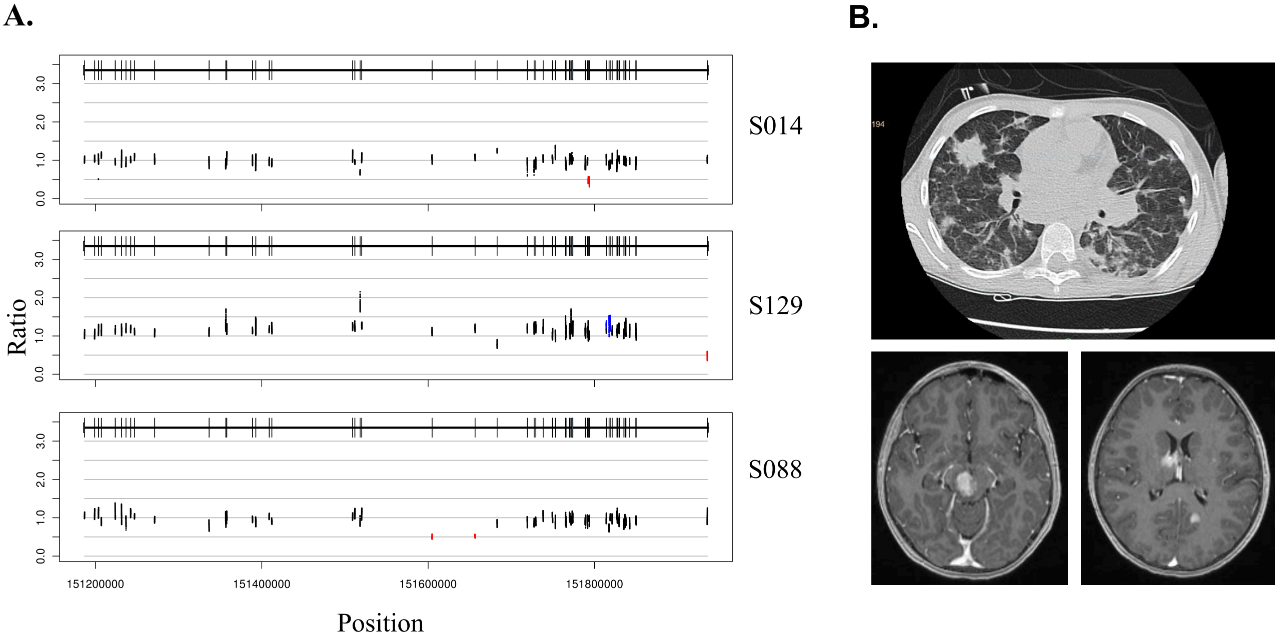


**Figure E1A, E1B. Mutations in *LRBA* in patients S14, S129, and S88**

**A.** Copy number mutations (CNVs) in patients S14, S129, and S88. Red elements on the *LRBA* genomic plots indicate deleted genomic regions. Minimal deletions are: exons 3-4, chr4:151,792,136 – 151,794,482 for S14; exon 2 including translation start, chr4:151,935,548 – 151,935,625 for S129; and exons 36-37, chr4:151,599,677 – 151,678,661 for S88. Each patient was compound heterozygous for a second, point mutation in *LRBA* (Table S2).

**B.** Patient S88 developed chronic interstitial lung disease, diagnosed at age 11 (top panel). He was started on abatacept with symptomatic improvement in his lung disease, but developed inflammatory brain lesions in his occipital lobe and midbrain (bottom panels). Following this diagnosis, he underwent HCT with excellent response, including improvement in his lung disease and resolution of most brain lesions.

