Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Kohn DB, Booth C, Shaw KL, et al. Autologous ex vivo lentiviral gene therapy for adenosine deaminase deficiency. N Engl J Med. DOI: 10.1056/NEJMoa2027675

Contents

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Methods

VECTOR, DRUG PRODUCT MANUFACTURE, TRANSPLANT, AND DRUG PRODUCT ATTRIBUTES FOR TRIALS NCT01852071 AND NCT02999984 (U.S. FRESH AND CRYO STUDIES)

VECTOR MANUFACTURE

The vector used in the United States (U.S.) studies was a self-inactivating lentiviral vector (LV) with codon-optimized human adenosine deaminase (ADA) complementary DNA (cDNA) driven by a shortened form of the human elongation factor α-1 gene (EFS) promoter (EFS-ADA LV), and using a Woodchuck hepatitis post-transcriptional regulatory element (WPRE) to stabilize vector transcripts and increase ADA expression (**Fig. S1**). The EFS-ADA LV was produced under Current Good Manufacturing Practice (cGMP) at the Indiana University Vector Production Facility under contract through the National Heart, Lung, and Blood Institute (NHLBI) Gene Therapy Resource Program (contract # HHSN2682012000051). The EFS-ADA LV was packaged by co-transfection of the transfer plasmid containing the lentiviral vector backbone and carrying the *ADA* cDNA, the plasmid encoding human immunodeficiency virus (HIV)-1 *GAG* and *POL*, the plasmid encoding HIV-1 Rev, and the plasmid encoding the vesicular stomatitis virus G (VSV-G) glycoprotein. The vector was produced and was fully characterized to meet release criteria agreed with the U.S. Food and Drug Administration (FDA), including purity, absence of contaminants (microbiological

control, absence of replication-competent lentivirus), potency (titer, expression of ADA enzyme activity), and identity (sequence confirmation).

DRUG PRODUCT MANUFACTURE

In both the U.S. Fresh and Cryo trials, the drug product was manufactured from $CD34^+$ hematopoietic stem and progenitor cells (HSPCs) isolated from bone marrow using immunomagnetic selection with CliniMACS® cell purification protocols (Miltenyi Biotec, Bergisch Gladbach, Germany). The cells were plated in serum-free medium supplemented with human serum albumin (HAS)and cytokines (stem cell factor [SCF] 300ng/ml], Flt-3 ligand 300 ng/ml, thrombopoietin [TPO] 100 ng/ml and IL-3 20 ng/ml) at a density of 1 x 10^6/ml for prestimulation overnight (20 hours). All cytokines (Peprotech) and culture reagents were approved for ex vivo clinical use. After prestimulation, the EF1αS-ADA lentiviral vector (EFS-ADA LV, Indiana University Vector Production Unit) was added for ~20 hours. Following transduction, the cells were washed and formulated. Patients treated in the U.S. Fresh Study received OTL-101 as a fresh formulation in which the drug product was formulated in Plasmalyte-A with 1% HSA shortly after harvest. Patients treated in the U.S. Cryo Study received OTL-101 as a cryopreserved formulation in which the drug product was formulated in 100% Cryostor CS5 (BioLife, Bothell, WA, U.S.) and cryopreserved in a control rate freezer.

TRANSPLANTATION

Patients treated in the U.S. Fresh Study received a single dose of intravenous (IV) weight-adjusted busulfan conditioning (4 mg/kg) on the day of stem cell harvest. Busulfan conditioning was initiated after confirmation that the required number of $CD34^+$ cells were isolated and in culture. After a 24-hour busulfan washout period, patients were infused intravenously with the fresh formulation of OTL-101. Drug product testing was completed in two stages, pre- and post-infusion.

Patients treated in the U.S. Cryo Study received 2 doses of busulfan conditioning after completion of drug product testing and certification. The first dose of busulfan was weight adjusted (3 mg/kg) and the second dose, given 24 hours later, was PK adjusted to a total target area under the concentration–time curve of 4900 µmol/l per minute. After a 24-hour washout period, OTL-101 was thawed at the bedside and infused intravenously.

The drug product was infused intravenously at a dose ≥1.0 x 10^6 (U.S. Fresh Study) or ≥2.0 x 10^6 (U.S. Cryo Study) $CD34^+$ cells/kg body weight. Pegylated adenosine deaminase enzyme replacement therapy (PEG-ADA ERT) was withdrawn 1 month (+/- 6 days) post infusion. If there was no bone marrow recovery by 6 weeks (absolute neutrophil count <0.5 x 10^9/l or platelets <20 x 10^9/l) the back-up harvest was re-infused.

DRUG PRODUCT ATTRIBUTES

Final drug product release criteria for infusion of the fresh formulation of OTL-101 were viability >70%; negative in-process bacterial and fungal stains and culture; and endotoxin <5 EU per kilogram. Additional characterization of the final drug product was performed after infusion and reported on the certificate of analysis, including mycoplasma test (BioReliance Corp., Rockville, MD, U.S.) and final sterility. DNA was extracted from a sample of drug product after 14 days *in vitro* culture using the PureLink genomic DNA mini-kit (Invitrogen, Carlsbad, CA, U.S.) and vector copy number (VCN) was determined by digital droplet

polymerase chain reaction (ddPCR). ADA enzyme activity was determined from cell lysates with the ADA enzyme assay by Diazyme (Poway, CA, U.S.). Transduction efficiency was determined by PCR as the percentage of vector-positive colonies after 14 days in methylcellulose culture.

Final drug product release criteria for infusion of the cryopreserved formulation were the same as for the fresh formulation; however, all release testing and certificates of analysis were issued prior to administration of the conditioning regimen and administration of the cryopreserved drug product.

One patient in the U.S. Fresh study and one U.K. study patient were infused with known contaminated fresh drug products (positive for coagulase-negative *Staphylococcus*) alongside antibiotic treatment following approval by the institutional review boards (U.S. studies), independent ethics committees (U.K.), FDA (U.S. studies), and investigators.

VECTOR, DRUG PRODUCT MANUFACTURE AND TREATMENT FOR NCT01380990 (U.K. STUDY)

VECTOR MANUFACTURE

As above for U.S. studies

DRUG PRODUCT MANUFACTURE

The cell product was manufactured from $CD34^+$ HSPCs isolated from bone marrow or mobilized peripheral blood. In total, 4 x 10^6 $CD34^+$ cells/kg were required for drug product manufacture, of which >1 x 10^6 cells/kg were used for transduction and the remainder (3 x 10^6 $CD34^+$ cells/kg) was cryopreserved without transduction as a backup sample for potential later use. Patients for whom 4x10^6 $CD34^+$ could not be harvested were withdrawn from the study.

Following harvest, $CD34^+$ HSPCs were purified, cultured, and transduced at Great Ormond Street Hospital using standard CliniMACs® cell purification protocols and seeded into fresh closed cell culture bags or flasks in serum free medium (X-VIVO-20, Lonza) supplemented with 1% human serum albumin (Baxter), and cytokines SCF (300 ng/ml), Flt-3 ligand (300 ng/ml), TPO (100 ng/ml) and IL-3 (20 ng/ml) at a density of 0.5 to 1 x 10^6/ml. All cytokines (Peprotech) and culture reagents were approved for ex vivo clinical use. A small culture sample was removed for sterility testing. After ~18 hours total pre-stimulation, cells were cultured with the EFS-ADA LV (Indiana University Vector Production Unit) for ~20 hours in the same complete medium at a cell concentration of 0.5 to 1 x 10^6 cells/ml. Following transduction, a portion of cells were removed for quality control i.e. analysis of transduction efficiency (using transgene polymerase chain reaction), viability (using trypan blue stain and 7AAD staining), sterility and replication competent lentivirus. The remaining cells were washed and resuspended in 0.9% saline and 2% human serum albumin for administration. Infusion was carried out within 6 hours of final formulation.

TRANSPLANTATION

Patients initiated IV weight-adjusted busulfan conditioning immediately after bone marrow or peripheral blood stem cell collection and pharmacokinetic monitoring of busulfan levels commenced. The drug product was infused intravenously at a dose >0.5 x 10^6 $CD34^+$ cells/kg body weight. Pegylated adenosine deaminase enzyme replacement therapy (PEG-ADA ERT)

was withdrawn 1 month (+/- 6 days) post infusion. If there was no bone marrow recovery by 6 weeks (absolute neutrophil count <0.5 x 10^9/l or platelets <20 x 10^9/l) the back-up harvest was re-infused.

DRUG PRODUCT ATTRIBUTES

Samples were collected during and at the end of the transduction procedure for cell viability (trypan blue stain, 7AAD staining) and sterility (bacteria, fungi, and mycoplasma). The course of action taken in the event of the $CD34^+$ HSPCs becoming contaminated with microbial agents during the transduction procedure depended on the status of the patient. If there was evidence of microbial agents and busulfan had already been administered, the cells were to be returned to the patient with appropriate antibiotic cover. If the contamination significantly affected cell viability, causing the total dose to be lower than the required $0.5x10^6$ $CD34^+$ cells/kg, the transduced cells were not to be infused, and the back-up sample was to be administered to the patient.

CLINICAL MONITORING AND FOLLOW-UP **(ALL STUDIES)**

In the U.S. Fresh Study, patients were seen for assessment and examination by their home physician, the principal investigator or a clinical investigator at months 1, 2, 3, 4, 5, 6, 8, 10, 12, 15, 18, 21, and 24 (±4 weeks). In the U.S. Cryo Study, assessments were completed at month 1, day 42, and months 3, 6, 9, 12, 18, and 24 (±2 to 4 weeks).

In the U.K. study, patients were followed up at 1, 1.5, 3, 6, 9, 12, 18, 24, 30, and 36 months post-gene therapy. If after 180 days there was no evidence of the transgene in peripheral blood mononuclear cells (PBMCs) by qPCR or no evidence of T-cell recovery, patients re-started PEG-ADA ERT and were withdrawn from the study.

For all studies, ADA enzymatic activity in hemolysates was determined by a radiochemical-thin layer chromatography method,[1] and expressed as nmol per hour per milligram (mg) hemolysate protein. For the U.S. studies, red blood cell ADA activity and total deoxyadenosine nucleotide (dAXP) measurements were performed at the Hershfield Laboratory at Duke University School of Medicine (Durham, NC, U.S.). For the U.K. study, red blood cell ADA activity and analysis of red blood cell dATP activity was performed at the Purine Research Laboratory at Guy's and St. Thomas' Hospitals, London, U.K.

ASSESSMENT OF IMMUNOLOGICAL RECONSTITUTION

Immune recovery following gene therapy was assessed using a lymphocyte immunophenotyping panel, to detect increases in T lymphocyte numbers and assess the distribution of cell populations. Percentages and absolute counts of $CD3^+$, $CD4^+$, naïve $CD4^+CD45RA^+$ (U.S. studies) or $CD4^+CD45RA^+CD27^+$ (U.K. study), $CD8^+$, $CD19^+$, and $CD56^+$ $CD16^+$ cells and were evaluated. Immunologic assays for lymphocyte counts and immunoglobulin levels were performed for the U.S. studies at laboratories certified by Clinical Laboratory Improvement Amendments (CLIA) at the Ronald Reagan Medical Center, University of California, Los Angeles, CA, U.S.; the Department of Laboratory Medicine, Clinical Center, National Institutes of Health, Bethesda, MD, U.S.; the Laboratory of Cell-Mediated Immunity, National Cancer Institute, SAIC-Frederick (currently Leidos Biomedical Research, Inc.), Frederick, MD, U.S.; or the clinical laboratories of the patient's primary care

physicians for the U.S. studies. For the U.K. study they were carried out at the Clinical Immunology Laboratory at Great Ormond Street Hospital, London, U.K.

T-cell receptor excision circle (TREC)s were used as a surrogate marker for new thymic emigrants following gene therapy and analysis was performed at the Great Ormond Street Hospital Laboratory, London, U.K.

TCR Vβ PHENOTYPING, VECTOR COPY NUMBER DETERMINATION, RCL EVALUATION AND INTEGRATION SITE ANALYSIS

Representation of T-cell receptor families by flow cytometric analysis (Vβ phenotyping), was used for monitoring both physiological and potentially pathological clonal expansions. For the U.K. study T cell receptor Vβ spectratyping was performed at the Clinical Immunology Laboratory at Great Ormond Street Hospital, London, U.K. and for the U.S. studies it was performed at UCLA and NIH Clinical Immunology laboratories.

For the U.S. studies, vector copy number (VCN) was determined by ddPCR on genomic DNA extracted from nucleated peripheral blood granulocytes and nucleated peripheral blood mononuclear cells at UCLA, CA, U.S.. For the U.K. study, VCN analysis was performed at University College London Great Ormond Street Institute of Child Health (London, U.K.) on sorted cell populations by real-time PCR methodology using the same primers and probe as in the U.S. studies. VCN in granulocytes, PBMCs, $CD34^+$ and $CD19^+$ cells were assessed at months 3, 6, 12, and 24 months (all studies) and 36 months (U.K. study) following gene therapy.

For all studies, tests for replication-competent lentivirus in peripheral blood were carried out at months 3, 6, 12, and 24 (and 36 months for the U.K. study). Analyses were performed at the National Gene Vector Biorepository at Indiana University Vector Production Facility (Indiana, Ind, U.S.) using qPCR for the VSV-G envelope (limits of detection 10 copies per 0.2 µg of genomic DNA). Large-scale vector integration site analysis (VISA), combining linear amplification–mediated polymerase chain reaction (PCR) and its nonrestrictive version [(nr)LAM-PCR] followed by subsequent deep sequencing, was used to determine the vector integration profile and potential clonal dominance (GeneWerk GmbH, Heidelberg, Germany). The frequency of the 10 most prominent integration sites detected in peripheral mononuclear cell DNA are presented in **Fig. S2**.[2-5]

ADVERSE EVENTS

Adverse events (AEs) and serious AEs (SAEs) were coded using the *Medical Dictionary for Regulatory Activities* version 20.0 and summarized by system organ class and preferred term.

LONG-TERM FOLLOW-UP

Patients were invited to participate in a long-term follow-up study that consists of semi-annual to annual visits and laboratory tests over the subsequent 13 (U.S. studies) and 12 (U.K. study) years.

STATISTICAL ANALYSIS

Gene transfer/engraftment parameters, ADA activity, adenosine nucleotides detoxification in red blood cells and lymphocyte subsets were summarized over time, along with changes from baseline. Descriptive statistics were used and presented in summary and individual plots. Incidence and rates of severe infections were summarized descriptively. Immunologic function was assessed through standard testing by clinical laboratories. These tests included quantitation of lymphocyte subsets and measurement of serum immunoglobulin levels. Use of immunoglobulin replacement therapy and evaluations of serum immunoglobulin levels were summarized descriptively over time.

Results

REPEAT INFUSIONS: PATIENT NARRATIVES

Three U.S. patients (2 from the U.S. Fresh Study, 1 from the U.S. Cryo study) and one U.K. patient were infused with the treatment twice (infusions were administered 1–6 hours apart for U.S. patients [Supplementary Table S2]).

The first patient treated in the U.S. Fresh study had a loss of $CD34^+$ HSPCs during cell processing of the initial bone marrow harvest and the product was formulated and cryopreserved. A second harvest was performed, and a fresh product was formulated, approximately 1 year later. Both products were administered to the patient one hour apart on the same day, with the fresh product infused first and the cryopreserved product infused subsequently.

The second patient in the U.S. Fresh study had two fresh products manufactured from the same harvest to compensate for insufficient vector availability on the day of transduction, which were administered 6 hours apart.

A patient in the U.S. Cryo study, had a repeat bone marrow harvest as the first cryopreserved product did not satisfy release criteria (total nucleated cell concentration was below the established limit). The second cryopreserved product was manufactured and administered to the patient 1.5 hours apart on the same day. This patient subsequently failed to engraft and withdrew from the study.

In the U.K. study, one patient received 2 infusions, 3 days apart, the second of which used cryopreserved product. An initial batch of product deemed unlikely to give a good outcome due to a low cell dose (1.44×10^6 $CD34^+$ cells/kg) was formulated and cryopreserved for future use. An additional harvest, performed at a later time, yielded a higher cell dose (3.6×10^6 $CD34^+$ cells/kg). The patient received both the cryopreserved and fresh formulation of EFS-ADA LV in order to maximize the total dose.

TREATMENT FAILURES: PATIENT NARRATIVES

There were only two treatment failures across all studies. One patient withdrew from the U.K. study 12.2 months post-treatment due to insufficient engraftment, poor T-cell recovery, and low ADA activity levels, and subsequently restarted ERT. ERT had been stopped for this

patient by the investigator 1 week prior to gene therapy in order to provide a survival advantage to gene-modified cells over endogenous cells as this patient had excellent immune recovery on PEG-ADA ERT. The patient had gone on to receive one fresh and one cryopreserved formulation as described above.

In the U.S. Cryo study, one patient restarted ERT and was withdrawn from the study 5.9 months post-infusion due to lack of engraftment. The patient had received two infusions of 2.99 x 10^6 $CD34^+$ cells/kg in a first infusion and 1.26 x 10^6 $CD34^+$ cells/kg in a second infusion, for a combined total cell dose of 4.25 x 10^6 $CD34^+$ cells/kg. Relevant past medical history included trimethoprim/sulfamethoxazole-induced granulocytopenia and positive coronavirus infection, mild pneumatosis intestinalis, and necrotizing enterocolitis that all resolved prior to gene therapy. The patient had a poor response to more than 10 months of treatment with PEG-ADA ERT with minimal increases in lymphocyte counts. The patient also had chronic neutropenia, which is consistent with findings showing ADA-SCID patients may be more susceptible to myeloid dysplasia,[6] potentially leading to drug-induced neutropenia and prolonged busulfan-induced myelosuppression.

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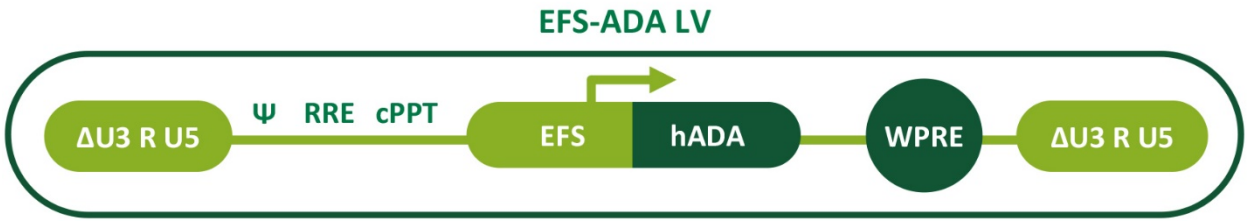
Fig. S1. Schematic of EFS-ADA LV.



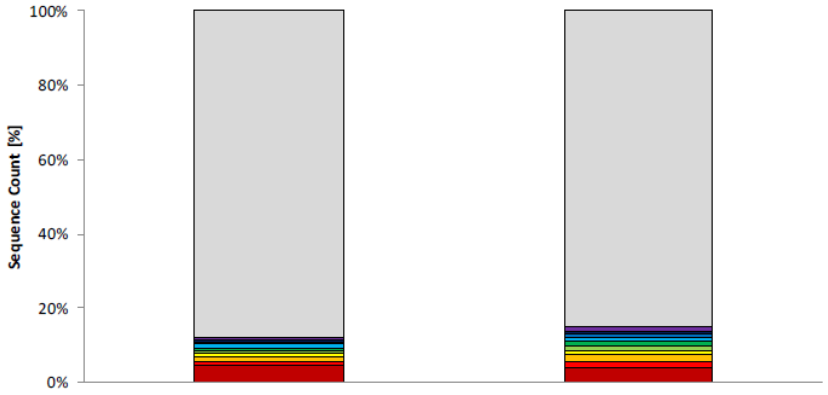
Elongation factor-1α shortened (EFS)-adenosine deaminase (ADA) lentivirus vector (LV) is a self-inactivating LV with codon-optimized human ADA complementary DNA (cDNA) driven by a shortened promoter sequence of the human elongation factor α-1 gene, and the Woodchuck hepatitis post-transcriptional regulatory element (WPRE), to stabilize vector transcripts and increase ADA expression. cPPT denotes central polypurine tract; hADA human adenosine deaminase, RRE Rev response element, U5 part of viral long terminal repeat, ΔU3 deletion in viral promoter region of long terminal repeat to render the vector as self-inactivating, and Ψ packaging signal.

Fig. S2. Vector Insertion Site Analysis.

Patients A to CC: Cumulative retrieval frequencies of the 10 most prominent integration sites detected in peripheral blood mononuclear cell (PBMC) DNA of all gene therapy-treated patients are presented. In most cases, the analysis of the drug product after 14-day culture (14D $CD34^+$) and longitudinal sampling during the follow-up period are presented. For individual samples at specific time points, sequence data from all linear nonrestrictive amplification-mediated polymerase chain reaction [(nr)LAM-PCR] amplicons are combined. The RefSeq name of genes closest to the respective integration sites are given in the table. The relative sequence count of all detected integration sites was calculated in relation to all sequences which could be mapped to a definite position in the genome (Total Seq Counts Used). Gene names highlighted with gray shading indicate integration sites that have been detected at different time points among the 10 most prominent integration sites detected. Top 10 integration sites from timepoints not shown in the figures, if applicable, are taken into account for repeated integration sites among the top 10. M denotes months.

U.S. studies

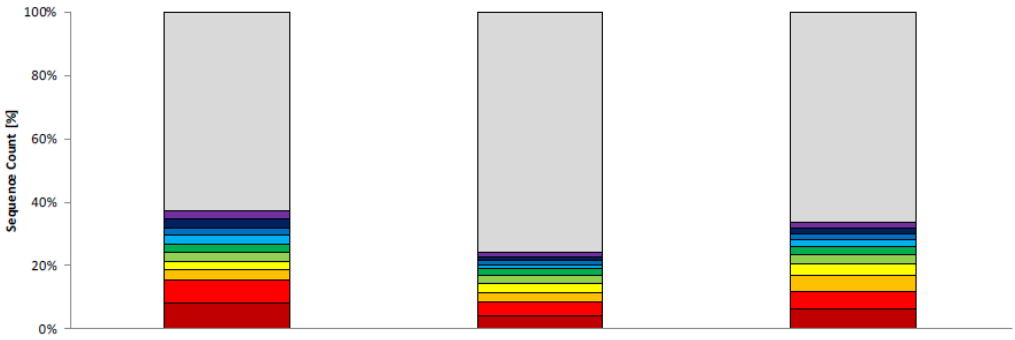
Patient A



Sample		10M PBMC			30M PBMC		
Rank		Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1		AKAP11	4.543	13+42316364	AKAP11	3.82	13+42316364
Top2		PDLIM5	1.15	4+94644050	LOC100130331	1.958	1-238073264
Top3		ZSCAN31	1.051	6-28316813	MPP6	1.535	7-24636952
Top4		AP3B1	0.922	5+78161774	HIVEP3	1.246	1+42025184
Top5		TNPO1	0.857	5-72820188	EIF4G3	1.147	1-21104532
Top6		MAP3K13	0.809	3-185388627	NEGR1	1.122	1+72241089
Top7		EZH1	0.74	17-42730324	GPR126	1.063	6-142372343
Top8		SIPA1L3	0.686	19+37959247	HSH2D	1.021	19+16142397
Top9		TANC2	0.671	17+63003820	CDH18	0.976	5-20329472
Top10		MIR8074	0.659	19+51208071	PRCC	0.899	1+156794888
#All Other mapp. IS		2750	87.912		3272	85.213	

Seq Count 10 Strongest	21564	26007
Seq Count all other mapp. IS	156828	149868
Total Seq Counts Used	178392	175875

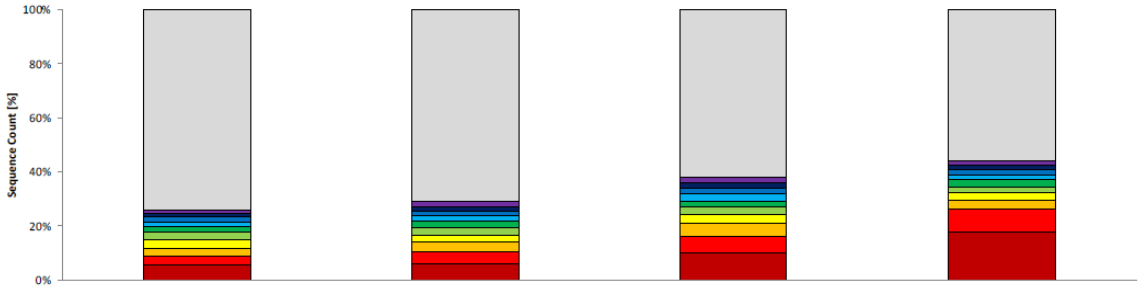
Patient B



Sample	10M PBMC			15M-18M PBMC			30M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	SETBP1	7.794	18+44985239	USP15	3.999	12+62360305	TMEM57	5.839	1+25475855
Top2	UBE2F	7.249	2+237998601	SIPA1L3	3.949	19-37959252	USP25	5.806	21-15767919
Top3	DHX15	3.318	4+24539778	CRYBA1	3.42	17+29254317	SNX13	5.081	7-17898357
Top4	USP15	2.802	12+62360305	GLCE	2.837	15-69205488	DLG1	3.583	3+197091847
Top5	MAPRE2	2.699	18-35115277	PCGEM1	2.477	2-192794178	C10orf107	2.794	10+61690880
Top6	MAP3K1	2.693	5-56856971	CRTC3	2.023	15+90574798	HDAC1	2.572	1-32305180
Top7	PCSK5	2.679	9+76005981	SETD2	1.419	3-47110159	CDH12	2.264	5+23153796
Top8	SETD2	2.649	3+47110576	OR1C1	1.35	1-247774894	PITPNA	1.964	17-1525031
Top9	C10orf107	2.499	10+61690880	POU1F1	1.187	3+87556318	SLC25A19	1.929	17-75277585
Top10	DEK	2.483	6+18236474	PPM1H	1.153	12-62840681	APLF	1.559	2+68538267
#All Other mapp. IS	163	63.135		881	76.186		389	66.609	

