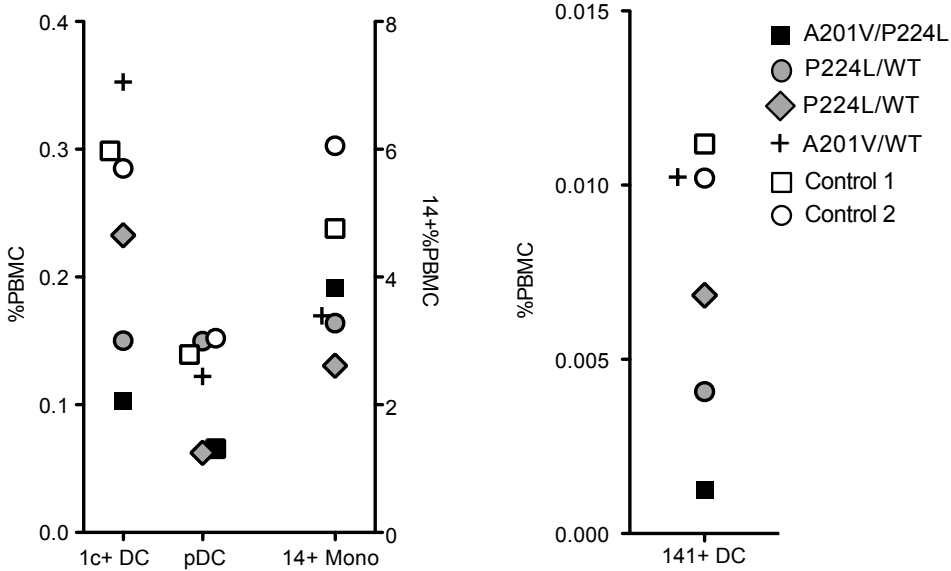
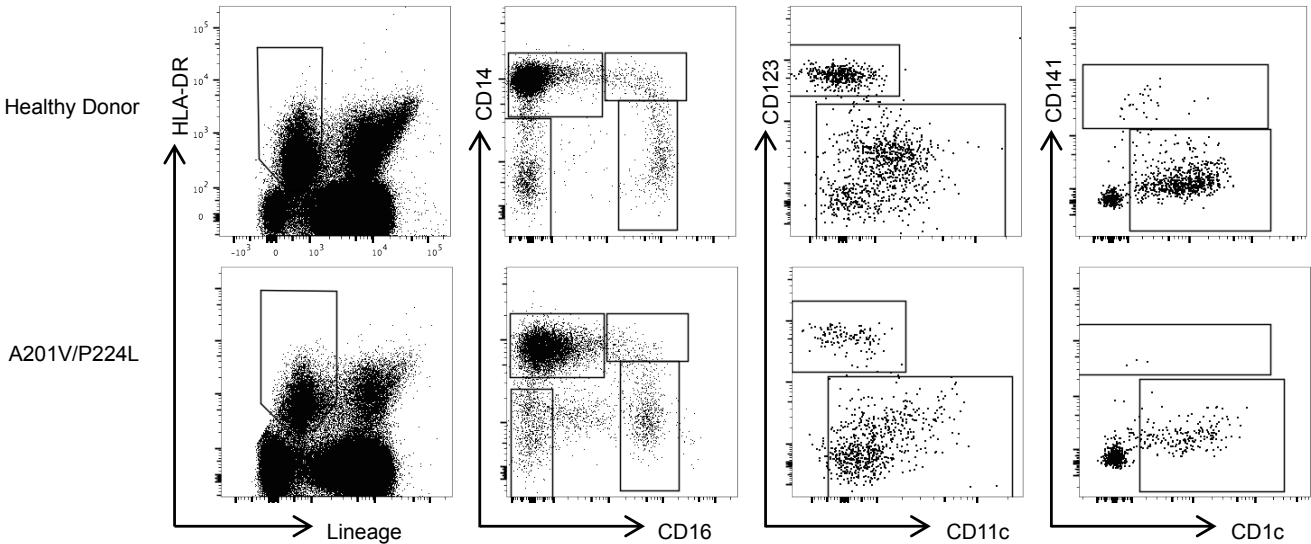


**Supplemental Figure 1. Confirmation of family member IRF8 variants by Sanger sequencing.** The proband's mother, son, brother and fraternal nephew were sequenced for the C602T (left traces) and C671T (right traces). DNA was extracted from material obtained from paraffin-embedded tissue from the now-deceased sister and the C671T variant was confirmed.



**Supplemental Figure 2. DC cell phenotype of patients with *IRF8* mutations.** DC phenotypes of heterozygous, homozygous, and healthy donor were evaluated by multi-parametric FACS phenotyping as described in Methods with the panel shown in Supplemental Table 4. Frequencies are shown as a percentage of cells found within peripheral blood mononuclear cells.

**Supplementary Table 1: Candidate gene variants from whole exome sequencing of Patient 1**

Gene	Coordinates	Zygoty	vR <sup>a</sup>	tR <sup>a</sup>	Type	ESP5400 <sup>b</sup>	1000G <sup>c</sup>	ExAC <sup>d</sup>	ExAC Count <sup>e</sup>	PhyloP <sup>f</sup>	SIFT <sup>g</sup>	Polyphen2 <sup>g</sup>	LRT <sup>g</sup>	Mut Tast
Recessive model variants:														
ELK1	X:47498442_G>A	Hemi	244	248	NS	0.0001	0	0.00009	1	0.95	T	D	N	N
IRF8	16:85952023_C>T	Het	39	112	NS	0.002	0.0046	0.0025	0	0.23	n/a	B	N	D
IRF8	16:85952092_C>T	Het	44	72	NS	0	0	0.000045	0	0.58	T	B	N	N
LRP2	2:169989127_A>G	Het	27	73	NS	0.003	0.0005	0.0019	1	-1.42	T	B	N	N
LRP2	2:170103472_G>A	Het	36	82	NS	0.002	0.0023	0.0037	5	0.80	T	D	D	D
SYNE2	14:64593458_C>T	Het	34	65	NS	0.0006	0	0.0006	0	-0.08	T	B	N	N
SYNE2	14:64687305_G>A	Het	32	60	NS	0.004	0.0023	0.0035	1	0.16	T	P	N	N
SYNE2	14:64688390_C>T	Het	69	121	NS	0.003	0.0023	0.0034	1	1.56	D	P	N	N
Dominant model variants:														
Variants not shared with unaffected family members														
TRIP12	2:230632449_GATTCA>G	Het	2	19	FS_del	0	0	0	0	0	n/a	n/a	n/a	n/a
TNRC18	7:5353412_TG>T	Het	2	10	FS_del	0	0	0	0	0	n/a	n/a	n/a	n/a
BRCC3	X:154348318_CCT>C	Het	2	19	FS_del	0	0	0	0	0	n/a	n/a	n/a	n/a
RGP1	9:35749729_T>C	Het	27	62	Splicing	0.000001	0	0.000039	3	0	n/a	n/a	n/a	n/a
ADAMTS17	15:100649248_G>T	Het	30	78	NS	0	0	0	0	-2.11	D	D	D	D
FSD2	15:83455641_C>T	Het	56	110	NS	0.0002	0	0.0000083	1	2.38	T	D	N	N
TYW5	2:200797842_C>T	Het	148	289	NS	0	0	0.000025	3	2.89	T	D	D	D
KCTD18	2:201369482_C>G	Het	29	53	NS	0.00009	0	0	0	2.94	T	D	D	N
FAT1	4:187525601_G>C	Het	32	65	NS	0	0	0.000017	2	1.01	T	B	N	n/a
SLC45A4	8:142228549_C>A	Het	11	20	NS	0.00009	0	0.000017	2	0.01	T	P	N	D

