Gene of Interest Report (GOI)

CART research group

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Introduction

This report presents an analysis of genes targeted during T cell therapy over 783 treated subjects (Described in Jadlowski et al.)

Lentiviral and gammaretroviral vectors integrate into genomes of targeted host cells in these studies T-cells. These genomic locations of vector integrations are identifiable through integration site sequencing. Abundances of individual cell clones can be inferred by the sonicLength method (Berry et al. 2012). In this report, we analyzed the data collected from integration site sequencing for subjects treated with engineered T cells.

We constructed 4 gene lists based on: 1 & 2) decreased (D) or enriched (E) integration site occurrence in patient samples relative to the initial transduction product, 3) peak clonal abundance (A), and 4) longitudinal clonal persistence (L).

More about each of these criteria is below:

Depleted (D)	Depleted genes show a significant decrease ($p \leq 0.05$) in integration frequency at later time points.
Enriched (E)	Enriched genes show a significant increase ($p \leq 0.05$) in integration frequency at later time points.
Abundant (A)	Abundant genes are genes associated with the top 1% of clonal abundance estimates at later time points.
Longitudinal (L)	Longitudinal genes are genes with ≥ 3 unique integrations from ≥ 3 patients recovered ≥ 90 days post-transduction.

Note that integration sites are sampled from a larger population, so that that sampling of each specimen is incomplete.

The assignment of genes to the Enriched and Depleted categories is dependent on gene specific Fisher's Exact tests (uncorrected p-values ≤ 0.05). Figure 1 below depicts the number of genes associated with more than one category.

Figure 1.
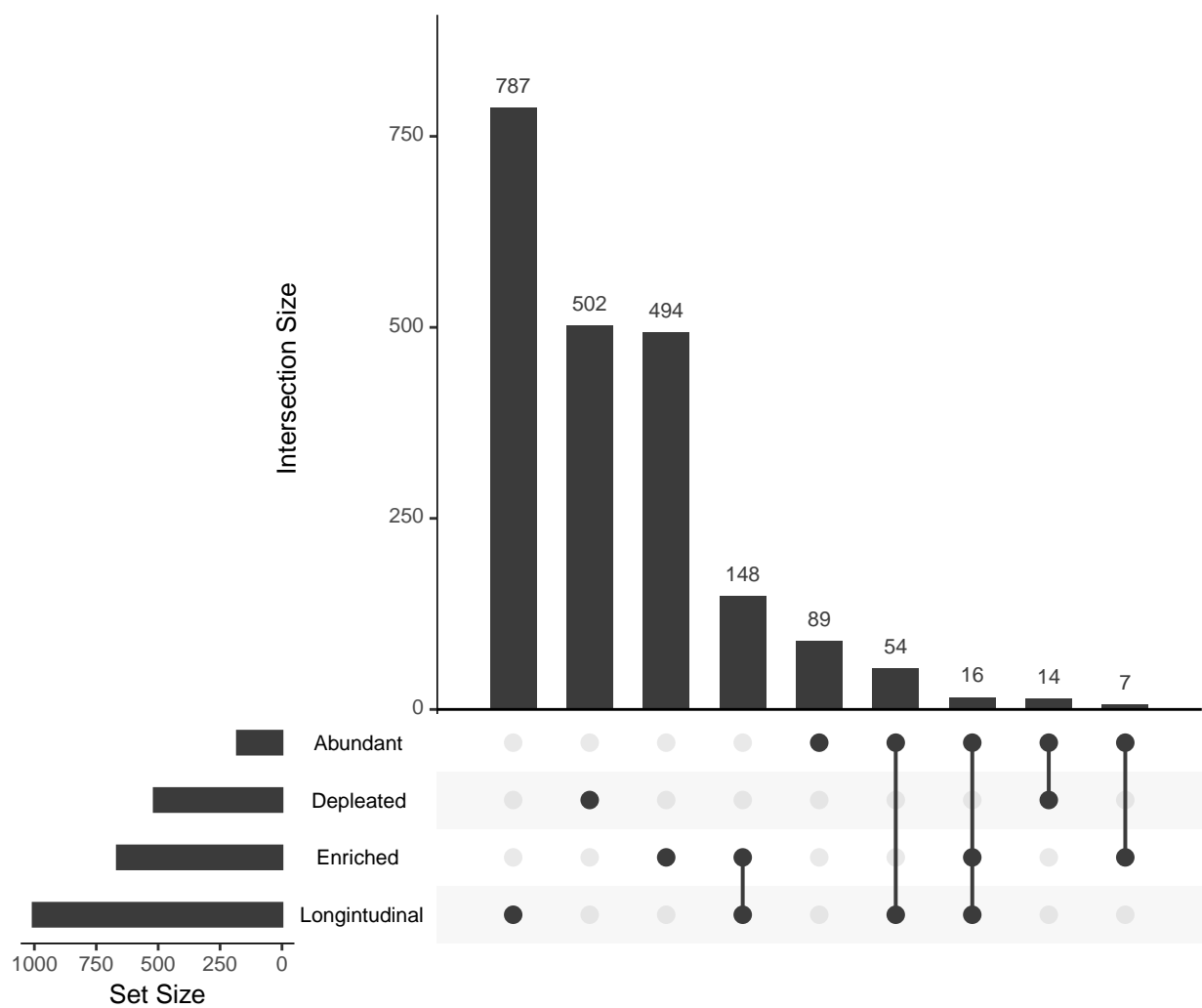
The table below contains gene that have been associated with the Enriched, Abundant, and Longintudinal categories. These genes are of particular interest since three separate metrics suggests that integration near these genes may bolster persistence and/or proliferation over time.