Seq Count 10 Strongest	63202	41051	34232
Seq Count all other mapp. IS	108240	131329	68288
Total Seq Counts Used	171442	172380	102520

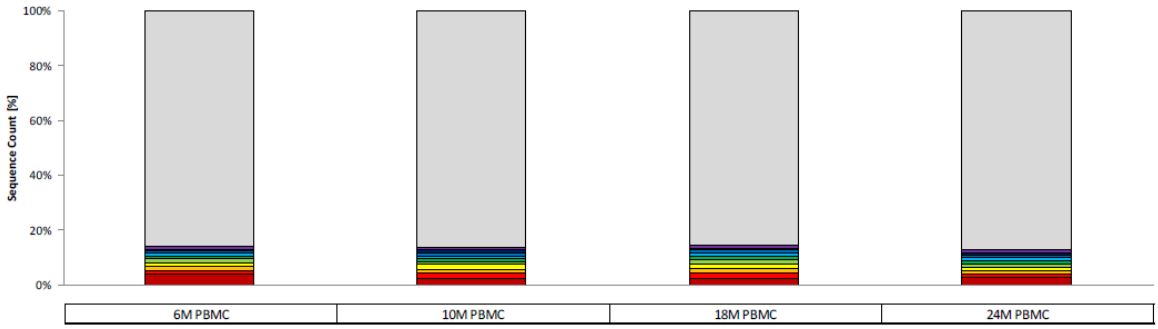
Patient C



Sample	4M-6M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	PITPNA	5.532	17+1530216	SUPT3H	6.043	6-45357863	SUPT3H	10.273	6-45357863	SUPT3H	17.573	6-45357863
Top2	PIEZO2	3.193	18+10794734	ZCCHC7	4.645	9-37194518	SARNP	5.868	12+55799213	SARNP	8.688	12+55799213
Top3	SUPT3H	3.051	6-45357863	TBC1D19	3.331	4+26748152	PITPNA	4.643	17+1530216	TEX2	3.216	17-64204766
Top4	EYA3	2.925	1-28055009	IL27RA	2.729	19-14040358	NUP93	3.614	16+56837545	NEMF	2.987	14-49811402
Top5	ZCCHC7	2.849	9-37194518	SARNP	2.645	12+55799213	IL27RA	2.635	19-14040358	ARFIP1	2.246	4-152888732
Top6	S100PBP	2.26	1+32828383	NEMF	2.312	14-49811402	CNTN5	2.306	11-98366585	GYPC	2.15	2+126630992
Top7	YTHDF2	1.782	1-28749672	CNTN5	2.061	11-98366585	NEMF	2.227	14-49811402	IL27RA	1.936	19-14040358
Top8	BMP2K	1.561	4+78817263	ARFIP1	1.764	4-152888732	HNRNPR	2.222	1-23311327	CNTN5	1.93	11-98366585
Top9	KIF18A	1.381	11-28057266	FBXO42	1.656	1+16329958	MKL1	2.22	22-40472014	ADK	1.823	10-74280468
Top10	BLM	1.354	15+90803336	MYH10	1.557	17+8626748	MYH10	1.948	17+8626748	MKL1	1.614	22-40472014
#All Other mapp. IS	766	74.112		605	71.257		499	62.044		817	55.837	

Seq Count 10 Strongest	42811	60464	78270	78818
Seq Count all other mapp. IS	122559	149898	127942	99652
Total Seq Counts Used	165370	210362	206212	178470

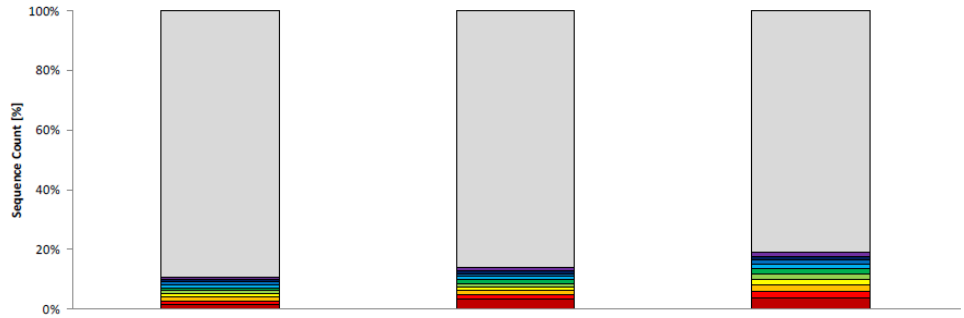
Patient D



Sample	6M PBMC			10M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	MAN2A1	3.813	5-109723376	MAN2A1	2.329	5-109723376	NCKAP1L	2.575	12+54507186	AGA	2.673	4-177438370
Top2	MIR181A1HG	1.572	1+198855921	MPP2	1.766	17-43890273	MAN2A1	1.788	5-109723376	NUP210L	1.375	1-154121986
Top3	TMEM131	1.418	2-97958221	IFI44L	1.71	1-78596551	UBR2	1.782	6-42635983	RLF	1.248	1-40221015
Top4	C7orf72	1.3	7-50136633	SLC25A17	1.455	22-40788873	RNU6-21P	1.663	16-63348182	CSNK1D	1.225	17-82256055
Top5	GLCCI1	1.281	7-8082111	SP1	1.203	12-53413471	TMEM2	1.291	9+71624690	FGF20	1.152	8-16724218
Top6	TNRC6C	1.082	17-78056782	CADM2	1.16	3+86373788	CREB1	1.266	2-207563891	RAB39B	1.069	X+155260082
Top7	C19orf48	1.019	19-50800206	SMG6	1.054	17-2196970	C2CD5	1.208	12-22514897	SPATS2	1.036	12+49492767
Top8	ANKRD12	0.907	18+9209144	CXCL1	1.025	4+73886075	RLF	1.025	1-40221015	PRKACA	1.009	19-14104964
Top9	PABPC4L	0.825	4-133724519	FAM115A	0.958	7-143913788	PPP1R9A	0.908	7+95284645	KNTC1	0.994	12+122545109
Top10	PHF21A	0.81	11+46069512	PACS1	0.954	11-66169829	VWDE	0.905	7+12346364	HNRNPUL1	0.993	19+41283692
#All Other mapp. IS	2734	85.973		5490	86.386		5969	85.589		1904	87.226	

Seq Count 10 Strongest	37963	35501	38961	27955
Seq Count all other mapp. IS	232676	225265	231393	190886
Total Seq Counts Used	270639	260766	270354	218841

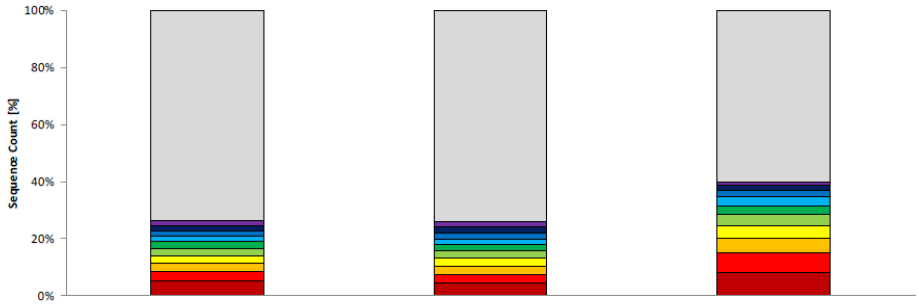
Patient E



Sample	12M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	ARAP2	1.32	4+35670030	UBE2G1	3.04	17-4318283	MS4A7	3.471	11+60393460
Top2	LMCD1-AS1	1.262	3-8399804	USP6NL	1.619	10+11593320	USP6NL	2.273	10+11593320
Top3	ZNF112	1.22	19-44351444	HIST1H2AC	1.437	6-26129759	ZNF337	2.208	20-25685302
Top4	SPOP	1.22	17-49636995	LOC100505817	1.389	18-73594514	MYCT1	2.032	6+152712881
Top5	STK3	1.102	8-98635092	PDE4B	1.137	1+66304980	ST3GAL3	1.667	1-43754749
Top6	MIR4426	1.002	16+61004248	RAB26	1.113	16-2152562	SETX	1.657	9+132317889
Top7	LPCAT3	0.963	12+7005857	LUZP2	1.051	11-24900999	YTHDC2	1.578	5-113526778
Top8	CAPN1	0.918	11+65194875	CYP7B1	0.995	8-64727575	TRIO	1.438	5+14196008
Top9	GNB1	0.882	1-1829052	ARL13B	0.976	3+94009423	INADL	1.417	1+61805184
Top10	METAP1	0.819	4-99026694	PRKAR2A	0.926	3+48830505	EDIL3	1.337	5+84108041
#All Other mapp. IS	5757	89.292		2633	86.317		1183	80.922	

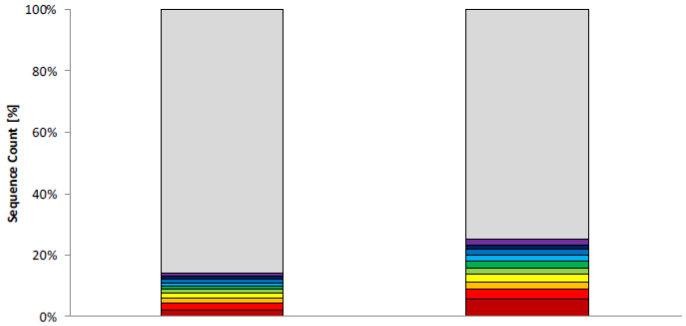
Seq Count 10 Strongest	22157	26454	27821
Seq Count all other mapp. IS	184759	166882	118007
Total Seq Counts Used	206916	193336	145828

Patient F



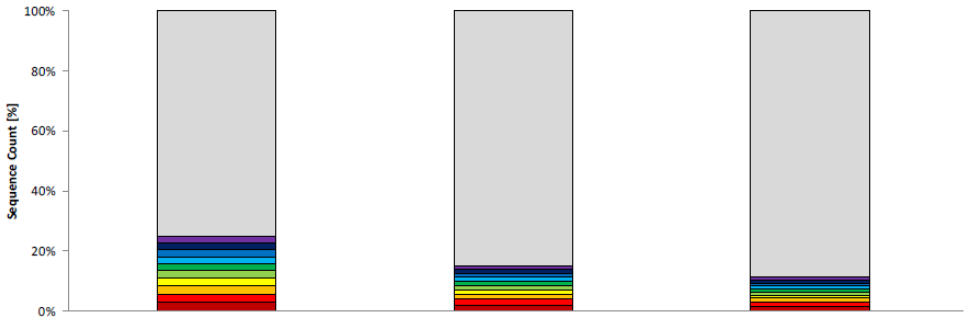
Sample	10M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	MIR99AHG	4.837	21-16431587	GMDS	4.119	6-2023776	PCDH9	7.834	13+67140744
Top2	AGTPBP1	3.181	9+85681189	RAP1A	3.085	1-111630122	RUNX2	7.025	6+45426337
Top3	MAML2	3.101	11+96287645	MIR99AHG	2.892	21-16431587	MIR99AHG	5.088	21-16431587
Top4	LPHN3	2.75	4+61497900	C10orf76	2.804	10+101967403	CBFB	4.265	16+67070013
Top5	GMDS	2.455	6-2023776	ZW10	2.698	11-113747420	KDM2A	4.085	11+67171604
Top6	XPO6	2.372	16-28160919	CBFB	2.177	16+67070013	ARL13B	3.209	3+94034790
Top7	CEP135	1.957	4+55971017	SCAI	2.124	9-125037550	PHKB	2.999	16-47477277
Top8	SOX2-OT	1.833	3+181578398	SOX2-OT	2.055	3+181578398	SCAI	2.047	9-125037550
Top9	GPKOW	1.791	X+49130525	CEP135	1.978	4+55971017	GPKOW	1.739	X+49130525
Top10	KCNV1	1.663	8-110070796	AGTPBP1	1.92	9+85681189	LCA5	1.63	6-79515934
#All Other mapp. IS	947	74.06		430	74.148		661	60.079	
Seq Count 10 Strongest	51018			49724			71328		
Seq Count all other mapp. IS	145658			142616			107345		
Total Seq Counts Used	196676			192340			178673		

Patient G



Sample	18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	PIBF1	2.271	13+72930692	NSUN3	5.682	3-94270459
Top2	PLSCR5	2.007	3+146637388	CSMD3	2.999	8+113638350
Top3	CHKB-AS1	1.565	22+50590383	NF1	2.568	17+31358402
Top4	HEATR5A	1.475	14+31357044	FAM173B	2.547	5-10241909
Top5	AK2	1.364	1+33023097	DST	2.177	6-56531158
Top6	LRBA	1.208	4+150751634	PIBF1	2.149	13+72930692
Top7	EXOC5	1.167	14+57232391	PLCB4	1.809	20-9096976
Top8	HSPA13	1.089	21+14414320	PEAK1	1.796	15-77363228
Top9	LPHN3-AS1	1.053	4+62500290	STX4	1.665	16+31024339
Top10	NSUN3	1.001	3-94270459	GBE1	1.553	3-81616537
#All Other mapp. IS	913	85.8		681	75.055	
Seq Count 10 Strongest	29401			55724		
Seq Count all other mapp. IS	177649			167665		
Total Seq Counts Used	207050			223389		

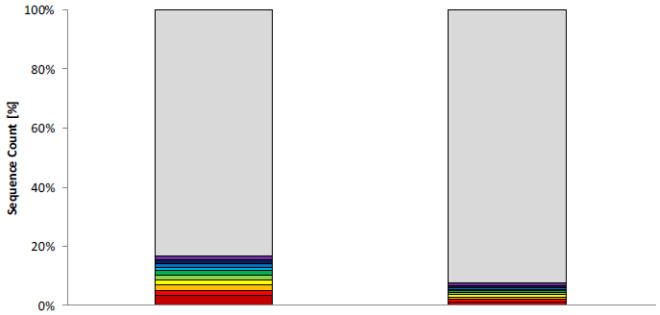
Patient H



Sample	12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ANAPC10	2.993	4+145095020	CNTNAP2	1.938	7-146990664	KIAA1109	1.44	4+122269504
Top2	ZNF264	2.66	19+57218589	POU2F1	1.895	1+167303421	DUSP6	1.404	12+89314883
Top3	GPR98	2.645	5-90637640	CHD9	1.7	16-53224791	MARCH10	1.325	17+62736172
Top4	EIF1AX	2.537	X+20139734	CDC42BPA	1.559	1-227114431	ZNF432	1.173	19+52036279
Top5	RAP1A	2.519	1+111672628	SSTR1	1.469	14+38152759	MAGEB16	1.056	X+35444683
Top6	LINC01036	2.376	1+188643465	MGA	1.367	15-41725106	ALMS1	1	2-73565317
Top7	HERC1	2.316	15-63808641	YES1	1.274	18+752144	SSTR1	0.97	14-38156035
Top8	DISP1	2.314	1+222921286	MOV10L1	1.265	22+50134397	LOC644919	0.966	14+41121790
Top9	WWP1	2.311	8+86353321	NRXN1	1.167	2+50124634	BRAF	0.956	7+140854831
Top10	PPP3CC	2.281	8+22503362	FOXJ3	1.107	1+42227200	PACRG	0.921	6-162733828
#All Other mapp. IS	166	75.048		955	85.259		743	88.789	

Seq Count 10 Strongest	28189	35611	14187
Seq Count all other mapp. IS	84783	205966	112360
Total Seq Counts Used	112972	241577	126547

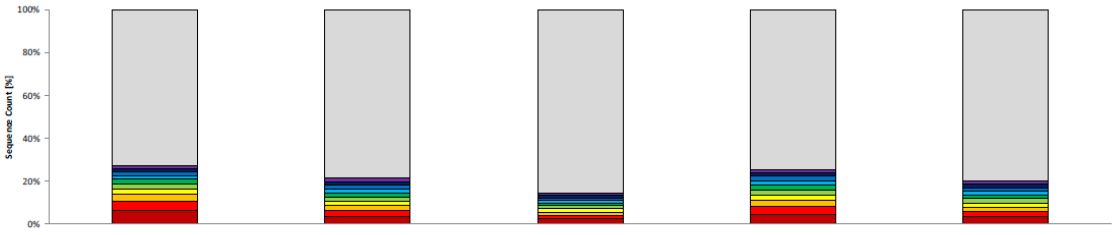
Patient I



Sample	18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	HS3ST3A1	3.036	17-13359893	RFX3	1.217	9-3500117
Top2	LINC00377	2.066	13-81634057	ST3GAL5	0.786	2-85868981
Top3	NNT	1.996	5+43656090	SPINT2	0.717	19+38280728
Top4	ZNF518B	1.516	4+10398154	PTPRM	0.703	18-8086970
Top5	ARSJ	1.506	4-114087169	CDC42SE2	0.693	5-131370757
Top6	OSBPL9	1.394	1+51654277	FBXO7	0.669	22+32491255
Top7	PCGEM1	1.339	2+193303488	IKZF2	0.662	2-213187302
Top8	MKL1	1.305	22-40612395	C16orf62	0.656	16+19584965
Top9	ST3GAL5	1.263	2-85868981	VPS13C	0.634	15+61992367
Top10	ZNF407	1.194	18-74643081	C1GALT1	0.626	7+7236843
#All Other mapp. IS	554	83.385		1388	92.637	

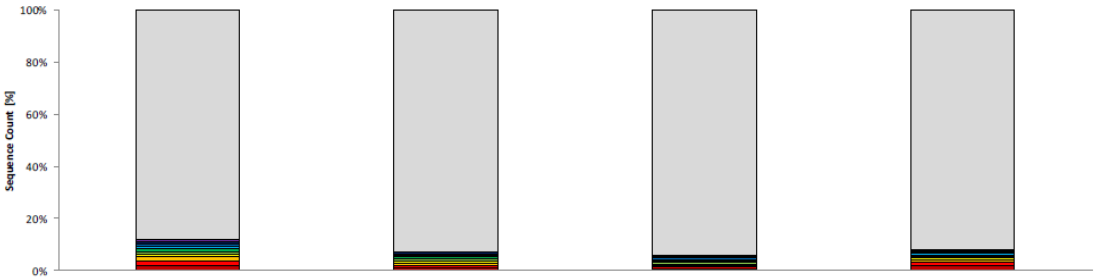
Seq Count 10 Strongest	18325	11106
Seq Count all other mapp. IS	91966	139734
Total Seq Counts Used	110291	150840

Patient J



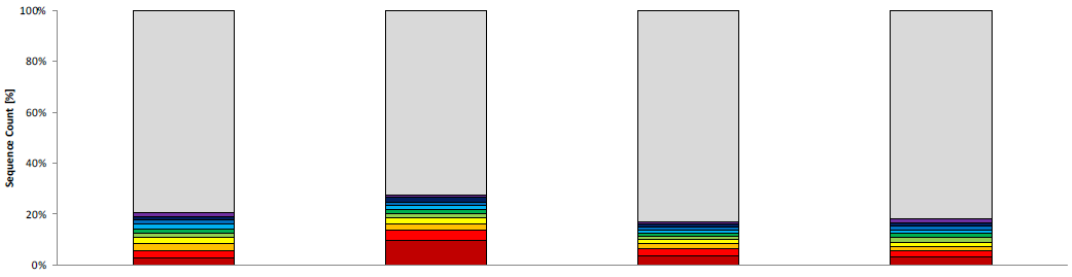
Sample	6M PBMC			8M PBMC			12M PBMC			15M-18MPBMC			30M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	PPHLN1	6.203	12+42379493	TRPM7	3.107	15-50627607	C19orf57	2.105	19-13894620	SOX5	4.328	12-23805932	PDE11A	3.194	2+177695033
Top2	MIR3169	4.103	13+61026648	PDZRN4	2.899	12+41566113	HINT1	1.664	5-130835717	NT5C2	3.727	10-103160829	LOC101928516	2.351	6+74649903
Top3	UBAP1	3.29	9+34207745	PKD2	2.289	4+88055842	SMAD2	1.639	18-47849258	C19orf57	2.929	19-13894620	MED13L	2.176	12-116210463
Top4	MAN1A2	2.8	1-117418204	MGA	2.141	15+41693864	KHDRBS2	1.583	6+62021604	SCAMP1	2.439	5+78395124	GBE1	1.926	3+81544866
Top5	GTSF1	2.389	12+54475282	LINC00379	2.011	13+91137559	LINC00630	1.332	X+102809101	HERC1	2.3	15-63709904	ASCC3	1.907	6+100654701
Top6	WWOX	1.907	16-78320650	NPHP3-ACAD11	1.927	3-132630661	EMB	1.306	5-50355870	FAT4	2.237	4+125359222	SSPN	1.895	12+26210651
Top7	LINC00290	1.862	4-180663817	LINC00333	1.842	13-84586247	KDM6A	1.253	X+45021480	LINC01526	2.157	6-81977861	ISPD	1.741	7-15988814
Top8	C7orf60	1.699	7+112872183	LOC101927378	1.687	7-84533670	SMC5	1.191	9+70287718	PER4	1.973	7-9280960	AP2B1	1.553	17+35678131
Top9	NOVA1	1.557	14-26141034	SMURF2	1.615	17-64581729	PER4	1.161	7-9280960	CBFA2T2	1.498	20-33496130	ALKBH8	1.512	11+107507035
Top10	MYO9B	1.417	19-17170327	ATF1	1.564	12-50821439	SP3	1.145	2+174007605	USP12	1.457	13-27117061	GLG1	1.462	16+74568248
#All Other mapp. IS	606	72.773		762	78.918		1124	85.621		357	74.955		1284	80.283	
Seq Count 10 Strongest	55054			43174			23876			31900			53777		
Seq Count all other mapp. IS	147151			161618			142171			95471			218969		
Total Seq Counts Used	202205			204792			166047			127371			272746		

Patient K



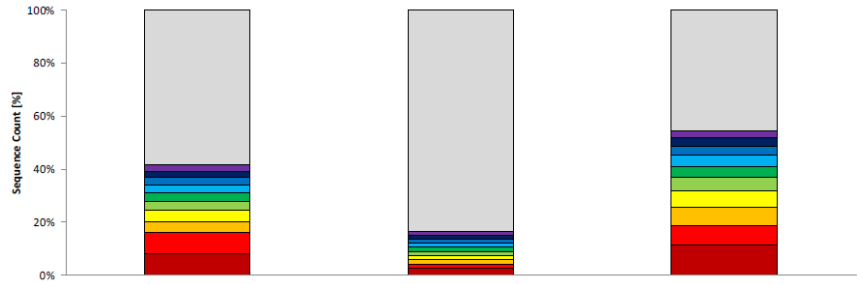
Sample	6M PBMC			12M PBMC			15M-18M PBMC			21M-24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	LINGO2	1.847	9+29565957	FOXP1	1.077	3-71452891	MRVI1	0.687	11+10609937	VPS53	1.643	17-676821
Top2	LOC101929147	1.725	1-119206979	MEIOB	0.994	16-1839102	ERGIC2	0.649	12-29364743	CCDC91	1.425	12+28256003
Top3	ATP8A1	1.658	4-42599106	LINC00251	0.871	8-65319487	TMEM57	0.636	1-25486179	SMARCC1	1.224	3+47607786
Top4	FAT4	1.28	4-125401794	NBEA	0.813	13-35094949	CCDC179	0.616	11+23057760	LSP1P3	0.67	5+28390372
Top5	ATP5G2	1.048	12-53665030	AHRR	0.729	5+406402	PCDH18	0.604	4+137664707	FOXK2	0.592	17+82538466
Top6	PEX11B	0.979	1+145914734	TAF12	0.678	1-28613679	ZNF804A	0.582	2-184588955	WAPAL	0.584	10+86510106
Top7	ANKRD11	0.93	16+89347631	SVIP	0.668	11+22834156	OR7A17	0.558	19-14878611	WBP1L	0.505	10+102746617
Top8	PTGR2	0.908	14+73883929	ZKSCAN1	0.603	7-100026836	MSC	0.543	8-71772291	IP6K1	0.489	3-49755367
Top9	KCNQ5	0.882	6+72632649	EYA3	0.556	1+28055740	NSD1	0.54	5+177226757	NDUFS4	0.475	5-53614370
Top10	MTMR3	0.874	22-29954693	L3MBTL4	0.539	18+6057470	PCDH15	0.53	10-53452377	PDIK1L	0.47	1+26120976
#All Other mapp. IS	1172	87.869		2429	92.472		3069	94.055		4260	91.923	
Seq Count 10 Strongest	16161			15308			12487			19711		
Seq Count all other mapp. IS	117057			188035			197555			224327		
Total Seq Counts Used	133218			203343			210042			244038		