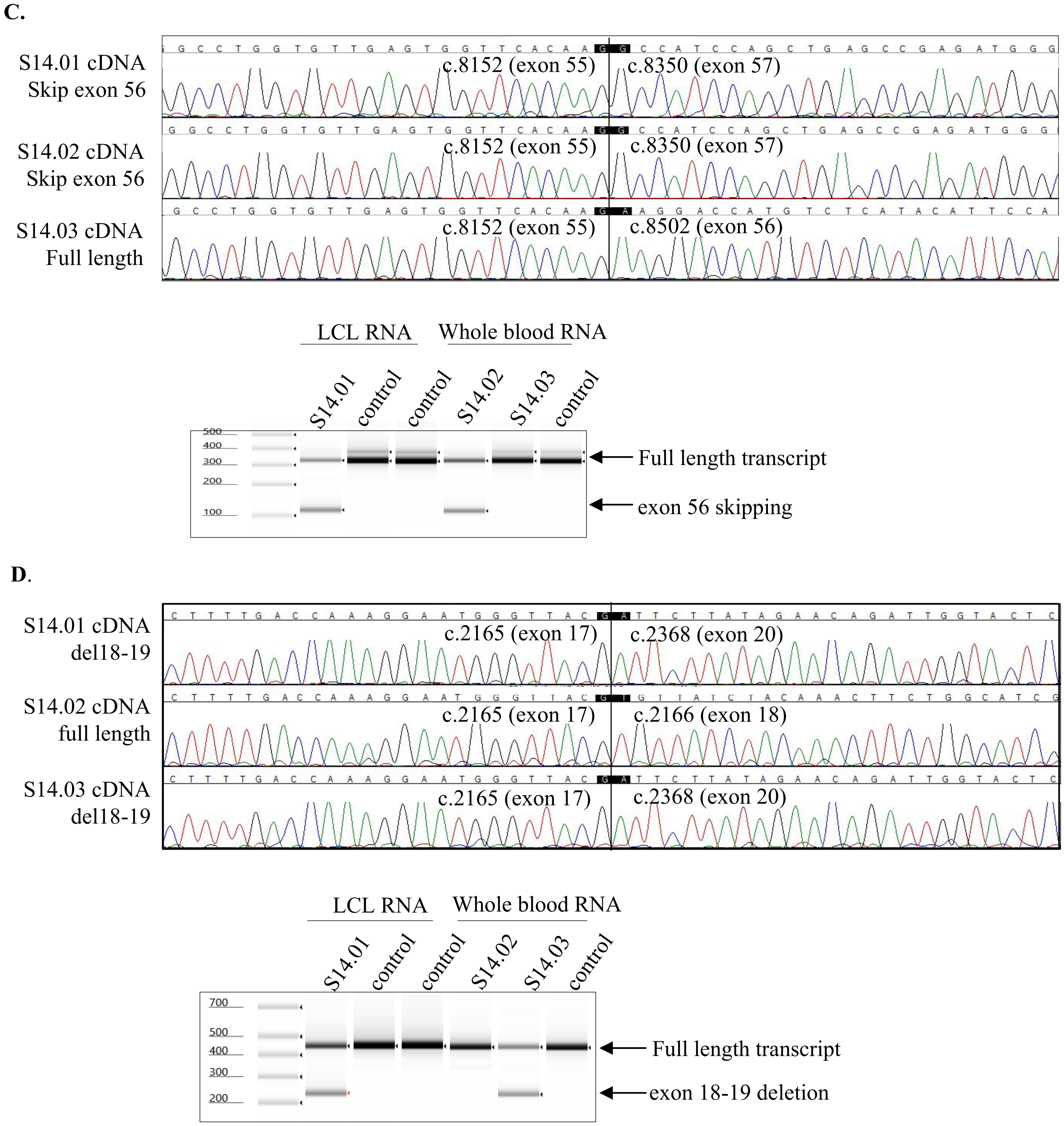


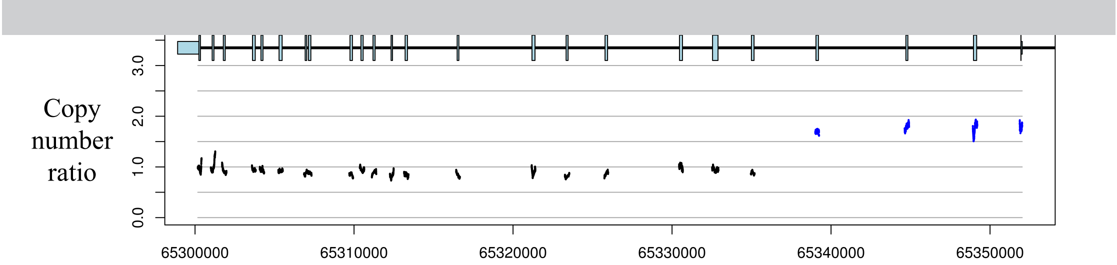
**Figure E1C, E1D. Mutations in *LRBA* in patient S14.01, father S14.02, and mother S14.03**

**C.** The paternal allele is an intronic deletion of 4bp, at *LRBA c.8349+4_8349+7del*. The mutation leads to transcriptional deletion of *LRBA* exon 56 (197bp) and premature stop at codon 2755 of 2864, validated by Sanger sequencing of cDNA and RT-PCR of RNA from whole blood and from lymphoblast cell lines (LCLs) of the patient and his father.

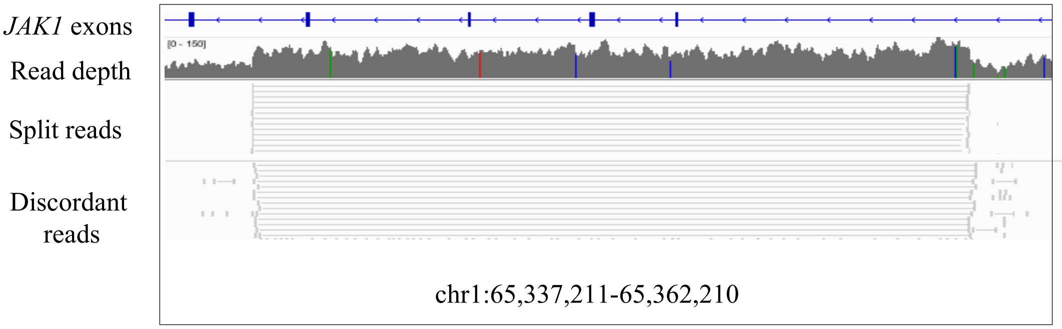
**D.** The maternal allele is a genomic deletion of at least 2347bp, leading to transcriptional deletion of exons 18-19 (202bp) and premature stop at codon 725 of 2864, validated as for panel C.

**Figure E2**

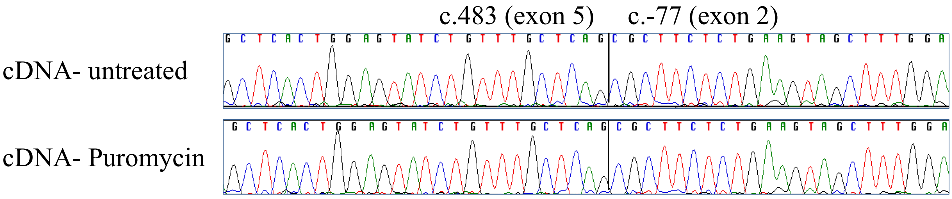
**A.**



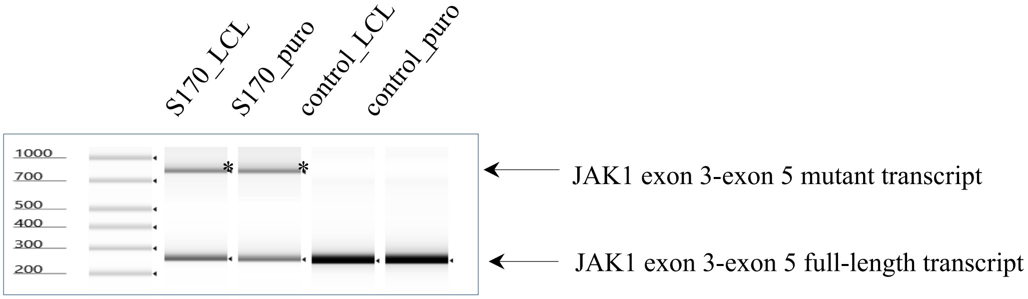
**B.**



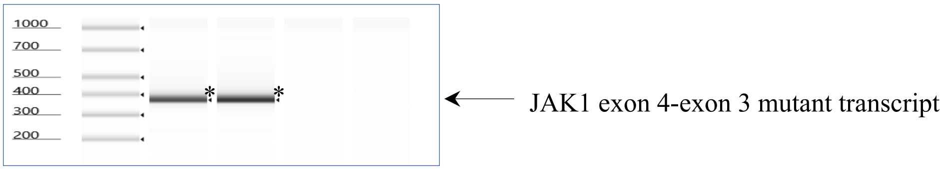
**C.**



**D.**



JAK1 exon 3-exon 5; c.158-414rev (257bp|817bp)



JAK1 exon 4-exon 3; c.215-34rev (380bp)

**Figure E2. *JAK1* triplication in patient S170**

**A.** Copy number on chr 1 of DNA from patient S170 normalized to other patients on the same run.

**B**. Alignment of *JAK1* mutant transcripts with in-tandem duplication spanning exons 2-5.

**C.** The mutant transcript is stable in patient lymphoblast RNA with or without treatment with puromycin to inhibit nonsense mediated decay