Table A. Genes annotated as EAL.

gene	subjects	totalSites	percentChange	maxAbund	longitudinalSites	oncoGene	categories
TRIO	35	52	121.4%	66	4		EAL
PPP6R3	124	642	58.4%	154	13		EAL
CLK4	102	324	52.4%	53	6		EAL
SRRM2	101	231	44.8%	33	6		EAL
NELL2	103	316	43.6%	441	6		EAL
SUPT3H	119	589	38.6%	31	4		EAL
MED13L	112	358	36.9%	38	4		EAL
FOXP1	120	431	35.6%	49	5	Yes	EAL
AKAP13	109	344	33.7%	27	4		EAL
VAV1	133	981	30.5%	37	9	Yes	EAL
ANKRD11	136	807	26.8%	25	14		EAL
ADD1	121	416	25.5%	43	5		EAL
RNF213	126	603	24.6%	76	7	Yes	EAL
PAFAH1B1	121	579	24.4%	33	11		EAL
SAE1	121	520	20.7%	24	5		EAL
CRAMP1	127	634	20.3%	31	7		EAL

The degree of integration near suspected oncogenes is important given that genotoxity through disruption of oncogene transcription units or over expression via promoter insertion can potentially lead to adverse events. Here we test for significance of overlap between select oncogene lists and genes near recovered integration events. Test data sets include:

allOnco [2,579 genes (link)]: A comprehensive list of oncogenes compiled from multiple projects and consortia.

cosmic [743 genes (link)]: "Catalogue Of Somatic Mutations In Cancer" is an expert-curated database encompassing the wide variety of somatic mutation mechanisms causing human cancer.

cosmic_tsg [320 genes]: This gene list is a subset of the cosmic gene list annotated as tumor suppressors.

Table B summarizes the size of each criteria gene list identified by the various methods. Significance of overlap between gene lists are displayed by asterisks before the percent of genes identified from the criteria list which overlap with the column specified group. The asterisk to the left of the "/" indicates a p-value below 0.05 before multiple comparison corrections, while an asterisk to the right of the "/" indicates a p-value below 0.05 after multiple comparison corrections. Significance was tested using Fisher's Exact test and multiple comparison corrections were made using a Benjamini-Hochberg (FDR) method for each criteria based list.

Table B.

Criteria	Genes	allOnco	cosmic	cosmic_tsg
Depleated	516	*/- 19.6%	*/- 9.3%	*/- 4.7%
Enriched	665	*/* 16.1%	*/* 7.2%	*/* 4.7%
Abundant	180	*/* 25.6%	*/* 11.1%	*/* 5.6%
Longitudinal	1005	*/* 22.7%	*/* 9.9%	*/* 5.1%

Genes associated with the Enriched category have greater integration frequencies at later time points compared to earlier time points which suggests that integration near these genes bolsters cell survival.

gene	Gene symbol.
subjects	Total number of subjects with an integration near gene.
earlyCount	Number of integration sites recovered from earlier time points ($\leq$ 0 days).
lateCount	Number of integration sites recovered from later time points ($>$ 0 days).
percentChange	Percent increase in integration frequency compared to earlier time period ($>$ 0 days).
pVal	p-value from Fisher's Exact test.
pVal.adj	BH corrected p-value from Fisher's Exact test.
oncoGene	Gene is found in a broad lists of oncogenes.
categories	DEAL categories associated with gene.

Table C. Top 100 enriched genes. p-Values are marked with an * if $\leq$ 0.05.

gene	subjects	earlyCount	lateCount	percentChange	pVal	pVal.adj	oncoGene	categories
EP300	115	249	243	85.21%	1.5e-11 *	8.4e-08 *	TSG	EL
KDM6A	107	178	185	97.25%	1.4e-10 *	4.7e-07 *	TSG	EL
CBFB	130	389	327	59.54%	7.2e-10 *	1.7e-06 *	TSG	EL
PPP6R3	124	357	298	58.42%	7.4e-09 *	1.2e-05 *		EAL
KMT2D	74	99	110	110.87%	8.1e-08 *	8.3e-05 *	TSG	EA
LRPPRC	68	52	69	151.83%	4.4e-07 *	3.8e-04 *		EL
NUCB2	47	28	44	198.23%	4.9e-06 *	2.7e-03 *		EL
CSMD1	45	12	28	342.83%	6.1e-06 *	3.2e-03 *		EL
CREBBP	123	300	233	47.40%	1.1e-05 *	5.3e-03 *	TSG	EL
LPP	116	184	155	59.87%	2.2e-05 *	9.1e-03 *	Yes	EL
PPP4R2	47	27	40	181.16%	2.8e-05 *	1.1e-02 *		EL
SMG1P7	68	56	64	116.90%	2.9e-05 *	1.1e-02 *		E
VAV1	133	605	416	30.50%	3.7e-05 *	1.3e-02 *	Yes	EAL
SUPT3H	119	345	252	38.62%	1.0e-04 *	3.1e-02 *		EAL
MICAL3	20	5	16	507.31%	1.2e-04 *	3.5e-02 *		EL
ATG5	77	78	77	87.35%	1.3e-04 *	3.7e-02 *		E
HELQ	40	22	33	184.68%	1.6e-04 *	4.3e-02 *		E
SMG1P1	110	127	110	64.38%	1.6e-04 *	4.3e-02 *		EL
CLK4	102	183	147	52.45%	1.6e-04 *	4.3e-02 *		EAL
SLC1A1	10	1	10	1797.84%	1.8e-04 *	4.5e-02 *		E
MPP2	30	14	25	238.90%	2.6e-04 *	5.5e-02		E
LCOR	81	102	92	71.18%	2.7e-04 *	5.6e-02		E
FANCL	46	27	36	153.04%	2.8e-04 *	5.6e-02		E
CSDE1	37	18	28	195.22%	2.9e-04 *	5.7e-02		E
A4GALT	12	2	11	943.81%	3.0e-04 *	5.9e-02		E
USP16	39	19	29	189.67%	3.5e-04 *	6.4e-02		E
MIR4435-2HG	19	6	16	406.09%	3.8e-04 *	6.7e-02		EL
CALN1	25	10	20	279.57%	3.8e-04 *	6.7e-02		EL
PTPRT	10	3	12	659.13%	4.1e-04 *	7.1e-02	TSG	E
NRXN3	24	9	19	300.65%	4.4e-04 *	7.5e-02		EL
TLL1	8	1	9	1608.05%	4.8e-04 *	7.8e-02		E
RHEB	25	11	21	262.31%	5.3e-04 *	8.2e-02		E
AGAP1	21	8	18	327.01%	5.7e-04 *	8.6e-02		EL
FRG1CP	57	48	51	101.64%	6.3e-04 *	9.3e-02		E
TCF12	84	110	94	62.18%	6.7e-04 *	9.6e-02	Yes	EL
FDX1	21	7	16	333.79%	7.1e-04 *	9.9e-02		E
LOC101927550	10	2	10	848.92%	7.5e-04 *	1.0e-01		E
RLIM	19	6	15	374.46%	7.6e-04 *	1.0e-01		E
EIF4H	29	16	25	196.54%	7.6e-04 *	1.0e-01		E
TAF2	62	54	55	93.30%	8.0e-04 *	1.0e-01		EL
PHF3	97	121	101	58.41%	8.6e-04 *	1.1e-01		EL
TIAM1	76	59	58	86.57%	8.8e-04 *	1.1e-01		EL