Patient L



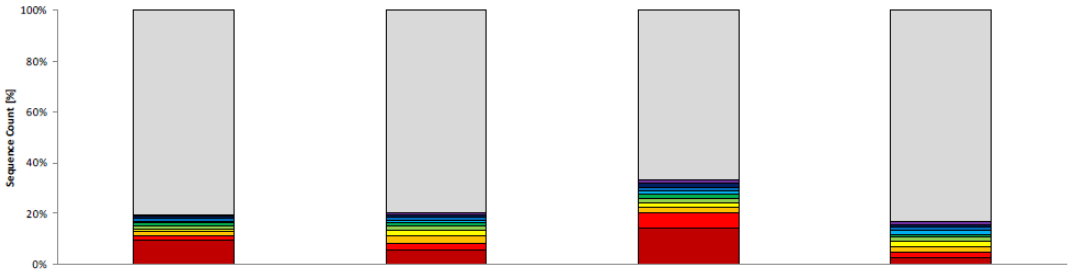
Sample	5M-6M PBMC			8M-10M PBMC			15M-18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	CWC22	2.998	2-179987600	TNRC6C	9.385	17+77999387	GCA	3.538	2+162359240	DDX19B	3.071	16+70311807
Top2	LRP1B	2.792	2-142175057	VMP1	4.035	17+59805309	GLYCTK	2.766	3-52284637	CDKL5	2.06	X+18597269
Top3	ODF3B	2.607	22-50537617	PCDH15	2.769	10+53929773	POLD1	2.079	19+50395998	CA8	1.923	8-60327461
Top4	PTPRD	2.113	9+8481809	DAZAP1	2.146	19+1427550	SLC6A16	1.574	19+49315579	AXIN1	1.829	16-312772
Top5	GPATCH2	1.848	1-217626814	SMOC1	1.883	14+70006434	SNTB1	1.269	8+120594840	GNG2	1.789	14-51928924
Top6	LOC101928767	1.831	14+86209791	TNRC6B	1.539	22+40134087	CLDN12	1.261	7+90415177	GCA	1.762	2+162359240
Top7	PCLO	1.805	7-82767467	PTPRA	1.537	20+2942774	CARD11	1.162	7+2987605	FOXJ3	1.458	1+42225402
Top8	SOGA3	1.517	6+127496852	SWAP70	1.494	11-9741549	ING4	1.099	12+6654464	GNG7	1.39	19-2673708
Top9	FAT4	1.513	4+125348684	CA8	1.482	8+59713029	PARP8	1.06	5+50752848	PPIL6	1.385	6+109433149
Top10	RNF157	1.451	17+76184806	SBF2	1.243	11+10126059	LRCH2	1.017	X+115215680	C4orf22	1.339	4-80755648
#All Other mapp. IS	507	79.525		1543	72.487		2460	83.175		1031	81.994	
Seq Count 10 Strongest	35690			59578			33492			68911		
Seq Count all other mapp. IS	138622			156968			165569			313802		
Total Seq Counts Used	174312			216546			199061			382713		

Patient M



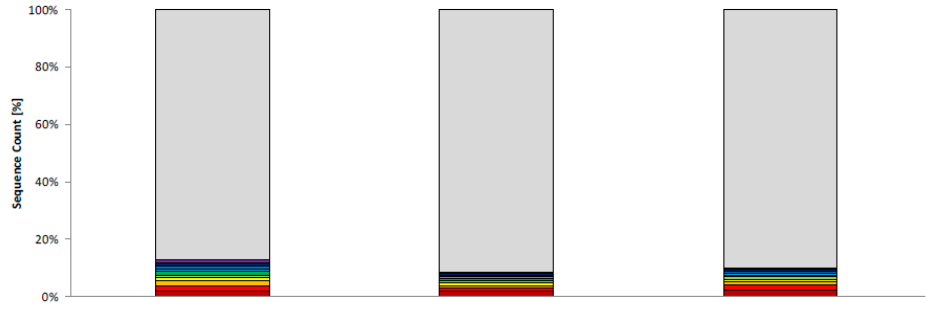
Sample	12M PBMC			21M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	STAT5B	8.25	17-42252951	UTY	2.375	Y-13408379	DEFB113	11.205	6+49974024
Top2	UTY	7.597	Y-13408379	CDKAL1	1.668	6+21119537	PPP1R9A	7.363	7+95006973
Top3	EXOC4	4.414	7+133474068	HACE1	1.663	6-104730201	PLIN3	6.844	19-4863715
Top4	ANKFY1	4.232	17+4228063	TRPC4AP	1.6	20-35062294	EPHA6	6.405	3-96823014
Top5	DDX6	3.243	11-118758441	SPEN	1.585	1-15900228	CLPB	4.872	11+72339512
Top6	DYNC2H1	3.154	11-103125117	EXOC4	1.545	7+133474068	C3orf84	4.334	3-49193367
Top7	ARHGEF12	2.84	11-120402092	ACAP2	1.432	3+195283378	PPP1R9A	3.946	7+94917832
Top8	UBR4	2.827	1+19134968	TTC37	1.431	5-95524141	NKHD1-EIF4EBF	3.533	5+140458114
Top9	TAOK1	2.71	17+29491139	CDH18	1.425	5-18695881	PTPN12	3.173	7+77598946
Top10	BIRC6	2.409	2+32600807	LOC101927869	1.345	21-24396393	CEP85L	2.686	6+118547303
#All Other mapp. IS	467	58.324		840	83.931		205	45.639	
Seq Count 10 Strongest	101324			27194			151785		
Seq Count all other mapp. IS	141799			142038			127431		
Total Seq Counts Used	243123			169232			279216		

Patient N



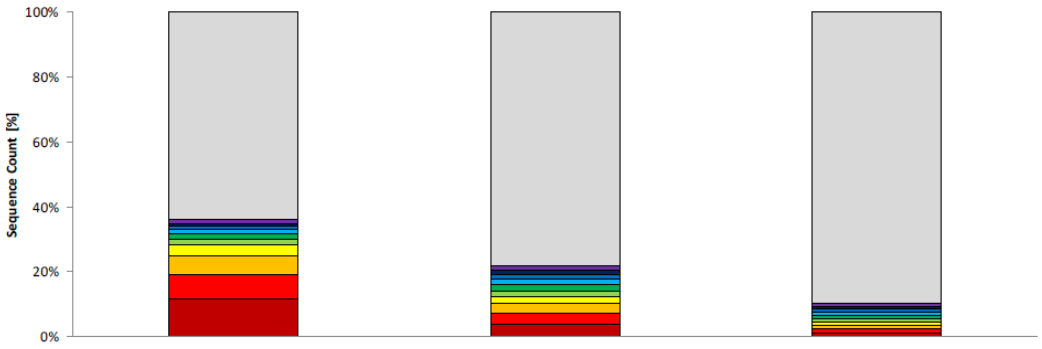
Sample	6M PBMC			10M-12M PBMC			15M-18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	IPO8	9.669	12-30648910	IPO8	5.412	12-30648910	UNK	14.258	17-75790504	IPO8	2.45	12-30648910
Top2	BTC	1.448	4+74614386	LINC00536	2.876	8+115823854	IPO8	5.969	12-30648910	CACNB2	2.223	10+18379621
Top3	LINC00536	1.419	8+115823854	CACNB2	2.695	10+18379621	PLEKHA5	2.089	12-19343585	GOLPH3L	2.048	1-150674522
Top4	FARP2	1.305	2-241370574	EPHA7	2.403	6+93042443	LINC00536	1.824	8+115823854	UNK	2.03	17-75790504
Top5	EPHA7	1.262	6+93042443	PLEKHA5	1.384	12-19343585	CDH19	1.675	18+66694628	MPP6	1.661	7+24621292
Top6	PHIP	1.047	6-79060220	CASC17	1.311	17-70872420	PHKB	1.579	16+47663005	LOC102467226	1.373	5+121288719
Top7	SETD2	0.853	3-47074918	PHKB	1.286	16-47597885	MIR4437	1.548	2+181286509	IFITM3	1.359	11+334265
Top8	BRWD3	0.817	X+80780589	ZBED4	1.042	22-49872295	IFITM3	1.449	11+334265	C12orf66	1.25	12-64235557
Top9	CDH19	0.816	18+66694628	PRKCB	0.919	16+24004321	LPHN3	1.443	4+61349477	GID8	1.144	20+62941891
Top10	SDCBP	0.811	8+58543107	ENOX1	0.893	13-43569103	LRBA	1.437	4-150486656	RPRD1A	1.041	18+36063055
#All Other mapp. IS	2033	80.553		1721	79.779		1077	66.729		2377	83.421	
Seq Count 10 Strongest	34068			24689			27872			49945		
Seq Count all other mapp. IS	141116			97407			55901			251308		
Total Seq Counts Used	175184			122096			83773			301253		

Patient O



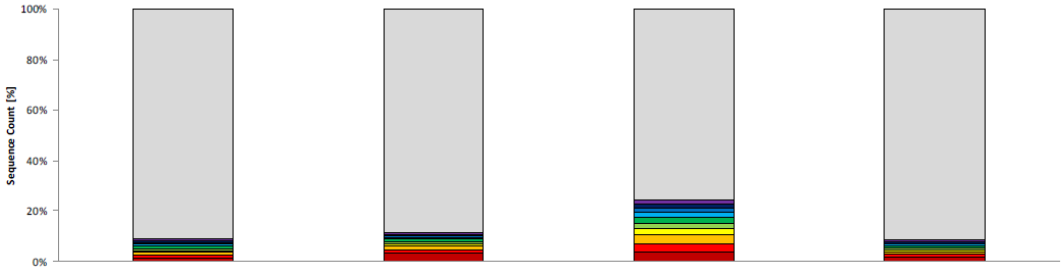
Sample	10M-12M PBMC			18M PBMC			21M-24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	LOC102724550	1.818	3-178027265	NRXN1	1.798	2+50074856	NTM	2.003	11-131835644
Top2	MIR4679-2	1.742	10+89131194	ZEB1	1.047	10+31376784	MIR3688-1	1.729	4-159143344
Top3	RIMS1	1.568	6+72116274	TFEC	0.841	7-115984855	ATP11B	1.085	3+182813699
Top4	LANCL1-AS1	1.244	2+210423594	NUP210	0.794	3-13361384	GRINA	0.939	8-144002654
Top5	NFIX	1.186	19+13005362	DDX10	0.782	11-108988359	LINC00971	0.871	3-84787796
Top6	TCF12	1.112	15+56978610	BTBD10	0.754	11-13437490	BRCA1	0.783	17+43089236
Top7	LINC01021	1.023	5+27707853	RUFY1	0.659	5+179581821	AP4B1-AS1	0.665	1+113839834
Top8	ARHGAP21	1.018	10-24731159	SMURF2	0.656	17-64613424	LINC01505	0.652	9+106656777
Top9	YES1	1.003	18+771345	CD163L1	0.632	12-7381326	TFR2	0.639	7+100624745
Top10	ZSWIM5	0.9	1+45172269	PPFIA3	0.59	19-49130889	ZNF589	0.629	3+48251119
#All Other mapp. IS	1094	87.386		5164	91.447		1878	90.005	
Seq Count 10 Strongest	11620			7965			31116		
Seq Count all other mapp. IS	80500			85160			280199		
Total Seq Counts Used	92120			93125			311315		

Patient P



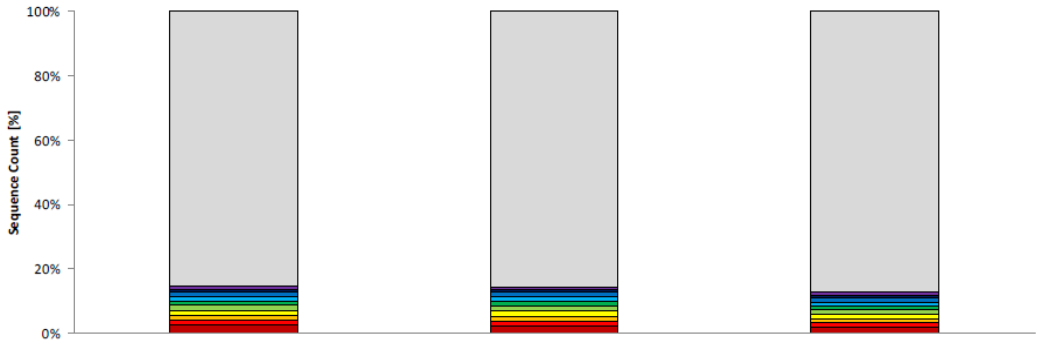
Sample	8M PBMC			12M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	USP15	11.794	12+62382533	GPR125	3.79	4+22442107	PHF12	1.236	17-28936503
Top2	HMGA2	7.199	12+65951273	IMMP2L	3.296	7-110977023	COL11A1	1.108	1+102669351
Top3	DNAL1	6.158	14-73658498	NR5A2	3.034	1+199743235	FAM172A	1.05	5+93879665
Top4	KLF11	3.096	2+10052026	IKZF1	2.15	7-50260214	USP48	1.01	1-21723588
Top5	NMBR	1.83	6+141515903	ZNF804A	1.919	2+184728522	PHTF2	1.009	7+77957055
Top6	SUB1	1.639	5-32570232	ALDH16A1	1.754	19-49458860	LOC339862	0.98	3+17958872
Top7	FBN2	1.304	5-128449187	ATG2B	1.613	14+96329608	PHF14	0.962	7-11122701
Top8	ZNF595	1.091	4+84757	KIAA1109	1.508	4+122210350	EVL	0.951	14-100089333
Top9	MUM1	0.94	19+1351242	LOC100133050	1.479	5+100456263	SUV39H2	0.947	10+14899780
Top10	CHIC2	0.859	4-54010588	TOM1L1	1.254	17+54917522	NAALAD2	0.936	11+90139747
#All Other mapp. IS	341	64.09		741	78.203		2295	89.811	
Seq Count 10 Strongest	29057			12824			29450		
Seq Count all other mapp. IS	51859			46009			259584		
Total Seq Counts Used	80916			58833			289034		

Patient Q



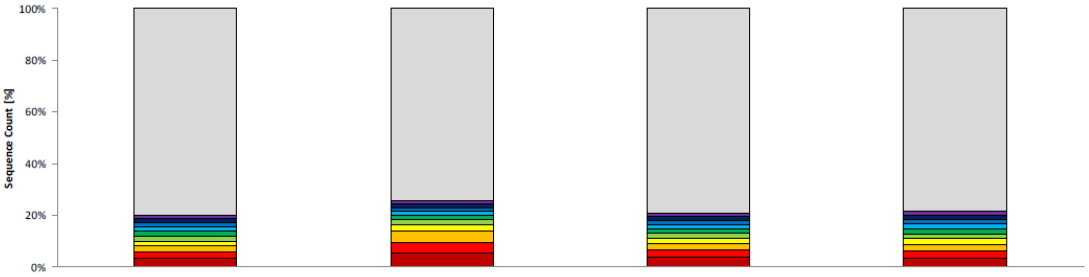
Sample	5M-6M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	CADM2	1.399	3+86208478	ZFPM2	3.057	8+105076606	FDX1L	3.682	19-10312444	UBR2	1.773	6-42578137
Top2	CYP2C8	1.084	10+95066831	NFATC3	1.519	16-68141115	TNFAIP8	3.535	5-119387344	CDKAL1	1.067	6+20624300
Top3	ACO1	0.913	9+32012229	EDC3	1.472	15+74662991	PPP6R3	3.365	11-68489773	PRKAR2A	0.86	3-48825704
Top4	MICU3	0.828	8+17125159	BIN1	0.889	2-127139409	FAM19A2	2.312	12+62035107	MGA	0.804	15-41729385
Top5	ZNF385B	0.827	2-179454463	SUPT5H	0.861	19-39454878	KDM2A	2.277	11+67181251	MAP3K5	0.725	6-136752888
Top6	KHDRBS2	0.82	6+62036228	ENTPD7	0.85	10-99697172	BCKDHA	2.267	19-41418919	DCAF16	0.705	4-17802164
Top7	AMBRA1	0.79	11+46566490	AKR1E2	0.758	10-4753448	LINGO2	1.917	9+29646497	FOLH1	0.693	11+49192900
Top8	USP14	0.771	18-198220	CHAMP1	0.665	13-114326574	NFAT5	1.839	16+69625395	CLK4	0.605	5+178614866
Top9	CBL	0.734	11-119251180	ZZEF1	0.656	17+4111292	SCAF11	1.543	12+45931401	CCDC88A	0.604	2+55401206
Top10	C3orf58	0.723	3+144298079	CPT1A	0.628	11+68796695	KCNV1	1.515	8-110344906	KIAA0556	0.599	16-27569955
#All Other mapp. IS	1040	91.111		4848	88.645		616	75.748		3013	91.565	
Seq Count 10 Strongest	8909			13970			25208			27422		
Seq Count all other mapp. IS	91315			109062			78735			297675		
Total Seq Counts Used	100224			123032			103943			325097		

Patient R



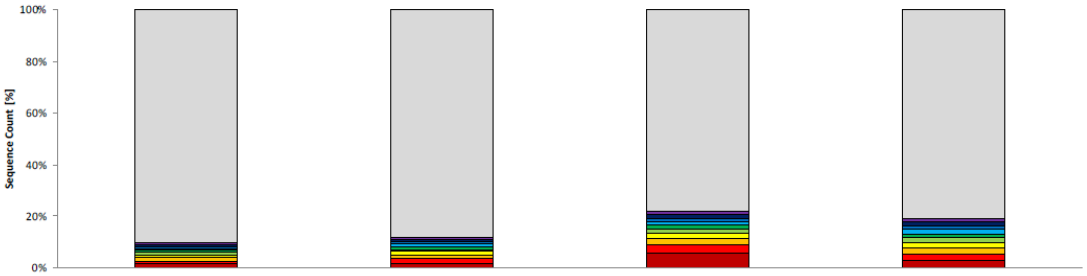
Sample	8M-10M PBMC			15M-18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	RAPGEF2	2.64	4+159243876	PCDH20	2.002	13+61431063	XPO7	1.771	8-21947045
Top2	ADAMTS3	1.646	4-72660987	CDK12	1.784	17-39514497	CDH19	1.537	18-66570903
Top3	PRKG1	1.501	10-51181961	ADAMTS3	1.687	4-72660987	LOC101929294	1.39	8-24355127
Top4	RALY	1.448	20-34054618	CREB1	1.495	2+207597857	ARPC1A	1.37	7+99331431
Top5	TCERG1	1.419	5+146462656	METTL15	1.493	11-28163985	SPATC1	1.32	8-144007483
Top6	TAOK3	1.329	12-118205610	CLIP1	1.461	12+122309876	MTRNR2L5	1.184	10-55672212
Top7	ZBED5	1.307	11-10855326	LOC101927305	1.406	4+130901224	EHMT1	1.118	9-137655832
Top8	NIN	1.264	14+50848966	RALGAPA1	1.204	14-35697552	MPP6	1.071	7-24622067
Top9	NCOA1	1.159	2-24628785	TRPS1	1.051	8-115586564	SH3GL1	0.951	19-4373697
Top10	USP54	1.14	10-73570099	ZNF75A	1.013	16-3314337	AP1S3	0.886	2-223768782
#All Other mapp. IS	924	85.147		1800	85.404		3459	87.402	
Seq Count 10 Strongest	14465			58740			29195		
Seq Count all other mapp. IS	82921			343699			202550		
Total Seq Counts Used	97386			402439			231745		

Patient S



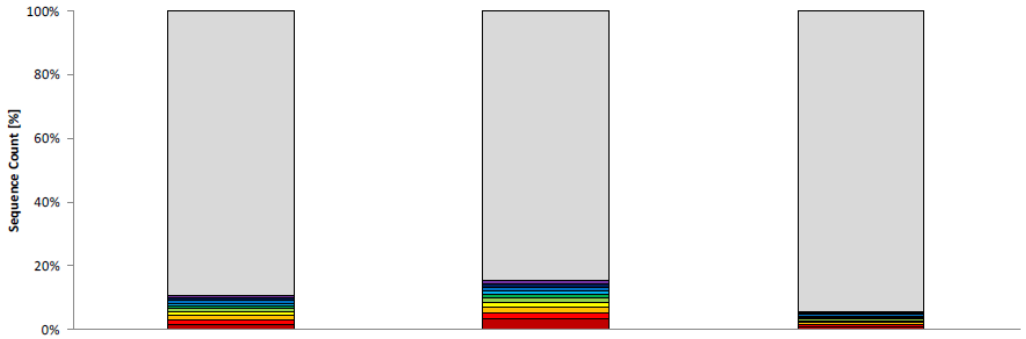
Sample	6M PBMC			12M PBMC			15M-18MPBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	GNAQ	3.023	9-77932587	SNX13	5.166	7-17821180	MMP16	3.839	8+88129841	LPCAT2	3.198	16-55531357
Top2	AGPAT4	2.499	6+161232897	XPO6	4.318	16-28162933	SPOPL	2.622	2-138509415	CORO1A	2.899	16-30181194
Top3	LINC00320	2.472	21-20129198	EYS	4.247	6+64488504	ALOX12-AS1	2.277	17+6946799	ANTXR2	2.371	4+80055550
Top4	AGMO	2.025	7+15332949	WASF2	2.37	1-27451883	CDH18	2.157	5+18706761	AP3B1	2.331	5-78210329
Top5	SCHLAP1	1.853	2-180506595	MIR23A	2.068	19+13849695	KLHL4	2.053	X+87862825	LOC644919	2.01	14+40421739
Top6	XPO6	1.774	16-28162933	RASSF9	1.631	12-85567035	LOC101927869	1.723	21+24226421	DIAPH2	1.93	X-96689733
Top7	WDR49	1.721	3-167571445	CEP44	1.58	4-174300578	CENPC	1.69	4+67458415	PHF21A	1.828	11+46100578
Top8	LYPLAL1-AS1	1.64	1-219123955	FAM168A	1.487	11-73589139	PFKP	1.548	10-2841621	LOC101927087	1.731	4-124601149
Top9	DENND1A	1.56	9+123844051	BTRC	1.425	10-101525446	MIR1268A	1.541	9+128461327	CLSTN1	1.692	1+9814524
Top10	IL6R	1.507	1+154452477	TAOK1	1.417	17+29482400	NUP188	1.488	9+128951480	SLC26A8	1.535	6+36007404
#All Other mapp. IS	608	79.926		637	74.291		395	79.062		3635	78.475	
Seq Count 10 Strongest	52973			61327			46474			43692		
Seq Count all other mapp. IS	210918			177214			175485			159289		
Total Seq Counts Used	263891			238541			221959			202981		

Patient T



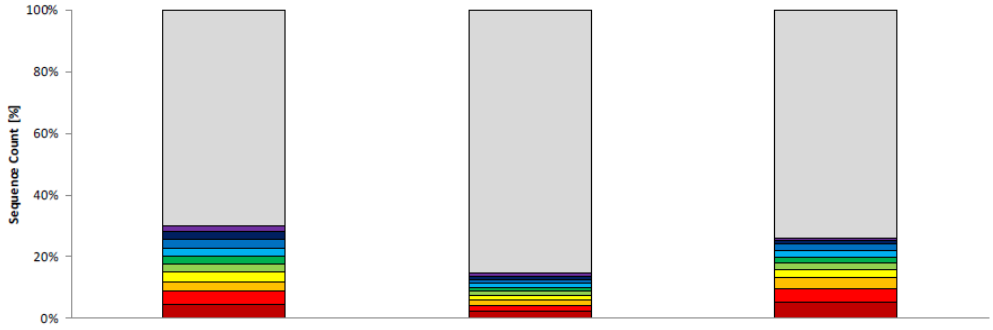
Sample	10M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	SLC9B2	1.343	4-103064620	NPHP4	1.832	1-5932745	ARRDC2	5.712	19-18027579	NEDD1	2.752	12-96931646
Top2	LOC729506	1.274	5+8351668	SLC30A9	1.63	4+42012154	METTL14	2.935	4-118701374	MIER1	2.499	1-66943511
Top3	HDAC1	1.183	1+32323924	AFF2	1.576	X-148909909	TMEFF2	2.644	2-191970583	TNRC6C	2.458	17+78026126
Top4	POLE	1.173	12+132653891	RICTOR	1.159	5-39058825	ERBB2IP	2.157	5+66048351	TRERF1	2.022	6-42415545
Top5	SHANK3	0.9	22-50662441	ADPGK	1.037	15+72760863	CHKA	1.558	11+68080251	SCLT1	1.787	4+128892621
Top6	LOC286190	0.803	8-70637086	UBE2E3	1.035	2+181019717	MIR6082	1.435	4-171421685	MIR548AE1	1.621	2-184031643
Top7	STX7	0.745	6+132498443	SPIDR	1.005	8-47334658	EPHA1-AS1	1.417	7-143475456	BCL7C	1.601	16+30872220
Top8	MC4R	0.7	18+60736386	UHRF1BP1L	0.826	12-100099855	NEDD1	1.332	12-96931646	ME3	1.582	11+86687721
Top9	LINC01139	0.684	1-238732814	MYLK4	0.76	6+2698153	IQGAP3	1.291	1-156518228	CLU1	1.48	12-92521944
Top10	DIP2B	0.68	12-50674334	SEPT7	0.73	7+35880439	GID4	1.249	17+18051303	KMT2E	1.328	7+105063833
#All Other mapp. IS	958	90.515		7317	88.41		5848	78.27		2898	80.87	
Seq Count 10 Strongest	22520			35921			63433			38503		
Seq Count all other mapp. IS	214907			274007			228481			162767		
Total Seq Counts Used	237427			309928			291914			201270		

