Analysis of integration site distributions and relative clonal abundance for subject pP9

August 13, 2019

Contents

Summary

Is there a rich population of progenitor cells delivering mature cells to the periphery?

To provide a simple measure, we ask whether there are $\geq$ 1000 descendants of independent progenitors (i.e. unique integration sites) in minimally fractionated cell specimens (Whole blood, T cells, B cells, NK cells, Neutrophils, Monocytes and PBMC). Cell specimens that pass these criteria are operationally designated Rich.

Time point	B CELLS	PBMC	T CELLS	Rich
M3	na	203	na	No
M16	na	2,098	na	Yes
M18	na	300	na	No
M24	na	201	na	No
M29	na	592	na	No
M60	na	238	na	No
M150.6	na	1,449	1,209	Yes
M174.4	na	1,711	na	Yes
M178	na	1,008	na	Yes
M183	na	673	na	No
M190	23	1,144	2,247	Yes
M195.9	na	706	na	No
M201	na	1,268	na	Yes

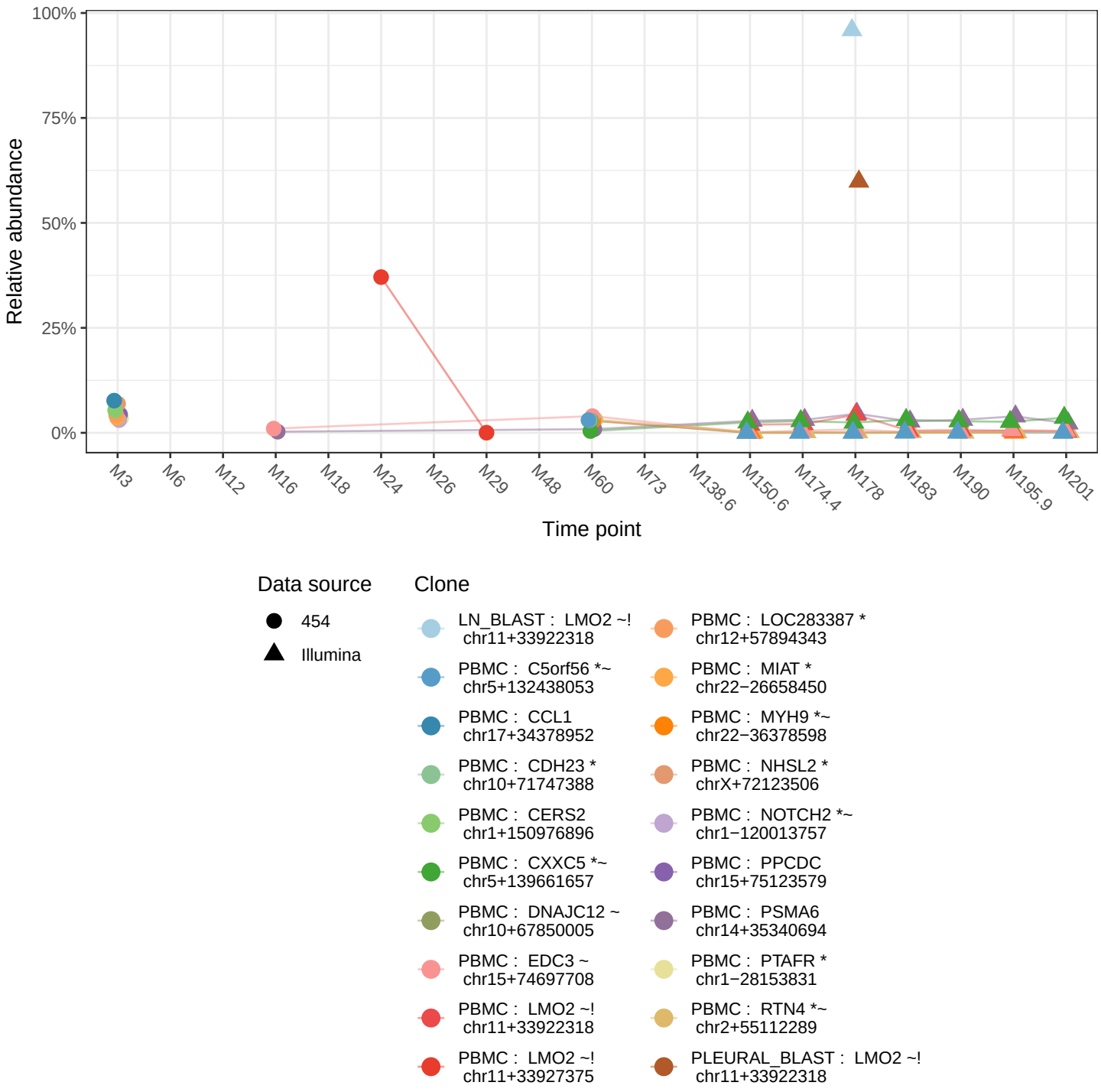
Do any cell clones account for more than 20% of all clones?

For some trials, a reporting criteria is whether any cell clones expand to account for greater than 20% of all clones. The table below highlights samples with relative abundances $\geq$ 20% considering only samples with 50 or more inferred cells.

IntSite	Abundance	Relative abudance	time point	Cell type	Nearest gene	Distance (KB)	Nearest oncogene	Distance (KB)
chr11+33927375	1	37.1%	M24	PBMC	LMO2	-35.10	LMO2	-35.10
chr11+33922318	578	29.7%	M178	BM_BLAST	LMO2	-30.00	LMO2	-30.00
chr11+33922318	1527	95.9%	M178	LN_BLAST	LMO2	-30.00	LMO2	-30.00
chr11+33922318	1446	59.9%	M178	PLEURAL_BLAST	LMO2	-30.00	LMO2	-30.00

Are any cell clones increasing in proportion over time?

The plot below details the longitudinal sample relative abundances of the most abundant 20 clones where only samples with 50 or more inferred cells are considered.



Introduction

The attached report describes results of analysis of integration site distributions and relative abundance for samples from gene therapy trials. For cases of gene correction in circulating blood cells, it is possible to harvest cells sequentially from blood to monitor cell populations. Frequency of isolation information can provide information on the clonal structure of the population. This report summarizes results for subject pP9 over time points M3, M6, M12, M16, M18, M24, M26, M29, M48, M60, M73, M138.6, M150.6, M174.4, M178, M183, M190, M195.9, M201 in UCSC genome draft .

The samples studied in this report, the numbers of sequence reads, recovered integration vectors, and unique integration sites available for this subject are shown below. We quantify population clone diversity using Gini coefficients, Shannon index, and UC50. The Gini coefficient provides a measure of inequality in clonal abundance in each sample. The coefficient equals zero when all sites are equally abundant (polyclonal) and increases as fewer sites account for more of the total (oligoclonal). Shannon index is another widely used measure of diversity and it accounts for both abundance and evenness of the integration events. Alternatively, the UC50 is the number of unique clones which make up the top 50% of the sample's abundance. For polyclonal samples, one may expect a low Gini coefficient, high Shannon Index, and high UC50 (proportional to the total number of unique sites identified in the sample).

Under most circumstances only a subset of sites will be sampled. We thus include an estimate of sample size based on frequency of isolation information from the SonicLength method (Berry, 2012). The 'S.chao1' column denotes the estimated lower bound for population size derived using Chao estimate (Chao, 1987). If sample replicates were present then estimates were subjected to jackknife bias correction.

We estimate the numbers of cell clones sampled using the SonicLength method (Berry, 2012); this is summarized in the column "Inferred cells". Integration sites were recovered using ligation mediated PCR after random fragmentation of genomic DNA, which reduces recovery biases compared with restriction enzyme cleavage. Relative abundance was not measured from read counts, which are known to be inaccurate, but from marks introduced into DNA specimens prior to PCR amplification using the SonicLength method PMID:22238265.

We quantify population diversity using Gini coefficients, Shannon index, and UC50. The Gini coefficient provides a measure of inequality in clonal abundance in each sample. The coefficient equals zero when all sites are equally abundant (polyclonal) and increases as fewer sites account for more of the total (oligoclonal). Shannon index is another widely used measure of diversity and it accounts for both abundance and evenness of the integration events. UC50 is the number of clones which make up the top 50% of the sample's abundance. For polyclonal samples, one may expect a low Gini coefficient, high Shannon Index, and high UC50 (proportional to the total number of unique sites identified in the sample).

Integration positions are reported with the format (nearest gene, chromosome, +/-, genomic position) where the nearest gene is the nearest transcriptional boundary to the integration position, '+' refers to integration in the positive orientation and '-' refers to integration in the reverse orientation. Reported distances are signed where where the sign indicates if integrationsare upstream (-) or downstream (+, no sign) of the nearest gene. Nearest genes possess additional annotations described in the table below.

Symbol	Meaning
*	site is within a transcription unit
~	site is within 50kb of a cancer related gene
!	nearest gene was assocaited with lymphoma in humans

Sample Summary

The table below provides population statistics for each analyzed sample. Occasionally multiple samples from the same cell fraction and time point are analyzed where only the sample with greatest number of inferred cells is considered in this report.