Table C. Top 100 enriched genes. p-Values are marked with an * if ≤ 0.05. *(continued)*

gene	subjects	earlyCount	lateCount	percentChange	pVal	pVal.adj	oncoGene	categories
UTY	72	95	83	65.81%	8.9e-04 *	1.1e-01		E
GOLT1B	26	11	20	245.06%	9.2e-04 *	1.1e-01		E
FAM81A	13	3	11	595.87%	9.7e-04 *	1.1e-01		E
GFRA1	12	3	11	595.87%	9.7e-04 *	1.1e-01		E
ANKRD11	136	488	326	26.78%	1.0e-03 *	1.2e-01		EAL
DNAAF4-CCPG1	25	8	17	303.29%	1.0e-03 *	1.2e-01		EL
FMR1	44	25	32	142.92%	1.1e-03 *	1.3e-01		E
WAC	72	67	63	78.45%	1.2e-03 *	1.3e-01		EL
ESRRG	8	1	8	1418.27%	1.3e-03 *	1.4e-01		EL
PPP3CA	108	191	144	43.08%	1.3e-03 *	1.4e-01		EL
CHD8	65	75	68	72.07%	1.5e-03 *	1.5e-01		E
CNTN5	16	6	14	342.83%	1.5e-03 *	1.5e-01		E
CRAT37	17	6	14	342.83%	1.5e-03 *	1.5e-01		E
HHAT	16	6	14	342.83%	1.5e-03 *	1.5e-01		EL
TTC7B	19	6	14	342.83%	1.5e-03 *	1.5e-01		E
NELL2	103	181	137	43.65%	1.7e-03 *	1.6e-01		EAL
KIAA1217	14	5	13	393.44%	1.7e-03 *	1.6e-01		E
KIF13A	15	5	13	393.44%	1.7e-03 *	1.6e-01		EL
PDCD6	14	5	13	393.44%	1.7e-03 *	1.6e-01		E
IFNGR2	9	2	9	754.03%	1.8e-03 *	1.7e-01		EA
PTPRN2	9	2	9	754.03%	1.8e-03 *	1.7e-01		E
ORC4	48	38	41	104.77%	1.9e-03 *	1.7e-01		E
FOXP1	120	252	180	35.56%	2.0e-03 *	1.8e-01	Yes	EAL
ATXN1	84	91	78	62.67%	2.0e-03 *	1.8e-01		EL
PPWD1	25	10	18	241.61%	2.1e-03 *	1.8e-01		E
CDK17	82	103	86	58.46%	2.1e-03 *	1.8e-01		E
ZNF148	78	103	86	58.46%	2.1e-03 *	1.8e-01		E
USP11	54	43	44	94.20%	2.2e-03 *	1.8e-01		E
LINC01687	12	3	10	532.61%	2.2e-03 *	1.8e-01		E
LTBP1	13	3	10	532.61%	2.2e-03 *	1.8e-01		E
NECAB1	13	3	10	532.61%	2.2e-03 *	1.8e-01		E
VAMP7	8	3	10	532.61%	2.2e-03 *	1.8e-01		E
RBPJ	50	33	37	112.79%	2.3e-03 *	1.8e-01		E
RASA2	114	185	137	40.54%	2.8e-03 *	2.1e-01		E
FRG1DP	35	23	28	131.04%	3.0e-03 *	2.2e-01		EL
ATP9A	16	6	13	311.20%	3.0e-03 *	2.2e-01		E
LINGO2	18	6	13	311.20%	3.0e-03 *	2.2e-01		E
TENM2	18	6	13	311.20%	3.0e-03 *	2.2e-01		EL
TPST1	15	6	13	311.20%	3.0e-03 *	2.2e-01		E
CDK8	37	26	31	126.28%	3.0e-03 *	2.2e-01		E
CEP128	71	74	65	66.70%	3.1e-03 *	2.3e-01		EL
PLEKHA1	65	65	59	72.27%	3.2e-03 *	2.3e-01		EL
ADCYAP1	7	1	7	1228.48%	3.3e-03 *	2.3e-01		E
DOK5	7	1	7	1228.48%	3.3e-03 *	2.3e-01		E
FAM83A	8	1	7	1228.48%	3.3e-03 *	2.3e-01		E
LINC01618	6	1	7	1228.48%	3.3e-03 *	2.3e-01		E
NEMP2	7	1	7	1228.48%	3.3e-03 *	2.3e-01		E
NFE2	8	1	7	1228.48%	3.3e-03 *	2.3e-01		E
NME6	7	1	7	1228.48%	3.3e-03 *	2.3e-01		E
SNAP91	7	1	7	1228.48%	3.3e-03 *	2.3e-01		E
TRAM2	8	1	7	1228.48%	3.3e-03 *	2.3e-01		E
DHX15	63	52	50	82.48%	3.3e-03 *	2.3e-01		E
ROCK1	99	134	104	47.29%	3.3e-03 *	2.3e-01		EL
FLJ42627	22	8	15	255.84%	3.4e-03 *	2.3e-01		E
NTAQ1	14	5	12	355.48%	3.4e-03 *	2.3e-01		E
DAZAP1	104	164	123	42.34%	3.5e-03 *	2.3e-01		EL
MYO10	21	10	17	222.63%	3.6e-03 *	2.4e-01		EL
TMPRSS11E	22	10	17	222.63%	3.6e-03 *	2.4e-01		E