**D.** The mutant transcript is specific to mutant *JAK1* and not present in controls with normal *JAK1*

**Figure E3**

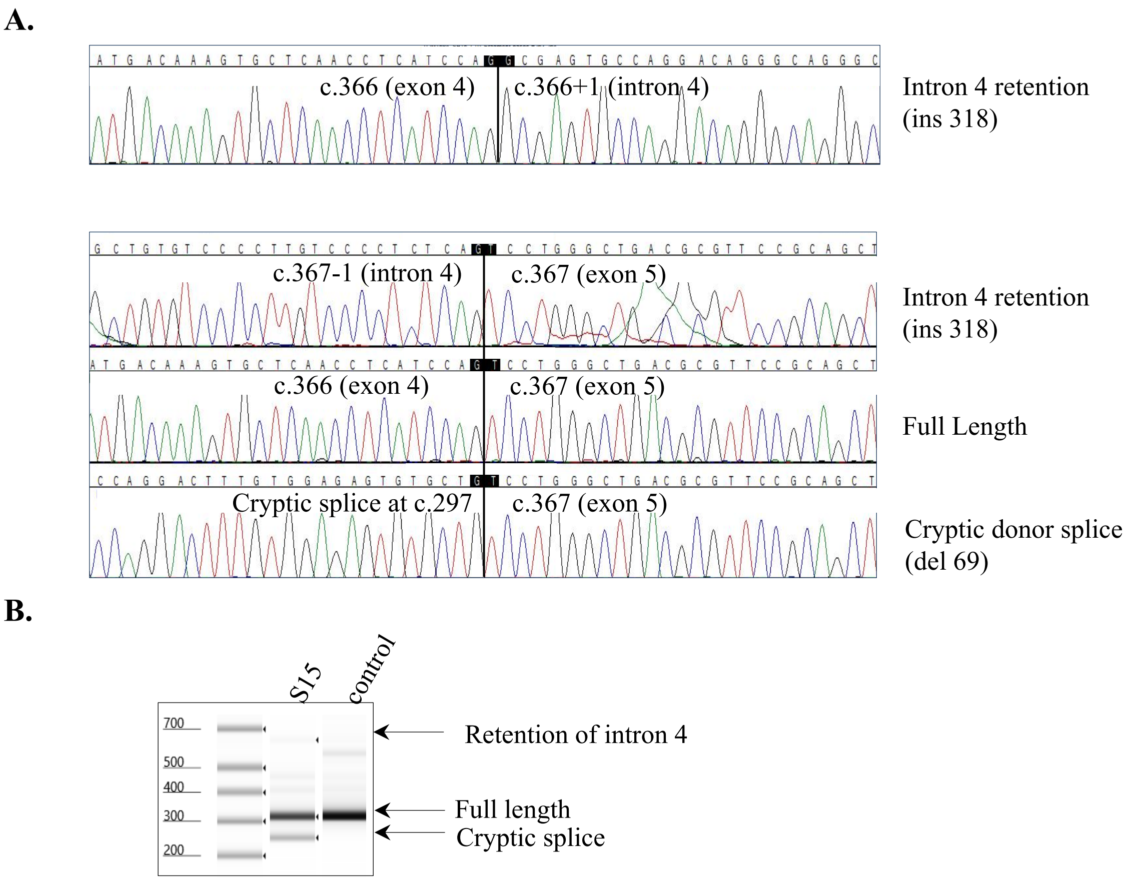


**Figure E3**. ***TOM1 c.366+2T>C*, yielding two mutant transcripts in patient S15.**

**A.** In RNA from patient's blood, *TOM1 c.366+2T>C* results in partial retention of intron 4 leading to a 318bp message insertion and a stop at codon 192 of 493, in about 5% of transcripts from the mutant allele; and a cryptic donor splice at *TOM1 c.297* in exon 4 resulting in a 69bp message deletion (del aa 100-122 within VHS domain involved in vesicular trafficking) in about 35% of transcripts from the mutant allele. *TOM1* transcripts resulting in intronic retention are predicted to undergo degradation by nonsense-mediated decay, so that a fraction of mutant message remains undetected in blood-based RNA.

**B.** RT PCR of *TOM1 c.153-476* (324bp, exons 3-5), demonstrating full-length transcript, mutant transcript with retained intron 4, and mutant transcript with cryptic splice. Relative intensities of these transcripts were 0.77 (full length), 0.02 (retained intron 4), and 0.21 (cryptic splice at c.297). Intensities of RT-PCR products corresponded to proportions of TOPO TA clones: 27 of 33 clones (0.72) had full-length transcript, 1 of 33 clones had retained intron 4 (0.03), and 5 of 33 clones (0.15) were from the TOM1 c.297 cryptic splice.

## Figure E4

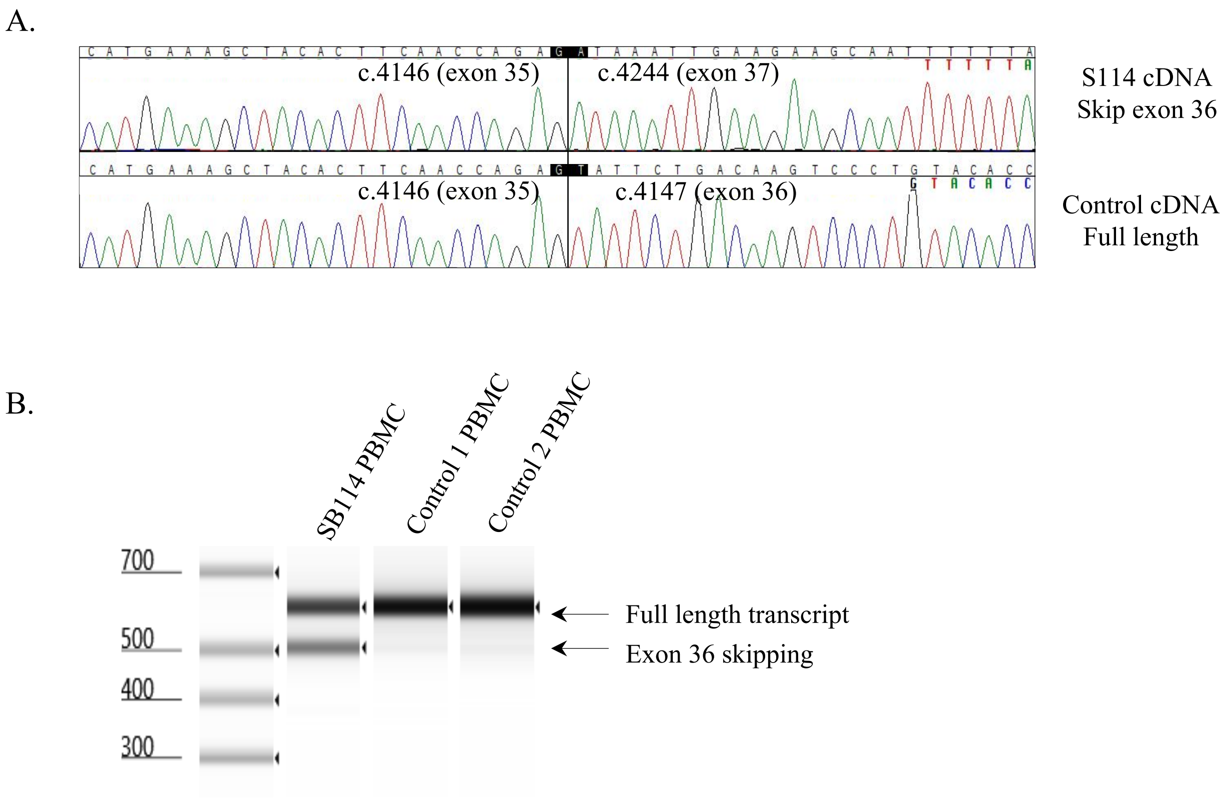


**Figure E4.** ***POLA1 c.4243+5G>A*** **in patient S114**

**A.** In RNA isolated from PBMCs of the patient, the mutant transcript is deleted for exon 36 (97bp), leading to a premature stop at codon 1385 of 1463.