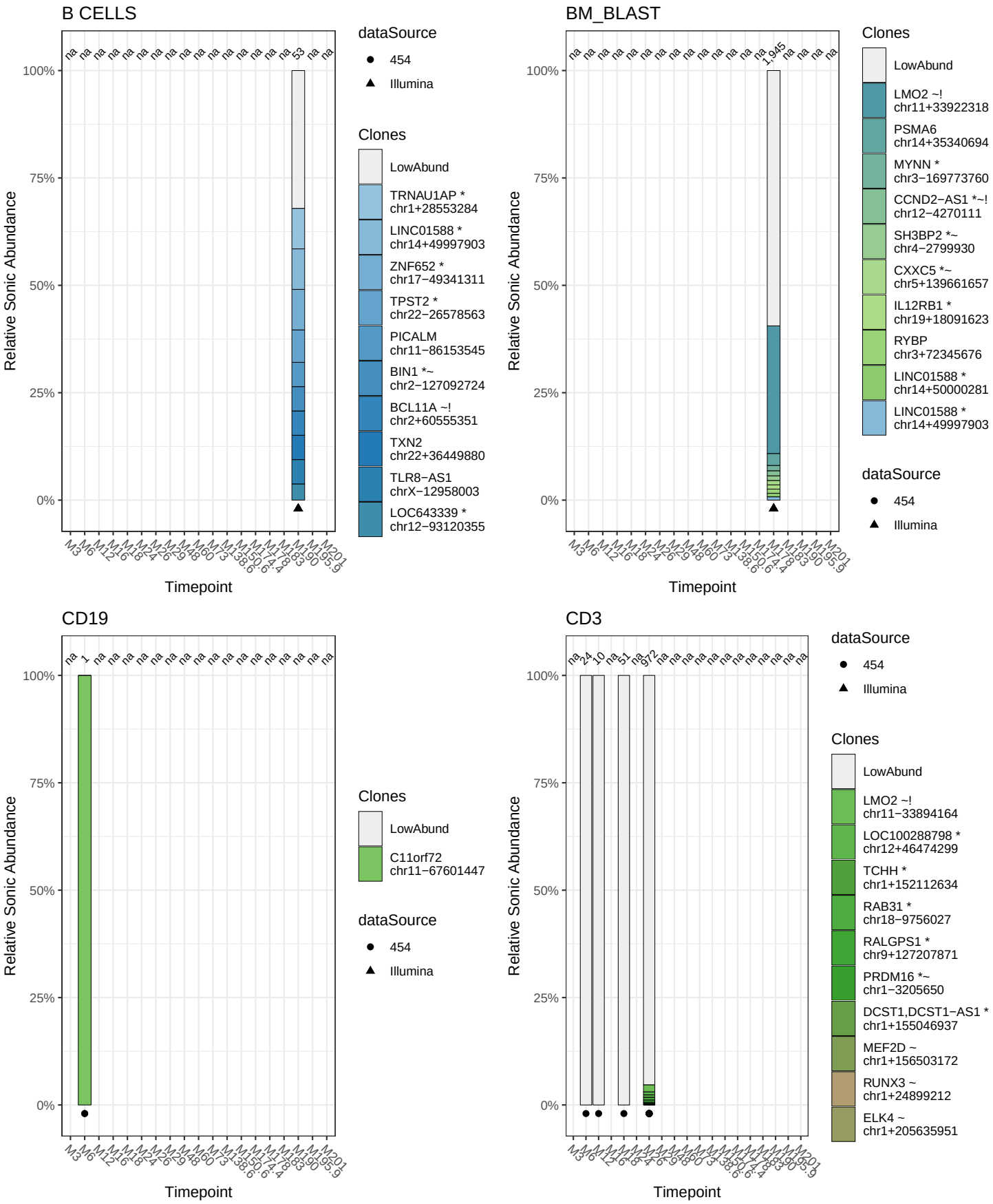
GTSP	dataSource	Patient	Timepoint	CellType	TotalReads	InferredCells	UniqueSites	Gini	Chao1	Shannon	Pielou	UC50	Included	VCN
LS-116	454	pP9	M3	PBMC	2,284	203	203	0.000	20,706	5.31	1.000	102	yes	NA
LS-104	454	pP9	M6	CD3	1,317	15	15	0.000	120	2.71	1.000	8	no	NA
LS-113	454	pP9	M6	CD19	1	1	1	0.000	1	0.00	NaN	1	yes	NA
LS-114	454	pP9	M6	CD3	1,893	24	24	0.000	300	3.18	1.000	13	yes	NA
LS-101	454	pP9	M12	CD3	1,041	10	10	0.000	55	2.30	1.000	6	yes	NA
LS-109	454	pP9	M16	PBMC	6,672	2,377	2,098	0.107	11,513	7.60	0.993	910	yes	NA
LS-102	454	pP9	M18	CD3	1,449	51	51	0.000	1,326	3.93	1.000	26	yes	NA
LS-115	454	pP9	M18	PBMC	3,819	300	300	0.000	45,150	5.70	1.000	151	yes	NA
LS-110	454	pP9	M24	PBMC	4,101	201	201	0.000	20,301	5.30	1.000	101	yes	NA
LS-103	454	pP9	M26	CD3	3,535.583	972	886	0.081	4,972	6.75	0.995	401	yes	NA
LS-111	454	pP9	M29	PBMC	3,948	592	592	0.000	175,528	6.38	1.000	297	yes	NA
LS-107	454	pP9	M48	PBL	3,746.5	937	850	0.085	4,973	6.71	0.995	382	yes	NA
LS-108	454	pP9	M60	PBL	3,890.917	744	652	0.108	2,602	6.44	0.993	281	yes	NA
LS-112	454	pP9	M60	PBMC	3,779	256	238	0.066	1,668	5.45	0.995	111	yes	NA
LS-105	454	pP9	M73	MEMORY	5,703	1,539	1,286	0.143	4,830	7.09	0.991	517	yes	NA
LS-106	454	pP9	M73	NAIVE	5,482	1,067	882	0.152	3,754	6.70	0.989	349	yes	NA
GTSP0269	Illumina	pP9	M138.6	CD4POSCD45ROPOS	606,274	284	182	0.277	376	5.04	0.969	51	yes	NA
GTSP0270	Illumina	pP9	M138.6	CD4POSCD45RAPOS	175,145	30	23	0.180	46	3.06	0.976	9	yes	NA
GTSP0271	Illumina	pP9	M138.6	CD8POSCD45ROPOS	489,310	86	47	0.342	88	3.62	0.940	12	yes	NA
GTSP0272	Illumina	pP9	M138.6	CD8POSCD45RAPOS	220,862	14	8	0.250	10	1.97	0.947	3	yes	NA
GTSP0273	Illumina	pP9	M138.6	TEMRA	552,741	243	90	0.505	175	3.94	0.876	12	yes	NA
GTSP0485	Illumina	pP9	M150.6	PBMC	115,928	5,279	1,449	0.623	3,171	6.31	0.867	97	yes	NA
GTSP0486	Illumina	pP9	M150.6	T CELLS	651,927	3,546	1,209	0.575	2,755	6.23	0.877	91	yes	NA
GTSP0487	Illumina	pP9	M150.6	CD4POSCD45ROPOS	589,416	652	376	0.356	959	5.59	0.943	81	yes	2.10
GTSP0488	Illumina	pP9	M150.6	CD4POSCD45RAPOS	780,007	1,224	403	0.537	752	5.38	0.897	47	yes	1.69
GTSP0489	Illumina	pP9	M150.6	CD8POSCD45ROPOS	440,410	752	320	0.496	685	5.05	0.876	37	yes	2.77
GTSP0490	Illumina	pP9	M150.6	CD8POSCD45RAPOS	776,392	1,141	446	0.509	1,037	5.49	0.900	54	yes	1.58
GTSP1313	Illumina	pP9	M174.4	PBMC	1,316,302	6,610	1,711	0.646	3,981	6.35	0.853	99	yes	0.68
GTSP1314	Illumina	pP9	M174.4	CD4NAIVE	1,844,520	10,424	1,486	0.759	3,108	5.79	0.793	47	yes	1.10
GTSP1315	Illumina	pP9	M174.4	CD4MEMORY	1,940,556	12,125	2,968	0.649	5,962	6.89	0.861	173	yes	1.50
GTSP1316	Illumina	pP9	M174.4	CD8NAIVE	1,824,595	6,001	1,158	0.711	2,465	5.75	0.815	50	yes	1.18
GTSP1317	Illumina	pP9	M174.4	CD8MEMORY	2,095,761	7,161	1,183	0.736	2,168	5.52	0.780	32	yes	1.54

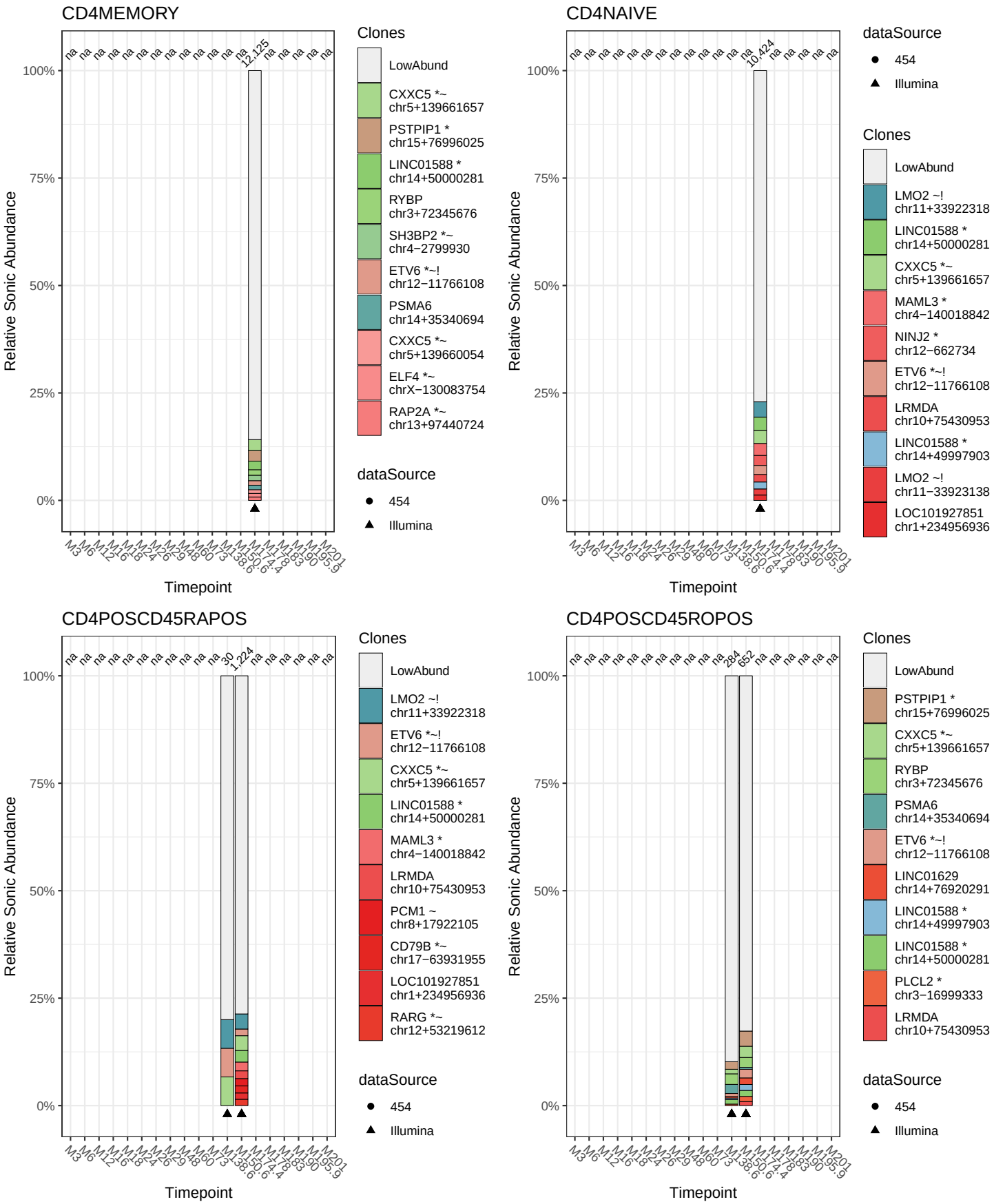
GTSP	dataSource	Patient	Timepoint	CellType	TotalReads	InferredCells	UniqueSites	Gini	Chao1	Shannon	Pielou	UC50	Included	VCN
GTSP1318	Illumina	pP9	M178	PBMC	1,183,023	3,183	1,008	0.602	2,628	5.93	0.857	68	yes	0.26
GTSP1319	Illumina	pP9	M178	BM_BLAST	1,351,413	1,945	626	0.616	1,385	4.77	0.741	30	yes	0.24
GTSP1320	Illumina	pP9	M178	LN_BLAST	1,683,840	1,592	54	0.947	154	0.33	0.083	1	yes	0.99
GTSP1321	Illumina	pP9	M178	PLEURAL_BLAST	1,799,844	2,416	515	0.752	1,109	3.03	0.485	1	yes	0.88
GTSP1532	Illumina	pP9	M178	MNC	320,790	774	332	0.495	1,056	5.17	0.890	39	yes	0.20
GTSP1533	Illumina	pP9	M183	PBMC	517,851	1,589	673	0.486	1,641	5.92	0.910	88	yes	0.51
GTSP2224	Illumina	pP9	M190	PBMC	550,264	3,437	1,144	0.571	2,519	6.22	0.883	97	yes	0.59
GTSP2225	Illumina	pP9	M190	B CELLS	1,001,764	53	23	0.318	29	2.97	0.947	7	yes	0.15
GTSP2226	Illumina	pP9	M190	T CELLS	708,376	9,577	2,247	0.667	4,655	6.58	0.853	117	yes	1.13
GTSP2227	Illumina	pP9	M195.9	PBMC	780,089	1,757	706	0.499	1,510	5.95	0.907	86	yes	0.00
GTSP2886	Illumina	pP9	M201	PBMC	1,152,427	3,780	1,268	0.569	2,927	6.31	0.884	108	yes	0.68