Genes associated with the Depleted category have lower integration frequencies at later time points compared to earlier time points which suggests that integration near these genes may be detrimental to cell survival.

gene	Gene symbol.
subjects	Total number of subjects with an integration near gene.
earlyCount	Number of integration sites recovered from earlier time points (≤ 0 days).
lateCount	Number of integration sites recovered from later time points (> 0 days).
percentChange	Percent increase in integration frequency compared to earlier time period (> 0 days).
pVal	p-value from Fisher's Exact test.
pVal.adj	BH corrected p-value from Fisher's Exact test.
oncoGene	Gene is found in a broad lists of oncogenes.
categories	DEAL categories associated with gene.

Table D. Top 100 depleated genes. p-Values are marked with an * if ≤ 0.05.

gene	subjects	earlyCount	lateCount	percentChange	pVal	pVal.adj	oncoGene	categories
RNPS1	135	590	146	-53.04%	2.5e-18 *	4.1e-14 *		D
CD4	85	167	24	-72.73%	7.6e-12 *	6.2e-08 *		D
PACS1	145	1881	751	-24.23%	6.1e-11 *	2.5e-07 *		DA
KDM2A	143	1378	531	-26.87%	4.0e-10 *	1.1e-06 *		D
EXOC2	111	314	81	-51.04%	1.2e-09 *	2.5e-06 *		D
IP6K1	139	609	199	-37.99%	1.4e-09 *	2.5e-06 *		D
SF3B2	80	142	25	-66.59%	1.9e-08 *	2.8e-05 *		D
TANK	144	641	221	-34.57%	2.5e-08 *	3.4e-05 *		D
MROH1	140	1305	518	-24.67%	2.7e-08 *	3.4e-05 *		D
RUVBL2	61	96	12	-76.28%	3.9e-08 *	4.5e-05 *		D
LONP1	71	98	13	-74.82%	6.2e-08 *	6.8e-05 *		D
QRICH1	134	461	149	-38.66%	8.9e-08 *	8.6e-05 *		D
LINC02569	107	313	91	-44.82%	1.9e-07 *	1.7e-04 *		D
TBC1D10C	56	87	12	-73.82%	6.6e-07 *	5.4e-04 *		D
ASH1L	142	789	300	-27.84%	1.0e-06 *	7.6e-04 *		D
ARHGDIA	120	281	82	-44.62%	1.0e-06 *	7.6e-04 *		D
UBE2J2	112	283	84	-43.67%	1.6e-06 *	1.1e-03 *		D
ANK3	94	186	47	-52.04%	2.3e-06 *	1.6e-03 *		D
NPLOC4	148	2175	956	-16.58%	2.4e-06 *	1.6e-03 *		D
WNK1	124	395	132	-36.58%	3.4e-06 *	2.1e-03 *		D
EIF2B3	124	344	111	-38.76%	4.1e-06 *	2.5e-03 *		D
KPNB1	83	129	28	-58.81%	4.7e-06 *	2.7e-03 *		D
NOSIP	133	655	247	-28.43%	5.0e-06 *	2.7e-03 *		DA
TNFSF12-TNFSF13	46	57	6	-80.02%	7.3e-06 *	3.7e-03 *		D
PRR12	125	447	157	-33.34%	8.0e-06 *	4.0e-03 *		D
TNFSF12	45	56	6	-79.67%	1.1e-05 *	5.3e-03 *		D
SDF4	75	122	27	-58.00%	1.3e-05 *	6.1e-03 *		D
STAG2	61	82	14	-67.60%	2.1e-05 *	9.0e-03 *	TSG	D
VMP1	123	443	159	-31.88%	2.1e-05 *	9.0e-03 *		DA
RBM6	134	511	189	-29.81%	2.4e-05 *	9.7e-03 *		D
TONSL	103	214	63	-44.13%	2.7e-05 *	1.1e-02 *		D
LSM2	99	238	73	-41.79%	2.8e-05 *	1.1e-02 *		D
CSGALNACT1	69	112	25	-57.64%	3.1e-05 *	1.1e-02 *		D
UBTF	53	74	12	-69.22%	3.2e-05 *	1.1e-02 *		D
IL6R	50	69	11	-69.74%	4.7e-05 *	1.6e-02 *		D
RETREG3	82	135	34	-52.20%	4.7e-05 *	1.6e-02 *		D
CCDC57	139	651	255	-25.66%	4.9e-05 *	1.6e-02 *		D
TBX21	35	42	4	-81.93%	7.4e-05 *	2.4e-02 *		D
PSMB9	104	294	99	-36.09%	8.2e-05 *	2.6e-02 *		D
WIPF1	63	81	16	-62.51%	1.0e-04 *	3.1e-02 *		D
LOC105369632	73	100	23	-56.35%	1.3e-04 *	3.8e-02 *		D