**B**. RT-PCR of a segment extending from *POLA1* exon 34 to the 3’UTR demonstrates aberrant splicing from the patient compared to controls.

**Table EI:** Genes included in the panel

| Gene | Genomic position (hg19) | Gene OMIM ID |
|---|---|---|
| *ACD* | chr11:6633996-6640692 | 609377 |
| *ACP5* | chr19:11685474-11689823 | 171640 |
| *ADA* | chr20:43248159-43280399 | 608958 |
| *ADA2/CECR1* | chr22:17,659,680-17,700,325 | 607575 |
| *ADAM17* | chr2:9628614-9695949 | 603639 |
| *ADAR* | chr1:154554532-154580724 | 146920 |
| *AICDA* | chr12:8754761-8765463 | 605257 |
| *AIM2* | chr1:159032274-159046647 | 604578 |
| *AIRE* | chr21:45705720-45718102 | 607358 |
| *AP1S3* | chr2:224620046-224702319 | 615781 |
| *AP3B1* | chr5:77298149-77590579 | 603401 |
| *AP3D1* | chr19:2100986-2151556 | 607246 |
| *ARPC1B* | chr7:98972297-98992424 | 604223 |
| *ATG16L1* | chr2:234160216-234204320 | 610767 |
| *ATM* | chr11:108093558-108239826 | 607585 |
| *ATP11C* | chrX:138808504-138914447 | 300516 |
| *ATP6AP1* | chrX:153656977-153664863 | 300197 |
| *B2M* | chr15:45003684-45010357 | 109700 |
| *BACH2* | chr6:90636246-91006627 | 605394 |
| *BANK1* | chr4:102711763-102995969 | 610292 |
| *BCL10* | chr1:85731458-85742587 | 603517 |
| *BCL11B* | chr14:99635623-99738050 | 606558 |
| *BCL2L11* | chr2:111878490-111926022 | 603827 |
| *BLK* | chr8:11351520-11422108 | 191305 |
| *BLM* | chr15:91260557-91358692 | 604610 |
| *BLNK* | chr10:97951454-98031333 | 604515 |
| *BLOC1S6* | chr15:45879757-45901914 | 604310 |
| *BRAF* | chr7:140433811-140624564 | 164757 |
| *BTK* | chrX:100604434-100641212 | 300300 |
| *C1QA* | chr1:22962998-22966175 | 120550 |
| *C1QB* | chr1:22979473-22988130 | 120570 |
| *C1QC* | chr1:22970109-22974604 | 120575 |
| *C1R* | chr12:7187512-7245043 | 613785 |
| *C1S* | chr12:7167964-7178336 | 120580 |
| *C2* | chr6:31895253-31913451 | 613927 |

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|---|---|---|
| *C3* | chr19:6677845-6720693 | 120700 |
| *C4A* | chr6:31949833-31970457 | 120810 |
| *C4B* | chr6:31982571-32003195 | 120820 |
| *C5* | chr9:123714612-123812554 | 120900 |
| *C6* | chr5:41142247-41213695 | 217050 |
| *C7* | chr5:40909353-40984742 | 217070 |
| *C8A* | chr1:57320442-57383894 | 120950 |
| *C8B* | chr1:57394882-57431813 | 120960 |
| *C8G* | chr9:139839697-139841426 | 120930 |
| *C9* | chr5:39284245-39364662 | 120940 |
| *CARD11* | chr7:2945708-3083579 | 607210 |
| *CARD14* | chr17:78152306-78183130 | 607211 |
| *CARD9* | chr9:139258407-139268133 | 607212 |
| *CASP10* | chr2:202047620-202086383 | 601762 |
| *CASP8* | chr2:202098165-202152434 | 601763 |
| *CCBE1* | chr18:57098170-57364644 | 612753 |
| *CCR7* | chr17:38710020-38721736 | 600242 |
| *CD19* | chr16:28943259-28950668 | 107265 |
| *CD247* | chr1:167399876-167487847 | 186780 |
| *CD27* | chr12:6554050-6560884 | 186711 |
| *CD28* | chr2:204571197-204603635 | 186760 |
| *CD36* | chr7:80267831-80308593 | 173510 |
| *CD38* | chr4:15779887-15854866 | 107270 |
| *CD3D* | chr11:118209788-118213459 | 186790 |
| *CD3E* | chr11:118175294-118186890 | 186830 |
| *CD3G* | chr11:118215058-118224497 | 186740 |
| *CD40* | chr20:44746892-44758384 | 109535 |
| *CD40LG* | chrX:135730335-135742549 | 300386 |
| *CD46* | chr1:207925382-207968861 | 120920 |
| *CD55* | chr1:207494816-207534311 | 125240 |
| *CD59* | chr11:33724555-33758025 | 107271 |
| *CD70* | chr19:6585849-6591163 | 602840 |
| *CD79A* | chr19:42381189-42385439 | 112205 |
| *CD79B* | chr17:62006095-62009714 | 147245 |
| *CD80* | chr3:119243139-119278481 | 112203 |
| *CD81* | chr11:2398546-2418649 | 186845 |
| *CD86* | chr3:121774208-121839990 | 601020 |
| *CD8A* | chr2:87011727-87018837 | 186910 |
| *CDCA7* | chr2:174219560-174233718 | 609937 |
| *CEBPE* | chr14:23586514-23588820 | 600749 |

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| *CFB* | chr6:31913720-31919861 | 138470 |
| *CFD* | chr19:859658-863569 | 134350 |
| *CFH* | chr1:196621007-196716634 | 134370 |
| *CFHR1* | chr1:196788860-196801319 | 134371 |
| *CFHR2* | chr1:196912897-196928356 | 600889 |
| *CFHR3* | chr1:196743929-196763203 | 605336 |
| *CFHR4* | chr1:196857143-196887843 | 605337 |
| *CFHR5* | chr1:196946666-196978804 | 608593 |
| *CFI* | chr4:110661847-110723381 | 217030 |
| *CFLAR* | chr2:201980876-202037411 | 603599 |
| *CFP* | chrX:47483611-47489704 | 300383 |
| *CHD7* | chr8:61591323-61780587 | 608892 |
| *CHUK* | chr10:101948054-101989367 | 600664 |
| *CIB1* | chr15:90773476-90777279 | 602293 |
| *CIITA* | chr16:10971054-11018840 | 600005 |
| *CISH* | chr3:50643884-50649262 | 602441 |
| *CLPB* | chr11:72003468-72145728 | 616254 |
| *COG6* | chr13:40229763-40326765 | 606977 |
| *COL7A1* | chr3:48601505-48632593 | 120120 |
| *COLEC11* | chr2:3642421-3692234 | 612502 |
| *COPA* | chr1:160258376-160313354 | 601924 |
| *CORO1A* | chr16:30194730-30200397 | 605000 |
| *CR2* | chr1:207627644-207663240 | 120650 |
| *CSF2RA* | chrX:1,387,693-1,428,828 | 306250 |
| *CSF3R* | chr1:36931643-36948915 | 138971 |
| *CTC1* | chr17:8128138-8151413 | 613129 |
| *CTLA4* | chr2:204732510-204738683 | 123890 |
| *CTPS1* | chr1:41444970-41478237 | 123860 |
| *CTSC* | chr11:88026759-88070955 | 602365 |
| *CXCR4* | chr2:136871918-136873805 | 162643 |
| *CYBA* | chr16:88709696-88717492 | 608508 |
| *CYBB* | chrX:37639269-37672714 | 300481 |
| *CYLD* | chr16:50775960-50835846 | 605018 |
| *DBR1* | chr3:137879829-137893791 | 607024 |
| *DCLRE1B* | chr1:114447914-114456708 | 609683 |
| *DCLRE1C* | chr10:14938795-14996900 | 605988 |
| *DEPTOR* | chr8:120885894-121063157 | 612974 |
| *DKC1* | chrX:153991016-154005964 | 300126 |
| *DNASE1L3* | chr3:58178352-58196730 | 602244 |
| *DNMT3B* | chr20:31350190-31397162 | 602900 |