FPGS	9:130566811_G>A	Het	53	115	NS	0	0	0.000033	4	0.57	T	P	N	D
F10	13:113777231_G>C	Het	59	121	NS	0	0	0.000034	4	0.06	T	B	N	N
Variants shared with mother but not other unaffected family members (dominant incomplete penetrance model)														
RTBDN	19:12936746_G>T	Het	8	21	Stopgain	0	0	0	0	0.25	D	D	N	n/a
FBXO47	17:37119112_A>T	Het	4	8	Stopgain	0	0	0	0	1.94	T	n/a	D	A
ODF3L2	19:472393_C>T	Het	49	93	Splicing	0	0	0	0	2.03	n/a	n/a	n/a	n/a
TRHDE	12:73046175_A>T	Het	16	41	NS	0	0	0	0	2.02	T	P	D	D
MYO5B	18:47511133_C>T	Het	71	122	NS	0	0	0.000017	2	2.58	T	D	D	D
PYGB	20:25276272_T>G	Het	8	21	NS	0	0	0.0000083	1	2.09	D	B	N	n/a
LIMD1	3:45637006_C>T	Het	48	76	NS	0	0	0.000033	4	-0.18	T	B	N	N
LOC402160	4:2438661_C>T	Het	53	117	NS	0	0	n/a	n/a	0	n/a	n/a	n/a	n/a
CEP78	9:80880802_A>G	Het	29	67	NS	0	0	0.00009	2	2.15	T	P	n/a	N
HELZ	17:65105372_G>A	Het	35	75	NS	0	0	0.000025	3	2.80	D	P	D	N

Footnotes:

<sup>a</sup> vR, variant reads; tR, total reads

<sup>b</sup> Minor allelic frequency in the ESP5400 database

<sup>c</sup> Minor allelic frequency in the 1000 Genomes database

<sup>d</sup> Minor allelic frequency in the ExAC database

<sup>e</sup> For recessive model, number of homozygotes (hemizygotes for X chromosome variants) in the ExAC database; for dominant model, allele count in the ExAC database

<sup>f</sup> PhyloP conservation score

<sup>g</sup> Damage predictions by the SIFT, PolyPhen2, LRT, and Mutation Taster algorithms: A, allowed; B, benign; D, damaging; N, neutral; P, possibly damaging; T, tolerated

Other abbreviations: FS\_del, frameshift deletion; Hemi, hemizygous; het, heterozygous; n/a, not available; NS, nonsynonymous

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

MEAN	SD	GENE ID	GENE	NAME	Gene Ontology
-39.67	8.57	NM_014511.3	KIR2DL1/KIR2DL3	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 3	other
-36.69	5.66	NM_032782.3	HAVCR2	hepatitis A virus cellular receptor 2	other
-31.21	14.70	NM_005810.3	KLRG1	killer cell lectin like receptor G1	other
-25.92	19.11	NM_001337.3	CX3CR1	chemokine (C-X3-C motif) receptor 1	G-protein coupled receptor
-15.08	5.37	NM_016260.2	IKZF2	IKAROS family zinc finger 2	transcription regulator
-12.92	4.59	NM_201563.4	FCGR2C	Fc fragment of IgG receptor IIc (gene/pseudogene)	transmembrane receptor
-12.84	14.43	NM_002460.1	IRF4	interferon regulatory factor 4	transcription regulator
-12.64	9.76	NM_002184.2	IL6ST	interleukin 6 signal transducer	transmembrane receptor
-12.38	7.41	NM_001557.2	CXCR2	chemokine (C-X-C motif) receptor 2	G-protein coupled receptor
-12.24	15.28	NM_002983.2	CCL3	chemokine (C-C motif) ligand 3	cytokine
-12.05	5.30	NM_004072.1	CMKLR1	chemerin chemokine-like receptor 1	G-protein coupled receptor
-11.44	1.70	NM_003820.2	TNFRSF14	tumor necrosis factor receptor superfamily member 14	transmembrane receptor
-11.23	2.85	NM_198157.1	UBE2L3	ubiquitin conjugating enzyme E2L 3	kinase
-10.04	3.91	NM_002385.2	MBP	myelin basic protein	other
-10.01	4.99	NM_001184714.1	SLAMF6	SLAM family member 6	transmembrane receptor
-9.31	2.10	NM_005745.7	BCAP31	B-cell receptor-associated protein 31	transporter
-9.20	0.53	NM_002880.2	RAF1	Raf-1 proto-oncogene, serine/threonine kinase	transcription regulator
-8.77	0.15	NM_002208.4	ITGAE	integrin subunit alpha E	other
-8.76	2.93	NM_014002.2	IKBKE	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon	kinase
-8.25	3.50	NM_198282.1	TMEM173	transmembrane protein 173	transmembrane receptor
-8.08	2.33	NM_000570.4	FCGR3A/FCGR3B	Fc fragment of IgG receptor IIIa	transmembrane receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

-7.88	3.59	NM_002609.3	PDGFRB	platelet derived growth factor receptor beta	growth factor
-7.77	1.11	NM_001066.2	TNFRSF1B	tumor necrosis factor receptor superfamily member 1B	transmembrane receptor
-7.68	2.99	NM_005384.2	NFIL3	nuclear factor, interleukin 3 regulated	transcription regulator
-7.17	2.34	NM_000873.3	ICAM2	intercellular adhesion molecule 2	other
-6.71	1.09	NM_000022.2	ADA	adenosine deaminase	enzyme
-6.55	7.87	NM_001083539.1	KIR3DS1	killer cell immunoglobulin-like receptor, three domains, short cytoplasmic tail, 1	other
-6.18	1.15	NM_000215.2	JAK3	Janus kinase 3	kinase
-6.15	0.77	NM_000175.2	GPI	glucose-6-phosphate isomerase	enzyme
-6.08	2.39	NM_004579.2	MAP4K2	mitogen-activated protein kinase kinase kinase kinase 2	transcription regulator
-6.01	2.51	NM_005903.5	SMAD5	SMAD family member 5	transcription regulator
-5.71	1.20	NM_005041.3	PRF1	perforin 1 (pore forming protein)	transcription regulator
-5.37	1.56	NM_005356.2	LCK	LCK proto-oncogene, Src family tyrosine kinase	other
-5.35	2.35	NM_080921.3	PTPRC	protein tyrosine phosphatase, receptor type C	phosphatase
-5.18	0.37	NM_004131.3	GZMB	granzyme B	peptidase
-5.07	1.44	NM_005157.3	ABL1	ABL proto-oncogene 1, non-receptor tyrosine kinase	kinase
-4.91	0.61	NM_005419.2	STAT2	signal transducer and activator of transcription 2	transcription regulator
-4.76	0.86	NM_005535.1	IL12RB1	interleukin 12 receptor subunit beta 1	transmembrane receptor
-4.65	0.24	NM_078481.2	ADGRE5	adhesion G protein-coupled receptor E5	G-protein coupled receptor
-4.59	0.62	NM_021602.2	CD79B	CD79b molecule	transmembrane receptor
-4.46	0.86	NM_006092.1	NOD1	nucleotide binding oligomerization domain containing 1	other
-4.43	0.44	NM_000210.1	ITGA6	integrin subunit alpha 6	transmembrane receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