Table D. Top 100 depleated genes. p-Values are marked with an * if ≤ 0.05. *(continued)*

gene	subjects	earlyCount	lateCount	percentChange	pVal	pVal.adj	oncoGene	categories
CISH	59	80	16	-62.04%	1.4e-04 *	4.0e-02 *		D
CD27-AS1	102	241	79	-37.79%	1.6e-04 *	4.3e-02 *		D
HCG20	118	494	190	-27.01%	1.8e-04 *	4.5e-02 *		D
HLA-DMB	32	40	4	-81.02%	1.8e-04 *	4.5e-02 *		D
LINC02332	30	32	2	-88.14%	1.8e-04 *	4.5e-02 *		D
LPCAT3	100	252	84	-36.74%	1.9e-04 *	4.5e-02 *		D
SH3GL1	69	105	25	-54.81%	2.0e-04 *	4.7e-02 *	Yes	D
LINC01970	35	43	5	-77.93%	2.0e-04 *	4.8e-02 *		D
GATAD2B	117	312	110	-33.09%	2.2e-04 *	5.1e-02		D
EMBP1	52	57	9	-70.03%	2.2e-04 *	5.1e-02		D
HLA-DPA1	41	53	8	-71.35%	2.3e-04 *	5.1e-02		D
NCAPH2	93	148	42	-46.14%	2.3e-04 *	5.2e-02		D
STAT3	113	276	95	-34.68%	2.5e-04 *	5.3e-02	Yes	D
ERN1	73	127	34	-49.19%	2.5e-04 *	5.3e-02		D
ENTHD1	80	133	36	-48.63%	2.5e-04 *	5.3e-02		D
ANTXR2	102	175	53	-42.52%	2.7e-04 *	5.6e-02		D
VRK3	106	229	75	-37.84%	2.8e-04 *	5.6e-02		D
GSDMD	21	25	1	-92.41%	3.1e-04 *	6.0e-02		D
EIF4A3	47	59	10	-67.83%	3.2e-04 *	6.0e-02		D
MAP3K14	90	137	38	-47.36%	3.2e-04 *	6.0e-02		D
RELA	105	191	60	-40.38%	3.2e-04 *	6.0e-02		D
EIF3B	48	55	9	-68.94%	3.2e-04 *	6.0e-02		D
ZNF764	28	34	3	-83.25%	3.7e-04 *	6.7e-02		D
KCTD13	73	104	26	-52.55%	4.1e-04 *	7.1e-02		D
PTPN11	48	61	11	-65.78%	4.3e-04 *	7.4e-02	Yes	D
FNBP1	130	516	204	-24.97%	4.7e-04 *	7.8e-02	Yes	DA
MDS2	33	40	5	-76.28%	4.8e-04 *	7.8e-02	Yes	D
EIF3L	80	150	44	-44.33%	4.8e-04 *	7.8e-02		D
HORMAD2	125	563	226	-23.82%	4.9e-04 *	7.8e-02		D
AKAP8	41	50	8	-69.63%	4.9e-04 *	7.8e-02		D
HSPA1B	35	51	8	-70.23%	5.0e-04 *	7.8e-02		D
PFKL	24	24	1	-92.09%	5.1e-04 *	7.9e-02		D
ADCK5	102	212	70	-37.34%	5.5e-04 *	8.4e-02		D
ABCF1	87	180	57	-39.90%	6.1e-04 *	9.1e-02		D
LINC00824	45	59	11	-64.62%	6.1e-04 *	9.1e-02		D
NCR3	73	115	31	-48.84%	6.3e-04 *	9.3e-02		D
PTK2	64	85	20	-55.35%	6.4e-04 *	9.3e-02		D
MYH9	97	175	55	-40.35%	6.4e-04 *	9.3e-02	TSG	D
SNRNP200	48	53	9	-67.77%	6.9e-04 *	9.8e-02		D
LINC02570	43	49	8	-69.01%	7.2e-04 *	9.9e-02		D
HGS	84	117	32	-48.09%	7.2e-04 *	9.9e-02		D
TYK2	70	111	30	-48.71%	7.2e-04 *	9.9e-02		D
RAB40C	106	229	78	-35.36%	7.4e-04 *	1.0e-01		D
UNK	112	238	82	-34.61%	7.7e-04 *	1.0e-01		D
PPP6R2	137	720	302	-20.40%	7.8e-04 *	1.0e-01		D
FLT3LG	103	224	76	-35.61%	8.0e-04 *	1.0e-01		D
DKC1	22	23	1	-91.75%	8.4e-04 *	1.1e-01		D
H2BC5	22	23	1	-91.75%	8.4e-04 *	1.1e-01		D
GPD2	70	84	20	-54.81%	8.7e-04 *	1.1e-01		D
PRKCH	90	143	43	-42.93%	8.8e-04 *	1.1e-01		D
OBSCN	60	89	22	-53.09%	9.1e-04 *	1.1e-01		D
ALG9	29	31	3	-81.63%	9.1e-04 *	1.1e-01		D
IFT140	126	401	155	-26.64%	9.4e-04 *	1.1e-01		DA
PYM1	80	122	35	-45.55%	1.0e-03 *	1.2e-01		D
ABCA7	48	63	13	-60.84%	1.0e-03 *	1.2e-01		D
MECP2	131	703	296	-20.09%	1.1e-03 *	1.2e-01		D
SPHK2	66	88	22	-52.55%	1.2e-03 *	1.3e-01		D
FKBP5	128	601	249	-21.37%	1.3e-03 *	1.4e-01		D
TAP2	88	165	53	-39.04%	1.3e-03 *	1.4e-01		D

Genes associated with the Abundant category reached high levels of clonal abundance measured by the sonic abundance method at later time points which suggests that integration near these genes may bolster cell division. For this analysis, the threshold for inclusion is an estimated abundances ≥ 24 cells.

gene	Gene symbol.
subjects	Total number of subjects with an integration near gene.
lateCount	Number of integration sites recovered from earlier time points (≤ 0 days).
maxAbund	Maximum estimated clonal abundance observered > 0 days.
maxRelAbund	Maximum relative sample clonal abundance observered > 0 days.
oncoGene	Gene is found in a broad lists of oncogenes.
categories	DEAL categories associated with gene.