Patient U



Sample	6M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	NCOA1	1.505	2+24569173	NRXN1	3.009	2-51239573	MIR548AG1	0.747	4-59471407
Top2	C10orf11	1.337	10-75678202	EDC3	2.061	15+74687712	VPS8	0.672	3-184917092
Top3	LOC102467213	1.257	5+106823366	NOSIP	1.81	19-49574306	FAM19A2	0.593	12+62132539
Top4	NCOA2	1.19	8+70189842	SLCO4A1	1.527	20+62640100	ENTHD1	0.516	22-39883899
Top5	DRC7	1.05	16-57710601	PCDH9	1.467	13+67998750	GRIA3	0.506	X-122935895
Top6	FTO	0.998	16+53823456	TANC2	1.186	17+63190918	SLC6A16	0.501	19-49322145
Top7	POM121L12	0.874	7+52510222	SOCS5	1.093	2+46747015	TBC1D32	0.483	6+120954251
Top8	NUP88	0.839	17-5410732	LINC01122	1.018	2-58644147	LOC400685	0.449	19-34829360
Top9	DNAJC13	0.804	3-132516936	MAP2K4	0.994	17+12091347	ASH1L	0.448	1-155471339
Top10	AUTS2	0.799	7+70783996	DPY19L1	0.878	7+34958374	PPP3CA	0.437	4+101218462
#All Other mapp. IS	1174	89.347		5006	84.957		8116	94.648	
Seq Count 10 Strongest	24064			30096			15147		
Seq Count all other mapp. IS	201828			169972			267875		
Total Seq Counts Used	225892			200068			283022		

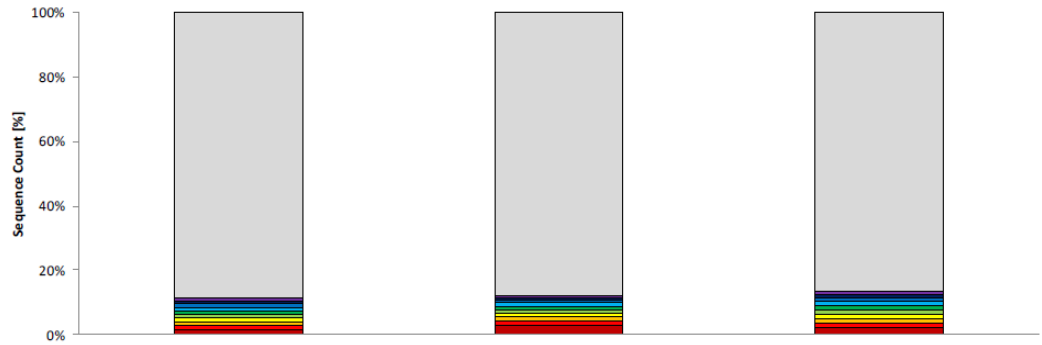
Patient V



Sample	6M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	HIST1H3G	4.305	6-26268330	PAWR	1.955	12-79647219	NAALADL2	4.976	3+175265326
Top2	UBE2G1	4.294	17-4320262	RGS18	1.953	1-191495252	NFIX	4.397	19+13074689
Top3	TGFBRAP1	3.115	2+105312404	RANBP17	1.701	5+171222690	GALNT3	3.535	2-165758690
Top4	GALNTL6	2.967	4-172132225	ATL2	1.472	2-38342320	CEP128	2.444	14-80902940
Top5	SSH2	2.695	17-29716060	DTNA	1.466	18-34933956	SMC5	2.296	9+70286105
Top6	LRP1B	2.69	2+141021409	ZMYND11	1.368	10-201927	ARHGEF12	2.188	11-120391492
Top7	VPS37A	2.645	8+17290961	FBXO34	1.219	14-55330690	CALN1	2.135	7+72067880
Top8	SCAPER	2.53	15+76442818	SPPL3	1.197	12+120810815	XPO7	1.851	8+21943363
Top9	CNTNAP2	2.501	7-147293867	PLOD2	1.001	3-145104751	SLC8A1	1.068	2+40744829
Top10	ATP6V1H	2.243	8+53747166	SETX	1	9+132302947	SSH2	1.018	17+29695847
#All Other mapp. IS	722	70.015		2465	85.668		2117	74.092	

Seq Count 10 Strongest	62278	49018	113212
Seq Count all other mapp. IS	145420	292997	323765
Total Seq Counts Used	207698	342015	436977

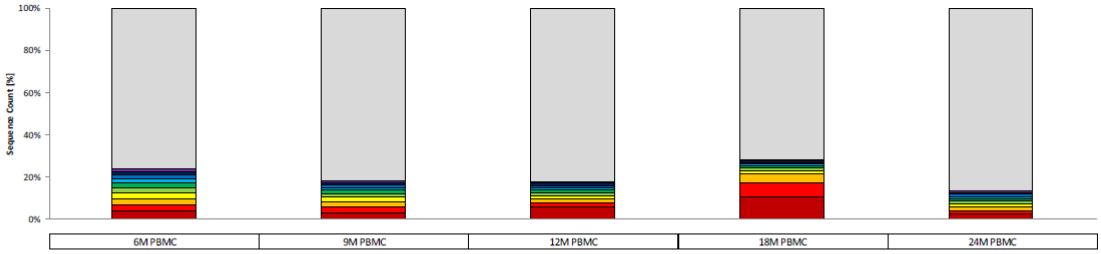
Patient W



Sample	6M PBMC			12M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ASH1L	1.416	1+155389236	GPHN	2.692	14-67011110	HMGA2	2.033	12-65946601
Top2	ZNF567	1.293	19-36708435	AP4S1	1.594	14+31036799	NUP35	1.501	2-183253513
Top3	SAMD9L	1.227	7+93164176	COPB1	1.345	11+14497658	ALOX12-AS1	1.471	17-6977812
Top4	BRIP1	1.218	17-61784998	CNTNAP5	1.241	2-123745689	HAAO	1.453	2+42874237
Top5	XXYLT1	1.153	3+195129136	USP40	1.006	2-233492622	SYNPO2	1.377	4-118914337
Top6	TTC17	1.11	11-43449000	SLC4A7	0.969	3+27406353	DNAJC12	1.223	10+67832241
Top7	CDT1	1.056	16+88798073	SBNO2	0.864	19-1182151	GPR174	1.175	X+79078675
Top8	LOC284788	0.973	20-22359077	CAPN1	0.82	11+65190647	MPZ	1.13	1-161295552
Top9	PSMF1	0.94	20-1140425	RNU6-81P	0.817	13+64045397	CASC6	1.096	6-91818449
Top10	USP3	0.861	15-63526896	RSRC1	0.804	3+158231074	EVI5	0.998	1+92704788
#All Other mapp. IS	1212	88.753		4284	87.848		3048	86.543	

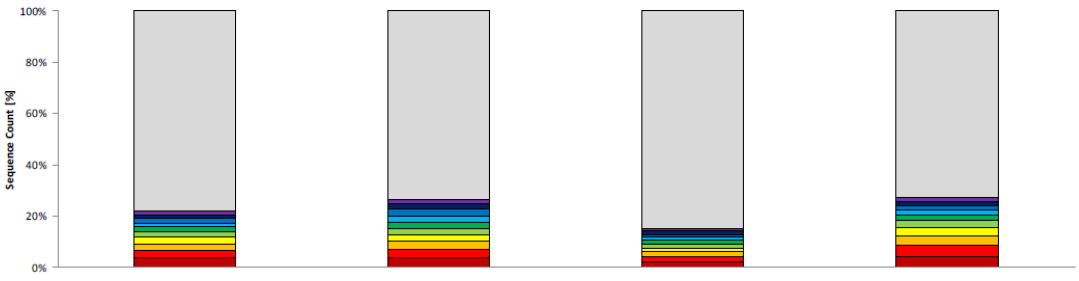
Seq Count 10 Strongest	26713	18076	55288
Seq Count all other mapp. IS	210799	130675	355559
Total Seq Counts Used	237512	148751	410847

Patient X



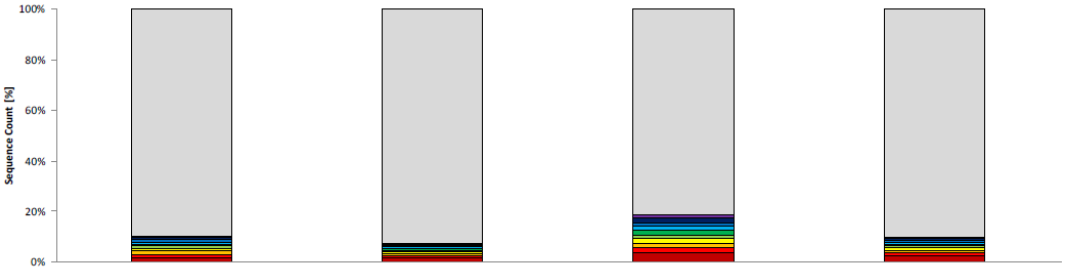
Sample	6M PBMC			9M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	RBFOX2	3.472	22-36013566	CCDC50	2.994	3-191348724	NUP50-AS1	5.759	22+45149620	GPM6A	10.647	4+175375357	CD84	2.033	1-160586173
Top2	GALNTL6	3.354	4-171607650	LINC01578	2.726	15+92897632	UBA6	1.997	4+67665436	ARL13B	6.25	3+94005165	PAFAH1B1	1.977	17+2610331
Top3	MIR1202	2.85	6+155873716	C12orf79	2.345	12+91589920	KANK2	1.752	19-11181014	MEIOB	4.603	16+1841354	C11orf80	1.614	11-66792900
Top4	DPYD	2.822	1+97345193	TBC1D19	2.072	4+26754267	SETD2	1.469	3+47031863	CELF1	1.588	11-47515908	MYCBP2	1.382	13+77218056
Top5	AGO3	2.446	1+36003251	RERE	1.884	1-8484326	PWRN1	1.34	15+24564313	NSD1	1.391	5-177142529	UBA2	1.314	19+34441504
Top6	GNB1L	2.126	22-19829783	LINC00669	1.703	18+39724021	CTSO	1.295	4+156313818	UN54	0.939	4+82946452	COX10	1.31	17+14129496
Top7	OR7A17	1.816	19+14901292	COG5	1.251	7-107371996	SAP30BP	1.181	17-75676199	CTSO	0.69	4+156313818	LRRC1	0.993	6+53887577
Top8	LUZP2	1.799	11-24831166	SRSF11	1.135	1+70235659	TAB3	1.072	X-30881918	RNF8	0.663	6+37367881	COLGALT1	0.925	19+17561627
Top9	SLC30A7	1.695	1+100978682	CPD	1.003	17-30397854	AP4B1-AS1	1.008	1+113815469	NPR2	0.555	9+35783857	BTBD3	0.922	20-11922465
Top10	SMG6	1.639	17+2220756	LINC00376	0.945	13+63110746	LINC01435	0.934	10+108367987	MYCBP2	0.536	13+77218056	SNHG1	0.9	11-62853878
#All Other mapp. IS	743	75.981		1938	81.942		3835	82.193		2791	72.138		3628	86.63	
Seq Count 10 Strongest	55723			45840			35678			134601			55676		
Seq Count all other mapp. IS	176271			208011			164680			348498			360751		
Total Seq Counts Used	231994			253851			200358			483099			416427		

Patient Y



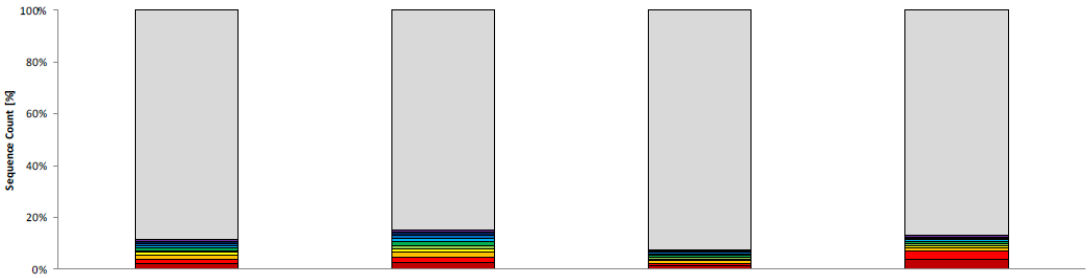
Sample	6M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	SETD3	3.394	14-99416384	PABPC4L	3.799	4-134674922	CRAMP1L	2.235	16-1635477	FKBP5	4.371	6+35667125
Top2	WRN	2.86	8-31133828	ZFC3H1	3.416	12-71655461	DNAJC7	2.023	17-42000607	TNRC6C	4.173	17-78036698
Top3	ARAP2	2.704	4-35522375	KLHL4	2.935	X-87853195	TAB2	1.717	6-149390132	DNAJC7	3.63	17-42000607
Top4	CSMD1	2.689	8+3335671	DYNC2H1	2.566	11+103190652	CAAP1	1.574	9+26847798	CSMD3	3.434	8-113565415
Top5	GATB	2.223	4-151880364	PSMA6	2.513	14-35301860	NCKAP1L	1.523	12+54516842	PSMA6	2.721	14-35301860
Top6	TNRC6B	1.964	22+40209106	RPGR	2.507	X-38308143	PLCB1	1.351	20-8661657	LINC01526	2.034	6-81794911
Top7	LINC01467	1.568	14-83349952	CPED1	2.504	7+121137119	CADM2	1.271	3+85070571	GRM3	1.871	7+86004339
Top8	KCNT2	1.567	1+194815529	RAB9BP1	2.293	5+105041352	CSNK2A2	1.168	16+58179034	ARHGAP6	1.753	X+11559255
Top9	LOC101927003	1.494	8-78558091	RNU6-30P	2.011	X-101631737	CPED1	1.151	7+121137119	SARNP	1.717	12-55754822
Top10	GAS2	1.402	11-22782468	VRK2	1.995	2-58084899	EPB41	1.148	1+28945761	KHDRBS2	1.407	6+61952684
#All Other mapp. IS	1388	78.135		1776	73.461		914	84.839		887	72.889	
Seq Count 10 Strongest	59289			51116			42708			97083		
Seq Count all other mapp. IS	211870			141491			238991			261011		
Total Seq Counts Used	271159			192607			281699			358094		

Patient Z



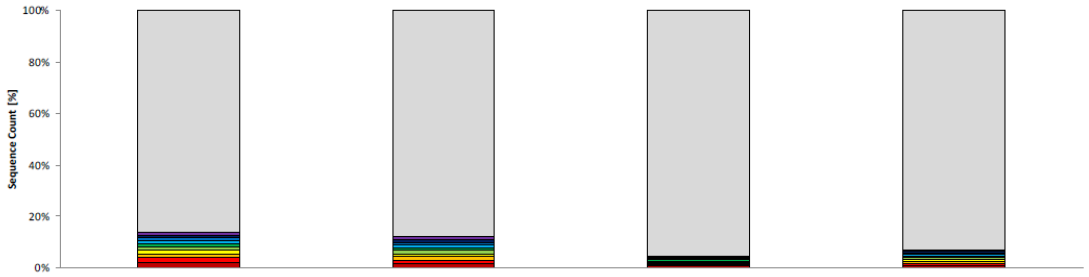
Sample	9M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	MIR6130	1.44	21+22607363	NXF1	1.59	11+62792983	UBE2E3	3.569	2+181028650	NXF1	2.323	11+62792983
Top2	NXF1	1.432	11+62792983	EIF4G3	0.826	1-20938058	NHLRC3	1.934	13+39062160	HIVEP1	1.294	6+12093610
Top3	ST18	1.311	8+52362824	ZHX3	0.788	20+41266428	MIR2054	1.835	4-125657246	WRN	1.023	8-31093978
Top4	INPP4B	1.054	4+142918008	MIR548AG1	0.737	4+60197845	PRKAR2B	1.723	7+107073364	PTPRO	0.855	12+15559839
Top5	DAZL	0.955	3-16595777	LCORL	0.684	4+17960658	VPS45	1.673	1+150094090	ITPR2	0.784	12+26534766
Top6	LOC1720	0.882	2-82775365	SDHB	0.666	1-17031043	EYA3	1.669	1+28075303	LOC101927058	0.73	12-42646304
Top7	LINC01162	0.838	7+21018033	IMMP2L	0.613	7-111303425	LCORL	1.648	4+17960658	BAI3	0.721	6-68738054
Top8	LINGO2	0.797	9+28885917	LOC101927058	0.58	12-42646304	TAOK3	1.588	12+118257883	GON4L	0.679	1-155809335
Top9	LOC100506393	0.711	12+19879934	LOC1720	0.543	2-82775365	LOC101926940	1.529	5-39520115	RERE	0.643	1+8570400
Top10	TBC1D1	0.704	4+38020795	FLNB	0.52	3+58015111	USP3	1.503	15-63526159	LCORL	0.627	4+17960658
#All Other mapp. IS	2270	89.876		3518	92.453		1226	81.329		2852	90.321	
Seq Count 10 Strongest	39183			12010			36677			36242		
Seq Count all other mapp. IS	347847			147125			159762			338200		
Total Seq Counts Used	387030			159135			196439			374442		

Patient AA



Sample	6M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	STT3B	2.187	3+31625656	DENND4C	2.599	9+19327774	LINC00992	1.404	5+117470480	TRHR	3.767	8+109091096
Top2	CX3CR1	1.828	3+39230960	BAZ1B	2.071	7-73495368	PKN1	0.891	19-14456200	IMMP1L	3.331	11+31437734
Top3	EDIL3	1.107	5-84575359	THRB	1.836	3-24434623	KIAA1109	0.877	4+122275502	KDM6A	0.939	X-45057608
Top4	RAB7A	1.059	3-128753548	UBN2	1.427	7-139281306	LRBA	0.704	4-150676365	DEPDC1-AS1	0.894	1-68604355
Top5	IL1RAPL2	1.039	X-104592072	KHDRBS2	1.347	6-62166282	NBEA	0.675	13+35433773	NBEA	0.774	13+35433773
Top6	FRMD6	1.018	14+51700562	FAM127B	1.244	X+135045280	MIR8060	0.615	3+96582392	MED21	0.74	12-27038160
Top7	PRDM9	0.958	5-23718539	MIR514A2	1.215	X+147544773	LONRF1	0.595	8-12742542	C9orf85	0.673	9+71944400
Top8	LONP2	0.774	16+48261795	ING3	1.214	7-120973407	CRISP2	0.583	6+49701265	ZC3H18	0.672	16+88592986
Top9	LARP4	0.711	12+50455377	LOC100129520	1.192	X+125490445	ACOX1	0.563	17+75975476	MIR514A2	0.584	X+147544773
Top10	POLDIP3	0.686	22+42590290	C9orf85	1.179	9+71944400	ZC3H18	0.543	16+88592986	CNTNAP5	0.559	2+123851657
#All Other mapp. IS	2417	88.633		2525	84.676		3978	92.55		1907	87.067	
Seq Count 10 Strongest	31493			52162			23346			69303		
Seq Count all other mapp. IS	245565			288233			290020			466557		
Total Seq Counts Used	277058			340395			313366			535860		

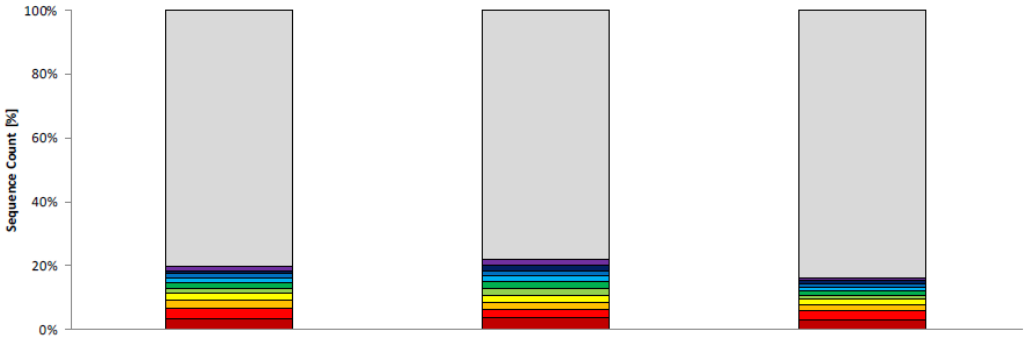
Patient BB



Sample	6M PBMC			12M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ZBTB46-AS1	2.049	20+63822821	SPRED1	1.713	15+38336859	GBE1	0.647	3-81361184	IKZF2	0.81	2-213108095
Top2	ZNF529	1.698	19+36587744	CTBP1	1.267	4-1242125	ALCAM	0.52	3-105386515	CIZ1	0.787	9+128184415
Top3	STX5	1.504	11+62820753	PAG1	1.245	8+81037268	C20orf194	0.508	20+3354894	AKTIP	0.778	16-53498841
Top4	SOCS5	1.457	2+46752393	PKD2L2	1.216	5-137905990	PPP1R1C	0.499	2+182039421	SPRED1	0.738	15+38336859
Top5	PSMD1	1.322	2-231085906	LRBA	1.19	4-150593228	CDH19	0.464	18+66785514	ANTXR2	0.695	4+79958529
Top6	NKAIN2	1.275	6+124151668	LOC101927196	1.142	2+185482490	FOCAD	0.46	9+20956216	SBF2	0.668	11-10275340
Top7	LINC01392	1.214	7-115460888	TMCO5A	1.124	15-37728492	AKTIP	0.418	16-53498841	ITPR1	0.647	3+4733446
Top8	PCGEM1	1.198	2-193109787	SUPT3H	1.085	6-45336726	SLC16A7	0.418	12+59675274	TSPAN2	0.567	1+115094959
Top9	SCAI	1.143	9+125028513	PTCHD4	1.035	6-48387101	BRWD3	0.392	X-80680420	LOC101929607	0.556	3-107426028
Top10	MIR4470	1.023	8-61913231	TDRD3	1.032	13+60540876	MRO	0.387	18+50828329	SLC10A7	0.556	4+146400241
#All Other mapp. IS	3585	86.117		5425	87.951		4209	95.287		3323	93.198	

Seq Count 10 Strongest	39957	38155	17559	38272
Seq Count all other mapp. IS	247852	278509	355008	524391
Total Seq Counts Used	287809	316664	372567	562663

Patient CC

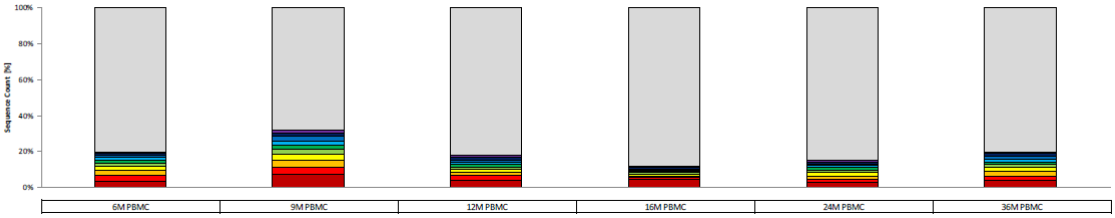


Sample	6M PBMC			18M PBMC			24M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	SULT1E1	3.315	4-69847665	MIR612	3.7	11+65439173	HLX	2.947	1+221064096
Top2	TAPBPL	2.912	12+6455044	CBFB	2.349	16-67082721	GMCL1	2.66	2+69862011
Top3	GPATCH8	2.867	17-44432581	ARPC1A	2.272	7+99336421	MACF1	2.206	1+39430316
Top4	ZNF521	2.22	18+25087839	ARL15	2.219	5+54101126	RABGAP1L	1.66	1-174698917
Top5	SLC35F5	1.537	2-113733772	LOC101929709	2.135	8+89752814	ATP6V0A1	1.283	17-42480443
Top6	LINC00669	1.503	18+39452034	PARP11	2.132	12+3830359	ARIH2	1.262	3-48982272
Top7	DNM2	1.501	19+10794796	SEMA3D	1.925	7+85850345	SAV1	1.16	14-50645909
Top8	SENP3-EIF4A1	1.272	17+7576664	KIAA0586	1.777	14-58461719	USP10	0.933	16+84717234
Top9	DCBLD2	1.241	3+98807861	CEP57L1	1.68	6+109103653	LRP1B	0.891	2+141118408
Top10	MIR8060	1.207	3-96098395	TEX41	1.546	2-144685367	MIR302F	0.891	18+29495338
#All Other mapp. IS	1043	80.425		1779	78.265		1106	84.107	