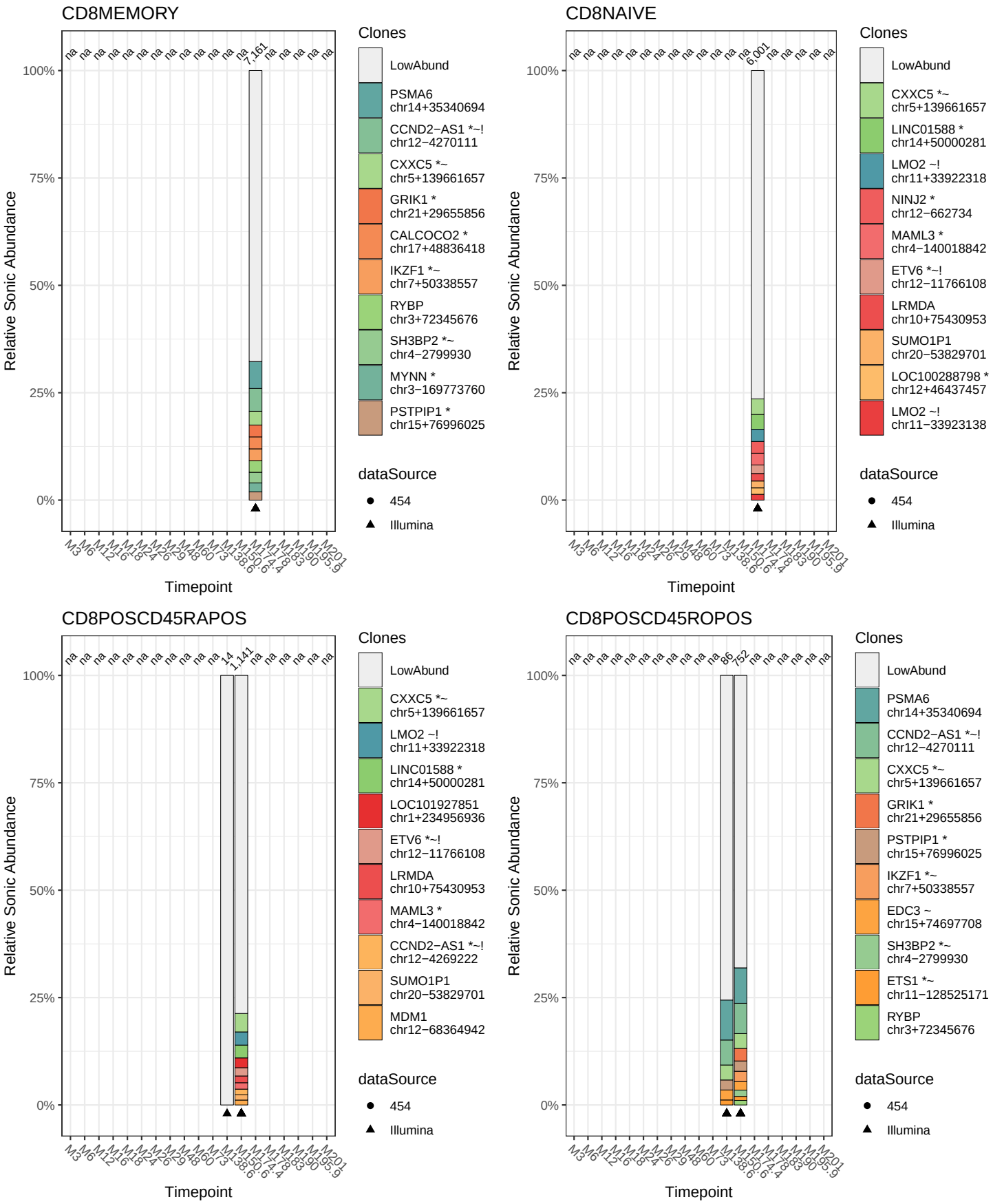
Tracking of clonal abundances

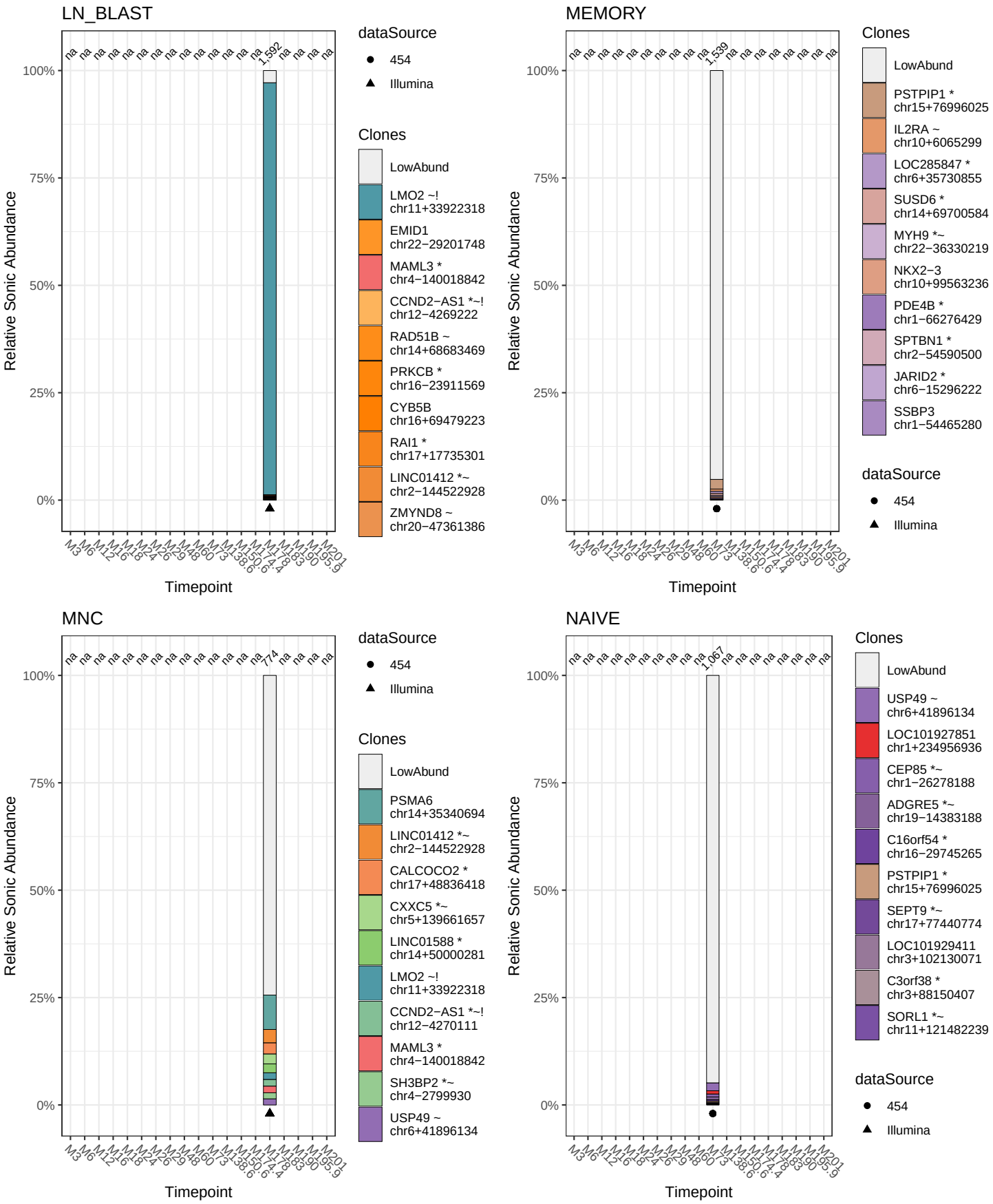
Relative abundance of cell clones

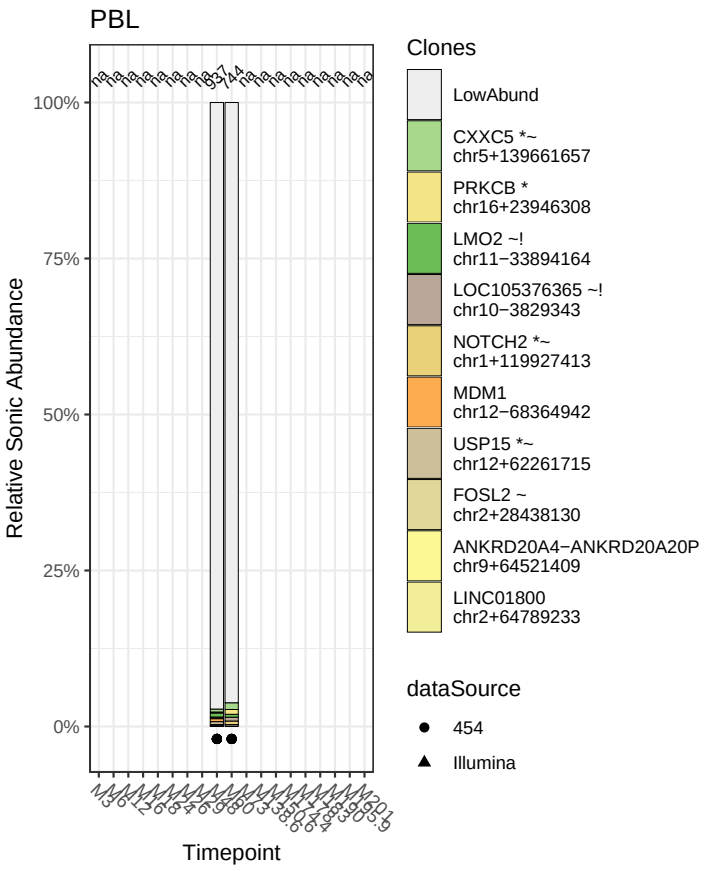
The relative abundances of cell clones is summarized in the stacked bar plots below. The cell fraction studied is named at the top of each plot and the time points are marked at the bottom. The different bars in each panel show the major cell clones, as marked by integration sites where the x-axis indicates time points and the y-axis is scaled by proportion of the total cells sampled. The top 10 most abundant clones from each cell type have been named by the nearest gene while the remaining sites are binned as low abundance (LowAbund; grey). The total number of genomic fragments used to identify integration sites are listed atop of each plot. These fragments are generated by restriction endonucleases in 454 sequencing experiments and by sonic shearing in Illumina sequencing experiments. Relative abundances are calculated using the total number of reads associated with clones in 454 sequencing experiments while the number of unique sonic breaks is used in Illumina sequencing experiments.

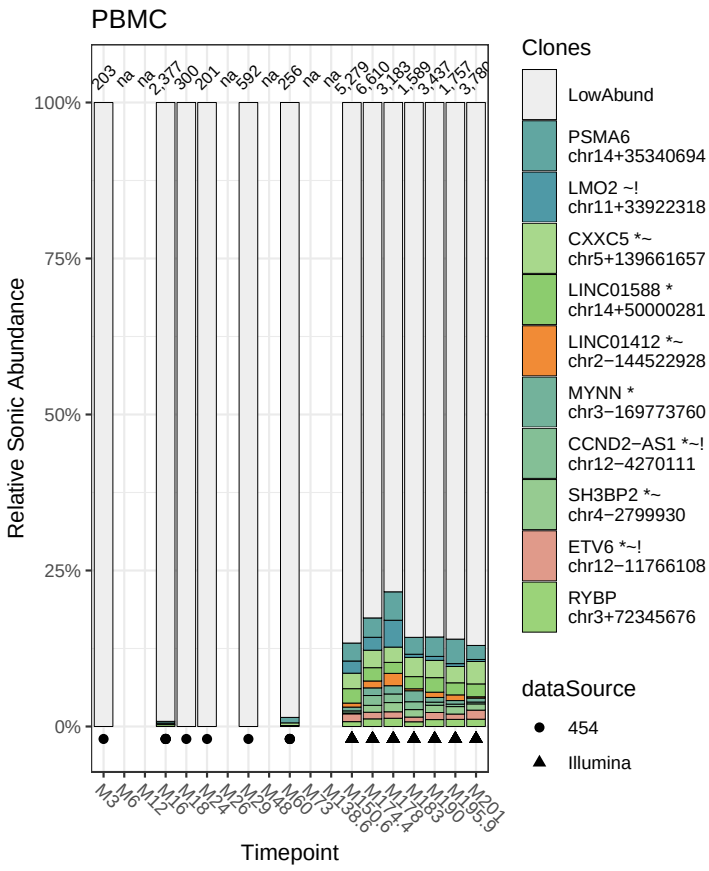

B CELLS
BM_BLAST
CD19
CD3
Relative Sonic Abundance
Timepoint
100%
75%
50%
25%
0%
dataSource
454
Illumina
Clones
LowAbund
TRNAU1AP * chr1+28553284
LINC01588 * chr14+49997903
ZNF652 * chr17−49341311
TPST2 * chr22−26578563
PICALM chr11−86153545
BIN1 *~ chr2−127092724
BCL11A ~! chr2+60555351
TXN2 chr22+36449880
TLR8−AS1 chrX−12958003
LOC643339 * chr12−93120355
LMO2 ~! chr11+33922318
PSMA6 chr14+35340694
MYNN * chr3−169773760
CCND2−AS1 *~! chr12−4270111
SH3BP2 *~ chr4−2799930
CXXC5 *~ chr5+139661657
IL12RB1 * chr19+18091623
RYBP chr3+72345676
LINC01588 * chr14+50000281
C11orf72 chr11−67601447
LMO2 ~! chr11−33894164
LOC100288798 * chr12+46474299
TCHH * chr1+152112634
RAB31 * chr18−9756027
RALGPS1 * chr9+127207871
PRDM16 *~ chr1−3205650
DCST1,DCST1−AS1 * chr1+155046937
MEF2D ~ chr1+156503172
RUNX3 ~ chr1+24899212
ELK4 ~ chr1+205635951