Table E. Top 100 abundant genes.

gene	subjects	lateCount	maxAbund	maxRelAbund	oncoGene	categories
TET2	73	60	858	99.00%	TSG	AL
TET2-AS1	71	48	858	99.00%		AL
PATL1	49	31	629	27.09%		A
PIKFYVE	53	33	460	28.64%		A
NELL2	103	137	441	14.85%		EAL
GLCCI1	88	61	425	14.31%		A
SRCAP	105	126	402	38.00%		AL
MTMR3	106	95	280	8.16%		AL
C1ORF159	119	125	176	11.21%		AL
IFNGR2	9	9	173	45.58%		EA
RC3H1	82	75	164	4.42%		A
PCNX1	111	112	156	1.06%		A
PPP6R3	124	298	154	5.43%		EAL
UHRF1	81	58	150	9.55%		AL
SSH2	122	170	146	6.29%		AL
RSRC1	75	55	115	1.47%		A
WDR7	111	96	113	44.84%		AL
MAPK14	96	93	98	1.28%		AL
SNHG12	5	4	98	5.74%		A
ZZEF1	127	247	92	50.00%		AL
MGA	105	128	91	5.05%		AL
RPA3	54	31	90	4.68%		AL
UMAD1	79	53	90	4.68%		AL
AQR	59	29	88	7.66%		A
LEF1	98	91	86	3.70%	TSG	A
MAN1B1	106	114	85	18.93%		A
ZNF573	50	20	85	63.43%		AL
LINC01473	17	8	84	8.18%		A
CARD8	132	244	82	8.17%		DA
BCAS3	96	69	81	32.14%		AL
IQCB1	46	19	80	2.86%		A
KANSL1	110	134	79	3.30%		AL
WWOX	68	51	78	69.03%		AL
LOC100294362	90	69	76	2.47%		AL
RNF213	126	241	76	2.86%	Yes	EAL
DNAJC13	77	60	73	0.56%		A
EXOSC10	60	31	69	0.77%		A
ATP2A2	77	48	67	2.89%		AL
TRIO	35	28	66	2.57%		EAL
SEC31A	64	40	65	3.23%		A
SMAP2	70	48	65	0.46%		A
GPN1	44	15	63	1.82%		A
EARS2	16	7	60	28.17%		A

Table E. Top 100 abundant genes. *(continued)*

gene	subjects	lateCount	maxAbund	maxRelAbund	oncoGene	categories
LINC01322	3	1	57	3.63%		A
JMJD6	32	22	54	1.56%		A
CLK4	102	147	53	6.08%		EAL
DERL2	64	38	52	14.29%		A
MEMO1	60	24	52	1.22%		A
PTBP1	102	116	52	4.48%		EA
FOXP1	120	180	49	36.57%	Yes	EAL
PPP3CC	120	117	49	52.13%		DA
DNM2	111	118	48	4.40%	TSG	AL
UBR1	94	82	48	42.11%		AL
EIF2AK4	50	28	47	0.85%		A
RASEF	6	5	47	0.60%		EA
DYNC1H1	77	59	46	0.38%		A
UXT-AS1	11	4	45	6.69%		A
GRB2	131	218	44	4.41%		AL
NGDN	36	19	44	0.57%		A
TAC3	34	10	44	1.86%		A
ZNF92	27	20	44	3.12%		EA
ADD1	121	168	43	16.28%		EAL
CPSF1	104	73	43	9.89%		DA
OPA1	49	28	43	1.40%		A
ZNF251	120	265	43	19.00%		AL
PHF12	52	18	42	2.21%		DA
ACTL6A	17	7	41	0.27%		A
POLG2	24	17	41	0.54%		EA
DIDO1	101	104	40	18.78%		AL
MICAL2	41	16	40	2.86%		A
LUC7L	135	357	39	22.41%		AL
PHF20	93	60	39	1.96%		DA
RNF157	134	485	39	7.58%		AL
DNAJC1	64	36	38	1.03%		A
ELMO1	88	45	38	0.98%		A
MED13L	112	150	38	2.38%		EAL
PA2G4	61	44	38	1.25%		A
HERC4	77	42	37	2.14%		A
MAD1L1	83	62	37	1.82%		AL
VAV1	133	416	37	15.69%	Yes	EAL
HRH1	10	6	36	16.90%		AL
KMT2B	97	77	36	28.07%		A
PDE3B	91	93	36	2.13%		AL
STAG3	87	70	36	0.53%		A
SUZ12	77	66	36	1.21%	TSG	A
CRTAP	6	5	35	0.35%		A
HSF5	81	46	35	1.92%		AL
KHDC4	95	83	35	2.23%		AL
LOC101927151	22	8	35	0.53%		A
MYH11	11	7	34	1.75%	Yes	A
NDE1	42	18	34	1.75%		A
PAM	61	25	34	3.77%		A
RHOD	7	3	34	23.40%		A
ZNF34	130	182	34	28.16%		AL
ZNF568	34	15	34	41.98%		A
C5	16	5	33	71.74%		A
DCUN1D4	62	31	33	4.88%		A
DNAJB5	41	23	33	21.71%		A
KMT2D	74	110	33	0.82%	TSG	EA
PAFAH1B1	121	234	33	5.17%		EAL

Genes are categorized as Longitudinal if ≥ 3 different integrations across ≥ 3 different subjects are observed ≥ 90 days post-transduction.

gene	Gene symbol.
totalSites	Total number of unique integrations associated with gene.
longitudinalSites	Total number of unique integrations associated with gene recovered ≥ 90 days.
longitudinalSubjects	Number of subjects associated with integrations associated with gene recovered ≥ 90 days.
longitudinalTimePoints	Number of time points sampled ≥ 90 days.
latestTimePointDays	Longest time point sampled.
oncoGene	Gene is found in a broad lists of oncogenes.
categories	DEAL categories associated with gene.