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| *DOCK2* | chr5:169064250-169510386 | 603122 |
| *DOCK8* | chr9:214000-466000 | 611432 |
| *ELANE* | chr19:852208-856246 | 130130 |
| *ENTPD1* | chr10:97515672-97637023 | 601752 |
| *EPG5* | chr18:43427573-43547305 | 615068 |
| *ERAP1* | chr5:96096513-96143892 | 606832 |
| *ERAP2* | chr5:96211642-96255420 | 609497 |
| *ERBIN* | chr5:65222381-65376851 | 606944 |
| *ERCC6L2* | chr9:98637899-98780735 | 615667 |
| *F12* | chr5:176829138-176836577 | 610619 |
| *FAAP24* | chr19:33463122-33468401 | 610884 |
| *FADD* | chr11:70049268-70053508 | 602457 |
| *FAS* | chr10:90750315-90776818 | 134637 |
| *FASLG* | chr1:172628147-172636013 | 134638 |
| *FAT1* | chr4:187508936-187644987 | 600976 |
| *FCGR1A* | chr1:149754249-149764074 | 146760 |
| *FCGR2A* | chr1:161475204-161489360 | 146790 |
| *FCGR2B* | chr1:161632904-161648444 | 604590 |
| *FCGR3A* | chr1:161511548-161519893 | 146740 |
| *FCGR3B* | chr1:161592985-161601252 | 610665 |
| *FCGRT* | chr19:50015535-50029685 | 601437 |
| *FCN3* | chr1:27695600-27701343 | 604973 |
| *FERMT1* | chr20:6055491-6104191 | 607900 |
| *FERMT3* | chr11:63974151-63991363 | 607901 |
| *FLG* | chr1:152274650-152297679 | 135940 |
| *FOS* | chr14:75745480-75748937 | 164810 |
| *FOXN1* | chr17:26850350-26866100 | 600838 |
| *FOXP3* | chrX:49105900-49122200 | 300292 |
| *FPR1* | chr19:52249022-52255150 | 136537 |
| *FUT2* | chr19:49199227-49209191 | 182100 |
| *FYN* | chr6:111981534-112194655 | 137025 |
| *G6PC3* | chr17:42148097-42153712 | 611045 |
| *G6PD* | chrX:153759604-153775233 | 305900 |
| *GATA2* | chr3:128197150-128213000 | 137295 |
| *GFI1* | chr1:92940317-92952433 | 600871 |
| *GIMAP5* | chr7:150434435-150440737 | 608086 |
| *GINS1* | chr20:25388318-25429191 | 610608 |
| *GRB2* | chr17:73314156-73401789 | 108355 |
| *GUCY2C* | chr12:14765565-14849519 | 601330 |
| *HAVCR2* | chr5:156512842-156536248 | 606652 |

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| *HAX1* | chr1:154245038-154248351 | 605998 |
| *HELLS* | chr10:96305523-96361856 | 603946 |
| *HIF1A* | chr14:62162118-62214977 | 603348 |
| *HPS1* | chr10:100175954-100206720 | 604982 |
| *HPS4* | chr22:26846847-26879829 | 606682 |
| *HPS6* | chr10:103825123-103827795 | 607522 |
| *ICOS* | chr2:204801470-204826300 | 604558 |
| *IFIH1* | chr2:163123588-163175218 | 606951 |
| *IFNAR1* | chr21:34697213-34732129 | 107450 |
| *IFNAR2* | chr21:34602199-34636818 | 602376 |
| *IFNGR1* | chr6:137518620-137540567 | 107470 |
| *IFNGR2* | chr21:34775201-34809828 | 147569 |
| *IGHM* | chr14:106,320,448-106,322,322 | 147020 |
| *IGLL1* | chr22:23915311-23922495 | 146770 |
| *IKBKB* | chr8:42128819-42190171 | 603258 |
| *IKBKG* | chrX:153775561-153793261 | 300248 |
| *IKZF1* | chr7:50344264-50472799 | 603023 |
| *IKZF2* | chr2:213864407-214015058 | 606234 |
| *IKZF3* | chr17:37913967-38020441 | 606221 |
| *IKZF4* | chr12:56414688-56432219 | 606239 |
| *IKZF5* | chr10:124750321-124768203 | 606238 |
| *IL10* | chr1:206940947-206945839 | 124092 |
| *IL10RA* | chr11:117857105-117872198 | 146933 |
| *IL10RB* | chr21:34638664-34669539 | 123889 |
| *IL12B* | chr5:158741790-158757481 | 161561 |
| *IL12RB1* | chr19:18169804-18197813 | 601604 |
| *IL12RB2* | chr1:67773046-67862583 | 601642 |
| *IL17A* | chr6:52051184-52055436 | 603149 |
| *IL17B* | chr5:148753829-148758838 | 604627 |
| *IL17C* | chr16:88705000-88706882 | 604628 |
| *IL17F* | chr6:52101483-52109298 | 606496 |
| *IL17RA* | chr22:17565848-17596584 | 605461 |
| *IL17RC* | chr3:9958757-9975305 | 610925 |
| *IL18RAP* | chr2:103035249-103069025 | 604509 |
| *IL1RN* | chr2:113885137-113891593 | 147679 |
| *IL21* | chr4:123533782-123542212 | 605384 |
| *IL21R* | chr16:27438578-27463363 | 605383 |
| *IL23R* | chr1:67632168-67725662 | 607562 |
| *IL2RA* | chr10:6052656-6104333 | 147730 |
| *IL2RG* | chrX:70327150-70331481 | 308380 |