-4.29	1.57	NM_001198.3	PRDM1	PR domain containing 1, with ZNF domain	enzyme
-4.06	0.59	NM_002468.3	MYD88	myeloid differentiation primary response 88	enzyme
-3.92	0.58	NM_012448.3	STAT5B	signal transducer and activator of transcription 5B	transcription regulator
-3.90	1.21	NM_014261.1	TICAM1	toll-like receptor adaptor molecule 1	other
-3.86	1.41	NM_002287.3	LAIR1	leukocyte-associated immunoglobulin-like receptor 1	transmembrane receptor
-3.82	0.45	NM_019009.2	TOLLIP	toll interacting protein	cytokine
-3.79	1.03	NM_001760.2	CCND3	cyclin D3	other
-3.78	2.56	NM_001081637.1	LILRB1	leukocyte immunoglobulin like receptor B1	transmembrane receptor
-3.72	0.57	NM_004849.2	ATG5	autophagy related 5	other
-3.62	0.99	NM_002120.3	HLA-DOB	major histocompatibility complex, class II, DO beta	transmembrane receptor
-3.56	1.10	NM_001131028.1	ATG10	autophagy related 10	enzyme
-3.53	0.84	NM_002117.4	HLA-C	major histocompatibility complex, class I, C	other
-3.52	4.98	NM_002415.1	MIF	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	transporter
-3.40	1.72	NM_002984.2	CCL4	chemokine (C-C motif) ligand 4	cytokine
-3.38	0.43	NM_006060.3	IKZF1	IKAROS family zinc finger 1	transcription regulator
-3.34	1.18	NM_002205.2	ITGA5	integrin subunit alpha 5	transmembrane receptor
-3.31	0.42	NM_005531.1	IFI16	interferon, gamma-inducible protein 16	transcription regulator
-3.31	1.19	NM_003640.3	IKBKAP	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein	other
-3.30	0.73	NM_005658.3	TRAF1	TNF receptor associated factor 1	other
-3.23	1.55	NM_006737.2	KIR3DL2	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 2	other

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

-3.19	0.65	NM_001114937.2	SH2D1A	SH2 domain containing 1A	other
-3.19	0.33	NM_003152.2	STAT5A	signal transducer and activator of transcription 5A	transcription regulator
-3.07	1.14	NM_013351.1	TBX21	T-box 21	transcription regulator
-3.03	0.68	NM_000611.4	CD59	CD59 molecule	other
-3.02	0.13	NM_198053.1	CD247	CD247 molecule	transmembrane receptor
-2.96	1.00	NM_007053.2	CD160	CD160 molecule	transmembrane receptor
-2.90	0.93	NM_006254.3	PRKCD	protein kinase C, delta	other
-2.85	0.44	NM_012340.3	NFATC2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	transcription regulator
-2.67	0.74	NM_004168.1	SDHA	succinate dehydrogenase complex subunit A, flavoprotein (Fp)	G-protein coupled receptor
-2.67	0.56	NM_016123.1	IRAK4	interleukin 1 receptor associated kinase 4	kinase
-2.62	0.66	NM_002985.2	CCL5	chemokine (C-C motif) ligand 5	cytokine
-2.59	0.33	NM_001556.1	IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta	kinase
-2.56	0.41	NM_001531.2	MR1	major histocompatibility complex, class I-related	peptidase
-2.54	0.45	NM_024318.2	LILRA6	leukocyte immunoglobulin like receptor A6	other
-2.52	0.36	NM_006433.2	GNLY	granulysin	other
-2.51	0.32	NM_000876.1	IGF2R	insulin like growth factor 2 receptor	transmembrane receptor
-2.49	0.87	NM_005533.3	IFI35	interferon induced protein 35	other
-2.47	0.25	NM_003639.2	IKBKG	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma	kinase
-2.45	0.54	NM_019839.4	LTB4R2	leukotriene B4 receptor 2	G-protein coupled receptor
-2.43	0.59	NM_002309.3	LIF	leukemia inhibitory factor	other
-2.43	0.25	NM_015089.2	CUL9	cullin 9	other



**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

-2.41	0.62	NM_019014.3	POLR1B	polymerase (RNA) I polypeptide B	transcription regulator
-2.37	0.51	NM_001172085.1	TBP	TATA-box binding protein	transcription regulator
-2.36	0.60	NM_002698.2	POU2F2	POU class 2 homeobox 2	enzyme
-2.33	0.24	NM_004555.2	NFATC3	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 3	transcription regulator
-2.31	0.56	NM_173799.2	TIGIT	T-cell immunoreceptor with Ig and ITIM domains	other
-2.26	0.51	NM_004585.3	RARRES3	retinoic acid receptor responder (tazarotene induced) 3	enzyme
-2.24	0.53	NM_001040033.1	CD53	CD53 molecule	other
-2.24	0.22	NM_003331.3	TYK2	tyrosine kinase 2	other
-2.22	0.16	NM_004707.2	ATG12	autophagy related 12	other
-2.19	0.32	NM_006144.2	GZMA	granzyme A	peptidase
-2.16	0.35	NM_000402.2	G6PD	glucose-6-phosphate dehydrogenase	enzyme
-2.15	0.47	NM_002182.2	IL1RAP	interleukin 1 receptor accessory protein	transmembrane receptor
-2.12	0.46	NM_000442.3	PECAM1	platelet/endothelial cell adhesion molecule 1	kinase
-2.11	0.23	NM_003809.2	TNFSF12	tumor necrosis factor superfamily member 12	cytokine
-2.08	0.28	NM_004862.3	LITAF	lipopolysaccharide-induced TNF factor	transmembrane receptor
-2.02	0.42	NM_001754.4	RUNX1	runt-related transcription factor 1	transcription regulator
-1.95	0.37	NM_003151.2	STAT4	signal transducer and activator of transcription 4	transcription regulator
-1.94	0.21	NM_138761.3	BAX	BCL2-associated X protein	transporter
-1.94	0.43	NM_052942.3	GBP5	guanylate binding protein 5	enzyme
-1.88	0.16	NM_021805.2	SIGIRR	single immunoglobulin and toll-interleukin 1 receptor (TIR) domain	other
-1.88	0.33	NM_006006.4	ZBTB16	zinc finger and BTB domain containing 16	G-protein coupled receptor
-1.86	0.33	NM_007360.1	KLRC4-KLRK1/KLRK1	killer cell lectin like receptor K1	other