Seq Count 10 Strongest	33603	77137	99892
Seq Count all other mapp. IS	138062	277760	528636
Total Seq Counts Used	171665	354897	628528

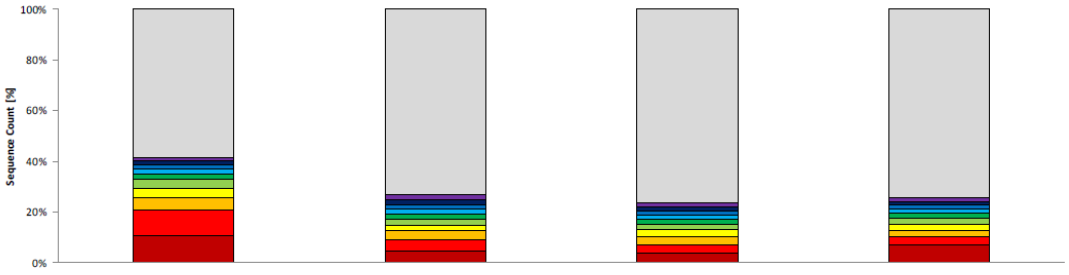
U.K. study

Patient A



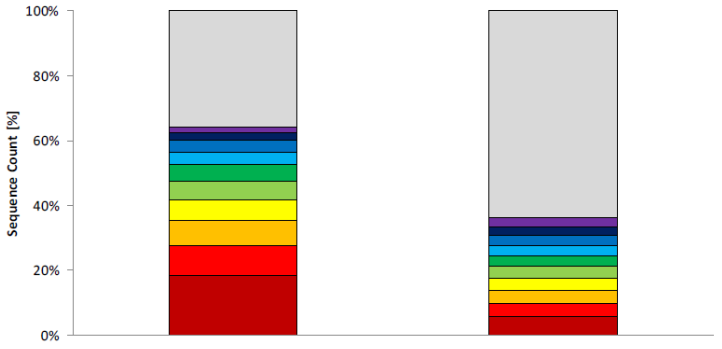
Sample	6M PBMC			9M PBMC			12M PBMC			16M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	PIAS1	3.53	15+68399701	MSRA	6.901	8+9939287	AKAP7	3.736	6+131530243	AKAP7	4.326	6+131530243	RUNDC1	2.501	17+41139626	C6orf10	3.998	6+32277644
Top2	STK38	3.032	6-36509768	SH2B3	4.541	12-111870936	PSMD3	3.012	17+38142491	ABCA5	1.199	17+67274649	SH2B3	1.972	12-111870936	DHRS4	2.364	14-24319889
Top3	PDUM1	2.859	10+97037992	TBCEL	3.682	11+129911854	USP4	1.598	3-49344881	CASC4	0.875	15+44623732	AKAP7	1.847	6+131530243	DNAJC1	2.349	10+22082157
Top4	SARNP	2.068	12+56172904	KDM2A	3.167	11+66945798	PLOD2	1.551	3-145361995	SH2B3	0.874	12-111870936	TNF	1.676	6+31546245	AKAP7	2.135	6+131530243
Top5	RASA1	1.837	5+86626975	PLCB3	2.854	11+64026889	PSMD1	1.453	2-232007001	PARL	0.851	3+183552045	ASXL2	1.608	2+25989462	TAF1B	1.768	2+10039685
Top6	NFYC	1.716	1+41177335	ZNF267	2.499	16+31898544	SULT1A3	1.449	16-29561363	TAF1B	0.749	2+10039685	RBM9	1.6	22+36307958	AKAP13	1.63	15+85937275
Top7	PKN2	1.409	1+89175814	FKBP5	2.236	6+35556734	GFOD2	1.269	16+67724593	WWP2	0.733	16+69917190	LRRC16A	1.017	6+25470396	TRIM39	1.566	6+30266309
Top8	SEPT9	1.186	17+75330714	RAB6A	2.209	11+73422652	BAZ2A	1.205	12+57017222	GFOD2	0.718	16+67724593	C4orf8	0.989	4+2679900	WWP2	1.467	16+69917190
Top9	SH2B3	0.982	12-111870936	FAM69B	1.976	9+139610211	TNF	1.187	6+31546245	PPIAL4G	0.647	1-143736734	AXIN1	0.949	16-385851	DDX46	1.353	5-134117184
Top10	SAP52	0.817	22+50794756	AKAP7	1.52	6+131530243	GABPB2	1.065	1-151062649	ATPAF1	0.626	1-47115139	TRIM38	0.814	6+25982885	PCDH9	1.267	13+68647215
#All Other mapp. IS	3684	80.564		2551	68.415		2814	82.475		2044	88.402		2074	85.027		871	80.103	
Seq Count 10 Strongest	24064			33014			14381			8654			36205			22281		
Seq Count all other mapp. IS	99748			71511			67679			65963			205598			89699		
Total Seq Counts Used	123812			104525			82060			74617			241803			111980		

Patient B



Sample	6M PBMC			12M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ZNF136	10.533	19+12281099	CCDC36	4.455	3+49289872	TNRC6C	3.753	17+76057147	TNRC6C	7.021	17+76057147
Top2	RARRES3	10.152	11-63309806	DPF2	4.223	11+65105300	PPHLN1	3.311	12-42764501	UBR4	3.061	1+19516904
Top3	EFR3A	4.963	8+132946485	RPTOR	3.975	17-78783225	C6orf10	3.264	6+32348298	ZFAND3	2.494	6+37996396
Top4	ZMYND8	3.674	20+45919494	OPN3	2.329	1-241763239	KDM5A	2.772	12+436131	RNF214	2.468	11-117134760
Top5	DNAH1	3.52	3-52372524	ANLN	2.113	7-36485160	CARM1	1.909	19+11011255	PRPSAP1	2.331	17-74328802
Top6	CRYBA4	2.183	22-27035682	NFAT5	1.978	16+69625369	TBC1D5	1.893	3-17985008	SLC8A1	2.112	2-41003238
Top7	SMG6	1.91	17-2103161	SPEN	1.976	1-16168242	RAP1B	1.824	12-68995298	RANBP9	1.749	6+13652807
Top8	COQ5	1.654	12-120954653	SLC38A2	1.908	12+46880620	DAP3	1.649	1+155669287	GRIN2D	1.576	19+48935644
Top9	GNL1	1.564	6-30492765	CCL5	1.874	17-34201980	NPLOC4	1.629	17-79563657	PRPSAP1	1.284	17-74322307
Top10	SLC6A16	1.521	19-49817898	ATRN	1.792	20+3543092	NIPA2	1.622	15-23019680	UVRAG	1.223	11-75681833
#All Other mapp. IS	1288	58.326		1006	73.377		1155	76.374		861	74.681	
Seq Count 10 Strongest	82625			73406			38881			161326		
Seq Count all other mapp. IS	115639			202317			125686			475846		
Total Seq Counts Used	198264			275723			164567			637172		

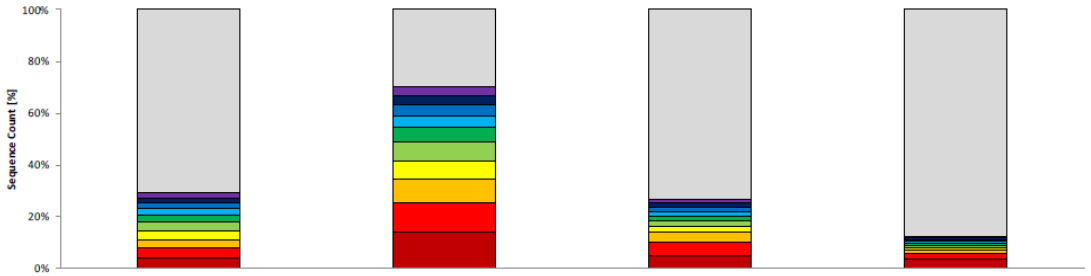
Patient C



Sample	6M PBMC			12M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	COL21A1	18.277	6+55859926	MED13L	5.755	12-116638821
Top2	PPP2R1A	9.254	19-52688600	FBXW7	4.083	4-153392551
Top3	GRLF1	7.769	19+47388776	LIN9	4.035	1-226434901
Top4	EIF4G3	6.381	1+21377078	SLC39A10	3.865	2-196063909
Top5	VRK1	5.787	14+97330951	GSPT1	3.39	16-12004415
Top6	BANP	5.038	16+88039854	MYH10	3.266	17-8528327
Top7	SETD2	4.049	3+47185070	KCNJ16	3.136	17+67998114
Top8	KDM2A	3.856	11+66964735	MARCH3	3.06	5+126287947
Top9	TMEM41B	2.053	11-9333144	RECQL5	2.92	17+73634212
Top10	TSC2	1.714	16+2099993	SAPS3	2.814	11+68285580
#All Other mapp. IS	180	35.822		161	63.676	

Seq Count 10 Strongest	103079	28149
Seq Count all other mapp. IS	57535	49346
Total Seq Counts Used	160614	77495

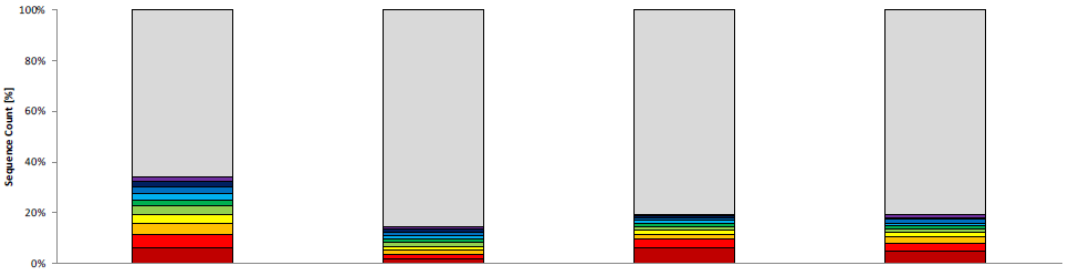
Patient D



Sample	6M PBMC			12M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	GATAD2B	4.035	1-153839203	EPAS1	13.867	2+46653353	GSDMC	5.031	8+130586964	IFT81	3.383	12-110653476
Top2	C9orf89	3.794	9+95864666	SEMA4A	11.08	1+156154157	FAM125B	5.017	9+129113681	VWA5A	2.307	11-123967755
Top3	FAM155A	3.283	13+107529248	HOPX	9.337	4-57526816	CLIC4	4.119	1+25146032	MYO9A	1.168	15+72218388
Top4	ZBTB8OS	3.247	1+33107075	RNF169	7.457	11+74526107	ANKFY1	2.193	17-4121021	C1R	0.896	12-7186332
Top5	SLAMF1	3.102	1+160583685	CD96	6.962	3-111320507	SEC11A	1.929	15-85249184	CHD3	0.852	17+7803738
Top6	SRFBP1	2.833	5-121352206	NF1	5.779	17+29580259	KDM5A	1.901	12-418762	ZNF383	0.831	19-37711823
Top7	CACNB1	2.611	17-37343452	CCNT1	4.33	12-49091996	SBF2	1.779	11+10074839	KDM2A	0.793	11+66980497
Top8	EDC3	2.128	15-74961630	C1orf83	4.175	1+54554871	C12orf4	1.715	12+4614153	CSK	0.791	15+75078403
Top9	PTK2	2.119	8-141908863	GATAD2B	3.561	1-153858600	HK2	1.48	2-75083521	FAM19A2	0.757	12+62461919
Top10	MYCBP2	2.063	13-77805271	UBOX5	3.489	20+3123593	C12orf65	1.15	12+123712480	SLC6A16	0.729	19-49829419
#All Other mapp. IS	854	70.785		83	29.963		725	73.686		2372	87.493	

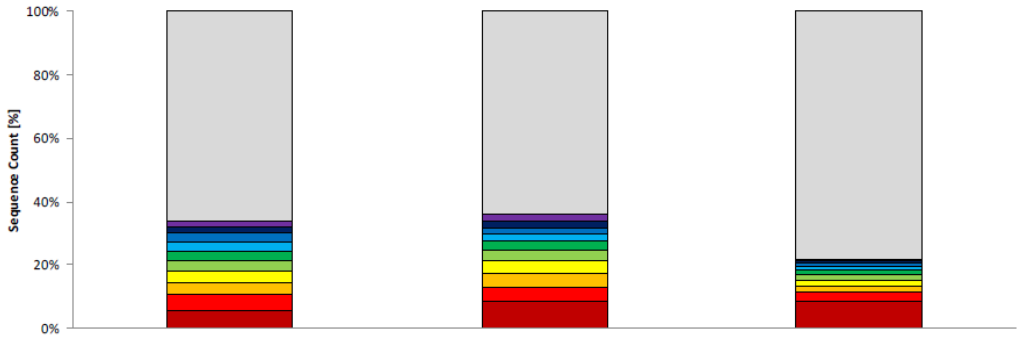
Seq Count 10 Strongest	75308	50663	36512	68773
Seq Count all other mapp. IS	182464	21674	102242	481107
Total Seq Counts Used	257772	72337	138754	549880

Patient E



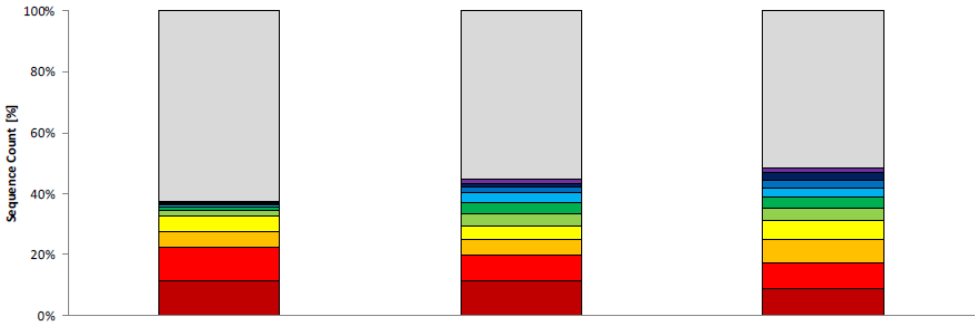
Sample	6M PBMC			12M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	MGAT5B	5.984	17-74980996	TAF2	1.857	8+120769633	TANC2	6.065	17-61285421	HSPA14	4.714	10-14896876
Top2	PSMG1	5.272	21-40379355	ETS2	1.712	21+40241557	KIAA1267	3.363	17-44204021	RBM9	3.193	22+36369163
Top3	KDM6B	4.211	17+7753846	SLC9A7	1.684	X+46588113	AKAP8	2.027	19-15433004	TCF4	2.395	18-52951201
Top4	KDM2A	4.071	11+66922316	NCOR1	1.586	17-16024411	GNAQ	1.561	9-80633044	BTRC	1.606	10+103151088
Top5	GOLIM4	2.87	3-168010026	EYA3	1.401	1-28420808	CDC27	1.528	17+45261941	INSR	1.454	19-7240918
Top6	GABPB1	2.591	15-50578470	AFMID	1.34	17+76184748	STAT5B	1.301	17+40382626	C16orf35	1.403	16-179211
Top7	RAD51L1	2.488	14-68477684	CDC27	1.3	17+45261941	UBE2O	1.174	17+74428540	GATAD2B	1.193	1-153873261
Top8	ODF2	2.429	9-131238903	AGGF1	1.24	5+76350163	C13orf18	0.871	13-46891911	KRTAP3-1	1.179	17+39169159
Top9	ATP6V0A1	2.367	17-40629297	SLC35D1	1.192	1-67492801	GSC2	0.739	22-19140137	B4GALT5	0.959	20+48315707
Top10	LRBA	2.07	4-151377749	ZBED4	1.148	22+50244336	GNG7	0.643	19+2707813	LOC102724874	0.896	8+78437548
#All Other mapp. IS	718	65.647		1112	85.54		2108	80.728		1219	81.008	
Seq Count 10 Strongest	72123			16963			25590			78725		
Seq Count all other mapp. IS	137824			100350			107192			335790		
Total Seq Counts Used	209947			117313			132782			414515		

Patient F



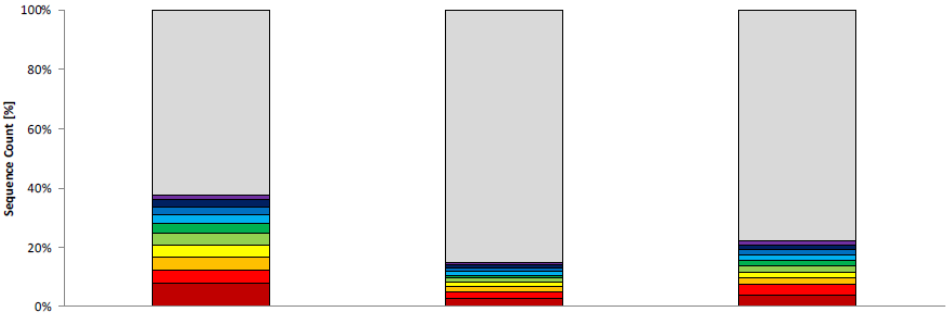
Sample	6M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ATP2A2	5.751	12+110756668	RAB2A	8.596	8-61452760	RAB2A	8.605	8-61452760
Top2	TSPAN8	4.777	12-71622166	YBX1	4.573	1+43159303	IPO9	2.736	1+201815823
Top3	UBR1	3.978	15-43285601	C9orf126	4.112	9-127797663	NF2	2.087	22-30049216
Top4	OSBP2	3.485	22-31141289	SH3TC1	3.923	4+8223661	PPFIA1	1.679	11-70158300
Top5	ARSG	3.234	17+66411628	NUDT3	3.431	6+34286398	SF1	1.653	11+64550115
Top6	UBR2	3.073	6+42617996	WDTC1	2.742	1+27574663	SMARCC1	1.517	3+47754113
Top7	KDM6A	3.013	X+44910760	BCL11A	2.272	2-60684594	NUP54	1.057	4-77047568
Top8	CD55	2.576	1+207547107	SPDYC	2.144	11+64925527	SMG1P2	0.948	16-30294562
Top9	FAM13B	2.058	5+137324396	ALOX15B	2.119	17+7938240	NBPF20	0.904	1+144925964
Top10	C19orf55	1.92	19-36253499	UNC13C	2.013	15+54790316	SIPA1L3	0.796	19-38459131
#All Other mapp. IS	870	66.135		748	64.075		2339	78.018	
Seq Count 10 Strongest	62194			70238			104520		
Seq Count all other mapp. IS	121459			125275			370958		
Total Seq Counts Used	183653			195513			475478		

Patient G



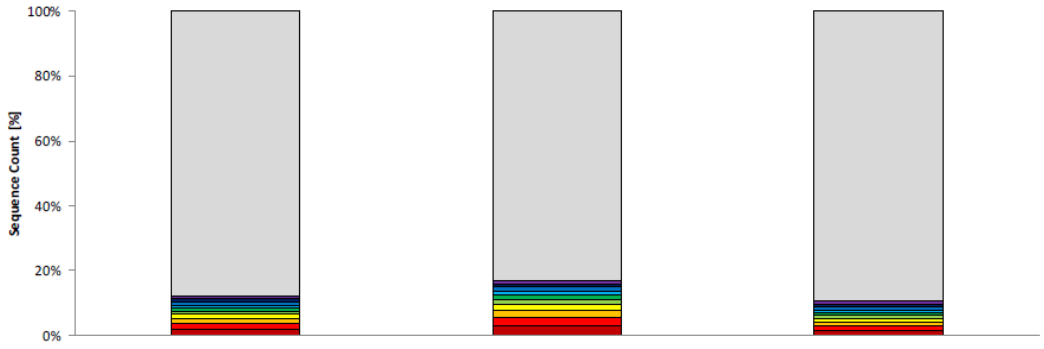
Sample	6M PBMC			12M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	BICD1	11.406	12+32404663	BICD1	11.422	12+32404663	FCHSD2	8.855	11-72692836
Top2	C6orf10	10.737	6-32311597	PIP5K1A	8.311	1-151178712	C3orf10	8.57	3+10173996
Top3	CALCRL	5.267	2+188304799	C6orf10	5.357	6-32311597	PLRG1	7.464	4-155469289
Top4	ADAM9	4.9	8+38878655	CALCRL	4.233	2+188304799	PRAGMIN	6.121	8+8202224
Top5	PARK2	2.304	6+163039170	ADAM9	3.865	8+38878655	CD72	4.218	9-35631227
Top6	PRAGMIN	0.897	8+8202224	PRAGMIN	3.831	8+8202224	TAP2	3.515	6+32793014
Top7	PLRG1	0.721	4-155469289	PARK2	3.281	6+163039170	HIPK2	2.927	7-139291239
Top8	TMEFF2	0.434	2+194132974	PLRG1	1.888	4-155469289	HLA-DMB	2.671	6+32875362
Top9	NF1	0.409	17+29440666	EPYC	1.292	12+91381344	BICD1	2.564	12+32404663
Top10	NSD1	0.402	5-176621190	CHIC1	1.276	X+73193702	FAM193B	1.42	5+176978297
#All Other mapp. IS	2401	62.523		2001	55.244		1368	51.675	
Seq Count 10 Strongest	67427			67469			231888		
Seq Count all other mapp. IS	112490			83279			247962		
Total Seq Counts Used	179917			150748			479850		

Patient H



Sample	6M PBMC			14M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	RTL1	7.621	14+101552592	SIPA1L3	3.004	19+38507338	EXOC6	3.985	10-94629435
Top2	ANTXR2	4.698	4+80952316	INPP4B	1.968	4+143407581	RBPMS	3.252	8+30345794
Top3	MYOZ1	4.397	10-75378645	GTF2I	1.594	7+74114410	NPTN	2.268	15+73914864
Top4	RPTOR	4.099	17+78542151	LILRA2	1.573	19+55094512	PRPF6	2.071	20-62624554
Top5	BTRC	3.958	10+103239500	CCDC146	1.371	7-76724637	SBNO2	2.01	19-1152405
Top6	ABCA3	3.459	16+2343746	SARNP	1.219	12-56176295	SPOP	1.856	17+47737864
Top7	TANC2	2.847	17-61372387	EFTUD1	1.213	15-82525274	FEM1B	1.756	15+68584619
Top8	KNTC1	2.491	12+123022726	HDAC9	1.07	7+18554306	SFXN1	1.72	5-174946608
Top9	LSM14A	2.252	19+34688325	SNRNP27	0.979	2-70123864	ARID3A	1.712	19-951053
Top10	SMG6	2.045	17-2116036	ZNRF1	0.86	16+75048526	PRPSAP1	1.474	17-74314650
#All Other mapp. IS	1819	62.133		1306	85.149		805	77.896	
Seq Count 10 Strongest	56393			29749			83235		
Seq Count all other mapp. IS	92531			170569			293327		
Total Seq Counts Used	148924			200318			376562		

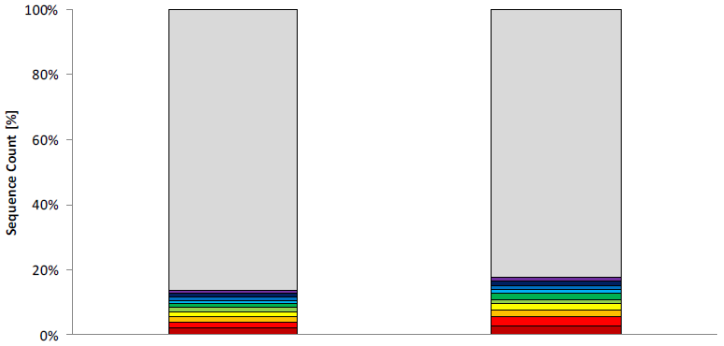
Patient I



Sample	6M PBMC			12M PBMC			36M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	UPF2	1.841	10-12081107	TCF12	2.929	15+57377126	C6orf182	1.476	6-109465692
Top2	CREBBP	1.664	16-3880825	PDS5A	2.435	4+39942265	C6orf10	1.276	6-32348653
Top3	USP36	1.511	17-76800641	GRK4	2.423	4+2996384	LOC102723854	1.209	2+43260921
Top4	ICAM2	1.187	17+62093095	CFAP70	1.897	10+75110034	LRRK1	1.026	15-101469949
Top5	ZNF706	1.128	8+102200178	AP3B1	1.323	5-77438667	PLEKHA5	0.981	12+19548234
Top6	CCM2	1.046	7-45082519	SETD2	1.298	3+47169033	KDM2A	0.951	11+66922792
Top7	INPP4B	0.967	4+143491555	C6orf182	1.236	6-109465692	MDC1	0.925	6+30681265
Top8	C6orf10	0.946	6-32297880	HDGFRP3	1.135	15-83866313	AATF	0.924	17-35335657
Top9	BTAF1	0.901	10+93717374	LOC100288637	1.097	15+31057329	RERE	0.915	1-8645637
Top10	PACS1	0.868	11-65967052	SUFU	1.083	10+104330994	MEGF8	0.891	19+42852724
#All Other mapp. IS	1518	87.941		2480	83.144		2347	89.426	