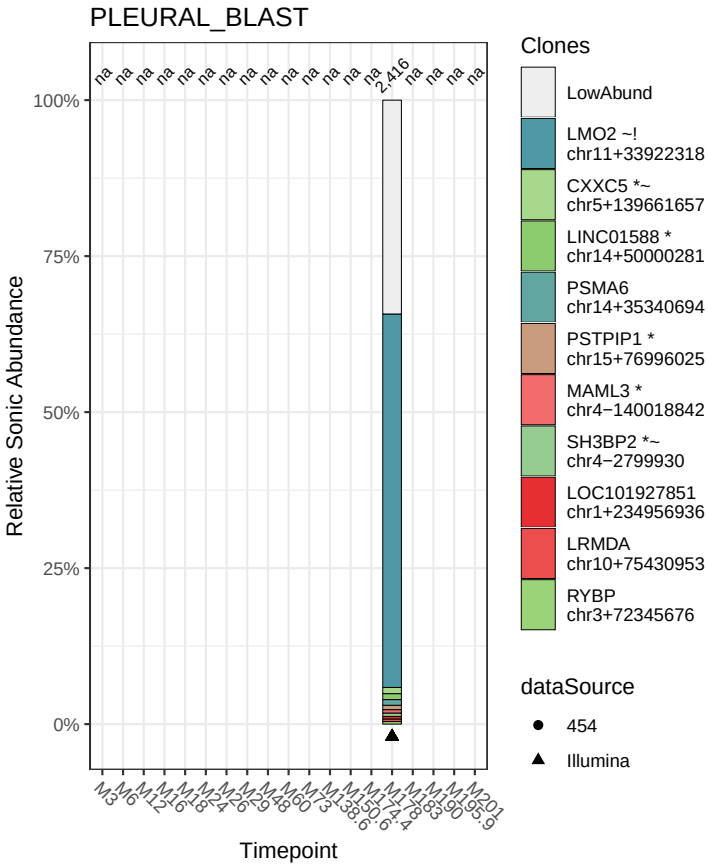

CD4MEMORY
CD4NAIVE
CD4POSCD45RAPOS
CD4POSCD45ROPOS
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
Clones
LowAbund
CXXC5 *~ chr5+139661657
PSTPIP1 * chr15+76996025
LINC01588 * chr14+50000281
RYBP chr3+72345676
SH3BP2 *~ chr4−2799930
ETV6 *~! chr12−11766108
PSMA6 chr14+35340694
CXXC5 *~ chr5+139660054
ELF4 *~ chrX−130083754
RAP2A *~ chr13+97440724
LMO2 ~! chr11+33922318
MAML3 * chr4−140018842
NINJ2 * chr12−662734
LRMDA chr10+75430953
LINC01588 * chr14+49997903
LMO2 ~! chr11−33923138
LOC101927851 chr1+234956936
PCM1 ~ chr8+17922105
CD79B *~ chr17−63931955
RARG *~ chr12+53219612
LINC01629 chr14+76920291
PLCL2 * chr3−16999333
dataSource
454
Illumina

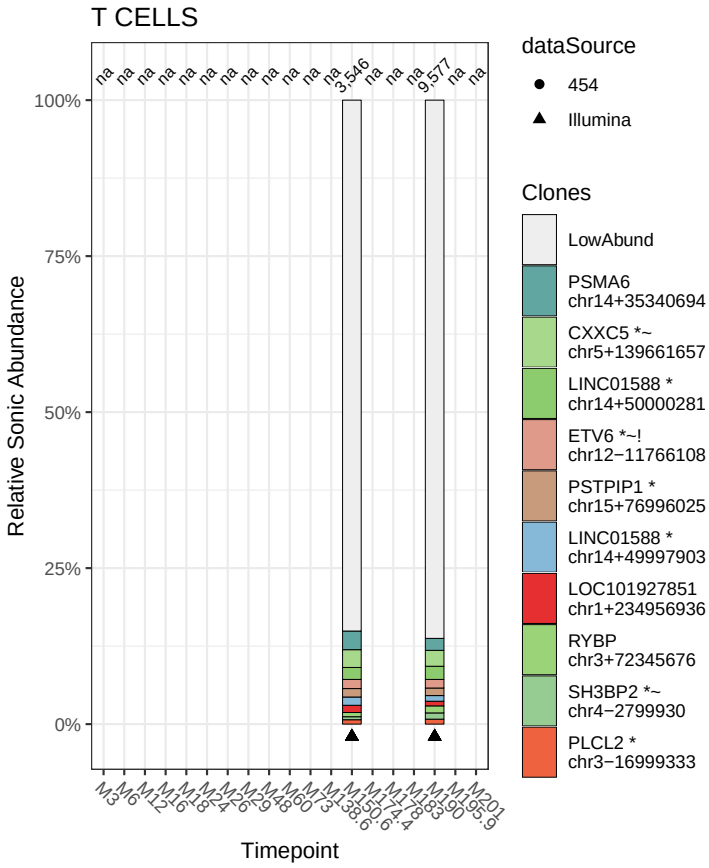

CD8MEMORY
CD8NAIVE
CD8POSCD45RAPOS
CD8POSCD45ROPOS
Relative Sonic Abundance
Timepoint
Clones
LowAbund
PSMA6 chr14+35340694
CCND2−AS1 *~! chr12−4270111
CXXC5 *~ chr5+139661657
GRIK1 * chr21+29655856
CALCOCO2 * chr17+48836418
IKZF1 *~ chr7+50338557
RYBP chr3+72345676
SH3BP2 *~ chr4−2799930
MYNN * chr3−169773760
PSTPIP1 * chr15+76996025
LINC01588 * chr14+50000281
LMO2 ~! chr11+33922318
NINJ2 * chr12−662734
MAML3 * chr4−140018842
ETV6 *~! chr12−11766108
LRMDA chr10+75430953
SUMO1P1 chr20−53829701
LOC100288798 * chr12+46437457
LMO2 ~! chr11−33923138
LOC101927851 chr1+234956936
CCND2−AS1 *~! chr12−4269222
MDM1 chr12−68364942
EDC3 ~ chr15+74697708
ETS1 *~ chr11−128525171
dataSource
454
Illumina

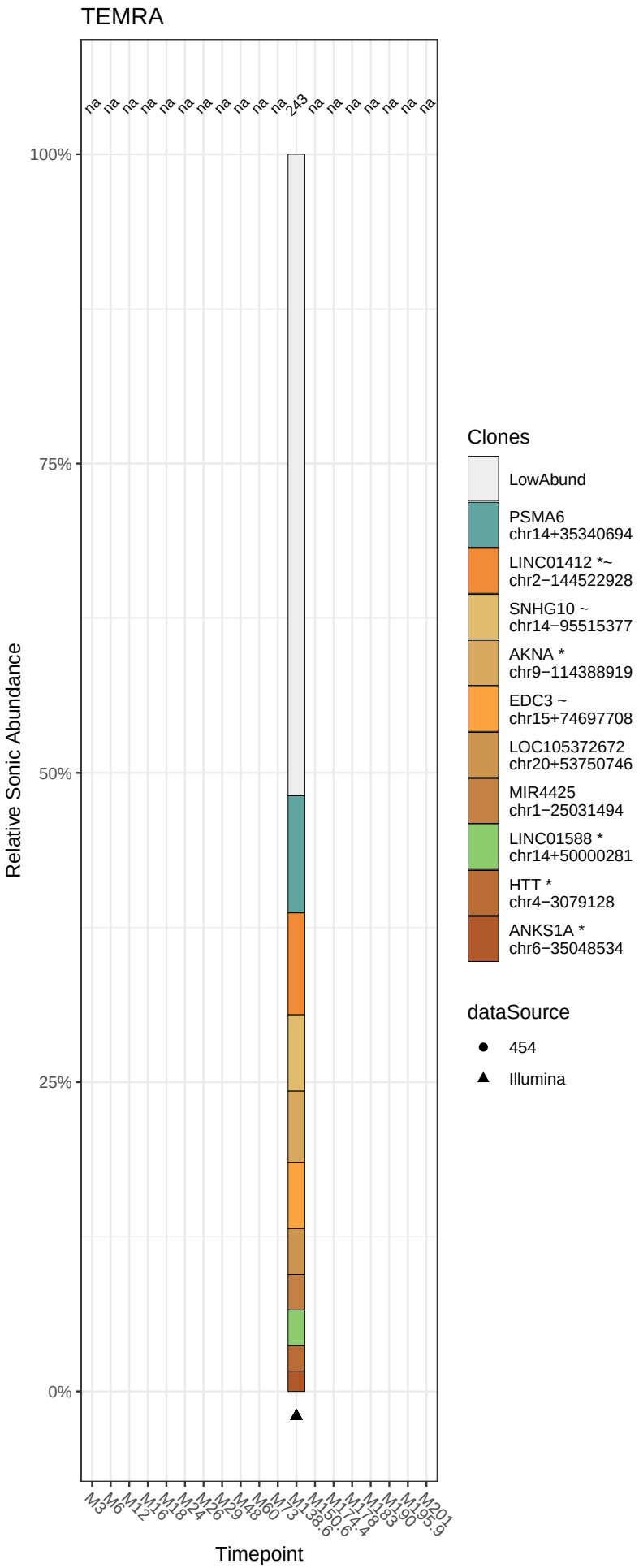

LN_BLAST
MEMORY
MNC
NAIVE
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
dataSource
454
Illumina
Clones
LowAbund
LMO2 ~!
chr11+33922318
EMID1
chr22−29201748
MAML3 *
chr4−140018842
CCND2−AS1 *~!
chr12−4269222
RAD51B ~
chr14+68683469
PRKCB *
chr16−23911569
CYB5B
chr16+69479223
RAI1 *
chr17+17735301
LINC01412 *~
chr2−144522928
ZMYND8 ~
chr20−47361386
PSTPIP1 *
chr15+76996025
IL2RA ~
chr10+6065299
LOC285847 *
chr6+35730855
SUSD6 *
chr14+69700584
MYH9 *~
chr22−36330219
NKX2−3
chr10+99563236
PDE4B *
chr1−66276429
SPTBN1 *
chr2−54590500
JARID2 *
chr6−15296222
SSBP3
chr1−54465280
PSMA6
chr14+35340694
CALCOCO2 *
chr17+48836418
CXXC5 *~
chr5+139661657
LINC01588 *
chr14+50000281
CCND2−AS1 *~!
chr12−4270111
SH3BP2 *~
chr4−2799930
USP49 ~
chr6+41896134
LOC101927851
chr1+234956936
CEP85 *~
chr1−26278188
ADGRE5 *~
chr19−14383188
C16orf54 *
chr16−29745265
SEPT9 *~
chr17+77440774
LOC101929411
chr3+102130071
C3orf38 *
chr3+88150407
SORL1 *~
chr11+121482239


PBL
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
Clones
LowAbund
CXXC5 *~ chr5+139661657
PRKCB * chr16+23946308
LMO2 ~! chr11−33894164
LOC105376365 ~! chr10−3829343
NOTCH2 *~ chr1+119927413
MDM1 chr12−68364942
USP15 *~ chr12+62261715
FOSL2 ~ chr2+28438130
ANKRD20A4−ANKRD20A20P chr9+64521409
LINC01800 chr2+64789233
dataSource
454
Illumina


PBMC
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
Clones
LowAbund
PSMA6 chr14+35340694
LMO2 ~! chr11+33922318
CXXC5 *~ chr5+139661657
LINC01588 * chr14+50000281
LINC01412 *~ chr2−144522928
MYNN * chr3−169773760
CCND2−AS1 *~! chr12−4270111
SH3BP2 *~ chr4−2799930
ETV6 *~! chr12−11766108
RYBP chr3+72345676
dataSource
454
Illumina