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

-1.82	0.10	NM_005902.3	SMAD3	SMAD family member 3	transporter
-1.76	0.08	NM_002037.3	FYN	FYN proto-oncogene, Src family tyrosine kinase	kinase
-1.74	0.16	NM_172350.1	CD46	CD46 molecule	other
-1.74	0.16	NM_001242.4	CD27	CD27 molecule	transmembrane receptor
-1.71	0.12	NM_002209.2	ITGAL	integrin subunit alpha L	transmembrane receptor
-1.66	0.13	NM_003805.3	CRADD	CASP2 and RIPK1 domain containing adaptor with death domain	other
-1.65	0.03	NM_002414.3	CD99	CD99 molecule	other
-1.17	2.45	NM_001177388.1	LGALS3	lectin, galactoside-binding, soluble, 3	transcription regulator
-0.71	2.07	NM_021138.3	TRAF2	TNF receptor associated factor 2	other
-0.66	2.03	NM_001001548.2	CD36	CD36 molecule	transmembrane receptor
0.49	2.17	NM_003265.2	TLR3	toll-like receptor 3	transmembrane receptor
1.13	2.57	NM_005178.2	BCL3	B-cell CLL/lymphoma 3	transcription regulator
1.50	3.70	NM_000733.2	CD3E	CD3e molecule	transmembrane receptor
1.81	0.28	NM_003177.3	SYK	spleen tyrosine kinase	transcription regulator
1.90	0.29	NM_172389.1	NFATC1	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1	enzyme
1.96	7.03	NM_000634.2	CXCR1	chemokine (C-X-C motif) receptor 1	G-protein coupled receptor
2.02	0.26	NM_002675.3	PML	promyelocytic leukemia	transmembrane receptor
2.03	0.18	NM_000194.1	HPRT1	hypoxanthine phosphoribosyltransferase 1	enzyme
2.22	7.46	NM_002965.2	S100A9	S100 calcium binding protein A9	other
2.27	0.23	NM_000201.2	ICAM1	intercellular adhesion molecule 1	transmembrane receptor
2.27	0.48	NM_002118.3	HLA-DMB	major histocompatibility complex, class II, DM beta	transmembrane receptor
2.47	1.14	NM_001024736.1	CD276	CD276 molecule	other
2.47	1.14	NM_001911.2	CTSG	cathepsin G	peptidase
2.51	0.74	NM_003701.2	TNFSF11	tumor necrosis factor superfamily member 11	cytokine

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

2.55	1.09	NM_001712.3	CEACAM1	carcinoembryonic antigen related cell adhesion molecule 1	other
2.55	1.09	NM_005211.2	CSF1R	colony stimulating factor 1 receptor	kinase
2.55	1.09	NM_018724.3	IL20	interleukin 20	cytokine
2.55	1.09	NM_000891.2	KCNJ2	potassium channel, inwardly rectifying subfamily J, member 2	ion channel
2.55	1.09	NM_001190765.1	KLRF2	killer cell lectin like receptor F2	transmembrane receptor
2.55	1.09	NM_006865.3	LILRA3	leukocyte immunoglobulin like receptor A3	other
2.55	1.09	NM_002438.2	MRC1	mannose receptor, C type 1	transmembrane receptor
2.55	1.09	NM_152942.2	TNFRSF8	tumor necrosis factor receptor superfamily member 8	transmembrane receptor
2.55	1.09	NM_005283.2	XCR1	chemokine (C motif) receptor 1	cytokine
2.58	0.83	NM_001504.1	CXCR3	chemokine (C-X-C motif) receptor 3	G-protein coupled receptor
2.63	0.56	NM_000615.5	NCAM1	neural cell adhesion molecule 1	other
2.73	0.71	NM_004295.2	TRAF4	TNF receptor associated factor 4	enzyme
2.73	0.25	NM_001025159.1	CD74	CD74 molecule	transmembrane receptor
2.74	0.90	NM_002483.4	CEACAM6	carcinoembryonic antigen related cell adhesion molecule 6	other
2.90	0.72	NM_002121.4	HLA-DPB1	major histocompatibility complex, class II, DP beta 1	transmembrane receptor
2.96	0.69	NM_004951.3	GPR183	G protein-coupled receptor 183	other
2.98	6.20	NM_000584.2	CXCL8	chemokine (C-X-C motif) ligand 8	cytokine
3.05	1.39	NM_194448.2	CLEC4A	C-type lectin domain family 4 member A	transmembrane receptor
3.18	7.67	NM_002964.3	S100A8	S100 calcium binding protein A8	transcription regulator
3.29	1.58	NM_001561.4	TNFRSF9	tumor necrosis factor receptor superfamily member 9	transmembrane receptor
3.39	2.54	NM_004107.4	FCGRT	Fc fragment of IgG receptor and transporter	transmembrane receptor
3.43	2.19	NM_002185.2	IL7R	interleukin 7 receptor	transmembrane receptor
3.48	1.44	NM_001192.2	TNFRSF17	tumor necrosis factor receptor superfamily member 17	transmembrane receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

3.52	0.53	NM_000958.2	PTGER4	prostaglandin E receptor 4	G-protein coupled receptor
3.54	1.22	NM_001001392.1	CD44	CD44 molecule (Indian blood group)	enzyme
3.59	0.67	NM_003745.1	SOCS1	suppressor of cytokine signaling 1	transcription regulator
3.84	1.46	NM_003202.2	TCF7	transcription factor 7 (T-cell specific, HMG-box)	transcription regulator
3.86	1.97	NM_006120.3	HLA-DMA	major histocompatibility complex, class II, DM alpha	transmembrane receptor
3.98	2.18	NM_006573.4	TNFSF13B	tumor necrosis factor superfamily member 13b	cytokine
4.06	6.28	NM_002704.2	PPBP	pro-platelet basic protein	ligand-dependent nuclear receptor
4.09	1.93	NM_006564.1	CXCR6	chemokine (C-X-C motif) receptor 6	G-protein coupled receptor
4.09	1.93	NM_148910.2	TIRAP	toll-interleukin 1 receptor (TIR) domain containing adaptor protein	other
4.16	1.82	NM_016232.4	IL1RL1	interleukin 1 receptor like 1	transmembrane receptor
4.16	1.54	NM_003839.2	TNFRSF11A	tumor necrosis factor receptor superfamily member 11a	transmembrane receptor
4.29	1.60	NM_000051.3	ATM	ATM serine/threonine kinase	kinase
4.41	1.40	NM_000419.3	ITGA2B	integrin subunit alpha 2b	transmembrane receptor
4.58	1.15	NM_000574.3	CD55	CD55 molecule (Cromer blood group)	other
4.59	0.49	NM_000389.2	CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	kinase
4.68	1.00	NM_001123041.2	CCR2	chemokine (C-C motif) receptor 2	G-protein coupled receptor
4.76	2.51	NM_001002295.1	GATA3	GATA binding protein 3	transcription regulator
4.81	4.58	NM_002188.2	IL13	interleukin 13	cytokine
4.87	1.35	NM_001145805.1	IRGM	immunity-related GTPase family, M	enzyme
5.00	1.60	NM_001838.2	CCR7	chemokine (C-C motif) receptor 7	G-protein coupled receptor
5.17	2.82	NM_005218.3	DEFB1	defensin beta 1	other

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

5.39	0.72	NM_000417.1	IL2RA	interleukin 2 receptor subunit alpha	transmembrane receptor
5.47	0.79	NM_031409.2	CCR6	chemokine (C-C motif) receptor 6	G-protein coupled receptor
5.49	4.19	NM_145659.3	IL27	interleukin 27	cytokine
5.49	4.19	NM_006864.2	LILRB3	leukocyte immunoglobulin like receptor B3	other
5.49	4.19	NM_002658.2	PLAU	plasminogen activator, urokinase	enzyme
5.49	4.19	NM_138554.2	TLR4	toll-like receptor 4	transmembrane receptor
5.58	2.72	NM_001244.3	TNFSF8	tumor necrosis factor superfamily member 8	cytokine
5.66	0.48	NM_000399.3	EGR2	early growth response 2	transcription regulator
5.69	3.94	NM_000043.3	FAS	Fas cell surface death receptor	transmembrane receptor
5.72	1.14	NM_016557.2	ACKR4	atypical chemokine receptor 4	G-protein coupled receptor
5.72	1.14	NM_001172.3	ARG2	arginase 2	enzyme
5.72	1.14	NM_006274.2	CCL19	chemokine (C-C motif) ligand 19	cytokine
5.72	1.14	NM_013230.2	CD24	CD24 molecule	other
5.72	1.14	NM_145071.2	CISH	cytokine inducible SH2-containing protein	other
5.72	1.14	NM_001081438.1	LILRB4	leukocyte immunoglobulin like receptor B4	transmembrane receptor
5.76	4.36	NM_001621.3	AHR	aryl hydrocarbon receptor	ligand-dependent nuclear receptor
5.78	3.83	NM_020661.1	AICDA	activation-induced cytidine deaminase	enzyme
5.78	3.83	NM_197954.2	CLEC7A	C-type lectin domain family 7 member A	transmembrane receptor
5.78	3.83	NM_001005376.1	PLAUR	plasminogen activator, urokinase receptor	peptidase
5.79	1.86	NM_033554.2	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	transmembrane receptor
5.82	4.20	NM_001710.5	CFB	complement factor B	peptidase
5.82	4.20	NM_001006658.1	CR2	complement component 3d receptor 2	transmembrane receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