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| *IL36RN* | chr2:113816684-113822321 | 605507 |
| *IL6ST* | chr5:55230922-55290821 | 600694 |
| *IL7R* | chr5:35856976-35880000 | 146661 |
| *INO80* | chr15:41271077-41408444 | 610169 |
| *IRAK1* | chrX:153275956-153285342 | 300283 |
| *IRAK4* | chr12:44152746-44183346 | 606883 |
| *IRF1* | chr5:131817300-131826465 | 147575 |
| *IRF2* | chr4:185308875-185395726 | 147576 |
| *IRF2BP2* | chr1:234740014-234745271 | 615332 |
| *IRF3* | chr19:50162825-50169132 | 603734 |
| *IRF4* | chr6:391738-411443 | 601900 |
| *IRF5* | chr7:128578270-128590096 | 607218 |
| *IRF7* | chr11:612554-615999 | 605047 |
| *IRF8* | chr16:85931050-85956212 | 601565 |
| *IRGM* | chr5:150226084-150281964 | 608212 |
| *ISG15* | chr1:948846-949920 | 147571 |
| *ITCH* | chr20:32951040-33099578 | 606409 |
| *ITGA3* | chr17:48133331-48167849 | 605025 |
| *ITGAE* | chr17:3617918-3704537 | 604682 |
| *ITGAM* | chr16:31271287-31344213 | 120980 |
| *ITGB2* | chr21:46305867-46340965 | 600065 |
| *ITK* | chr5:156607906-156682109 | 186973 |
| *ITPKB* | chr1:226819390-226926876 | 147522 |
| *JAGN1* | chr3:9932270-9936033 | 616012 |
| *JAK1* | chr1:65298905-65432252 | 147795 |
| *JAK2* | chr9:4985244-5128183 | 147796 |
| *JAK3* | chr19:17935590-17958841 | 600173 |
| *JUN* | chr1:59246462-59249785 | 165160 |
| *JUNB* | chr19:12902309-12904125 | 165161 |
| *KDM6A* | chrX:44732420-44971857 | 300128 |
| *KMT2D* | chr12:49411750-49450000 | 602113 |
| *KRAS* | chr12:25357722-25403865 | 190070 |
| *LAG3* | chr12:6881669-6887621 | 153337 |
| *LAMTOR2* | chr1:156024516-156028301 | 610389 |
| *LAT* | chr16:28996386-29002104 | 602354 |
| *LCK* | chr1:32739711-32751768 | 153390 |
| *LIG1* | chr19:48618701-48673860 | 126391 |
| *LIG4* | chr13:108859789-108867130 | 601837 |
| *LPIN2* | chr18:2916991-3011945 | 605519 |
| *LRBA* | chr4:151185810-151936419 | 606453 |

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| *LRRC8A* | chr9:131644780-131680318 | 608360 |
| *LYN* | chr8:56792385-56925006 | 165120 |
| *LYST* | chr1:235824330-236030227 | 606897 |
| *MAGT1* | chrX:77081860-77151065 | 300715 |
| *MAL* | chr2:95691399-95719737 | 188860 |
| *MALT1* | chr18:56338617-56417371 | 604860 |
| *MAP2K1* | chr15:66679210-66783882 | 176872 |
| *MAP3K14* | chr17:43340485-43394430 | 604655 |
| *MAPK8* | chr10:49514681-49647403 | 601158 |
| *MASP1* | chr3:186933872-187009810 | 600521 |
| *MASP2* | chr1:11086579-11107296 | 605102 |
| *MCM10* | chr10:13203553-13253104 | 609357 |
| *MCM4* | chr8:48872762-48890720 | 602638 |
| *MEFV* | chr16:3292027-3306627 | 608107 |
| *MOGS* | chr2:74688183-74692537 | 601336 |
| *MPO* | chr17:56347216-56358296 | 606989 |
| *MS4A1* | chr11:60223281-60238225 | 112210 |
| *MSH5* | chr6:31707724-31730455 | 603382 |
| *MSH6* | chr2:48010220-48034092 | 600678 |
| *MSN* | chrX:64887510-64961793 | 309845 |
| *MTHFD1* | chr14:64854758-64926725 | 172460 |
| *MVK* | chr12:110011499-110035075 | 251170 |
| *MYD88* | chr3:38179968-38184513 | 602170 |
| *MYO5A* | chr15:52599479-52821247 | 160777 |
| *MYO5B* | chr18:47349155-47721451 | 606540 |
| *MYSM1* | chr1:59120410-59165747 | 612176 |
| *NBN* | chr8:90945563-90996899 | 602667 |
| *NCF1* | chr7:74188308-74203720 | 608512 |
| *NCF2* | chr1:183524696-183559739 | 608515 |
| *NCF4* | chr22:37257029-37274059 | 601488 |
| *NEIL3* | chr4:178230990-178284092 | 608934 |
| *NFAT5* | chr16:69599868-69738569 | 604708 |
| *NFATC1* | chr18:77155771-77289323 | 600489 |
| *NFATC2* | chr20:50003493-50159258 | 600490 |
| *NFATC3* | chr16:68119268-68263162 | 602698 |
| *NFATC4* | chr14:24836116-24848810 | 602699 |
| *NFKB1* | chr4:103422485-103538459 | 164011 |
| *NFKB2* | chr10:104154334-104162286 | 164012 |
| *NFKBIA* | chr14:35870715-35873960 | 164008 |
| *NFKBIB* | chr19:39390569-39399534 | 604496 |

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|---|---|---|
| *NFKBID* | chr19:36378853-36391564 | |
| *NFKBIZ* | chr3:101568357-101579869 | 608004 |
| *NHEJ1* | chr2:219940045-220025587 | 611290 |
| *NHP2* | chr5:177576463-177580961 | 606470 |
| *NLRC4* | chr2:32449517-32490812 | 606831 |
| *NLRP1* | chr17:5417437-5487832 | 606636 |
| *NLRP12* | chr19:54296837-54327657 | 609648 |
| *NLRP3* | chr1:247581350-247612410 | 606416 |
| *NLRP7* | chr19:55434876-55458873 | 609661 |
| *NOD2* | chr16:50731049-50766988 | 605956 |
| *NOP10* | chr15:34633916-34635362 | 606471 |
| *NRAS* | chr1:115247084-115259515 | 164790 |
| *NSMCE3* | chr15:29560352-29562020 | 608243 |
| *NT5E* | chr6:86159301-86205509 | 129190 |
| *ORAI1* | chr12:122064454-122079946 | 610277 |
| *OTULIN* | chr5:14664753-14699959 | 615712 |
| *PARN* | chr16:14529556-14724128 | 604212 |
| *PAX1* | chr20:21686296-21699124 | 167411 |
| *PAX5* | chr9:36833271-37034476 | 167414 |
| *PDCD1* | chr2:242792032-242801058 | 600244 |
| *PGM3* | chr6:83874591-83903655 | 172100 |
| *PIAS1* | chr15:68346913-68483802 | 603566 |
| *PIAS2* | chr18:44395672-44497495 | 603567 |
| *PIAS3* | chr1:145575987-145586546 | 605987 |
| *PIAS4* | chr19:4007595-4039384 | 605989 |
| *PIK3CD* | chr1:9711789-9789172 | 602839 |
| *PIK3CG* | chr7:106505722-106549423 | 601232 |
| *PIK3R1* | chr5:67511583-67597649 | 171833 |
| *PLCG2* | chr16:81812862-81996298 | 600220 |
| *PMM2* | chr16:8891669-8943194 | 601785 |
| *PMS2* | chr7:6010555-6048737 | 600259 |
| *PNP* | chr14:20937537-20946165 | 164050 |
| *POLA1* | chrX:24711949-25015103 | 312040 |
| *POLE* | chr12:133200347-133264110 | 174762 |
| *POLE2* | chr14:50110269-50155098 | 602670 |
| *POLR3A* | chr10:79734906-79789298 | 614258 |
| *POMP* | chr13:29233140-29253094 | 613386 |
| *PRF1* | chr10:72357103-72362531 | 170280 |
| *PRKCD* | chr3:53195222-53226733 | 176977 |
| *PRKCQ* | chr10:6469104-6622263 | 600448 |