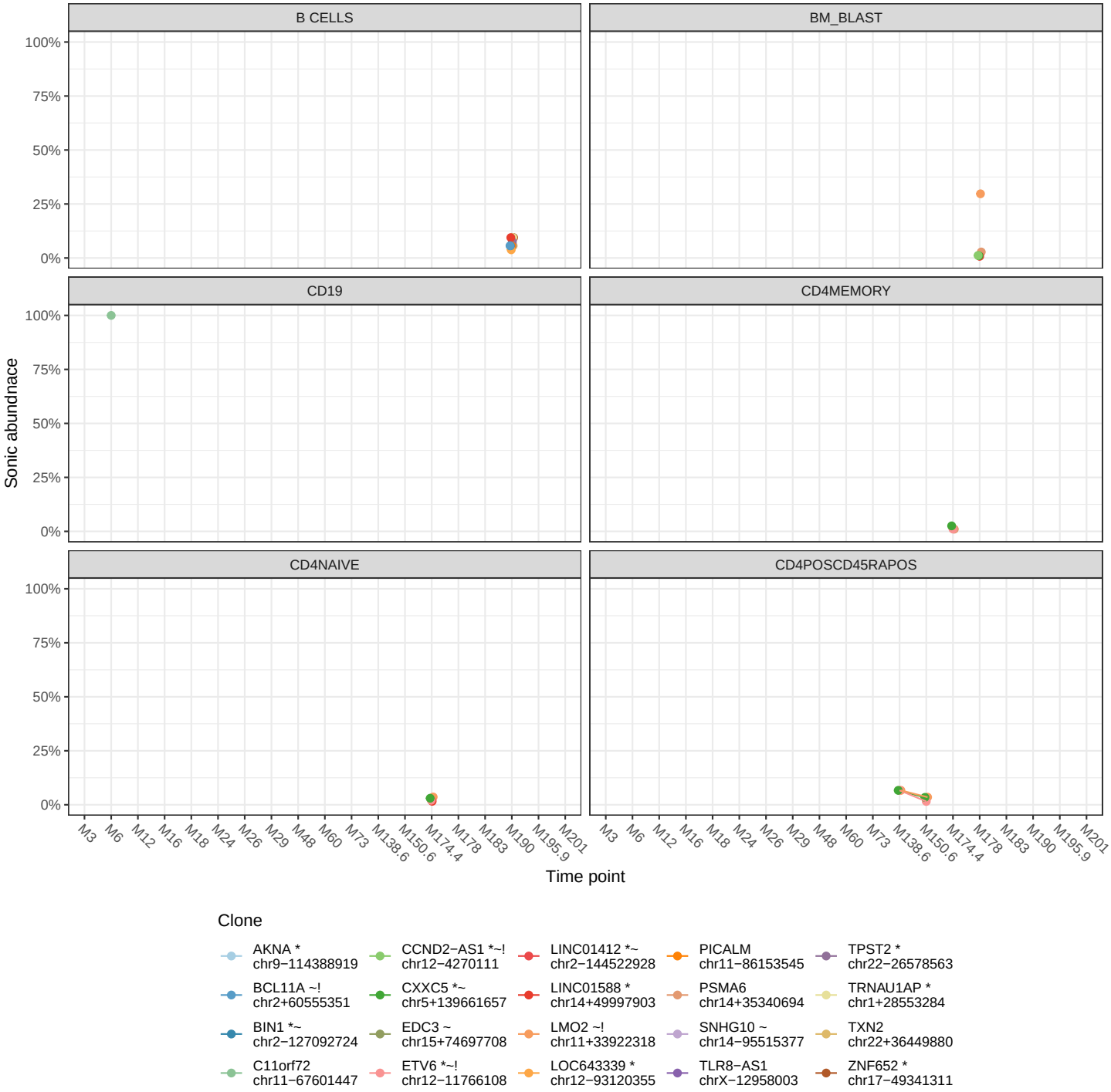

PLEURAL_BLAST
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
Clones
LowAbund
LMO2 ~! chr11+33922318
CXXC5 *~ chr5+139661657
LINC01588 * chr14+50000281
PSMA6 chr14+35340694
PSTPIP1 * chr15+76996025
MAML3 * chr4−140018842
SH3BP2 *~ chr4−2799930
LOC101927851 chr1+234956936
LRMDA chr10+75430953
RYBP chr3+72345676
dataSource
454
Illumina

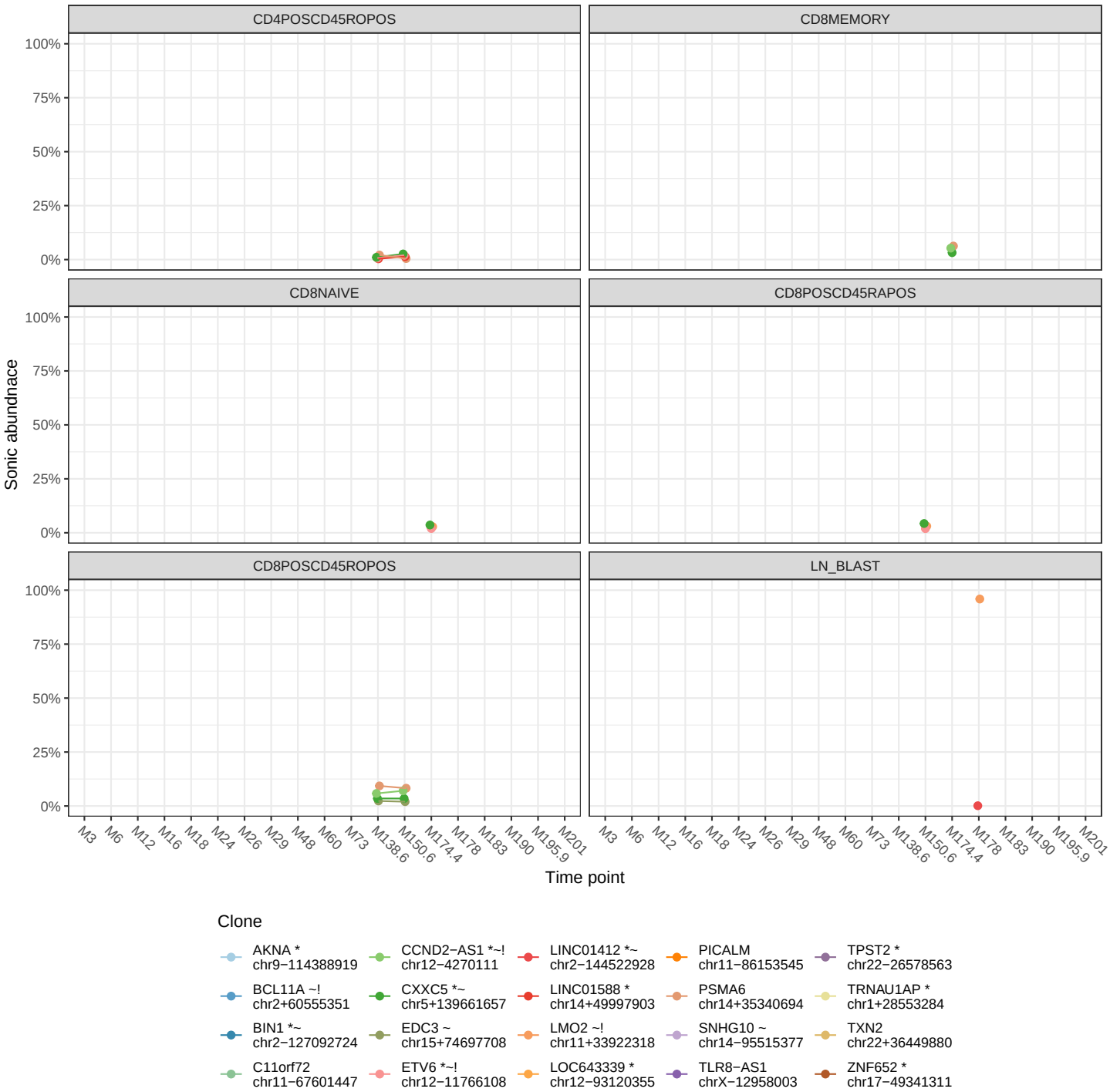

T CELLS
Relative Sonic Abundance
100%
75%
50%
25%
0%
Timepoint
dataSource
454
Illumina
Clones
LowAbund
PSMA6 chr14+35340694
CXXC5 *~ chr5+139661657
LINC01588 * chr14+50000281
ETV6 *~! chr12−11766108
PSTPIP1 * chr15+76996025
LINC01588 * chr14+49997903
LOC101927851 chr1+234956936
RYBP chr3+72345676
SH3BP2 *~ chr4−2799930
PLCL2 * chr3−16999333

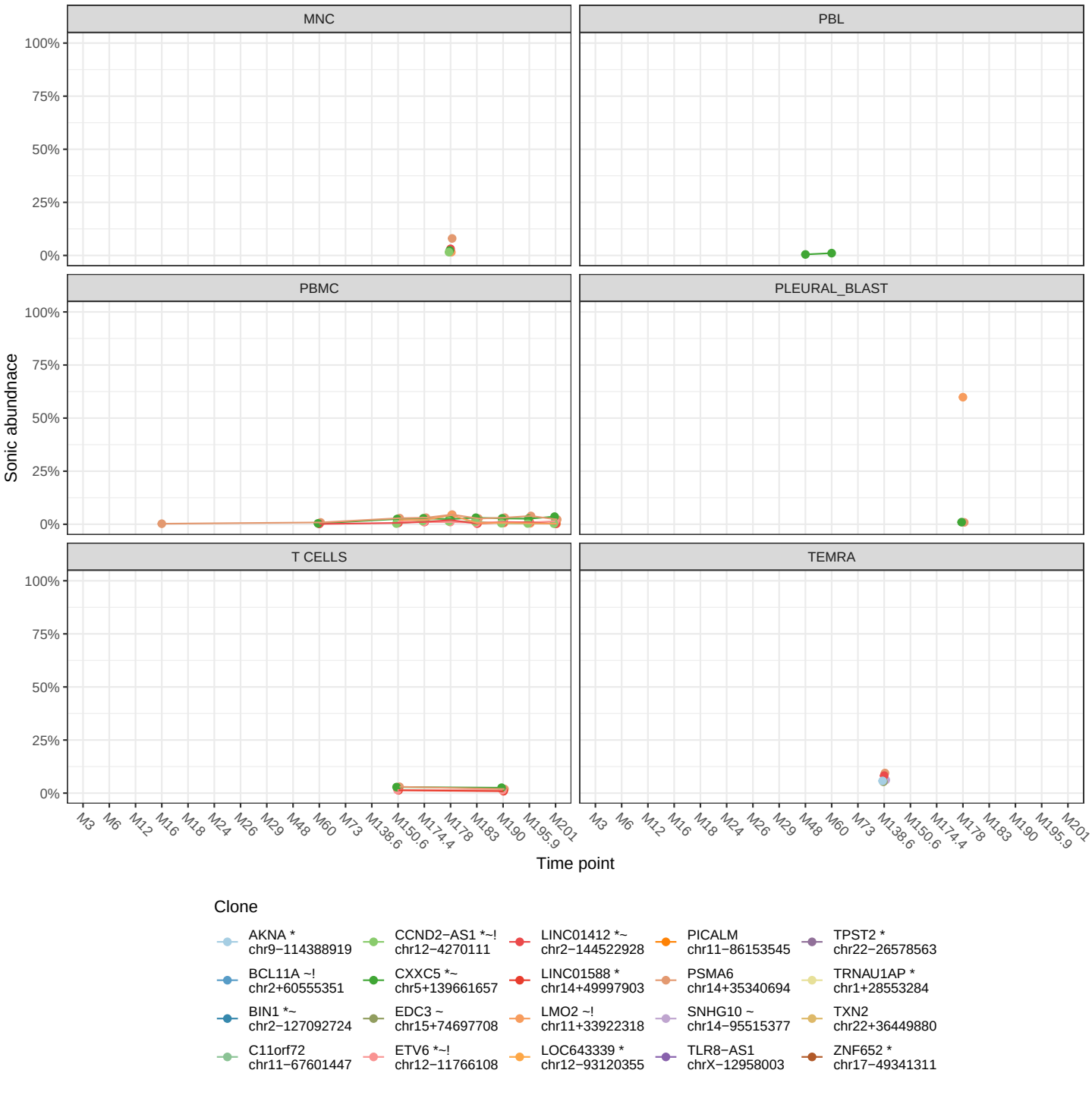

TEMRA
na
243
100%
75%
50%
25%
0%
Relative Sonic Abundance
M3
M6
M12
M16
M18
M24
M26
M29
M48
M60
M73
M138.9
M150.6
M174.4
M178.3
M190
M195.9
M201
Timepoint
Clones
LowAbund
PSMA6
chr14+35340694
LINC01412 *~
chr2−144522928
SNHG10 ~
chr14−95515377
AKNA *
chr9−114388919
EDC3 ~
chr15+74697708
LOC105372672
chr20+53750746
MIR4425
chr1−25031494
LINC01588 *
chr14+50000281
HTT *
chr4−3079128
ANKS1A *
chr6−35048534
dataSource
454
Illumina

Longitudinal behavior of major clones

When multiple time points are available, it is of interest to track the behavior of the most abundant clones across different cell types. A plot of the relative abundances of the most abundant 20 clones is shown below. For cases where only a single time point is available, the data is plotted as unlinked points.