5.82	4.20	NM_000609.5	CXCL12	chemokine (C-X-C motif) ligand 12	cytokine
5.82	4.20	NM_014398.3	LAMP3	lysosomal associated membrane protein 3	transmembrane receptor
5.82	1.73	NM_002995.1	XCL1	chemokine (C motif) ligand 1	transcription regulator
5.95	3.46	NM_000065.2	C6	complement component 6	other
6.13	3.44	NM_001014975.2	CFH	complement factor H	other
6.13	4.12	NM_144701.2	IL23R	interleukin 23 receptor	transmembrane receptor
6.14	3.74	NM_001771.2	CD22	CD22 molecule	transmembrane receptor
6.14	3.74	NM_002176.2	IFNB1	interferon, beta 1, fibroblast	cytokine
6.14	3.74	NM_016584.2	IL23A	interleukin 23 subunit alpha	cytokine
6.18	1.87	NM_001243078.1	CD28	CD28 molecule	transmembrane receptor
6.18	1.87	NM_003824.2	FADD	Fas associated via death domain	other
6.18	1.87	NM_024013.1	IFNA1/IFNA13	interferon, alpha 1	cytokine
6.18	1.87	NM_015869.3	PPARG	peroxisome proliferator-activated receptor gamma	transcription regulator
6.19	3.82	NM_173343.1	IL1R2	interleukin 1 receptor, type II	transmembrane receptor
6.22	6.60	NM_002990.3	CCL22	chemokine (C-C motif) ligand 22	cytokine
6.23	0.58	NM_003965.4	CCRL2	chemokine (C-C motif) receptor-like 2	G-protein coupled receptor
6.23	0.58	NM_002342.1	LTBR	lymphotoxin beta receptor	G-protein coupled receptor
6.23	2.85	NM_022555.3	HLA-DRB3	major histocompatibility complex, class II, DR beta 3	other
6.29	3.69	NM_021155.2	CD209	CD209 molecule	other
6.58	3.03	NM_002996.3	CX3CL1	chemokine (C-X3-C motif) ligand 1	cytokine
6.58	3.03	NM_000536.3	RAG2	recombination activating gene 2	enzyme
6.58	3.03	NM_000358.2	TGFBI	transforming growth factor beta induced	transcription regulator
6.58	3.03	NM_003327.2	TNFRSF4	tumor necrosis factor receptor superfamily member 4	transmembrane receptor
6.65	4.42	NM_014143.3	CD274	CD274 molecule	enzyme
6.79	2.90	NM_001296.3	ACKR2	atypical chemokine receptor 2	G-protein coupled receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_000045.2	ARG1	arginase 1	enzyme
6.79	2.90	NM_018664.2	BATF3	basic leucine zipper transcription factor, ATF-like 3	transcription regulator
6.79	2.90	NM_001196.2	BID	BH3 interacting domain death agonist	other
6.79	2.90	NM_013314.2	BLNK	B-cell linker	other
6.79	2.90	NM_004334.2	BST1	bone marrow stromal cell antigen 1	enzyme
6.79	2.90	NM_000061.1	BTK	Bruton tyrosine kinase	kinase
6.79	2.90	NM_015991.2	C1QA	complement component 1, q subcomponent, A chain	other
6.79	2.90	NM_007293.2	C4A/C4B	complement component 4B (Chido blood group)	other
6.79	2.90	NM_001735.2	C5	complement component 5	cytokine
6.79	2.90	NM_000587.2	C7	complement component 7	other
6.79	2.90	NM_000562.2	C8A	complement component 8, alpha polypeptide	other
6.79	2.90	NM_000066.2	C8B	complement component 8, beta polypeptide	other
6.79	2.90	NM_000606.2	C8G	complement component 8, gamma polypeptide	transporter
6.79	2.90	NM_001737.3	C9	complement component 9	other
6.79	2.90	NM_004345.3	CAMP	cathelicidin antimicrobial peptide	other
6.79	2.90	NM_052813.4	CARD9	caspase recruitment domain family member 9	other
6.79	2.90	NM_032977.3	CASP10	caspase 10	peptidase
6.79	2.90	NM_002986.2	CCL11	chemokine (C-C motif) ligand 11	cytokine
6.79	2.90	NM_004590.2	CCL16	chemokine (C-C motif) ligand 16	cytokine
6.79	2.90	NM_002988.2	CCL18	chemokine (C-C motif) ligand 18	cytokine
6.79	2.90	NM_002982.3	CCL2	chemokine (C-C motif) ligand 2	cytokine
6.79	2.90	NM_145898.1	CCL23	chemokine (C-C motif) ligand 23	cytokine
6.79	2.90	NM_002991.2	CCL24	chemokine (C-C motif) ligand 24	cytokine
6.79	2.90	NM_006072.4	CCL26	chemokine (C-C motif) ligand 26	cytokine
6.79	2.90	NM_016602.2	CCR10	chemokine (C-C motif) receptor 10	G-protein coupled receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_005201.2	CCR8	chemokine (C-C motif) receptor 8	G-protein coupled receptor
6.79	2.90	NM_004244.4	CD163	CD163 molecule	transmembrane receptor
6.79	2.90	NM_001763.2	CD1A	CD1a molecule	other
6.79	2.90	NM_001025109.1	CD34	CD34 molecule	other
6.79	2.90	NM_012099.1	CD3EAP	CD3e molecule associated protein	other
6.79	2.90	NM_000616.4	CD4	CD4 molecule	transmembrane receptor
6.79	2.90	NM_014207.2	CD5	CD5 molecule	transmembrane receptor
6.79	2.90	NM_001252.2	CD70	CD70 molecule	cytokine
6.79	2.90	NM_005191.3	CD80	CD80 molecule	transmembrane receptor
6.79	2.90	NM_002231.3	CD82	CD82 molecule	other
6.79	2.90	NM_175862.3	CD86	CD86 molecule	transmembrane receptor
6.79	2.90	NM_001769.2	CD9	CD9 molecule	other
6.79	2.90	NM_001795.3	CDH5	cadherin 5	other
6.79	2.90	NM_001816.3	CEACAM8	carcinoembryonic antigen related cell adhesion molecule 8	other
6.79	2.90	NM_001928.2	CFD	complement factor D (adipsin)	peptidase
6.79	2.90	NM_002621.2	CFP	complement factor properdin	other
6.79	2.90	NM_000246.3	CIITA	class II, major histocompatibility complex, transactivator	transcription regulator
6.79	2.90	NM_013252.2	CLEC5A	C-type lectin domain family 5 member A	other
6.79	2.90	NM_001007033.1	CLEC6A	C-type lectin domain family 6 member A	transmembrane receptor
6.79	2.90	NM_001831.2	CLU	clusterin	other
6.79	2.90	NM_000757.4	CSF1	colony stimulating factor 1	cytokine
6.79	2.90	NM_000758.2	CSF2	colony stimulating factor 2	cytokine
6.79	2.90	NM_000395.2	CSF2RB	colony stimulating factor 2 receptor beta common subunit	transmembrane receptor
6.79	2.90	NM_001511.1	CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	cytokine
6.79	2.90	NM_001565.1	CXCL10	chemokine (C-X-C motif) ligand 10	cytokine