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|---|---|---|
| *PRKDC* | chr8:48685668-48872743 | 600899 |
| *PSMA3* | chr14:58711522-58738727 | 176843 |
| *PSMB10* | chr16:67968406-67970780 | 176847 |
| *PSMB4* | chr1:151372040-151374412 | 602177 |
| *PSMB8* | chr6:32808493-32812712 | 177046 |
| *PSMB9* | chr6:32821937-32827628 | 177045 |
| *PSME1* | chr14:24605366-24608176 | 600654 |
| *PSME2* | chr14:24612573-24615855 | 602161 |
| *PSTPIP1* | chr15:77287425-77329816 | 606347 |
| *PTEN* | chr10:89623194-89731687 | 601728 |
| *PTPN11* | chr12:112856701-112947722 | 601728 |
| *PTPN22* | chr1:114356432-114414381 | 600716 |
| *PTPRC* | chr1:198608097-198726605 | 151460 |
| *RAB27A* | chr15:55495163-55562592 | 603868 |
| *RAC2* | chr22:37621300-37640339 | 602049 |
| *RAG1* | chr11:36589562-36601312 | 179615 |
| *RAG2* | chr11:36613492-36619829 | 179616 |
| *RASGRP1* | chr15:38780301-38857007 | 603962 |
| *RBCK1* | chr20:388693-412783 | 610924 |
| *RC3H1* | chr1:173900221-173962210 | 609424 |
| *REL* | chr2:61108629-61155306 | 164910 |
| *RELA* | chr11:65421066-65430443 | 164014 |
| *RELB* | chr19:45504706-45541456 | 604758 |
| *RFX5* | chr1:151313115-151319769 | 601863 |
| *RFXANK* | chr19:19303007-19312678 | 603200 |
| *RFXAP* | chr13:37393338-37403740 | 601861 |
| *RHOH* | chr4:40198526-40246384 | 602037 |
| *RIT1* | chr1:155867598-155880706 | 609591 |
| *RLTPR* | chr16:67679029-67691472 | 610859 |
| *RMRP* | chr9:35,657,748-35,658,015 | 157660 |
| *RNASEH2A* | chr19:12917427-12924462 | 606034 |
| *RNASEH2B* | chr13:51483813-51530901 | 610326 |
| *RNASEH2C* | chr11:65485143-65488409 | 610330 |
| *RNF168* | chr3:196195653-196230639 | 612688 |
| *RNF31* | chr14:24616658-24629870 | 612487 |
| *RNU4ATAC* | chr2:122,288,441-122,288,598 | 601428 |
| *RORC* | chr1:151778546-151804348 | 602943 |
| *RPSA* | chr3:39448179-39454033 | 150370 |
| *RTEL1* | chr20:62289162-62327606 | 608833 |
| *SAMD9* | chr7:92728825-92747336 | 610456 |

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|---|---|---|
| *SAMD9L* | chr7:92759366-92777701 | 611170 |
| *SAMHD1* | chr20:35520226-35580246 | 606754 |
| *SBDS* | chr7:66452689-66460588 | 607444 |
| *SBNO2* | chr19:1107632-1174282 | 615729 |
| *SEC61A1* | chr3:127771211-127790526 | 609213 |
| *SEMA3E* | chr7:82993221-83278479 | 608166 |
| *SERPING1* | chr11:57365026-57382326 | 606860 |
| *SH2B3* | chr12:111843751-111889427 | 605093 |
| *SH2D1A* | chrX:123480131-123507010 | 300490 |
| *SH3BP2* | chr4:2820540-2842823 | 602104 |
| *SHARPIN* | chr8:145153535-145159140 | 611885 |
| *SKIV2L* | chr6:31926580-31937532 | 600478 |
| *SLC11A1* | chr2:219246751-219261617 | 600266 |
| *SLC29A3* | chr10:73079009-73123147 | 612373 |
| *SLC35C1* | chr11:45826640-45834567 | 605881 |
| *SLC37A4* | chr11:118895060-118901616 | 602671 |
| *SLC46A1* | chr17:26721660-26733230 | 611672 |
| *SLC7A7* | chr14:23242430-23285107 | 603593 |
| *SMARCAL1* | chr2:217277136-217347776 | 606622 |
| *SMARCD2* | chr17:61909440-61920351 | 601736 |
| *SOCS1* | chr16:11348273-11350039 | 603597 |
| *SOCS2* | chr12:93963597-93970521 | 605117 |
| *SOCS3* | chr17:76352857-76356160 | 604176 |
| *SOCS4* | chr14:55493843-55516207 | 616337 |
| *SOCS5* | chr2:46926098-46989927 | 607094 |
| *SOCS6* | chr18:67956136-67997434 | 605118 |
| *SOCS7* | chr17:36508006-36561846 | 608788 |
| *SP110* | chr2:231033633-231084827 | 604457 |
| *SPINK5* | chr5:147443534-147516925 | 605010 |
| *SPPL2A* | chr15:50999729-51057910 | 608238 |
| *STAT1* | chr2:191833761-191878976 | 600555 |
| *STAT2* | chr12:56735380-56754037 | 600556 |
| *STAT3* | chr17:40465342-40540513 | 102582 |
| *STAT4* | chr2:191894301-192016322 | 600558 |
| *STAT5A* | chr17:40439565-40463960 | 601511 |
| *STAT5B* | chr17:40351194-40428424 | 604260 |
| *STAT6* | chr12:57489186-57505196 | 601512 |
| *STIM1* | chr11:3876932-4114440 | 605921 |
| *STK4* | chr20:43595114-43708618 | 604965 |
| *STN1* | chr10:105637315-105678045 | 613128 |