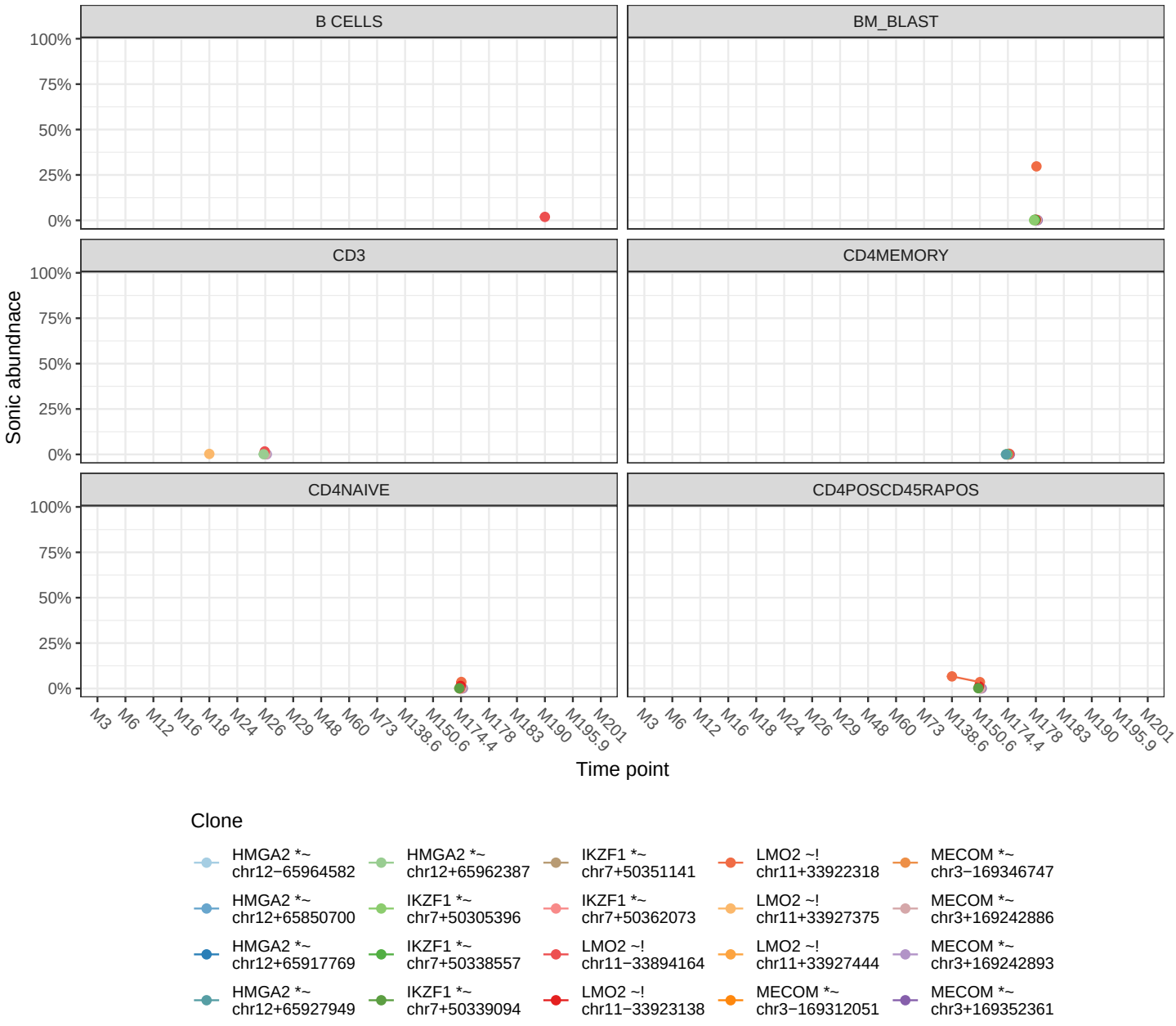


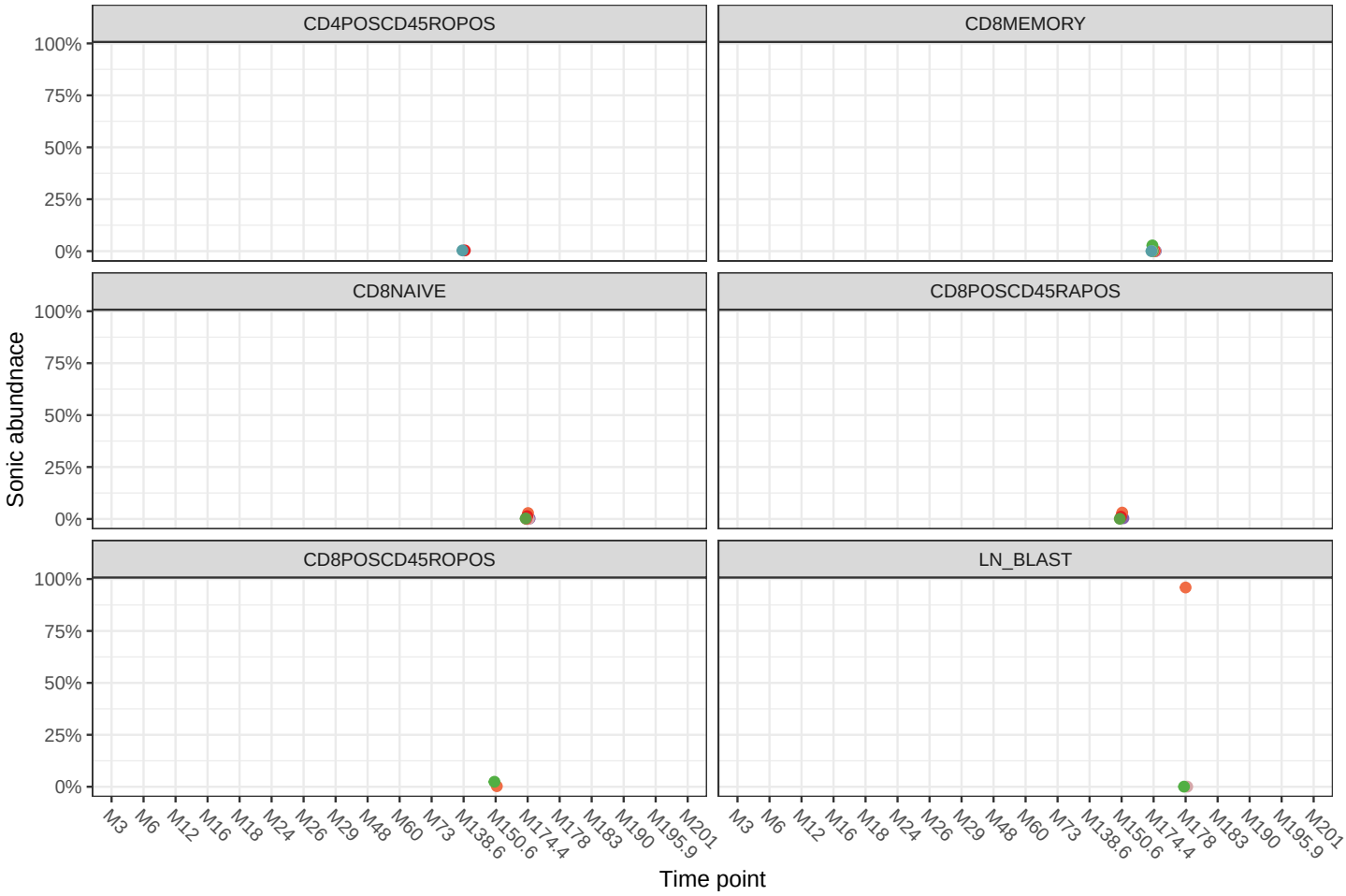

CD4POSCD45ROPOS
CD8MEMORY
CD8NAIVE
CD8POSCD45RAPOS
CD8POSCD45ROPOS
LN_BLAST
Sonic abundnace
100%
75%
50%
25%
0%
M3
M6
M12
M16
M18
M24
M26
M29
M48
M60
M73
M138.6
M150.6
M174.4
M178
M183
M190
M195.9
M201
Time point
Clone
AKNA * chr9−114388919
CCND2−AS1 *~! chr12−4270111
LINC01412 *~ chr2−144522928
PICALM chr11−86153545
TPST2 * chr22−26578563
BCL11A ~! chr2+60555351
CXXC5 *~ chr5+139661657
LINC01588 * chr14+49997903
PSMA6 chr14+35340694
TRNAU1AP * chr1+28553284
BIN1 *~ chr2−127092724
EDC3 ~ chr15+74697708
LMO2 ~! chr11+33922318
SNHG10 ~ chr14−95515377
TXN2 chr22+36449880
C11orf72 chr11−67601447
ETV6 *~! chr12−11766108
LOC643339 * chr12−93120355
TLR8−AS1 chrX−12958003
ZNF652 * chr17−49341311


MNC
PBL
PBMC
PLEURAL_BLAST
T CELLS
TEMRA
100%
75%
50%
25%
0%
Sonic abundnace
M3
M6
M12
M16
M18
M24
M26
M29
M48
M60
M73
M138.6
M150.6
M174.4
M178
M183
M190
M195.9
M201
Time point
Clone
AKNA * chr9−114388919
CCND2−AS1 *~! chr12−4270111
LINC01412 *~ chr2−144522928
PICALM chr11−86153545
TPST2 * chr22−26578563
BCL11A ~! chr2+60555351
CXXC5 *~ chr5+139661657
LINC01588 * chr14+49997903
PSMA6 chr14+35340694
TRNAU1AP * chr1+28553284
BIN1 *~ chr2−127092724
EDC3 ~ chr15+74697708
LMO2 ~! chr11+33922318
SNHG10 ~ chr14−95515377
TXN2 chr22+36449880
C11orf72 chr11−67601447
ETV6 *~! chr12−11766108
LOC643339 * chr12−93120355
TLR8−AS1 chrX−12958003
ZNF652 * chr17−49341311