**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_005409.4	CXCL11	chemokine (C-X-C motif) ligand 11	cytokine
6.79	2.90	NM_006419.2	CXCL13	chemokine (C-X-C motif) ligand 13	cytokine
6.79	2.90	NM_002089.3	CXCL2	chemokine (C-X-C motif) ligand 2	cytokine
6.79	2.90	NM_002416.1	CXCL9	chemokine (C-X-C motif) ligand 9	cytokine
6.79	2.90	NM_000397.3	CYBB	cytochrome b-245, beta polypeptide	enzyme
6.79	2.90	NM_018661.3	DEFB103A/DEFB103B	defensin beta 103B	other
6.79	2.90	NM_004942.2	DEFB4A/DEFB4B	defensin beta 4A	other
6.79	2.90	NM_005755.2	EBI3	Epstein-Barr virus induced 3	cytokine
6.79	2.90	NM_003991.2	EDNRB	endothelin receptor type B	G-protein coupled receptor
6.79	2.90	NM_001964.2	EGR1	early growth response 1	transcription regulator
6.79	2.90	NM_001098175.1	ENTPD1	ectonucleoside triphosphate diphosphohydrolase 1	enzyme
6.79	2.90	NM_133280.1	FCAR	Fc fragment of IgA receptor	other
6.79	2.90	NM_000566.3	FCGR1A	Fc fragment of IgG receptor Ia	transmembrane receptor
6.79	2.90	NM_212482.1	FN1	fibronectin 1	enzyme
6.79	2.90	NM_014009.3	FOXP3	forkhead box P3	transcription regulator
6.79	2.90	NM_000407.4	GP1BB	glycoprotein Ib platelet beta subunit	other
6.79	2.90	NM_021175.2	HAMP	hepcidin antimicrobial peptide	other
6.79	2.90	NM_139011.2	HFE	hemochromatosis	transmembrane receptor
6.79	2.90	NM_001039132.1	ICAM4	intercellular adhesion molecule 4 (Landsteiner-Wiener blood group)	other
6.79	2.90	NM_003259.3	ICAM5	intercellular adhesion molecule 5	other
6.79	2.90	NM_012092.2	ICOS	inducible T-cell co-stimulator	transmembrane receptor
6.79	2.90	NM_002164.3	IDO1	indoleamine 2,3-dioxygenase 1	enzyme
6.79	2.90	NM_000605.3	IFNA2	interferon, alpha 2	cytokine
6.79	2.90	NM_172140.1	IFNL1	interferon, lambda 1	cytokine
6.79	2.90	NM_172139.2	IFNL3	interferon, lambda 3	other
6.79	2.90	NM_000572.2	IL10	interleukin 10	cytokine
6.79	2.90	NM_002187.2	IL12B	interleukin 12B	cytokine

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_002190.2	IL17A	interleukin 17A	cytokine
6.79	2.90	NM_013371.3	IL19	interleukin 19	cytokine
6.79	2.90	NM_000575.3	IL1A	interleukin 1 alpha	cytokine
6.79	2.90	NM_000576.2	IL1B	interleukin 1 beta	cytokine
6.79	2.90	NM_000877.2	IL1R1	interleukin 1 receptor, type I	transmembrane receptor
6.79	2.90	NM_003854.2	IL1RL2	interleukin 1 receptor like 2	transmembrane receptor
6.79	2.90	NM_000577.3	IL1RN	interleukin 1 receptor antagonist	cytokine
6.79	2.90	NM_000586.2	IL2	interleukin 2	cytokine
6.79	2.90	NM_021803.2	IL21	interleukin 21	cytokine
6.79	2.90	NM_020525.4	IL22	interleukin 22	cytokine
6.79	2.90	NM_181310.1	IL22RA2	interleukin 22 receptor subunit alpha 2	transmembrane receptor
6.79	2.90	NM_018402.1	IL26	interleukin 26	cytokine
6.79	2.90	NM_000588.3	IL3	interleukin 3	cytokine
6.79	2.90	NM_000589.2	IL4	interleukin 4	cytokine
6.79	2.90	NM_000879.2	IL5	interleukin 5	cytokine
6.79	2.90	NM_000600.1	IL6	interleukin 6	cytokine
6.79	2.90	NM_000565.2	IL6R	interleukin 6 receptor	transmembrane receptor
6.79	2.90	NM_000880.2	IL7	interleukin 7	cytokine
6.79	2.90	NM_000590.1	IL9	interleukin 9	cytokine
6.79	2.90	NM_007199.1	IRAK3	interleukin 1 receptor associated kinase 3	kinase
6.79	2.90	NM_017625.2	ITLN1	intelectin 1 (galactofuranose binding)	other
6.79	2.90	NM_080878.2	ITLN2	intelectin 2	other
6.79	2.90	NM_153443.3	KIR3DL3	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 3	other
6.79	2.90	NR_028045.1	KLRAP1	killer cell lectin like receptor A1, pseudogene	other
6.79	2.90	NM_002286.5	LAG3	lymphocyte-activation gene 3	other
6.79	2.90	NM_006863.1	LILRA1	leukocyte immunoglobulin like receptor A1	cytokine

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_006866.2	LILRA2	leukocyte immunoglobulin like receptor A2	transmembrane receptor
6.79	2.90	NM_012276.3	LILRA4	leukocyte immunoglobulin like receptor A4	other
6.79	2.90	NM_001081442.1	LILRB5	leukocyte immunoglobulin like receptor B5	other
6.79	2.90	NM_002343.2	LTF	lactotransferrin	transmembrane receptor
6.79	2.90	NM_006770.3	MARCO	macrophage receptor with collagenous structure	kinase
6.79	2.90	NM_139125.3	MASP1	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)	transmembrane receptor
6.79	2.90	NM_139208.1	MASP2	mannan-binding lectin serine peptidase 2	peptidase
6.79	2.90	NM_000242.2	MBL2	mannose-binding lectin (protein C) 2, soluble	peptidase
6.79	2.90	NM_000902.2	MME	membrane metallo-endopeptidase	cytokine
6.79	2.90	NM_002445.3	MSR1	macrophage scavenger receptor 1	other
6.79	2.90	NM_000631.4	NCF4	neutrophil cytosolic factor 4	other
6.79	2.90	NM_000625.4	NOS2	nitric oxide synthase 2	other
6.79	2.90	NM_005018.1	PDCD1	programmed cell death 1	transcription regulator
6.79	2.90	NM_025239.3	PDCD1LG2	programmed cell death 1 ligand 2	phosphatase
6.79	2.90	NM_002644.2	PIGR	polymeric immunoglobulin receptor	other
6.79	2.90	NM_000300.2	PLA2G2A	phospholipase A2 group IIA	transporter
6.79	2.90	NM_014589.1	PLA2G2E	phospholipase A2 group IIE	enzyme
6.79	2.90	NM_000952.3	PTAFR	platelet-activating factor receptor	peptidase
6.79	2.90	NM_000963.1	PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	G-protein coupled receptor
6.79	2.90	NM_000450.2	SELE	selectin E	enzyme
6.79	2.90	NM_003037.2	SLAMF1	signaling lymphocytic activation molecule family member 1	transmembrane receptor
6.79	2.90	NM_000582.2	SPP1	secreted phosphoprotein 1	other