Table F. Top 100 longitudinaly persistant genes.

| gene	totalSites	longitudinalSites	longitudinalSubjects	longitudinalTimePoints	latestTimePointDays	oncoGene
ZNF251	719	17	10	9	4015	
RAB11FIP3	589	11	8	6	4015	
KANSL1	419	10	5	6	4015	
NELL2	316	6	5	3	4015	
RFX2	217	6	6	7	4015	
CD96	163	5	4	6	4015	
AP2A2	229	4	3	2	4015	
EHBP1	112	4	4	4	4015	
HIVEP3	149	4	3	4	4015	
FOXP1	431	5	4	12	3285	Yes
CENPP	100	4	4	4	3285	
DYM	205	4	3	3	3285	
GAK	176	4	3	3	3285	
SHANK2	22	4	4	4	3285	
LOC730100	16	3	3	3	3285	
MGAT4C	8	3	3	3	3285	
MYO3B	16	3	3	3	3285	
SLC9A7	97	3	3	4	3285	
UHRF1	174	7	4	4	3042	
USP25	342	7	6	6	3042	
ACACA	262	6	5	4	3042	
TRAT1	100	6	3	6	3042	
CLEC16A	308	5	5	4	3042	
GXYLT1	49	5	3	4	3042	
MACROD2	73	5	3	4	3042	
NTM	16	5	4	5	3042	
ABCD2	208	4	4	4	3042	
HRAS	19	4	3	4	3042	Yes
KIFC1	159	4	4	4	3042	
KLHL6	35	4	3	3	3042	
SDHC	100	4	3	4	3042	TSG
SHISA6	10	4	4	3	3042	
WDR45B	170	4	3	4	3042	
ZNF254	55	4	4	5	3042	
HROB	45	3	3	2	3042	
LCMT1	21	3	3	3	3042	
LOC100289333	78	3	3	5	3042	
MKKS	35	3	3	3	3042	
PTPRM	64	3	3	3	3042	
SDCCAG8	73	3	3	2	3042	
UBE2H	135	3	3	3	3042	
RNF157	1361	15	7	7	2920	
VAPB	39	4	3	2	2920	
FANCA	1757	19	12	5	2555	TSG

Table F. Top 100 longitudinaly persistant genes. *(continued)*

gene	totalSites	longitudinalSites	longitudinalSubjects	longitudinalTimePoints	latestTimePointDays	oncoGene
FCHSD2	704	17	9	7	2555	
ANKRD11	807	14	10	9	2555	
SMARCC1	736	14	9	8	2555	
PPP6R3	642	13	9	4	2555	
SMG1P5	500	10	7	6	2555	
VAV1	981	9	5	8	2555	Yes
AP3B1	177	8	7	3	2555	
MTOR	290	8	6	7	2555	Yes
EYS	39	7	4	5	2555	
MPP7	148	7	6	3	2555	
CAMKMT	86	6	3	5	2555	
HHAT	20	6	6	4	2555	
KMT2C	271	6	6	5	2555	TSG
RAP1GDS1	129	6	4	4	2555	Yes
ZBTB8OS	49	6	3	5	2555	
ZZEF1	706	6	5	19	2555	
BAZ1A	182	5	4	3	2555	TSG
ACOX1	332	4	4	3	2555	
ATAD2B	128	4	3	3	2555	
DNAAF4-CCPG1	25	4	4	4	2555	
ECPAS	83	4	3	3	2555	
MED13L	358	4	4	4	2555	
NUP160	84	4	4	4	2555	
PHF21A	247	4	4	3	2555	
PPHLN1	84	4	3	4	2555	
TENM2	19	4	4	3	2555	
UNKL	199	4	3	4	2555	
ARSK	27	3	3	3	2555	
ATAD3B	196	3	3	2	2555	
COL21A1	10	3	3	3	2555	
CUX1	109	3	3	3	2555	TSG
FAM114A2	29	3	3	2	2555	
GRK6	69	3	3	3	2555	
IQCJ-SCHIP1	20	3	3	3	2555	
KCNB1	7	3	3	3	2555	
LRPPRC	121	3	3	3	2555	
MACO1	207	3	3	3	2555	
MALRD1	21	3	3	3	2555	
MAP3K20	33	3	3	3	2555	
POLR3K	154	3	3	3	2555	
SH3BP4	7	3	3	3	2555	
STX2	33	3	3	3	2555	
TIAM1	117	3	3	3	2555	
UBR3	151	3	3	2	2555	
SMG1P2	418	10	5	6	2372	
RBFOX1	50	7	5	6	2372	
ARHGAP15	533	5	4	3	2372	
IQGAP1	385	5	5	4	2372	
POLR2A	729	5	3	4	2372	Yes
RIGI	91	5	4	3	2372	
SARNP	468	4	4	3	2372	
A1BG	16	3	3	2	2372	
AKAP10	124	3	3	2	2372	
HYCC1	105	3	3	3	2372	
TCERG1	111	3	3	3	2372	
EHMT1	858	14	9	6	2190	

Volcano plot analysis

Changes in gene integration frequencies between pre- and post- transfusion samples and their significance is shown below in Figure 2. Changes in integration frequency is defined as *(f - fo) / fo* where *f* is the integration frequency post-transfusion and *fo* is the integration of preinfused transduction material. The significance of these changes is assessed using Fisher's Exact tests corrected for multiple comparisons.