Integration sites near particular genes of interest

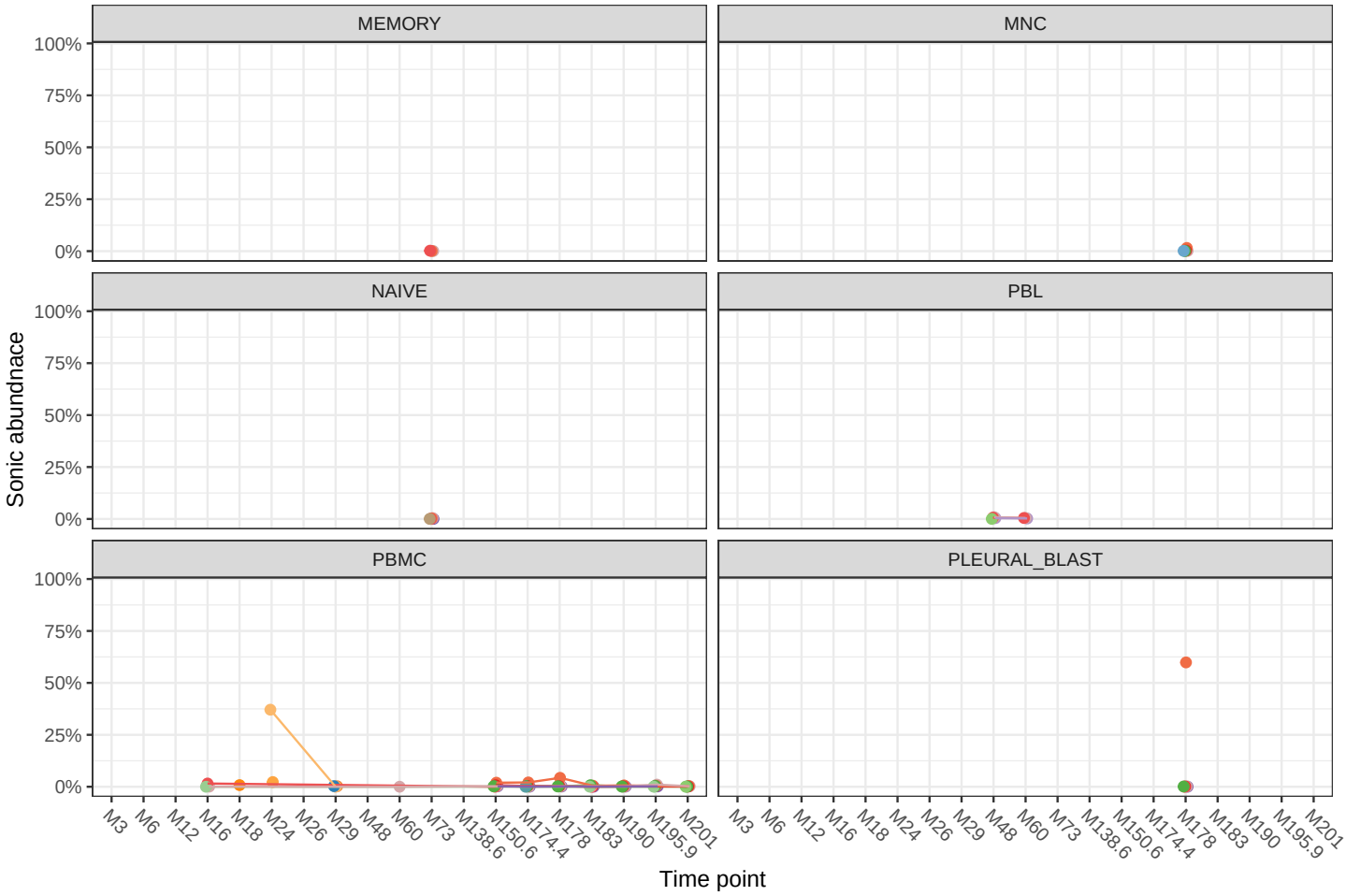
Integration sites near genes that have been associated with adverse events are of particular interest. Below are longitudinal relative abundance plots that focus on the most abundant 5 clones whoes nearest genes are LMO2, IKZF1, CCND2, HMGA2, and MECOM.





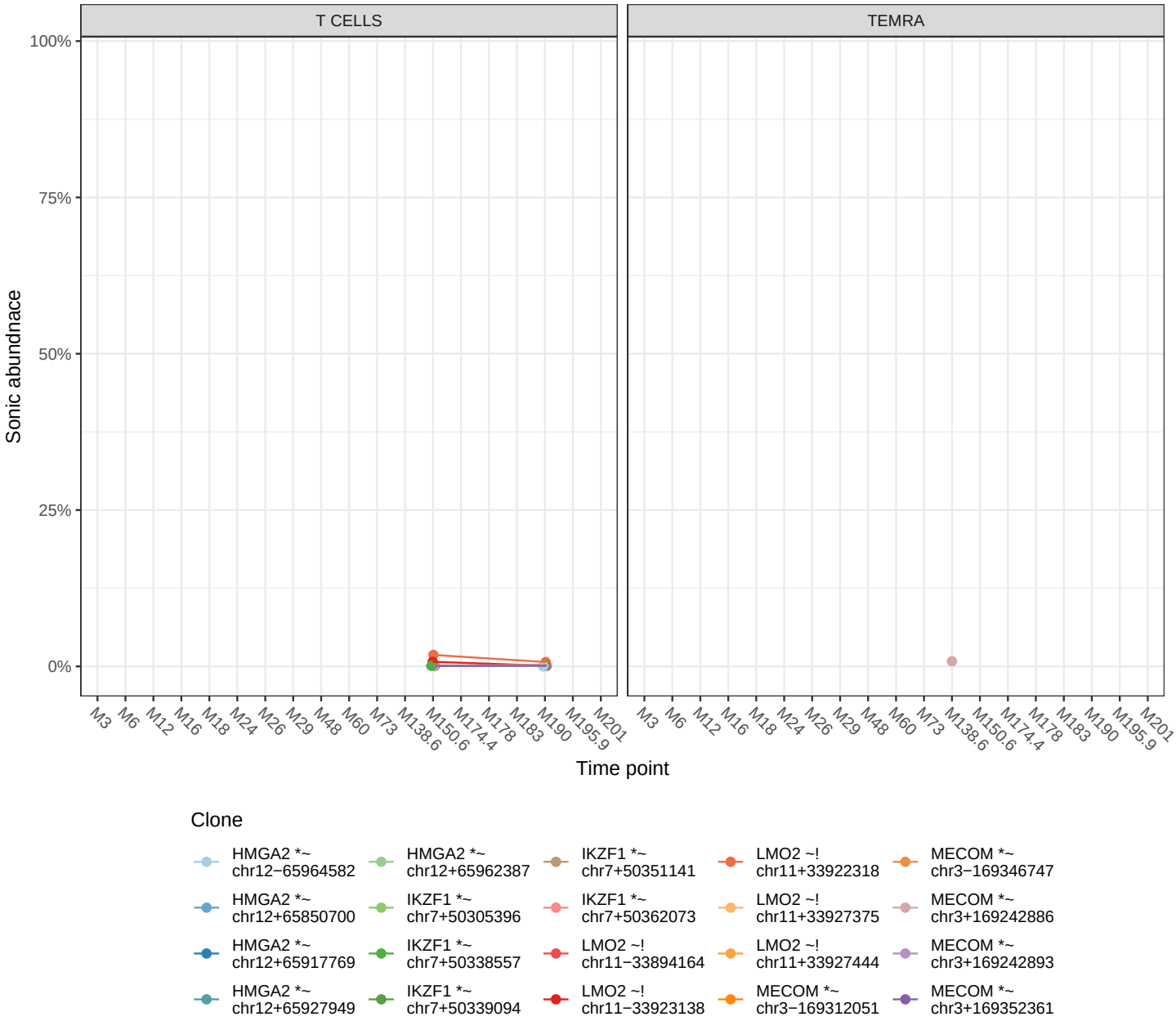
Clone

HMGA2 *~ chr12−65964582
HMGA2 *~ chr12+65850700
HMGA2 *~ chr12+65917769
HMGA2 *~ chr12+65927949
HMGA2 *~ chr12+65962387
IKZF1 *~ chr7+50305396
IKZF1 *~ chr7+50338557
IKZF1 *~ chr7+50339094
IKZF1 *~ chr7+50351141
IKZF1 *~ chr7+50362073
LMO2 ~! chr11−33894164
LMO2 ~! chr11−33923138
LMO2 ~! chr11+33922318
LMO2 ~! chr11+33927375
LMO2 ~! chr11+33927444
MECOM *~ chr3−169312051
MECOM *~ chr3−169346747
MECOM *~ chr3+169242886
MECOM *~ chr3+169242893
MECOM *~ chr3+169352361