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

6.79	2.90	NM_003189.2	TAL1	T-cell acute lymphocytic leukemia 1	Type(s)
6.79	2.90	NM_006288.2	THY1	Thy-1 cell surface antigen	kinase
6.79	2.90	NM_003268.3	TLR5	toll-like receptor 5	transmembrane receptor
6.79	2.90	NM_016562.3	TLR7	toll-like receptor 7	transmembrane receptor
6.79	2.90	NM_012452.2	TNFRSF13B	tumor necrosis factor receptor superfamily member 13B	transmembrane receptor
6.79	2.90	NM_052945.3	TNFRSF13C	tumor necrosis factor receptor superfamily member 13C	transmembrane receptor
6.79	2.90	NM_001204344.1	TNFSF15	tumor necrosis factor superfamily member 15	cytokine
6.79	2.90	NM_001078.3	VCAM1	vascular cell adhesion molecule 1	enzyme
6.79	2.90	NM_000638.3	VTN	vitronectin	transmembrane receptor
7.08	2.63	NM_002526.2	NT5E	5'-nucleotidase ecto	enzyme
7.17	2.76	NM_017442.2	TLR9	toll-like receptor 9	transmembrane receptor
7.30	2.40	NM_000074.2	CD40LG	CD40 ligand	cytokine
7.30	2.40	NM_014358.2	CLEC4E	C-type lectin domain family 4 member E	other
7.30	2.40	NM_014443.2	IL17B	interleukin 17B	cytokine
7.30	2.40	NM_007115.2	TNFAIP6	TNF alpha induced protein 6	cytokine
7.30	2.40	NM_003841.3	TNFRSF10C	tumor necrosis factor receptor superfamily member 10c	other
7.51	4.95	NM_004233.3	CD83	CD83 molecule	transmembrane receptor
7.94	5.27	NM_181780.2	BTLA	B and T lymphocyte associated	other
8.23	3.17	NM_000491.3	C1QB	complement component 1, q subcomponent, B chain	other
8.23	3.17	NM_005408.2	CCL13	chemokine (C-C motif) ligand 13	cytokine
8.23	3.17	NM_032965.3	CCL15	chemokine (C-C motif) ligand 15	cytokine
8.23	3.17	NM_001770.4	CD19	CD19 molecule	transmembrane receptor
8.23	3.17	NM_000204.3	CFI	complement factor I	peptidase
8.23	3.17	NM_000651.4	CR1	complement component 3b/4b receptor 1 (Knops blood group)	transmembrane receptor
8.23	3.17	NM_001037631.1	CTLA4	cytotoxic T-lymphocyte associated protein 4	transmembrane receptor

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

8.23	3.17	NM_021642.3	FCGR2A	Fc fragment of IgG receptor IIa	transmembrane receptor
8.23	3.17	NM_015259.4	ICOSLG/LOC102723996	inducible T-cell co-stimulator ligand	other
8.23	3.17	NM_172138.1	IFNL2	interferon, lambda 2	other
8.23	3.17	NM_181879.2	LILRA5	leukocyte immunoglobulin like receptor A5	other
8.23	3.17	NM_015364.2	LY96	lymphocyte antigen 96	peptidase
8.23	3.17	NM_152866.2	MS4A1	membrane-spanning 4-domains subfamily A member 1	transmembrane receptor
8.23	3.17	NM_001018017.1	MUC1	mucin 1, cell surface associated	transmembrane receptor
8.23	3.17	NM_016734.1	PAX5	paired box 5	phosphatase
8.23	3.17	NM_000448.2	RAG1	recombination activating gene 1	kinase
8.23	3.17	NM_000062.2	SERPING1	serpin peptidase inhibitor, clade G (C1 inhibitor), member 1	transmembrane receptor
8.42	4.72	NM_000222.2	KIT	KIT proto-oncogene receptor tyrosine kinase	transmembrane receptor
9.33	3.98	NM_000064.2	C3	complement component 3	peptidase
9.33	3.98	NM_004591.1	CCL20	chemokine (C-C motif) ligand 20	cytokine
9.33	3.98	NM_002123.3	HLA-DQB1	major histocompatibility complex, class II, DQ beta 1	other
9.73	8.10	NM_001295.2	CCR1	chemokine (C-C motif) receptor 1	G-protein coupled receptor
10.59	12.11	NM_000595.2	LTA	lymphotoxin alpha	transcription regulator
11.32	4.36	NM_016610.2	TLR8	toll-like receptor 8	transmembrane receptor
12.33	10.92	NM_001560.2	IL13RA1	interleukin 13 receptor subunit alpha 1	transmembrane receptor
12.39	9.44	NM_000688.4	ALAS1	5'-aminolevulinate synthase 1	enzyme
12.49	22.47	NM_014512.1	KIR2DS4 (includes others)	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 2	transmembrane receptor
14.01	15.99	NM_016269.3	LEF1	lymphoid enhancer binding factor 1	other
15.62	7.20	NM_033016.2	PDGFB	platelet derived growth factor subunit B	enzyme
21.96	15.76	NM_001935.3	DPP4	dipeptidyl-peptidase 4	peptidase

**Supplementary Table 2: Genes up- and down-regulated in Patient 1 relative to 3 healthy donors**

22.71	20.11	NM_000882.2	IL12A	interleukin 12A	cytokine
22.91	9.77	NM_001766.3	CD1D	CD1d molecule	other
24.44	20.42	NM_019111.3	HLA-DRA	major histocompatibility complex, class II, DR alpha	transmembrane receptor
24.61	7.88	NM_003264.3	TLR2	toll-like receptor 2	other
24.62	8.11	NM_198508.2	KLRG2	killer cell lectin like receptor G2	other
26.44	20.34	NM_002751.5	MAPK11	mitogen-activated protein kinase 11	kinase
28.77	13.27	NM_002001.2	FCER1A	Fc fragment of IgE receptor 1a	transmembrane receptor
36.49	15.56	NM_000383.2	AIRE	autoimmune regulator	transcription regulator
52.04	57.90	NM_002124.2	HLA-DRB1	major histocompatibility complex, class II, DR beta 1	transmembrane receptor
107.68	49.65	NM_002122.3	HLA-DQA1	major histocompatibility complex, class II, DQ alpha 1	transmembrane receptor