Figure 2.
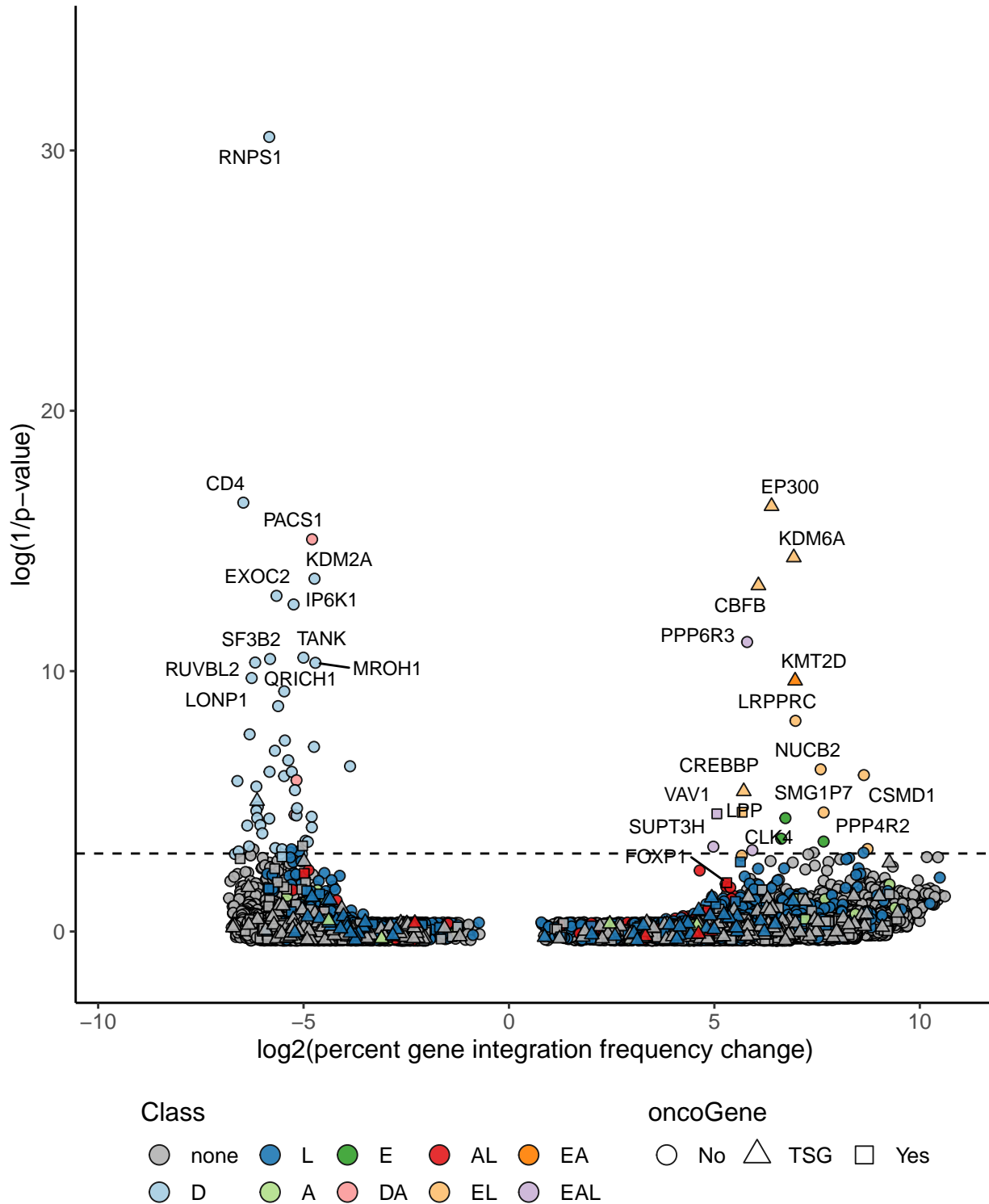
The following table reports clusters of integration sites identified by comparing sites recovered on or before day 0 and those recovered afterwards. Clusters are identified using the geneRxCluster (ScanStatistics) software package (Berry et al. 2014). The cluster ranges in the first column are links to the UCSC genome browser where integrations with positive orientations are shown with blue tick marks while integrations with reverse orientations are shown with red tick marks. Tick marks are shaded my maximum estimated abundance values where darker shades indicated higher abundance values.

cluster	start	end	width	earlySites	lateSites	target.min	nearestGenes
chr1:1721712-1728387	1721712	1728387	6676	1	14	2.222	CDK11A (11) SLC35E2A (4)
chr1:114720961-114739676	114720961	114739676	18716	6	21	3.452	CSDE1 (27)
chr1:150684318-150688833	150684318	150688833	4516	28	0	4.584	GOLPH3L (28)
chr1:154415643-154436337	154415643	154436337	20695	31	0	1.966	IL6R (31)
chr6:134986795-135007478	134986795	135007478	20684	32	0	1.966	HBS1L (32)
chr9:136888757-136890709	136888757	136890709	1953	30	0	1.966	TANK (30)
chr11:65341483-65342694	65341483	65342694	1212	31	0	1.966	DPF2 (31)
chr11:68562951-68567256	68562951	68567256	4306	2	15	4.696	PPP6R3 (17)
chr12:6805542-6810736	6805542	6810736	5195	40	0	1.966	CD4 (40)
chr12:49028268-49035158	49028268	49035158	6891	9	26	4.192	KMT2D (35)
chr12:96281185-96289669	96281185	96289669	8485	2	15	4.696	CDK17 (17)
chr16:949519-956366	949519	956366	6848	3	18	1.258	LMF1 (21)
chr16:3752170-3754358	3752170	3754358	2189	1	14	2.222	CREBBP (15)
chr16:18885572-18887014	18885572	18887014	1443	3	17	3.141	SMG1 (20)
chr17:64521318-64525828	64521318	64525828	4511	3	17	3.141	CEP95 (20)
chr19:5692907-5707131	5692907	5707131	14225	28	0	4.584	LONP1 (28)
chr19:15304884-15317081	15304884	15317081	12198	28	0	4.584	BRD4 (28)
chr22:37839722-37855774	37839722	37855774	16053	30	0	1.966	EIF3L (26) ANKRD54 (4)
chrX:154086640-154087398	154086640	154087398	759	28	0	4.584	MECP2 (28)

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Software parameters

parameter	value
earlyVsLateCutoffDays	0
inputDataPath	../data/intSiteData.tsv.gz
minSampleAbund	25
minGeneSubjects	2
maxDistNearestGene	50000
longitudinal_minNumSubjects	3
longitudinal_minNumSites	3
longitudinal_minNumTimepoints	3
longitudinal_minTimeDays	90
volcanoPlot_numTopGeneLabels	12
HGNC_symbols	../data/HGNC_symbols.tsv
COSMIC_oncogene_table	../data/COSMIC_oncogenes.txt
COSMIC_tsg_table	../data/COSMIC_oncogenes_tumor_suppressors.txt
allOnco_oncogene_table	../data/allOnco.txt
geneNameReassignment_table	../data/geneNameReassignments.tsv
scanStatsBEDfileURL	http://genome.ucsc.edu/cgi-bin/hgTracks?org=human&db=hg38&hgt.customText=https://m