Seq Count 10 Strongest	20691	98502	33391
Seq Count all other mapp. IS	150891	485869	282391
Total Seq Counts Used	171582	584371	315782

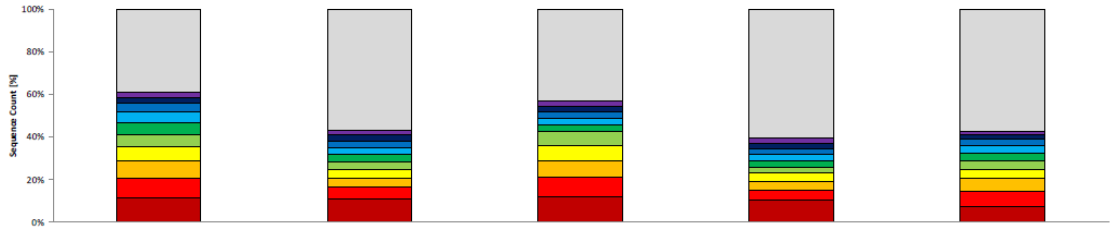
Patient J



Sample	6M PBMC			12M PBMC		
Rank	**Gene Name**	**Frequency [%]**	**Location**	**Gene Name**	**Frequency [%]**	**Location**
Top1	KIAA1715	2.067	2+176879216	HIVEP3	2.806	1+42267001
Top2	HEATR7A	1.886	8+145226580	LINC01122	2.778	2-58890936
Top3	KCNJ3	1.745	2-156243462	NCOA6	2.316	20-33391487
Top4	CRISP2	1.399	6+49635117	METTL16	1.611	17-2386478
Top5	PIK3C3	1.28	18-39636939	FKBP5	1.601	6-35615036
Top6	LRRC27	1.202	10+134151243	UBR2	1.476	6+42545294
Top7	STAT5B	1.159	17+40389259	MBD5	1.414	2-148858632
Top8	RP2	1.041	X-46740530	MTOR	1.282	1+11280931
Top9	GFPT1	1.034	2+69513996	LINC01231	1.272	9-3077050
Top10	CYTSB	1.003	17+20038142	CAPN1	1.251	11+64963121
#All Other mapp. IS	1541	86.184		2386	82.193	

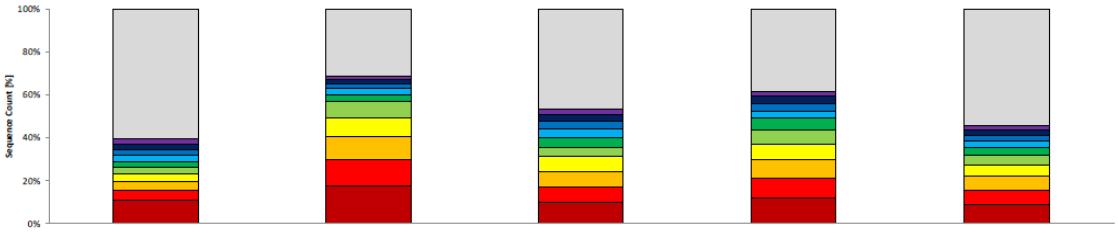
Seq Count 10 Strongest	22777	87989
Seq Count all other mapp. IS	142086	406137
Total Seq Counts Used	164863	494126

Patient K



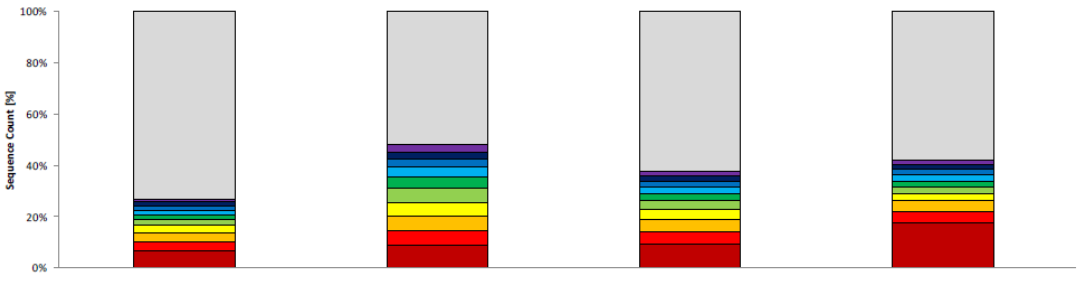
Sample	7M PBMC			10M PBMC			18M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	GRB14	11.414	2+165360433	GRB14	10.973	2+165360433	SEPT9	12.108	17+75363330	DIAPH2	10.215	X-95991891	PLEC1	7.493	8-144988218
Top2	BRWD1	8.868	21-40630039	GNA12	5.284	7-2867740	TFCP2	9.157	12+51560751	MSLN	4.649	16+801565	POLR2E	6.641	19-1096654
Top3	ELMO1	8.766	7-37281793	TFCP2	4.196	12+51560751	GRB14	7.417	2+165360433	TFCP2	4.304	12+51560751	NUP107	6.149	12+69111437
Top4	ABHD2	6.235	15+89653814	KLHL28	3.951	14-45427263	KLHL28	7.019	14-45427263	SLC26A4	3.607	7+107294552	KIAA0319L	4.562	1+35991469
Top5	EIF2C3	5.755	1+36522943	NUP107	3.687	12+69111437	FANCL	6.596	2-59005622	GRB14	3.01	2+165360433	STARD10	3.988	11+72511752
Top6	AKT3	5.374	1+243776968	ARID3A	3.649	19-973695	TAF15	3.275	17+34151864	RRM2B	2.921	8+103228563	FCHSD2	3.578	11+72659623
Top7	ZNF772	5.121	19+57981176	ZNF407	3.267	18-72447998	DISP2	3.129	15-40668807	ZP4	2.902	1-238271498	GRB14	3.216	2+165360433
Top8	TFCP2	4.576	12+51560751	MBD5	3.089	2+149219027	PUM1	3.095	1+31492044	IL12RB1	2.737	19-18149838	DHX58	3.008	17-40236854
Top9	SLC9A9	2.486	3+143510073	ZNF778	2.969	16-89292004	GNA12	2.597	7-2867740	KLHL28	2.498	14-45427263	FANCL	2.123	2-59005622
Top10	FCHSD2	2.303	11+72769839	CPD	1.886	17-28708949	RFFL	2.193	17+33344813	SACM1L	2.476	3-45766233	FAF2	1.886	5+175898075
#All Other mapp. IS	148	39.102		514	57.049		821	43.414		636	60.681		255	57.356	
Seq Count 10 Strongest	24329			41777			47974			38150			52556		
Seq Count all other mapp. IS	15622			55489			36807			58878			70687		
Total Seq Counts Used	39951			97266			84781			97028			123243		

Patient L



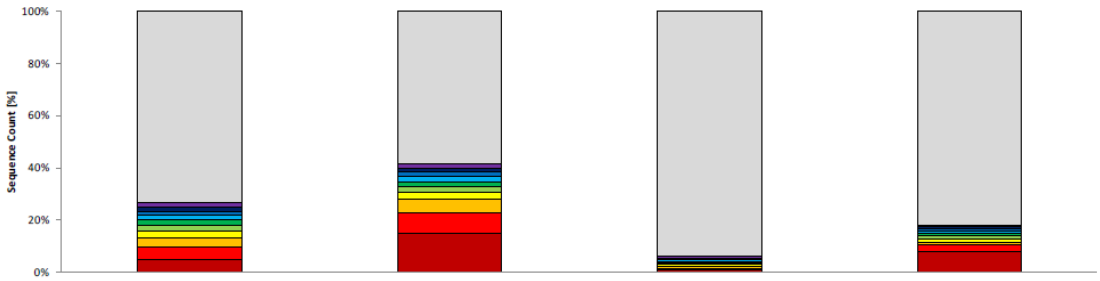
Sample	6M PBMC			12M PBMC			18M PBMC			24M PBMC			40M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ELMO1	10.956	7+36951242	VPS13B	17.792	8-100376523	VPS13B	9.472	8-100376523	PACS1	11.743	11-65889905	VPS13B	8.829	8-100376523
Top2	CAMSAP1L1	4.271	1-200748373	RERE	12.022	1-8594402	PACS1	7.494	11-65889905	KLF7	9.567	2-208017213	KLF7	6.488	2-208017213
Top3	HIVEP3	4.16	1+42374891	CDC42	10.883	1-22410296	RBM9	7.133	22+36233368	PHF7	8.171	3-52454596	RNASEH2B	6.456	13-51535265
Top4	NFATC3	3.435	16-68158094	CDC27	8.485	17-45242218	RBM4B	6.832	11+66428579	TARBP1	7.573	1-234540160	TARBP1	5.413	1-234540160
Top5	MARK2	3.372	11-63609682	PHACTR4	7.624	1-28792020	SMG6	4.848	17-2189191	VPS13B	6.279	8-100376523	CHD9	4.501	16+53297091
Top6	MAP2	2.827	2+210153227	UQCC	3.27	20+33958484	CD27	4.301	12-6546960	SEC16A	5.495	9+139362514	TCF12	4.03	15-57446619
Top7	VPS13A	2.762	9+79852780	EIF4EBP2	2.954	10-72173892	BAT3	3.882	6-31612084	PCDH15	3.518	10+56429606	EYA3	2.698	1-28385016
Top8	CISH	2.634	3+50634073	BAT3	2.239	6-31612084	G2E3	3.788	14+31057947	SPCS3	3.411	4-177245233	P2RY1	2.484	3+152458496
Top9	BHLHE40	2.634	3+5034774	EYA3	1.813	1-28385016	TARBP1	3.114	1-234540160	P2RY1	3.376	3+152458496	ZNF148	2.44	3+124996740
Top10	CRHBP	2.426	5-76271046	HN1L	1.728	16-1738896	MYO9A	2.27	15+72261148	USHBP1	2.552	19-17374380	SEC16A	2.16	9+139362514
#All Other mapp. IS	140	60.523		222	31.19		544	46.866		448	38.315		272	54.501	
Seq Count 10 Strongest	30214			26833			58168			51831			66075		
Seq Count all other mapp. IS	46322			12163			51306			32194			79148		
Total Seq Counts Used	76536			38996			109474			84025			145223		

Patient M



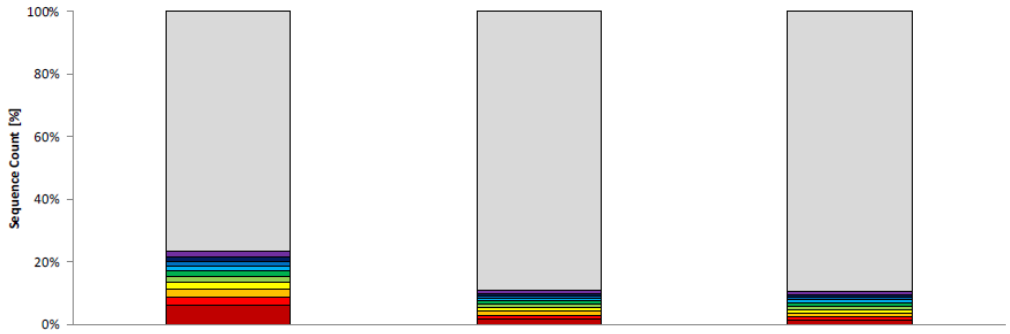
Sample	9M PBMC			12M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	SMAD2	6.625	18-45387264	RCAN3	8.853	1+24852485	SMAD2	9.024	18-45387264	SMAD2	17.543	18-45387264
Top2	MAP3K10	3.645	19-40714081	SMAD2	5.633	18-45387264	IP6K1	5.207	3+49817042	RCAN3	4.28	1+24852485
Top3	SPEN	3.457	1-16241050	CD2AP	5.553	6-47565996	PREX2	4.897	8+68908916	PAM	4.164	5-102328292
Top4	R3HDM2	3.012	12+57724333	R3HDM2	5.472	12+57724333	GNAT3	3.731	7+80001010	SPEN	2.786	1-16241050
Top5	GRB2	1.982	17-73354139	RPL10L	5.371	14-46720822	MNAT1	3.475	14+61340782	STARD13	2.662	13-33734716
Top6	TAPBPL	1.964	12+6569244	STX5	4.881	11-62584951	NLN	2.583	5+65024144	R3HDM2	2.448	12+57724333
Top7	PAM	1.893	5-102328292	SPEN	3.679	1-16241050	CHEK1	2.515	11-125516982	FST	2.287	5-52593318
Top8	PREX2	1.566	8+68908916	CHEK1	2.81	11-125516982	UBE2G1	2.365	17+4257546	MARK3	2.213	14+103926250
Top9	STAT3	1.44	17-40530480	FRK	2.799	6+115396447	ZMYND8	2.039	20+45976954	NAV2	1.797	11+20138800
Top10	NLRC3	1.224	16-3619077	PREX2	2.789	8+68908916	PAM	1.929	5-102328292	GNAT3	1.732	7+80001010
#All Other mapp. IS	1556	73.192		333	52.16		262	62.235		644	58.088	
Seq Count 10 Strongest	22631			61606			34763			68832		
Seq Count all other mapp. IS	61786			67170			57287			95399		
Total Seq Counts Used	84417			128776			92050			164231		

Patient N



Sample	6M PBMC			12M PBMC			24M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	NDC80	4.809	18+2591172	SLC37A1	14.895	21+43981289	PAPOLA	0.806	14-96978742	HORMAD2	7.831	22+30563510
Top2	ARHGAP23	4.596	17-36644655	DHRS2	7.654	14+24151522	PCDH15	0.726	10+56127981	MACF1	2.257	1+39673631
Top3	TRDN	3.599	6+123867402	DMC1	5.257	22+38933071	CCDC99	0.679	5-169032009	PCDH9	1.243	13-67182944
Top4	EDIL3	2.749	5+83576458	N4BP1	2.772	16+48595990	CDH18	0.679	5+20501456	AMOT	1.202	X+112784343
Top5	MED13L	2.25	12+116675799	CDH10	2.148	5-25554783	DHRS2	0.572	14+24151522	THBS3	1.1	1-155174645
Top6	PDGFC	2.085	4-157714373	CTNNA3	1.993	10-67410060	SPA17	0.515	11+124550286	ARPC1A	1.088	7+98935706
Top7	CD109	1.69	6+74394984	CNN2	1.919	19+1037071	CEACAM3	0.505	19-42323009	KIAA0430	1.034	16+15722766
Top8	PACS1	1.653	11+65871764	FCHSD2	1.743	11+72699357	UBR4	0.49	1-19462290	ATL1	0.734	14+51059185
Top9	C6orf10	1.616	6-32316646	SMARCA1	1.44	X+128599684	HNMT	0.475	2+138888819	AGPAT3	0.728	21-45384140
Top10	TBCB	1.547	19+36608305	FXYD5	1.415	19-35676107	SUV420H1	0.449	11+67947559	DPY19L3	0.681	19-32951787
#All Other mapp. IS	2970	73.406		1397	58.764		2762	94.104		3553	82.102	
Seq Count 10 Strongest	34485			59870			6972			32469		
Seq Count all other mapp. IS	95187			85318			111284			148941		
Total Seq Counts Used	129672			145188			118256			181410		

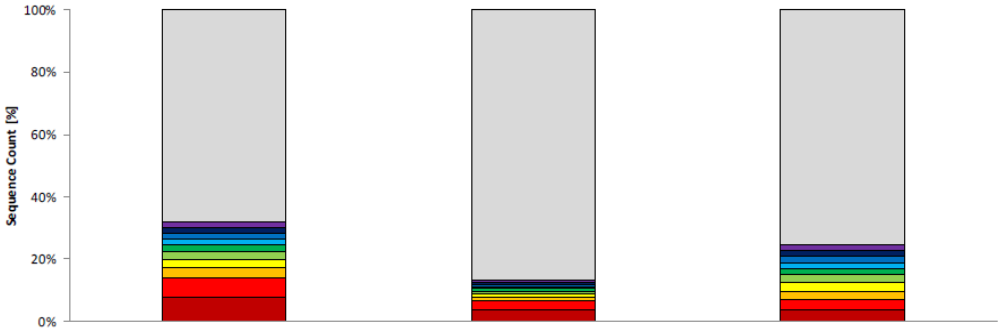
Patient O



Sample	6M PBMC			12M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	NSUN4	6.101	1-46836283	VPS13D	1.691	1-12448895	ACTRT1	1.248	X+126989883
Top2	CREBBP	2.583	16+3839602	PRDM2	1.248	1+14086005	C9orf3	1.226	9-97666513
Top3	TMEM49	2.583	17+57807366	ERP44	1.238	9-102850107	MARK3	1.129	14-103952386
Top4	ACACA	2.267	17-35549677	PIGV	1.106	1+27123220	TSPAN16	1.094	19+11406210
Top5	TNPO3	1.779	7-128687075	C9orf126	1.094	9-127784227	CNOT6	1.042	5-179980317
Top6	FAM33A	1.734	17+57195653	RSRC2	1.025	12+123007538	ANKS1A	1.03	6+34975661
Top7	MED25	1.625	19-50344770	SLITRK1	0.891	13+84311169	PCGF3	1.002	4+720401
Top8	HERC1	1.551	15-63994943	ANUBL1	0.877	10+46146516	PLPP7	0.928	9-134202882
Top9	HOMEZ	1.46	14-23740937	INSR	0.84	19+7286644	UHRF1BP1	0.894	6-34795859
Top10	GYS1	1.451	19+49490960	SLC25A33	0.816	1-9608410	PTBP3	0.885	9-114989745
#All Other mapp. IS	1305	76.866		1037	89.174		824	89.522	

Seq Count 10 Strongest	29399	11296	27029
Seq Count all other mapp. IS	97684	93050	230929
Total Seq Counts Used	127083	104346	257958

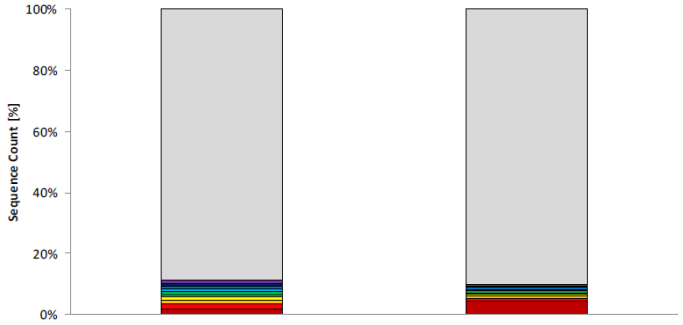
Patient P



Sample	6M PBMC			12M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	NOC3L	7.861	10-96098369	SYDE2	3.59	1-85657466	DR1	3.555	1-93833953
Top2	VPS37B	6.029	12+123384369	CDC42BPB	2.88	14+103418477	GOSR1	3.125	17+28814410
Top3	TIMELESS	3.39	12+56822750	MECP2	1.265	X-153324862	NFIX	2.936	19-13153164
Top4	MTMR3	2.452	22+30313670	POU3F3	0.962	2-105316071	ADCK4	2.746	19-41218707
Top5	MATR3	2.33	5-138642716	SRCAP	0.949	16-30722867	MLLT10	2.578	10+21963362
Top6	HEATR7A	2.212	8+145253565	TSC2	0.795	16+2120694	OR4E1	1.937	14+22484355
Top7	CLEC9A	2.087	12-10218291	MCTP2	0.643	15-94808105	PDGFC	1.933	4+157762131
Top8	RNF34	1.983	12+121840265	MED13L	0.638	12-116644726	F8A1	1.893	X-154677815
Top9	ZBED4	1.732	22+50237885	FAM164A	0.6	8-79621146	FLJ37201	1.734	10-91457755
Top10	EYA3	1.619	1-28409517	RAD54L2	0.59	3+51647801	KMT5B	1.722	11-67944842
#All Other mapp. IS	2409	68.305		1526	87.088		866	75.841	

Seq Count 10 Strongest	47716	25563	119200
Seq Count all other mapp. IS	102832	172415	374196
Total Seq Counts Used	150548	197978	493396

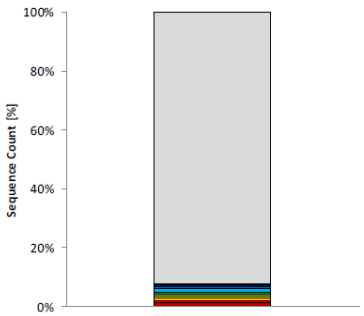
Patient Q



Sample	12M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	ZGPAT	1.707	20+62348527	STAM2	4.299	2-152981952
Top2	SARNP	1.669	12+56173416	RBM6	0.888	3-50089068
Top3	FERMT3	1.127	11+63983165	NEK11	0.757	3+130853712
Top4	STX17	1.018	9+102677191	LOC101927869	0.652	21-25557722
Top5	PTPRD	0.983	9-8356267	KDM2A	0.618	11-66974519
Top6	HNRNPUL1	0.978	19-41789384	CLIC4	0.539	1+25148488
Top7	AMBRA1	0.924	11+46461139	KIAA0753	0.534	17+6520787
Top8	TCF4	0.923	18+53222966	DIP2B	0.532	12+50933675
Top9	ASH1L	0.917	1+155349899	YAF2	0.531	12-42612166
Top10	SMC5	0.91	9-72885020	HLA-DMB	0.523	6-32891949
#All Other mapp. IS	1913	88.844		4141	90.127	

Seq Count 10 Strongest	76744	23084
Seq Count all other mapp. IS	611175	210721
Total Seq Counts Used	687919	233805

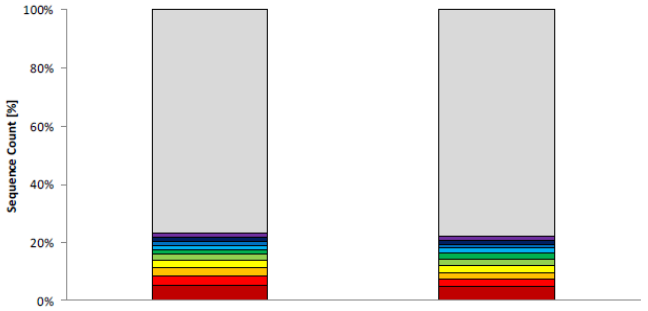
Patient R



Sample	12M PBMC		
Rank	Gene Name	Frequency [%]	Location
Top1	KLRF2	1.251	12+10039098
Top2	ERCC6L2	0.801	9+98677045
Top3	HS3ST1	0.785	4-11610208
Top4	LINC01375	0.768	10-91675254
Top5	INCENP	0.759	11-61838569
Top6	RERE	0.738	1+8547142
Top7	AGO3	0.729	1+36404338
Top8	MUT	0.72	6-49257720
Top9	DIDO1	0.689	20-61564865
Top10	STK35	0.687	20-2111757
#All Other mapp. IS	3378	92.073	

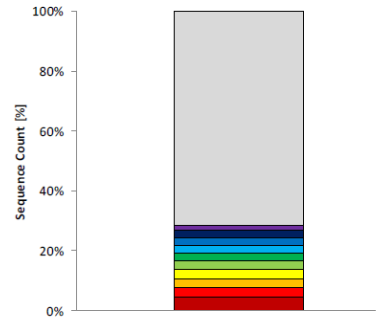
Seq Count 10 Strongest	31137
Seq Count all other mapp. IS	361666
Total Seq Counts Used	392803