**Supplemental Table 3. Overlap of IR8 binding sites with deregulated genes in A201/P224L IRF8 patient NK cells**

Peak Distance from TSS	Diff%Exp	No.%Overlap with%ChIP	No.%Diffi Exp%Genes	Total%ChIP% Bound	Total%Genes% Examined	Random Avg	Random SD	Z%score	Probability	FDR	Genes
5Gkb	FC2_UP	38	269	887	27189	8.776	2.899	10.0799	3.08E014	1.23E013	CCL2 CD74 CD1D IL1RL2 IL12B IL12A CCR2 CCR6 CCR7 IL1R1 MS4A1 TLR2 LILRB3 BID BTLA C9 VCAM1 TNFSF13B DPP4 TAL1 CD44 IL6R CYBB PPARG CCL13 LTF BATF3 CXCL12 KCNJ2 IL13RA1 TLR9 AHR TLR7 TLR4 TGFB1 LILRA5 CFP TNFRSF11A
	FC7_UP	8	32	887	27189	1.044	1.004	6.9258	6.52E006	1.30E005	CD1D CCL13 IL13RA1 IL12A TLR2 LILRA5 DPP4 MS4A1
	FC2_DN	10	98	887	27189	3.197	1.755	3.8752	0.00136482	0.00136482	LIF IL6ST IKBKB TNFRSF14 LAIR1 IKBKE TYK2 IGF2R MBP TMEM173
	FC7_DN	5	25	887	27189	0.816	0.888	4.7130	0.00112714	0.00136482	TNFRSF14 IKBKE MBP TMEM173 IL6ST
10Gkb	FC2_UP	44	269	1287	27189	12.733	3.466	9.0219	6.13E013	2.45E012	CCL2 CD74 CD1D CCR6 IL1RL2 IL12B IL12A CCR1 CCR2 IL27 CCR7 IL1R1 TNFSF13B TLR2 LILRB3 BID BTLA C9 CXCR6 MS4A1 DPP4 TNFRSF11A TAL1 CD44 IL6R CYBB PPARG CCL13 LTF BATF3 CXCL13 CXCL12 TNFRSF13B KCNJ2 IL13RA1 TLR9 CSF1 AHR TLR7 TLR4 TGFB1 LILRA5 CFP VCAM1
	FC7_UP	8	32	1287	27189	1.515	1.201	5.4018	9.37E005	0.00018747	CD1D CCL13 IL13RA1 IL12A TLR2 LILRA5 DPP4 MS4A1
	FC2_DN	13	98	1287	27189	4.639	2.098	3.9844	0.00071856	0.00090582	LIF CMKLR1 IL6ST IKBKB TNFRSF14 LAIR1 PRDM1 IKBKE LGALS3 TYK2 IGF2R MBP TMEM173
	FC7_DN	6	25	1287	27189	1.183	1.061	4.5384	0.00090582	0.00090582	MBP IL6ST TNFRSF14 IKBKE CMKLR1 TMEM173
20Gkb	FC2_UP	60	269	1825	27189	18.056	4.084	10.2706	9.38E017	3.75E016	CD74 CSF2RB CD1D CCR6 TNFSF15 IL12B TNFSF11 IL12A C1QB CCR1 CCR2 IL27 CCR7 MSR1 LILRA5 HFE CXCL13 IL1R1 MS4A1 AHR LILRB3 IL1RL2 BID BTLA XCR1 XCL1 IFNB1 C9 CXCR6 BST1 TNFSF13B DPP4 BLNK TNFRSF11A PDGFB TAL1 ENTPD1 CD44 IL6R CYBB PPARG LTF TGFB1 CCL2 CXCL12 TNFRSF13B KCNJ2 IL13RA1 CCL13 IL20 ARG1 CSF1 TLR2 SPP1 TLR7 TLR4 BATF3 TLR9 CFP VCAM1
	FC7_UP	10	32	1825	27189	2.148	1.415	5.5502	2.97E005	2.97E005	PDGFB CD1D CCL13 IL13RA1 IL12A C1QB TLR2 LILRA5 DPP4 MS4A1
	FC2_DN	21	98	1825	27189	6.578	2.473	5.8323	1.75E006	2.33E006	BCAP31 CD53 LIF CX3CR1 CCL4 MBP NFIL3 PRKCD IL6ST IKBKB TNFRSF14 LAIR1 PRDM1 IKBKE LGALS3 TYK2 IGF2R CMKLR1 TMEM173 HAVCR2 IKZF2
	FC7_DN	11	25	1825	27189	1.678	1.251	7.4538	2.24E007	4.47E007	BCAP31 CX3CR1 MBP NFIL3 IL6ST TNFRSF14 IKBKE CMKLR1 TMEM173 HAVCR2 IKZF2

For comparison of differentially expressed genes to previously identified IRF8 binding sites, published ChIP-seq data generated from mouse macrophages was used (<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSM2060952>). Genes were mapped to human where unambiguous mappings could be made and then the mouse data was filtered to all peaks within 5, 10 or 20 kB of transcriptional start sites. These were compared to differentially expressed genes with an absolute fold change of  $\geq 2$  or  $\geq 7$  split into up/down fold change (FC) or sets of random genes. Each gene considered is split into 2 groups: those containing  $\geq 1$  IRF8 peak or those that have 0. The significance of overlap of differentially expressed genes was determined using a hypergeometric distribution and resulting p-values adjusted using Benjamini-Hochberg correction.

#### Supplemental Table 4. Antibodies used for flow cytometry

##### NK cell panel

Fluorophore	Marker	Clone, Source
APC	CD94	DX22, Biolegend
APC Cy7	CD34	581, Biolegend
Pacific Blue	CD57	NC1, Beckman Coulter
QD605	CD56	HCD56, Biolegend
QD655	CD62L	DREG56, Biolegend
QD711	CD3	SK7, Biolegend
FITC	Perforin	<sup>TM</sup> G9, BD Pharmingen
PE Cy7	CD117	104D2, Biolegend
CF 594	CD16	3G8, Biolegend
APC	CD18	6.7, BD Pharmingen
Bv421	CD158e	DX9, Biolegend
FITC	CD158b	DX27, Biolegend
AlexaFluor 700	NKG2A	131411, R&D Systems
PE	NKG2C	134591, R&D Systems
PE-Cy7	NKG2D	1D11, Biolegend
AlexaFluor 700	IFN $\gamma$	4S.B3, Biolegend
QD655	TNF $\alpha$	Mab11, Biolegend
PE-Cy5	CD107a	eBioH4A3, eBioscience

##### Dendritic cell panel

Fluorophore	Marker	Clone, Source
Pacific Blue	Lineage*	Biolegend
QD605	HLA-DR	L243, Biolegend
QD655	CD11c	N418, Biolegend
FITC	CD14	M5E2, BD Biosciences
PE	CD34	4H11, eBioscience
CF594	CD16	3G8, Biolegend
PE-Cy7	CD141	M80, Biolegend
APC	CD123	6H6, Biolegend
APC-Cy7	CD1c	L161, Biolegend



**Supplemental Table 4 continued. Antibodies used for flow cytometry**

Mouse panel

<b>Fluorophore</b>	<b>Marker</b>	<b>Clone, Source</b>
AF700	CD45	30-F11, <a href="#">Biolegend</a>
BV 421	CD3	17A2, <a href="#">Biolegend</a>
APC/Cy7	NKp46	29A1.4, <a href="#">eBioscience</a>
Bv650	CD4	RM4-5, <a href="#">Biolegend</a>
Bv785	CD8a	53-6.7, <a href="#">Biolegend</a>
PE	CD25	3C7, <a href="#">Biolegend</a>
APC	CD11c	N418, <a href="#">Biolegend</a>
PE/Cy7	CD11b	M1/70, <a href="#">Biolegend</a>
FITC	CD19	6D5, <a href="#">Biolegend</a>
AmCyan	CD27	LG.3A10, <a href="#">BD Biosciences</a>
QDOT 605	CD62L	MEL-14, <a href="#">Biolegend</a>
Bv711	Ly-6G/Ly-6C(Gr-1)	RB6-8C5, <a href="#">Biolegend</a>
PE TX Red	CD14	rmC5-3, <a href="#">BD Biosciences</a>
PE Cy5	NK1.1	PK136, <a href="#">Biolegend</a>