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|---|---|---|
| *STX11* | chr6:144471653-144513076 | 605014 |
| *STXBP2* | chr19:7701986-7712760 | 601717 |
| *SYK* | chr9:93563961-93660842 | 600085 |
| *TALDO1* | chr11:747431-765024 | 602063 |
| *TAP1* | chr6:32812985-32821748 | 170260 |
| *TAP2* | chr6:32793186-32806547 | 170261 |
| *TAPBP* | chr6:33267470-33282164 | 601962 |
| *TAZ* | chrX:153639853-153650065 | 300394 |
| *TBC1D8B* | chrX:106045918-106119380 | 301027 |
| *TBK1* | chr12:64845839-64895899 | 604834 |
| *TCF3* | chr19:1609288-1652328 | 147141 |
| *TCN2* | chr22:31003069-31023047 | 613441 |
| *TERC* | chr3:169,482,398-169,482,848 | 602322 |
| *TERT* | chr5:1253281-1295162 | 187270 |
| *TFRC* | chr3:195776154-195808961 | 190010 |
| *TGFBR1* | chr9:101867370-101916474 | 190181 |
| *TGFBR2* | chr3:30647993-30735634 | 190182 |
| *THBD* | chr20:23026269-23030301 | 188040 |
| *TICAM1* | chr19:4815935-4831754 | 607601 |
| *TIGIT* | chr3:114012832-114029135 | 612859 |
| *TINF2* | chr14:24708848-24711880 | 604319 |
| *TIRAP* | chr11:126152981-126163071 | 606252 |
| *TLR3* | chr4:186990308-187006252 | 603029 |
| *TLR4* | chr9:120466452-120479769 | 603030 |
| *TLR7* | chrX:12885201-12908480 | 300365 |
| *TLR9* | chr3:52255095-52260179 | 605474 |
| *TMC6* | chr17:76108998-76124875 | 605828 |
| *TMC8* | chr17:76126858-76139049 | 605829 |
| *TMEM173* | chr5:138855112-138862375 | 612374 |
| *TNFAIP3* | chr6:138188324-138204451 | 191163 |
| *TNFRSF11A* | chr18:59992519-60054943 | 603499 |
| *TNFRSF13B* | chr17:16842397-16875402 | 604907 |
| *TNFRSF13C* | chr22:42321035-42322821 | 606269 |
| *TNFRSF18* | chr1:1138887-1142089 | 603905 |
| *TNFRSF1A* | chr12:6437922-6451283 | 191190 |
| *TNFRSF4* | chr1:1146705-1149548 | 600315 |
| *TNFSF12* | chr17:7452374-7461207 | 602695 |
| *TNFSF4* | chr1:173152869-173176452 | 603594 |
| *TOM1* | chr22:35695796-35743987 | 604700 |
| *TPP2* | chr13:103249285-103332308 | 190470 |

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|---|---|---|
| *TRAF1* | chr9:123664670-123689173 | 601711 |
| *TRAF2* | chr9:139780964-139821067 | 601895 |
| *TRAF3* | chr14:103243815-103377837 | 601896 |
| *TRAF3IP2* | chr6:111880142-111927154 | 607043 |
| *TRAF6* | chr11:36505316-36531863 | 602355 |
| *TREX1* | chr3:48506918-48509044 | 606609 |
| *TRNT1* | chr3:3168599-3190707 | 612907 |
| *TTC37* | chr5:94799598-94890709 | 614589 |
| *TTC7A* | chr2:47168312-47303275 | 609332 |
| *TYK2* | chr19:10461203-10491248 | 176941 |
| *UNC13D* | chr17:73823305-73840798 | 608897 |
| *UNC93B1* | chr11:67758570-67771595 | 608204 |
| *UNG* | chr12:109535922-109548798 | 191525 |
| *USB1* | chr16:58035276-58055527 | 613276 |
| *USP18* | chr22:18632757-18660164 | 607057 |
| *VPS13B* | chr8:100025493-100889814 | 607817 |
| *VPS45* | chr1:150039349-150117505 | 610035 |
| *WAS* | chrX:48542185-48549818 | 300392 |
| *WASF2* | chr1:27730729-27816698 | 300392 |
| *WDR1* | chr4:10075962-10118573 | 604734 |
| *WIPF1* | chr2:175424301-175499307 | 602357 |
| *XIAP* | chrX:122994016-123047829 | 300079 |
| *ZAP70* | chr2:98330030-98356323 | 176947 |
| *ZBTB1* | chr14:64971291-64991669 | 616578 |
| *ZBTB24* | chr6:109783718-109804440 | 614064 |
| *ZBTB46* | chr20:62375020-62436856 | 614639 |
| *ZNF341* | chr20:32319565-32380075 | 618269 |

**Table EII.** Recommendations for therapy, gene-by-gene, for patients with genetic diagnoses

| ***Gene*** | **N*** | **Recommendations for therapy** |
|---|---|---|
| *AIRE* | 1 | Consider azathioprine and rituximab. Recommend pneumococcal vaccination; pulmonary, thyroid, parathyroid, liver screening labs and imaging |
| *BACH2* | 1 | Consider pulmonary and immunoglobulin level screening |
| *BCL11B* | 2 | Neurologic screening. Consider HCT |
| *CARD11* | 4 | No clear therapeutic or screening recommendations |
| *CARD14* | 2 | Consider TNF-alpha inhibitors and IL12/IL23 inhibitors. Unlikely amenable to HCT |
| *CTLA4* | 4 | Consider abatacept, sirolimus, or hct. Recommend regular screening for malignancy |
| *IRF2BP2* | 1 | Recommend screening for pulmonary and GI disease, and for antibody defects |
| *ITCH* | 1 | No clear therapeutic or screening recommendations |
| *JAK1* | 3 | Consider JAK inhibitors |
| *KMT2D* | 1 | Recommend screening for antibody defects and cardiac defects |
| *LRBA* | 4 | Consider abatacept, sirolimus, or HCT. Recommend regular screening for malignancy. |
| *MYO5B* | 1 | Unlikely amenable to HCT |
| *NFKB1* | 1 | Recommend screening for renal, thyroid, pulmonary, and hematologic disease. Also recommend screening for malignancy. |
| *NLRC4* | 1 | Consider recombinant IL-18-binding protein (in trials) |
| *POLA1* | 2 | Recommend regular ophthalmologic screening exams |
| *POMP* | 1 | No clear therapeutic or screening recommendations |
| *RAG1* | 2 | Consider HCT. Recommend screening for renal, thyroid, pulmonary, and hematologic disease |
| *SH2D1A* | 1 | Consider HCT. Recommend regular screening for malignancy |
| *SKIV2L* | 1 | Unlikely amenable to HCT |
| *STAT1* | 2 | Consider JAK inhibitors. Consider screening for cranial aneurysms |
| *STAT3* | 4 | Consider JAK inhibitors, IL-6 inhibitors, or HCT. Consider screening for pulmonary disease and malignancy. |
| *TNFAIP3* | 2 | TNF-alpha inhibitors |
| *TNFRSF6 /FAS* | 1 | Consider sirolimus. Recommend regular screening for malignancy. |
| *TNFRSF13B* | 1 | No clear therapeutic or screening recommendations |
| *TOM1* | 1 | Consider pulmonary screening |
| *TTC37* | 2 | Unlikely amenable to HCT |
| *XIAP* | 1 | Consider recombinant IL-18-binding protein (in trials) and HCT |

*N: number of patients in this study with a damaging mutation in the indicated gene