Patient S



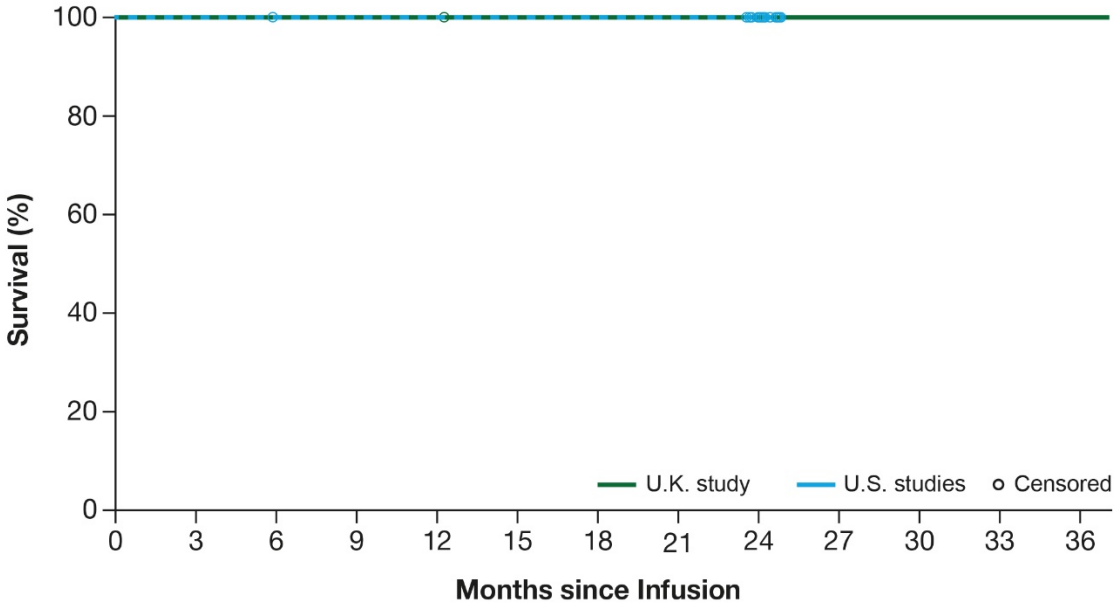
Sample	12M PBMC			36M PBMC		
Rank	Gene Name	Frequency [%]	Location	Gene Name	Frequency [%]	Location
Top1	SLC2A5	5.126	1-9141047	LOC101927269	4.787	7-79954958
Top2	PROM1	3.183	4-16030352	CHKA	2.473	11-67856190
Top3	METTL16	2.825	17+2357780	SLC2A5	2.423	1-9141047
Top4	NUDT3	2.476	6+34327534	CDC40	2.421	6-110508163
Top5	CAPN1	2.224	11-64962076	PBX3	2.101	9-128516263
Top6	PBX3	1.743	9-128516263	KANSL1	2.07	17-44164284
Top7	RASSF9	1.633	12+86212879	NUDT3	1.918	6+34327534
Top8	SLC25A36	1.363	3+140574486	DNAH2	1.339	17-7680076
Top9	C5	1.362	9-123721112	PRKACA	1.272	19-14205833
Top10	LOXL1-AS1	1.245	15-74210155	CD55	1.262	1+207497430
#All Other mapp. IS	960	76.82		1086	77.934	
Seq Count 10 Strongest	69310			50628		
Seq Count all other mapp. IS	229697			178810		
Total Seq Counts Used	299007			229438		

Patient T



Sample	12M PBMC		
Rank	Gene Name	Frequency [%]	Location
Top1	PCNX1	4.477	14+71459251
Top2	MLLT10	3.131	10+21860091
Top3	NCOR2	3.08	12-125082509
Top4	PTGES3	2.98	12-57067196
Top5	PALM2	2.897	9+112363668
Top6	SYN3	2.698	22-33344482
Top7	EIF4G3	2.532	1-21381737
Top8	PKN2	2.499	1-89176950
Top9	CCDC47	2.406	17-61844823
Top10	EIF4G3	1.953	1-21382621
#All Other mapp. IS	382	71.347	
Seq Count 10 Strongest	91951		
Seq Count all other mapp. IS	228961		
Total Seq Counts Used	320912		

Fig. S3. Kaplan-Meier Curves for Overall Survival

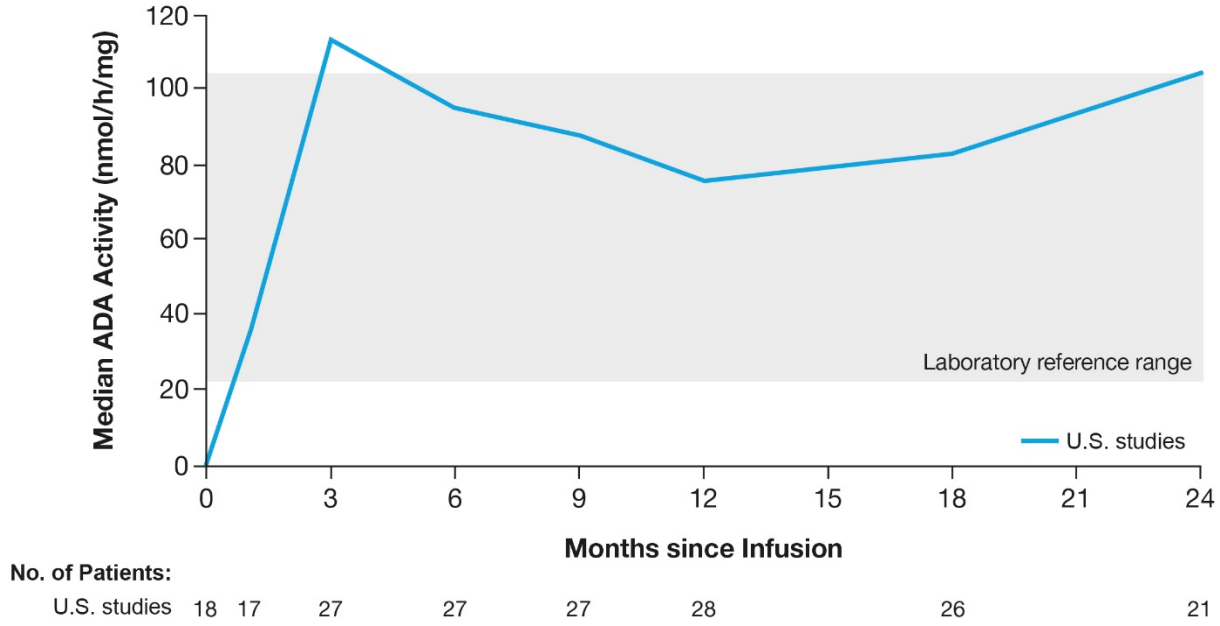


No. of Patients:													
U.K. study	20	20	20	20	20	19	19	19	19	19	19	19	19
U.S. studies	30	30	29	29	29	29	29	29	21				

Overall survival over 24 (U.S. studies) and 36 (U.K. study) months in patients who received gene therapy. At 12, 24, and 36 months, overall survival was 100.0% for both U.S. and U.K. patients.

Fig. S4. Median ADA Enzyme Activity in Peripheral Red Blood Cells

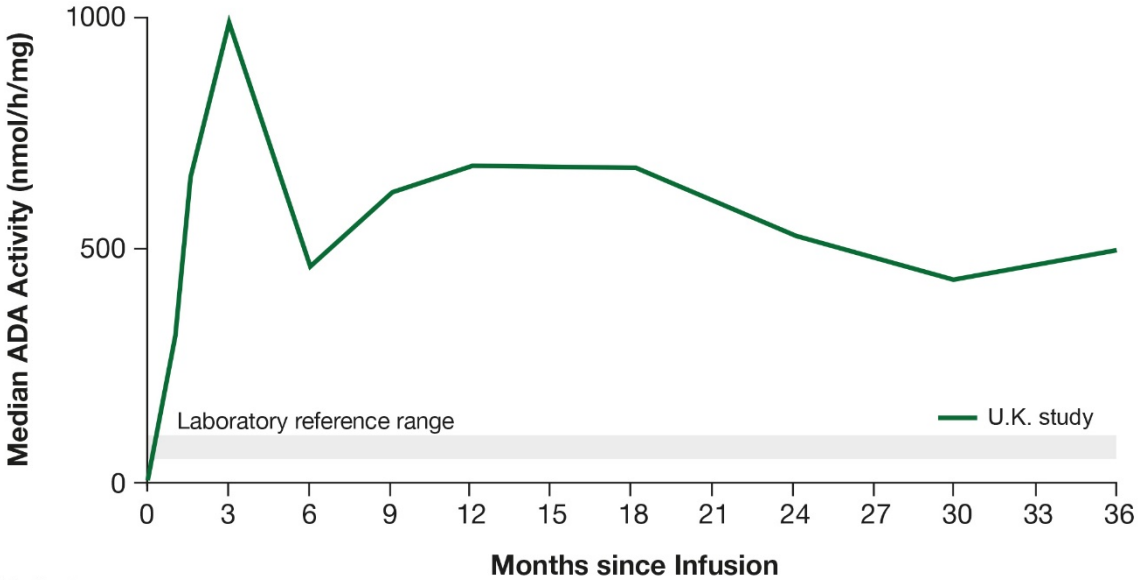
A



No. of Patients:

U.S. studies	18	17	27	27	27	28	26	21

B

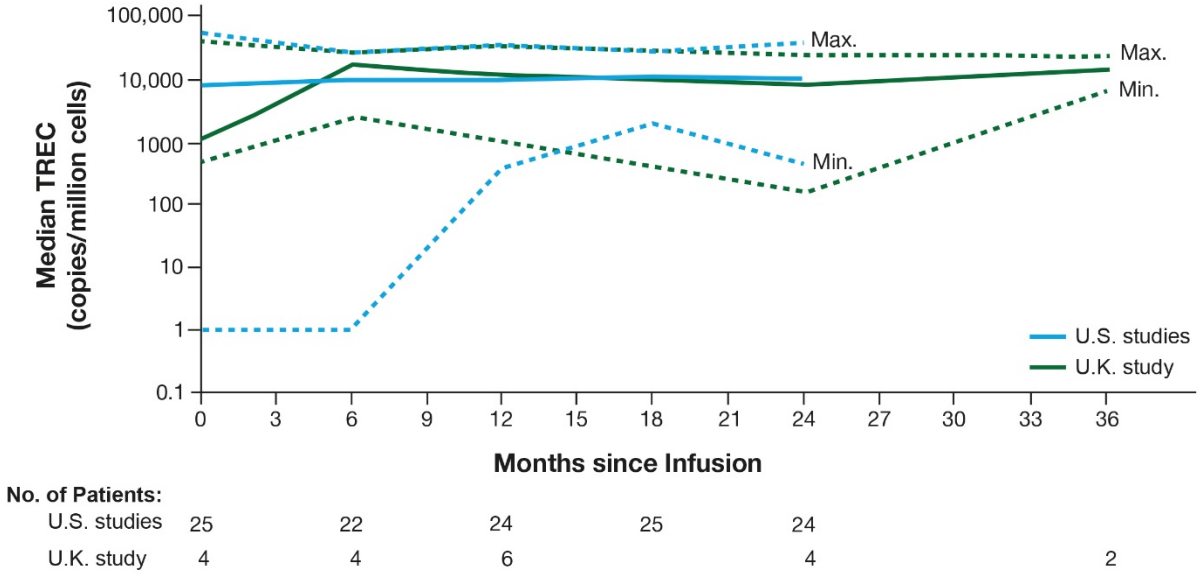


No. of Patients:

U.K. study	18	19	11	18	19	18	20	18	18	16	18

ADA activity over 24 months (U.S. studies, Panel A) and 36 months (U.K. study, Panel B) in OTL-101–treated Patients. Median adenosine deaminase (ADA) enzyme activity in peripheral red blood cells. Assays using different systems were employed in the U.S. and U.K. sites.

Fig. S5. TREC Counts in Peripheral Blood

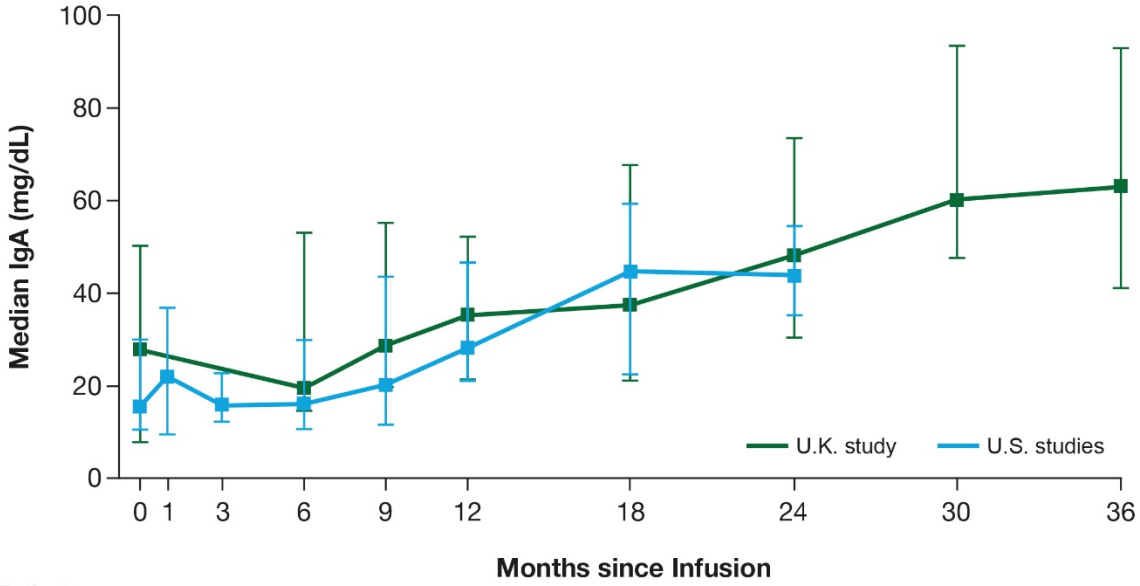


No. of Patients:													
U.S. studies	25		22		24		25		24				
U.K. study	4		4		6				4				2

TREC counts over 24 months (U.S. studies) and 36 months (U.K. study) in OTL-101–treated Patients. Median (solid line) and minimum and maximum values (dotted lines) are plotted for all patients. Values of 0 are adjusted to 1. TREC denotes T-cell receptor excision circle.

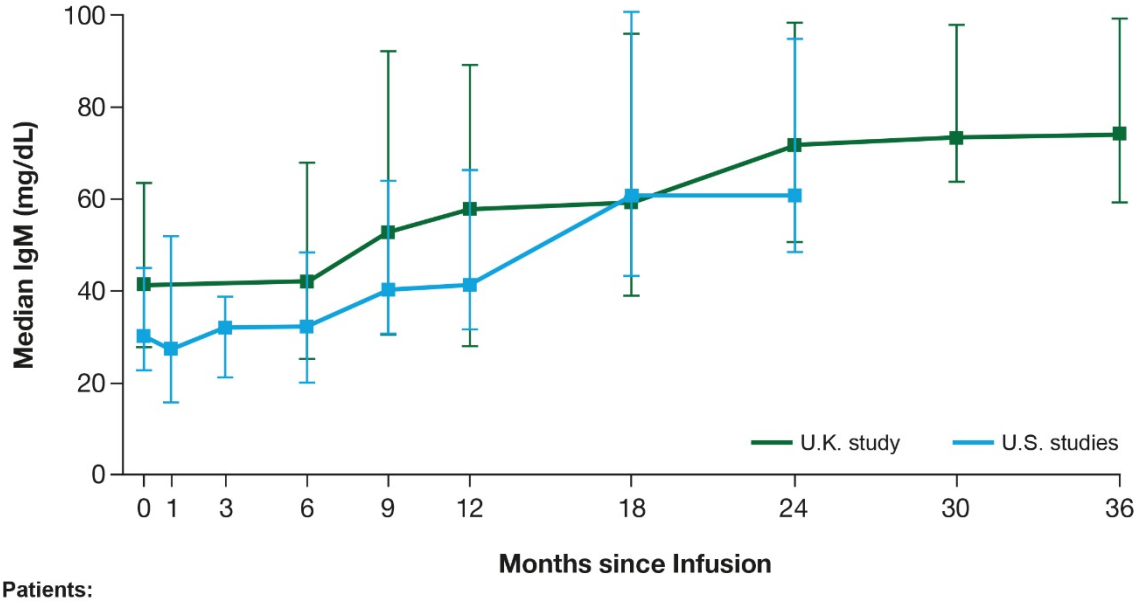
Fig. S6. Serum IgA and IgM Levels and Serum IgG Levels Following IgRT Cessation

A Serum IgA Levels



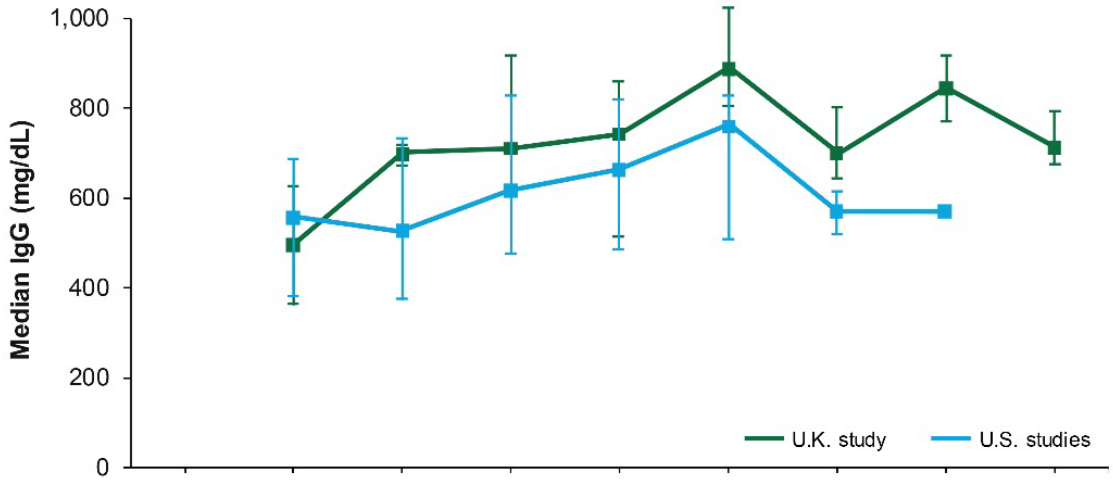
No. of Patients:									
U.K. study	17		20	20	20	18	18	16	19
U.S. studies	30	15 22	27	25	25	23	25		

B Serum IgM Levels



No. of Patients:									
U.K. study	17		20	20	20	18	18	16	19
U.S. studies	30	15 23	26	25	26	23	25		

C IgG after IgRT Cessation



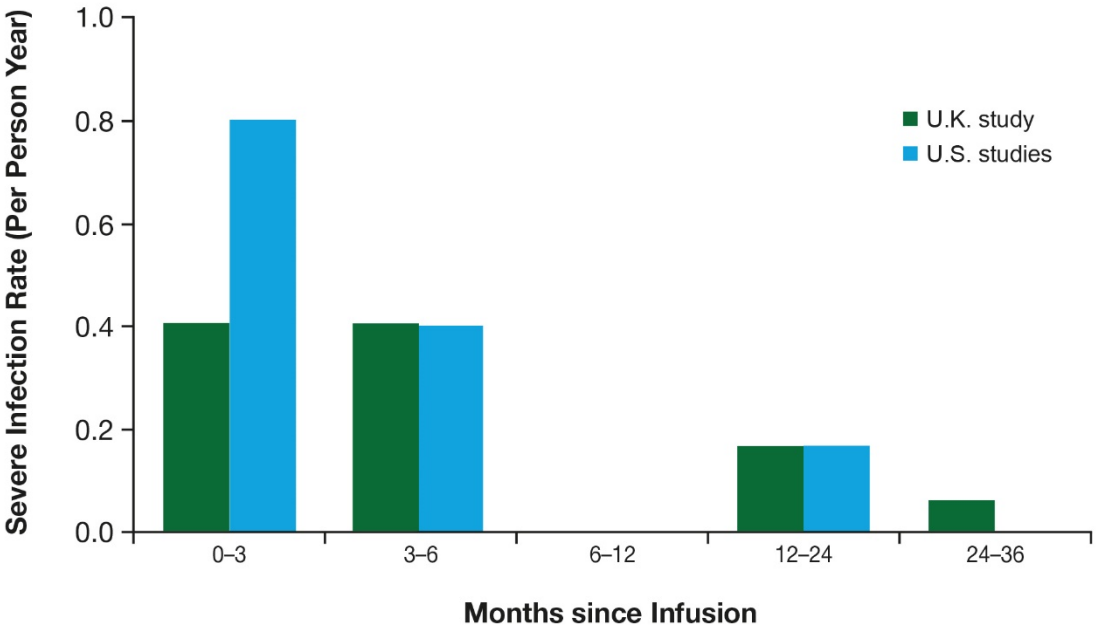
No. of Patients:								
U.K. study	2	8	4	10	5	8	2	7
U.S. studies	13	13	11	12	8	2	1	

Serum IgA (Panel A), IgM (Panel B) and IgG (Panel C) over 24 months (U.S. studies) and 36 months (U.K. study). Medians and interquartile ranges are plotted. Treatment improved serum IgM and IgA levels, resulting in most patients achieving levels within or above normal limits over time. Median IgG levels remained high following cessation of IgRT.

Ig denotes immunoglobulin and IgRT denotes immunoglobulin replacement therapy.

Fig. S7. Severe Infection Rate by Time Period

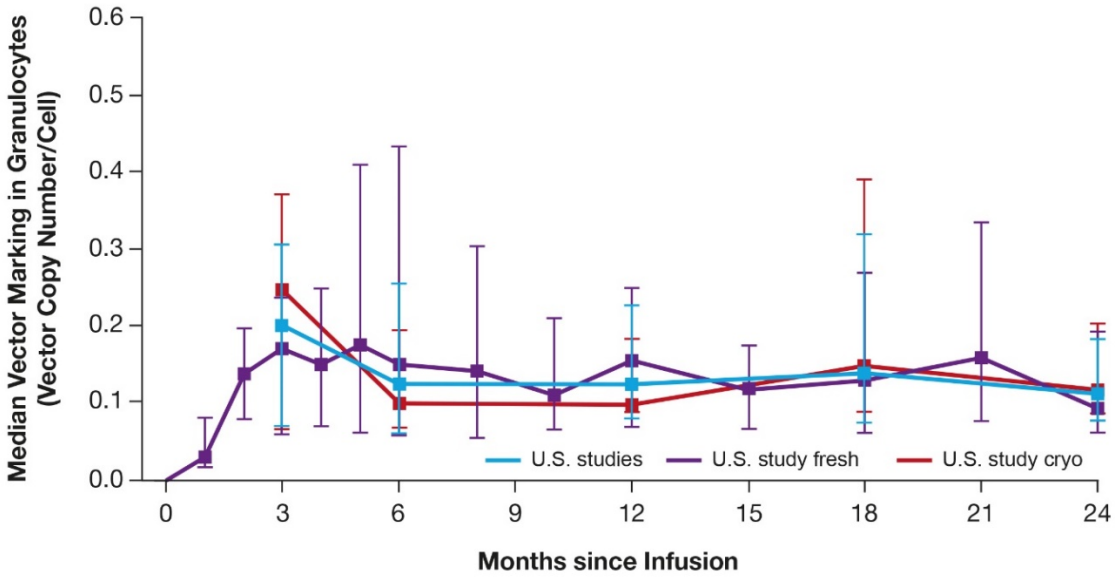
Severe infections, ie SAEs coded to Infections and Infestations MedDRA system organ class, were assessed up to 24 months' (U.S. studies) or 36 months' (U.K. study) follow up. Starting at three months post-treatment to last follow-up severe infection rates were similar in the U.S. and U.K. studies.



No. of Patients:					
U.K. study	20	20	20	20	19
U.S. studies	30	30	29	29	

Fig. S8. Comparison of the U.S. Studies Integrated Fresh and Cryopreserved Data for (A) Median VCN in granulocytes (B) Median VCN in PBMCs (C) Median CD3⁺ T Cell Counts and (D) Median ADA activity.

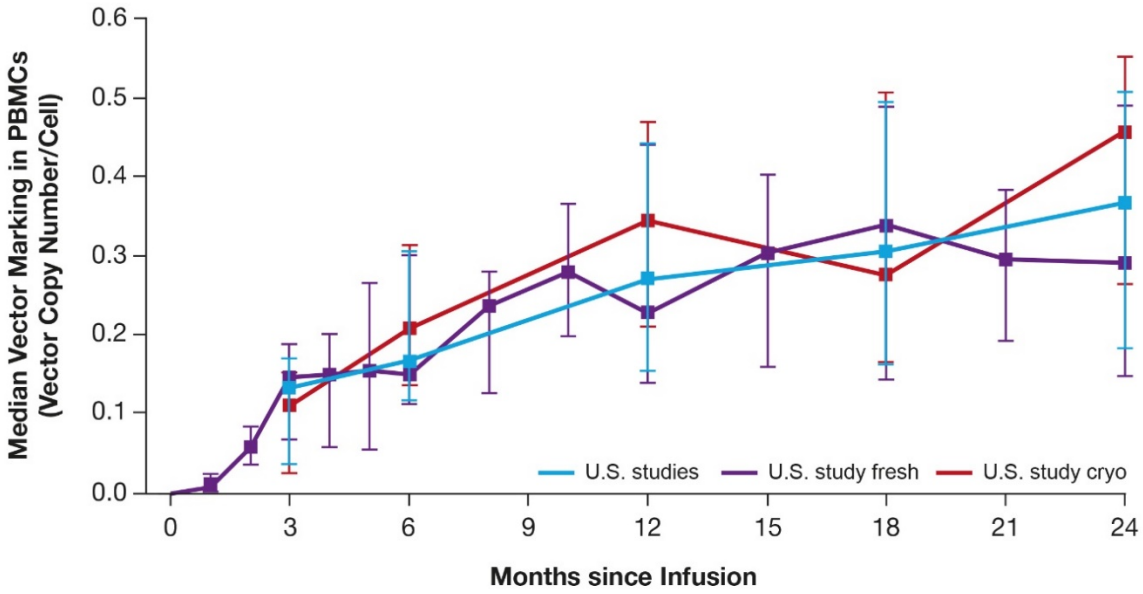
A



No. of Patients:

U.S. studies				27			26			28			25			27
U.S. study fresh	19	17	16	17	17	19	17	18	18	19	20		18	20		18
U.S. study cryo				10			9			9			7			9

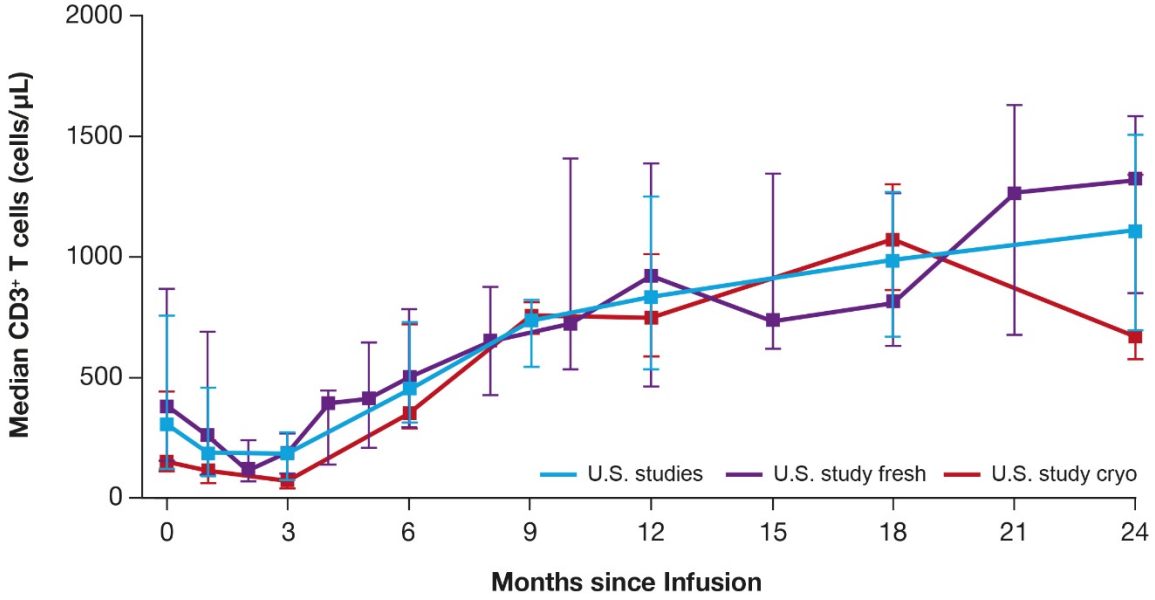
B



No. of Patients:

U.S. studies				22			24			25			26			27
U.S. study fresh	18	17	18	13	17	19	16	18	19	18	20		19	20		18
U.S. study cryo				9			8			7			7			9

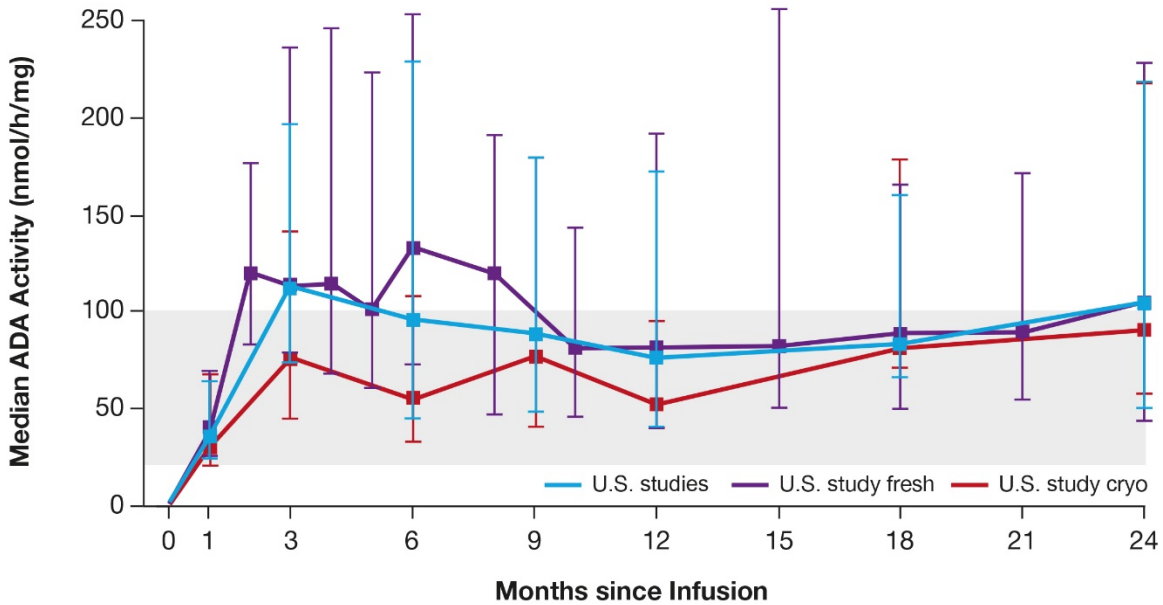
C



No. of Patients:

U.S. studies	28	27		28			25			25			24				23					24		
U.S. study fresh	18	17	18	19	18	17	18		18		19		17		16		15		19			16		
U.S. study cryo	10	10		9			7			7			7				8					8		

D



No. of Patients:

U.S. studies	18	17		27			27			27			28				26					21		
U.S. study fresh	11	9	16	17	19	20	17		20		20		19		19		18		18			14		
U.S. study cryo	6	8		10			10			7			9				8					7		

ADA adenosine deaminase, PBMC peripheral blood mononuclear cell, VCN vector copy number

Table S1. Inclusion and Exclusion Criteria.*

Inclusion Criteria		
NCT01852071 (U.S. Fresh Study)	**NCT02999984 (U.S. Cryopreserved Study)**	**NCT01380990 (U.K. study)**
1: Children ≥1.0 months of age with a diagnosis of ADA-SCID, based on:	**1: Children ≥30 days and <18 years of age with a diagnosis of ADA-SCID, based on:**	**1. Male or female Subject, below 5 years of age OR male or female subjects 5 to 15 years of age who have preserved thymic function, as evidenced by presence of >10% naïve T cells ($CD4^+$ $CD45RA^+$ $CD27^+$ cells)**
2. Evidence of ADA deficiency, defined as: Decreased ADA enzymatic activity in erythrocytes, leukocytes, skin fibroblasts, or cultured fetal cells to levels consistent with ADA-SCID as determined by the reference laboratory, **or** identified mutations in ADA alleles consistent with a severe reduction in ADA activity **Evidence of ADA-SCID based on either:** i. Family history of a first-order relative with ADA deficiency and clinical and laboratory evidence of severe immunologic deficiency, **or** ii. Evidence of severe immunologic deficiency in subjects prior to the institution of immune restorative therapy, based on: - Lymphopenia (ALC <400 cells/µl) OR absence or low number of T cells (absolute $CD3^+$ count <300 cells/µl), **or** - Severely decreased T-lymphocyte blastogenic responses to phytohemagglutinin (<10% of lower limit of normal for the diagnostic laboratory, or <10% of the response of the normal control of the day, or stimulation index <10), **or** - Identification of SCID by neonatal screening revealing low TREC levels	**2. Evidence of ADA deficiency, defined as:** i. Decreased ADA enzymatic activity in erythrocytes, leukocytes, skin fibroblasts, or in cultured fetal cells to levels consistent with ADA-SCID as determined by the reference laboratory, or ii. Identified mutations in ADA alleles consistent with a severe reduction in ADA activity, **Evidence of ADA-SCID based on either:** i. Family history of a first order relative with ADA deficiency and clinical and laboratory evidence of severe immunologic deficiency, **or** ii. Evidence of severe immunologic deficiency in subjects prior to the institution of immune restorative therapy, based on - Lymphopenia (absolute lymphocyte count (ALC) <400 cells/µL) OR absence or low number of T cells (absolute CD3+ count < 300 cells/µL), or - Severely decreased T lymphocyte blastogenic responses to phytohem-agglutinin (either <10% of lower limit of normal for the diagnostic laboratory, or <10% of the response of the normal	**2. Diagnosis of ADA-SCID** confirmed by DNA sequencing OR by confirmed absence of <3 % of ADA enzymatic activity in peripheral blood (PB) or (for neonates) in umbilical cord blood erythrocytes and/or leucocytes or in cultured fetal cells derived from either chorionic villus biopsy or amniocentesis, prior to institution of PEG-ADA ERT

	control of the day, or stimulation index <10), **or** - Identification of SCID by neonatal screening revealing low TREC levels.	
3. Ineligible for matched sibling allogeneic bone marrow transplantation Absence of a medically eligible HLA-identical sibling, with normal immune function, who may serve as an allogeneic bone marrow donor	**3. Ineligible for matched family allogeneic BM transplantation,** defined as the absence of a medically eligible HLA-identical sibling or family donor, with normal immune function, who could serve as an allogeneic bone marrow donor	**3. Patients who lack a fully HLA-matched family donor**
4. Signed written informed consent according to guidelines of the institutional review board (UCLA Office of Human Research Protection Program and NHGRI Institutional Review Board)	**4. Provision of written informed consent** prior to any study-related procedures. In this study, consent must be provided by the parents/legal guardians and, where applicable according to local laws, a signed assent from the child	**4. Informed consent** signed by a parent/guardian
	5. Females of childbearing age will be required to provide a negative pregnancy test 30 days prior to Visit 2	
	Subjects and their parents/legal guardians must be willing and able to comply with study restrictions, to remain at the clinic for the required duration during the study period, and to return to the clinic for the follow-up evaluation as specified in the protocol	
Exclusion Criteria		
1. Hematologic		
Anemia (hemoglobin <10.5 g/dl at <2 years of age, or <11.5 g/dl at >2 years of age)	Anemia (hemoglobin <8.0 g/dl)	
Neutropenia: absolute granulocyte count <500/mm^3	Neutropenia (ANC <500/mm^3). Note: ANC <500/mm^3 with absence of myelodysplastic syndrome on bone marrow aspirate and biopsy and normal marrow cytogenetics are acceptable for eligibility	
Thrombocytopenia (platelet count <150,000/mm^3 at any age)	Thrombocytopenia (platelet count <50,000/mm^3 at any age)	

INR or PT >2xULN, or PTT >2.33xULN (subjects with a correctable deficiency controlled on medication will not be excluded)	PT or INR and PTT >2xULN (subjects with a correctable deficiency controlled on medication will not be excluded)	
Cytogenetic abnormalities in peripheral blood, bone marrow (or amniotic fluid [if available])	Cytogenetic abnormalities in peripheral blood, bone marrow (or amniotic fluid [if available])	**1. Cytogenetic abnormalities on peripheral blood**
Prior allogeneic HSCT with cytoreductive conditioning	Prior allogeneic HSCT with cytoreductive conditioning	
3. Infections		
Evidence of infection with HIV-1, Hepatitis B, Hepatitis C, or Parvovirus B 19 by DNA PCR within 90 days prior to bone marrow harvest. If other infection is present, it must be under control (e.g., stable or decreasing viral load) at the time of screening	Confirmation of an infectious disease by deoxyribonucleic acid (DNA) PCR positive at time of screening assessment for the following: HIV-1, Hepatitis B, Parvovirus B19	
4. Pulmonary		
Resting O_2 saturation by pulse oximetry <95% on room air	Resting O_2 saturation by pulse oximetry <90% on room air	
Chest X-ray indicating active or progressive pulmonary disease	Chest X-ray indicating active or progressive pulmonary disease. Note: Chest X ray indicating residual signs of treated pneumonitis is acceptable for eligibility	
5. Cardiac		
Abnormal ECG indicating cardiac pathology	Abnormal ECG indicating cardiac pathology	
Uncorrected congenital cardiac malformation with clinical symptomatology	Uncorrected congenital cardiac malformation with clinical symptomatology	
Active cardiac disease, including clinical evidence of congestive heart failure, cyanosis, hypotension	Active cardiac disease, including clinical evidence of congestive heart failure, cyanosis, hypotension	
Poor cardiac function as evidenced by left ventricular ejection fraction <40% on echocardiogram	Poor cardiac function as evidenced by left ventricular ejection fraction <40% on echocardiogram	
6. Neurologic		
Significant neurologic abnormality by examination	Significant neurologic abnormality by examination	
Uncontrolled seizure disorder	Uncontrolled seizure disorder	
7. Renal		
Renal insufficiency: serum creatinine ≥1.2 mg/dl (10^6 µmol/l) or ≥3+ proteinuria	Renal insufficiency: serum creatinine ≥1.2 mg/dl (10^6 µmol/l) or ≥3+ proteinuria	

Abnormal serum sodium, potassium, calcium, magnesium, phosphate (fresh: at grade III or IV by Division of AIDS Toxicity Scale; cryopreserved: >2xULN)	Abnormal serum sodium, potassium, calcium, magnesium or phosphate levels at >2 x ULN.	
8. Hepatic/gastrointestinal		
Serum transaminases >5xULN	Serum transaminases >5xULN	
Serum bilirubin >2xULN	Serum bilirubin >2xULN	
Serum glucose >1.5xULN	Serum glucose >1.5xULN	
Intractable severe diarrhea		
9. Oncologic† (see below)		
Evidence of active malignant disease other than DFSP	Evidence of active malignant disease other than DFSP	**2. Evidence of active malignant disease**
Evidence of DFSP expected to require antineoplastic therapy within 5 years following infusion of genetically corrected cells (if anti-neoplastic therapy has been completed, a subject with a history of DFSP can be included)	Evidence of DFSP expected to require anti-neoplastic therapy within the 5 years following the infusion of genetically corrected cells (if anti-neoplastic therapy has been completed, a subject with a history of DFSP can be included)	
Evidence of DFSP expected to be life limiting within 5 years following infusion of genetically corrected cells	Evidence of DFSP expected to be life limiting within 5 years following infusion of genetically corrected cells	
10. Known sensitivity to busulfan	**10. Known sensitivity to busulfan**	**3. Known sensitivity to busulfan**
11. General		
Age ≤1.0 months		
Appropriate organ function as outlined below must be observed within 60 days of entering this trial		
Pregnant	The subject is pregnant or has a major congenital anomaly	4. **If applicable, confirmed pregnancy** (tested in subjects above 12 years old)
Major congenital anomaly		
Ineligible for autologous HSCT by the criteria at the clinical site	Ineligible for autologous HSCT by the criteria at the clinical site	
Expected survival <6 months	Likely to require treatment during the study with drugs that are not permitted by the study protocol	

Other conditions that, in the opinion of the principal investigator and/or co-investigators, contraindicate the bone marrow harvest, administration of busulfan, or infusion of OTL-101 or indicate the subject or their parent/primary caregiver's inability to follow protocol	Other conditions that, in the opinion of the principal investigator and/or co-investigators, contraindicate the harvest of bone marrow, the administration of busulfan and the infusion of transduced cells, or that indicate an inability of the subject or subject's parent/legal guardian to comply with the protocol	
	The subject has previously received another form of gene therapy	

*ADA denotes adenosine deaminase, AIDS acquired immune deficiency syndrome, ALC absolute lymphocyte count, ANC absolute neutrophil count, DFSP dermatofibrosarcoma protuberans, ECG electrocardiogram, HIV human immunodeficiency virus, HLA human leukocyte antigen, HSCT hematopoietic stem cell transplant, INR international normalized ratio, NHGRI National Human Genome Research Institute, PB, peripheral blood, PCR polymerase chain reaction, PEG-ADA ERT pegylated adenosine deaminase enzyme replacement therapy, PT prothrombin time, PTT partial thromboplastin time, SCID severe combined immunodeficiency, TREC T-cell receptor excision circle, UCLA University of California, Los Angeles; and ULN upper limit of normal.

†Subjects receiving active antineoplastic therapy or radiation for any cancer, including DFSP, were not eligible. Subjects with DFSP not being treated with active antineoplastic therapy at the time of enrollment AND who had no plans to receive active antineoplastic therapy in the absence of progressive malignant disease AND whose DFSP was not expected to be life limiting within 5 years following the infusion of genetically corrected cells would have been eligible.

Table S2. Summary of Gene Therapy Infusion.

	U.S. studies (N=30)	U.K. study (N=20)
Number of patients treated	30	20
Busulfan AUC, µmol/l·min*		
Median	4542.5	4418.0
Minimum, maximum	2360, 5673	2567, 7513
Number of infusions		
1	27	19
2	3	1
Patient weight, kg		
Median	7.9	9.2
Minimum, maximum	5.3, 17.6	4.9, 43.3
Total $CD34^+$ HSPCs infused by body weight, $x10^6$ $CD34^+$ cells/kg		
Median	7.4	14.4[a]
Minimum, maximum	2.1, 10.9	3.0, 71.4[b]

*AUC denotes area under the concentration–time curve, and HSPC hematopoietic stem and progenitor cell.
†Statistics were obtained using the sum of each patient's results.
[a]The median according to the clinical database was 14.43 x 10^6 $CD34^+$ cells/kg. A data entry error was confirmed by the site after database lock. After correcting for the error, the median was 12.62 x 10^6 $CD34^+$ cells/kg.
[b]The maximum according to the clinical database was 71.4 x 10^6 $CD34^+$ cells/kg. A data entry error was confirmed by the site after database lock. After correcting for the error, the maximum was 28.7 x 10^6 $CD34^+$ cells/kg.

Table S3. Primary and Secondary Endpoints.

U.S. Fresh Study	U.S. cryopreserved study	U.K. study
Primary Endpoints:		
Safety Incidence and grade of serious adverse events (SAEs). SAEs could manifest as: • Clinical toxicities • Exposure to replication competent lentivirus (RCL) • Development of monoclonal expansion or leukoproliferative complications from vector insertional effects	**Safety** Assessments of adverse events (AEs, including infections), clinical laboratory test results, vital signs measurements, physical examination results, and use of concomitant medications	**Safety** Clinical, hematological, and immunological progress of subjects, assessed by evaluating AEs and SAEs, the results of physical examination, and laboratory values (biochemistry and hematology)

	Emergence of RCL, and monoclonal expansion or leukemia due to vector integration	Analysis of the frequency of clonal expansion associated with vector integration near proto-oncogenes
		Analysis of the frequency of vector integration into known proto-oncogenes
Efficacy		
	Evaluation of the gene therapy at 6 months post infusion based on the following parameters and their thresholds: • Erythrocyte ADA enzyme activity above baseline/pre-treatment level (i.e.>0 Units) • Absolute $CD3^+$ T cell counts ≥200/µl • Granulocyte samples positive for vector sequences by qPCR (≥1/10,000 cells) Subjects must meet all 3 criteria. Subjects not meeting these criteria will be designated a failure (nonresponder) and will be withdrawn from the study. These data will be used to compare subject data from one of the ongoing phase 1/2 studies using the fresh formulation	
Overall and event-free survival by 12 months post-treatment where a treatment failure event is defined by one of the following endpoints: death; reinstitution of PEG-ADA; or need for rescue allogeneic HSCT	Overall and event-free survival by 12 months post-treatment. Overall survival was defined as the proportion of subjects alive. Event-free survival was defined as the proportion of subjects alive with no 'event'; an 'event' was the resumption of PEG-ADA ERT or the need for a rescue allogeneic HSCT	Overall survival of subjects treated with the gene therapy, assessed at 12 months of follow up Event-free survival of subjects treated with the gene therapy, assessed at 12 months of follow up. An ‘event’ was defined as death, reinstitution of pegylated adenosine deaminase (PEG-ADA) enzyme replacement therapy (ERT), or need for a rescue allogeneic hematopoietic stem cell transplant (HSCT)
		Success of engraftment and resulting immunological and metabolic effects in subjects who received gene therapy, determined by assessing: • Vector copy number in peripheral blood leukocytes at month 3, 6, 12, 24, and 36 • Cellular and humoral immune system recovery, determined as changes in T-

		cell numbers, T-cell function (proliferation to phytohemagglutinin and anti-CD3 antibodies), circulating immunoglobulin levels and number of subjects requiring immunoglobulin replacement therapy (IgRT) at each study visit • ADA activity and reduction in deoxyadenosine triphosphate (dATP) in erythrocytes at Baseline and month 1, 1.5, 3, 6, 9, 12, 18, 24, 30, and 36
Key Secondary Endpoints:		
Overall and event-free survival at 24 months	Overall and event-free survival at 24 months	
Efficacy of gene transfer/engraftment of HSPCs, expressed as: vector copy number (VCN)		Overall survival and event-free survival outcomes at 2 and 3 years in subjects treated with gene therapy
ADA expression and purine metabolite detoxification, characterized by: • ADA enzyme activity in red blood cells • deoxyadenosine nucleotides (dAXP) levels in red blood cells		
Examine the effects of treatment on immune reconstitution characterized by: • Absolute lymphocyte and lymphocyte subset counts • Measures of B cell function (use of IgRT; serum immunoglobulin [Ig] levels; specific antibody responses) • Measures of T-cell reconstitution and function (T-cell receptor excision circles [TRECs] in peripheral blood; T-cell receptor [TCR] Vβ panel; lymphocyte proliferation)	Immune reconstitution, assessed as counts of T, B, and natural killer (NK) cells in peripheral blood, response to tetanus vaccinations, and use of IgRT	
Assess severe infection rates	Rates of severe infections/opportunistic infectious episodes, defined as infections requiring or prolonging hospitalization and/or documented infections by opportunistic pathogens	Reduction in the frequency of infections, evaluated at 1, 2, and 3 years post treatment on the basis of clinical history and examination. The infections of interest in this study were severe infections or opportunistic infectious episodes, defined as infections requiring hospitalization or prolonging

		hospitalization and/or documented infections by opportunistic pathogens
	Performance outcomes and quality of life, measured by the Karnofsky/Lansky scale and questions relevant to the subjects' general well-being, school attendance and ability to practice sports	
		Assessment of the longitudinal clinical effects of treatment, by evaluation of: • TRECs, as a marker of improved thymic function, 2 years after gene therapy administration • Serum levels of immunoglobulin IgA, IgG, and IgM and the number of subjects requiring immunoglobulin replacement therapy, recorded dichotomously
		Growth of pathogenic microorganisms over 3 years, evaluated through the assessment of AEs and SAEs related to infections
		Tolerability of the conditioning regimen, determined by assessing whether hematopoietic recovery has taken place within 6 weeks (absolute neutrophil count >0.5 x 10^9 cells/l)
		Feasibility of the transduction procedure, assessed by: • Availability of greater than 0.5 x 10^6 $CD34^+$ cells/kg after transduction • Undetectable replication competent lentivirus (determined retrospectively) • $CD45^+$ cell viability after transduction equal to or greater than 50%, in accordance with the final product release criteria
Exploratory endpoints		
	Assess the level of gene correction, engraftment and immune reconstitution: • Vector copy number (VCN) in peripheral blood cells	

	• ADA enzyme activity and total adenosine nucleotides in red blood cells • Further indicators of immune reconstitution: – Serum immunoglobulin (Ig) levels – TRECs analysis – TCR Vβ repertoire – Lymphocyte proliferative responses	
	Exploratory safety endpoints included vector integration site analysis and quantification of the clonal diversity of vector integrants	
PEG-ADA ERT use	PEG-ADA ERT use	PEG-ADA ERT use
		T cell receptor Vβ repertoire
		Morphology (Normal/Abnormal), vector integration (Normal/Abnormal), and vector copy number in bone marrow (bone marrow) mononuclear cells, performed in bone marrow aspirate samples, if collected
		Tetanus vaccination response

ADA, adenosine deaminase, AE adverse event, dATP deoxyadenosine triphosphate, BMT bone marrow transplantation, dATP deoxyadenosine triphosphate, ERT, enzyme replacement therapy, IgRT, immunoglobulin replacement therapy, PEG pegylated, qPCR quantitative polymerase chain reaction, RCL, replication competent lentivirus, SAE serious adverse events, TREC T cell receptor excision circles

Table S4. Summary of Events, Including Rescue Treatment and Death.

Events	U.S. studies	U.K. study
Patients/patients — no. (%)	30 (100.0)	20 (100.0)
Death — no. (%)		
Month 12	0 (0)	0 (0)
Unknown at month 12[†]	1 (3)	0 (0)
Month 24	0 (0)	0 (0)
Unknown at month 24[†]	1 (3)	0 (0)
Month 36		
Unknown at month 24[†]		
Rescue allogeneic HSCT required — no. (%)		
Month 12	0 (0)	0 (0)
Unknown at month 12[†]	1 (3)	0 (0)
Month 24	0 (0)	0 (0)
Unknown at month 24[†]	1 (3)	1 (5)
Month 36		0 (0)
Unknown at month 36[†]		1 (5)
Re-institution of PEG-ADA ERT — no. (%)		
Month 12		0 (0)
Unknown at month 12[†]	1 (3)	0 (0)
Month 24	0 (0)	1 (5)
Unknown at month 24[†]	1 (3)	0 (0)
Month 36	0 (0)	1 (5)
Unknown at month 36[†]		0 (0)

ADA denotes adenosine deaminase, ERT enzyme replacement therapy, HSCT hematopoietic stem cell transplant, PEG pegylated.

[†]A patient's status was classed as 'unknown' if they had not reached this time point or withdrew prior to the visit while still alive.