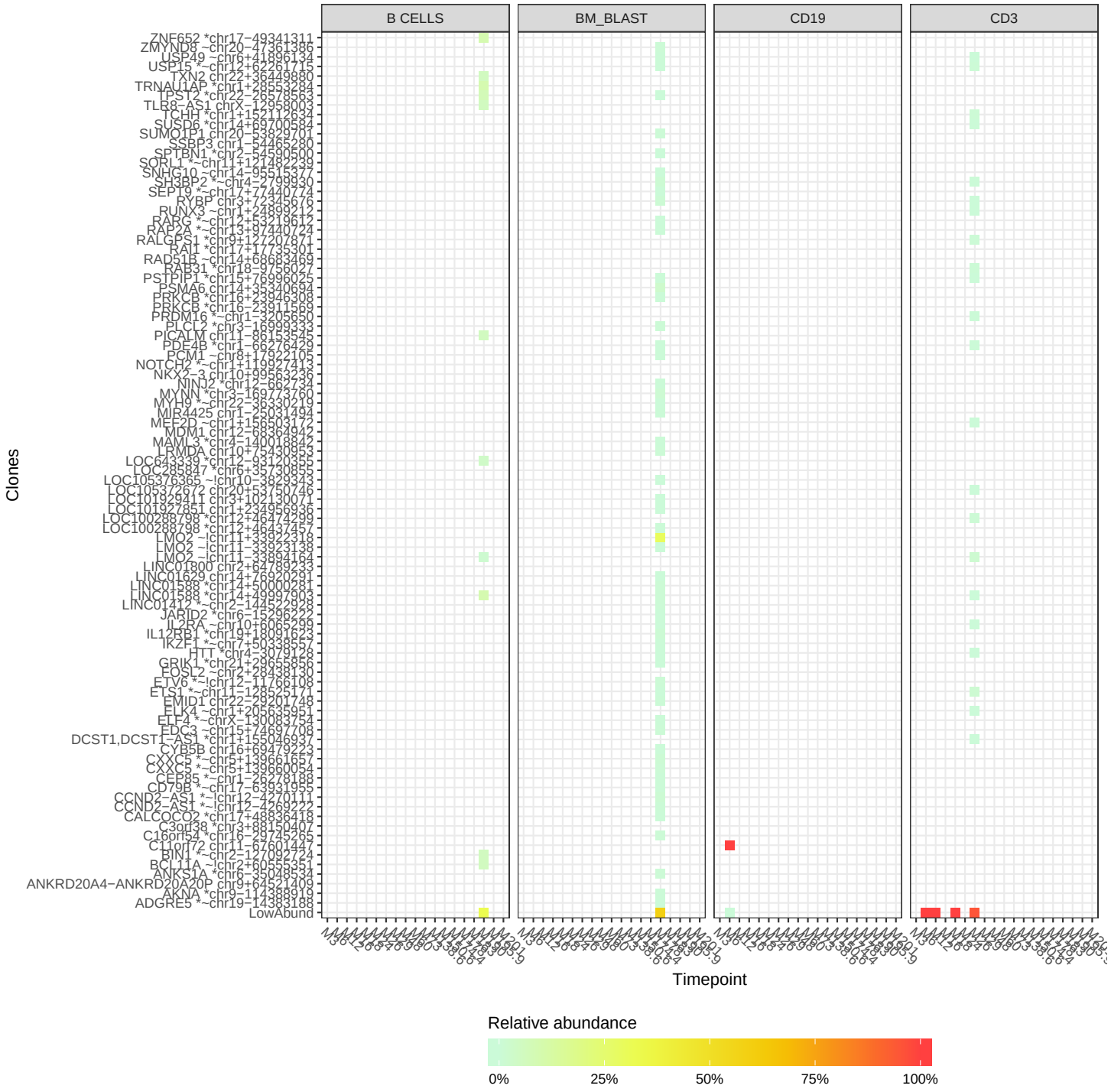
Clone

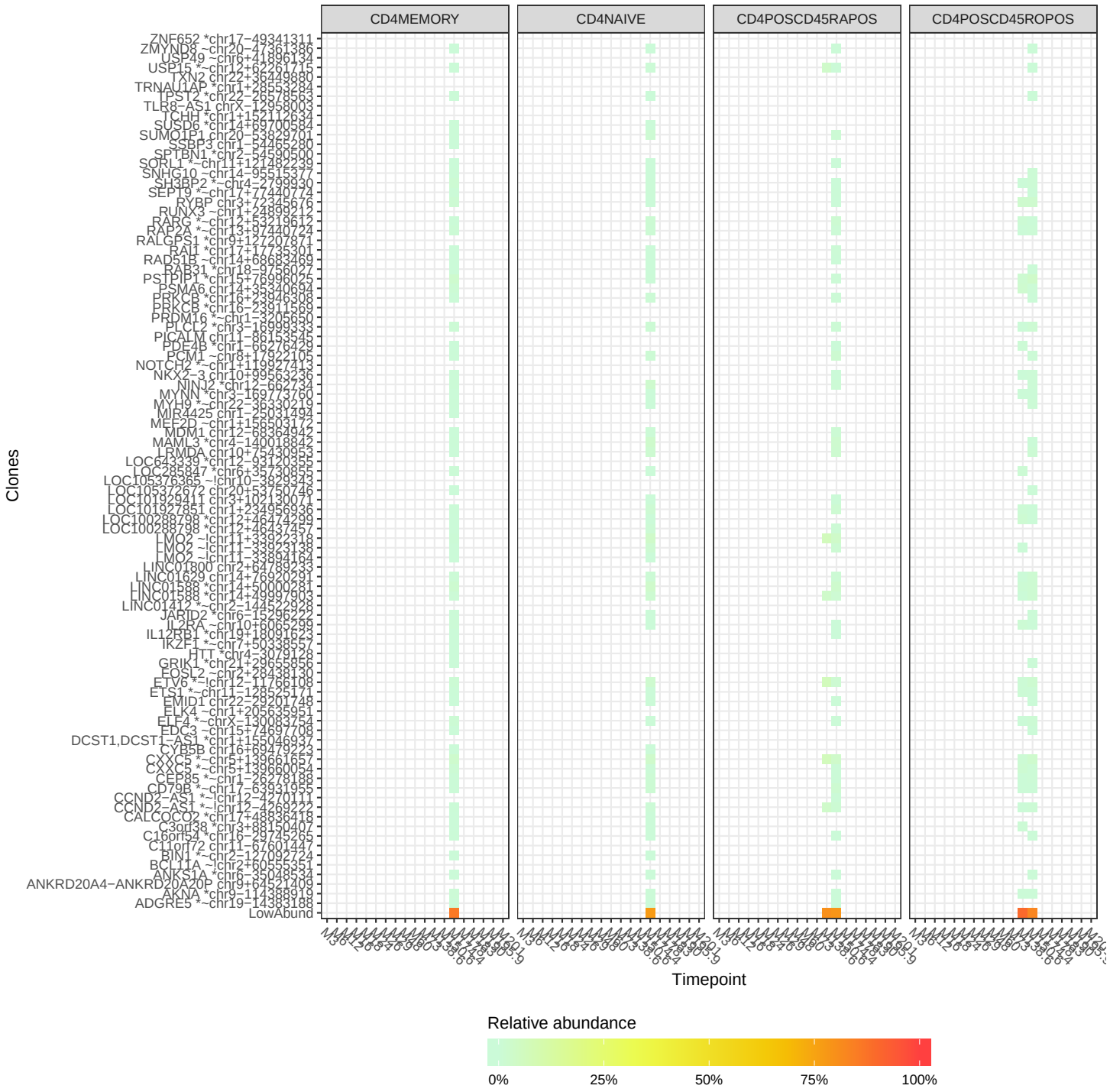
HMGA2 *~ chr12−65964582
HMGA2 *~ chr12+65850700
HMGA2 *~ chr12+65917769
HMGA2 *~ chr12+65927949
HMGA2 *~ chr12+65962387
IKZF1 *~ chr7+50305396
IKZF1 *~ chr7+50338557
IKZF1 *~ chr7+50339094
IKZF1 *~ chr7+50351141
IKZF1 *~ chr7+50362073
LMO2 ~! chr11−33894164
LMO2 ~! chr11−33923138
LMO2 ~! chr11+33922318
LMO2 ~! chr11+33927375
LMO2 ~! chr11+33927444
MECOM *~ chr3−169312051
MECOM *~ chr3−169346747
MECOM *~ chr3+169242886
MECOM *~ chr3+169242893
MECOM *~ chr3+169352361

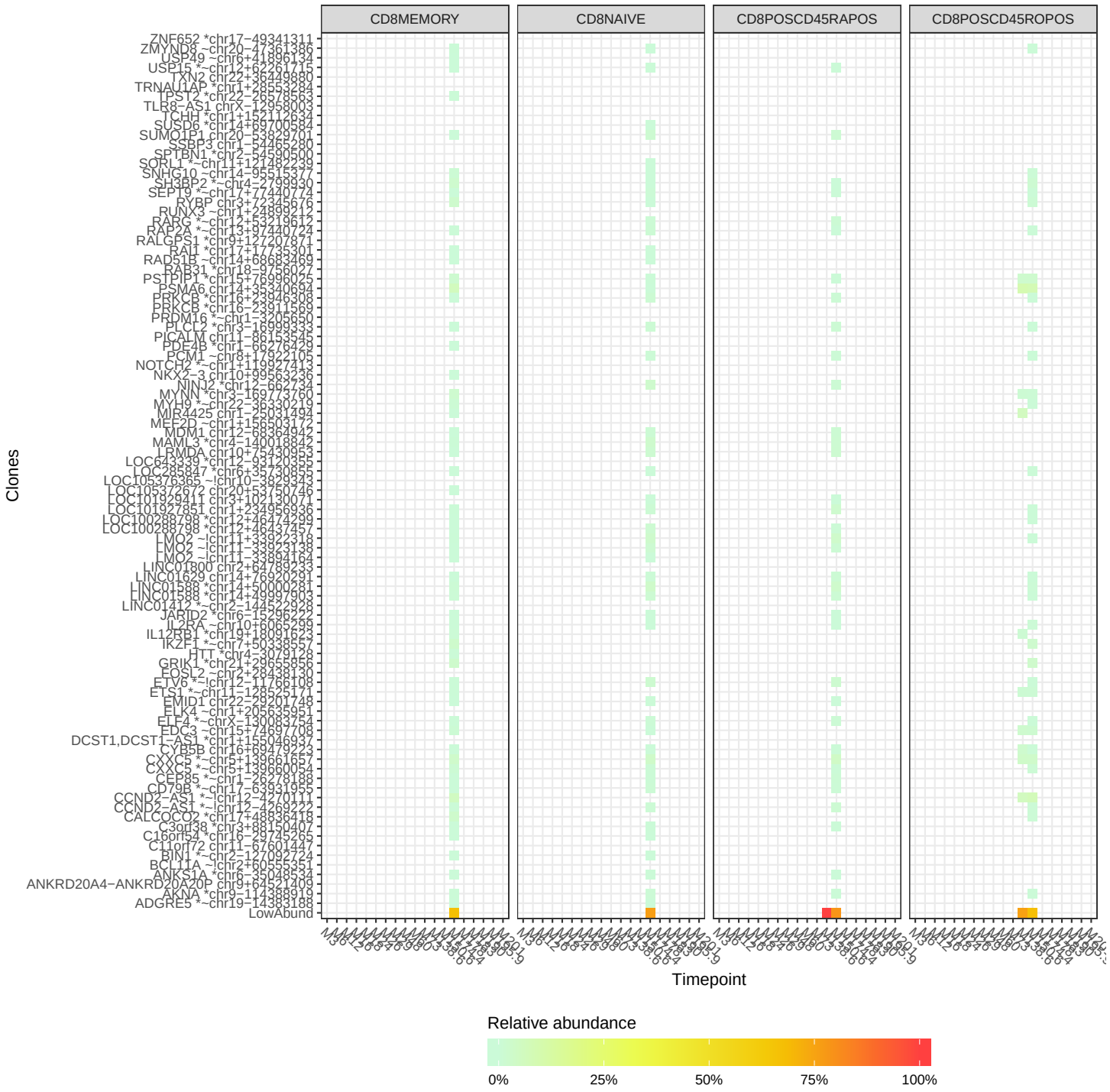

T CELLS
TEMRA
100%
75%
50%
25%
0%
Sonic abundnace
M3
M6
M12
M16
M18
M24
M26
M29
M48
M60
M73
M138.6
M150.6
M174.4
M178
M183
M190
M195.9
M201
Time point
Clone
HMGA2 *~ chr12−65964582
HMGA2 *~ chr12+65962387
IKZF1 *~ chr7+50351141
LMO2 ~! chr11+33922318
MECOM *~ chr3−169346747
HMGA2 *~ chr12+65850700
IKZF1 *~ chr7+50305396
IKZF1 *~ chr7+50362073
LMO2 ~! chr11+33927375
MECOM *~ chr3+169242886
HMGA2 *~ chr12+65917769
IKZF1 *~ chr7+50338557
LMO2 ~! chr11−33894164
LMO2 ~! chr11+33927444
MECOM *~ chr3+169242893
HMGA2 *~ chr12+65927949
IKZF1 *~ chr7+50339094
LMO2 ~! chr11−33923138
MECOM *~ chr3−169312051
MECOM *~ chr3+169352361

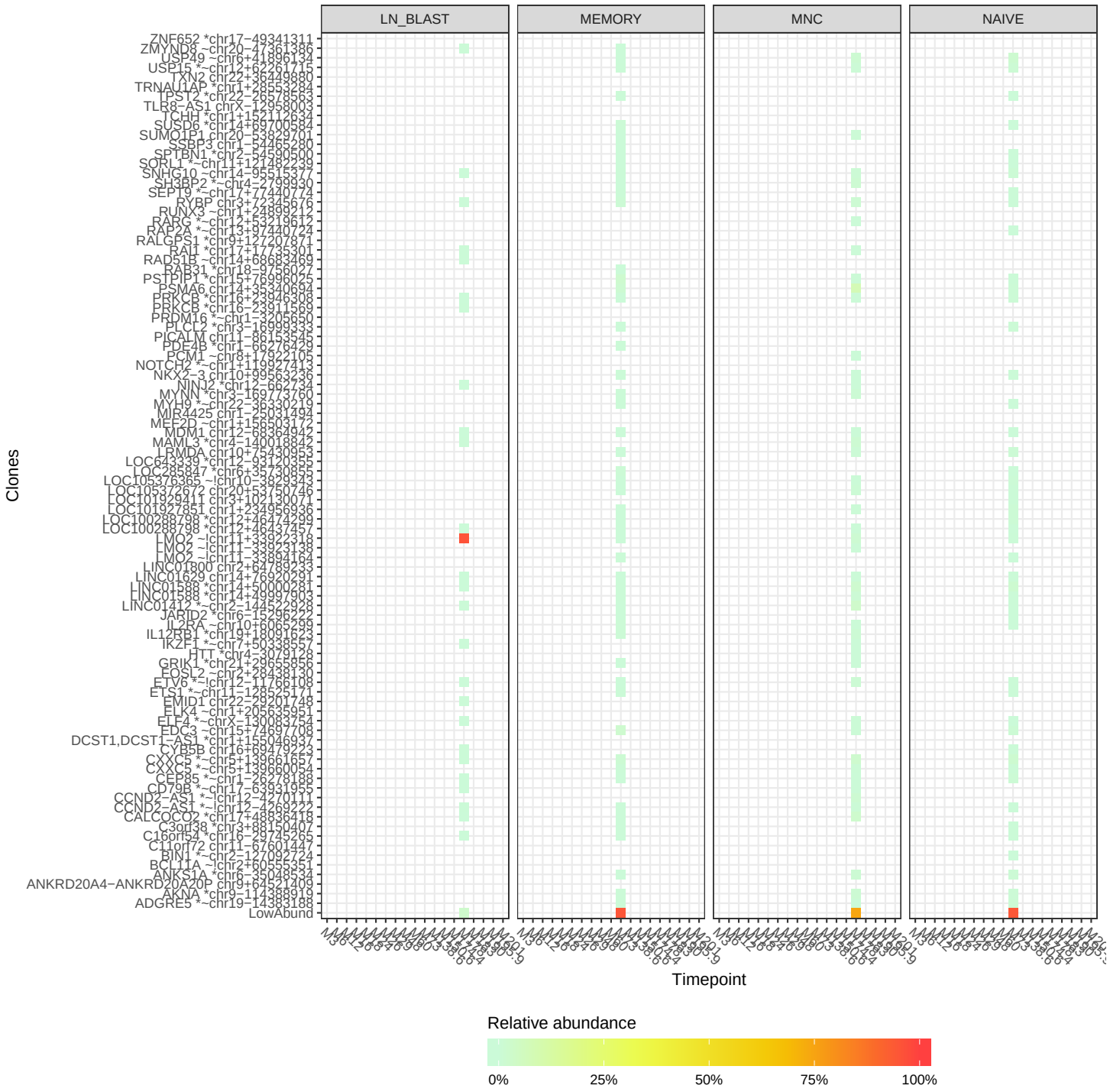
Sample relative abundance heatmap

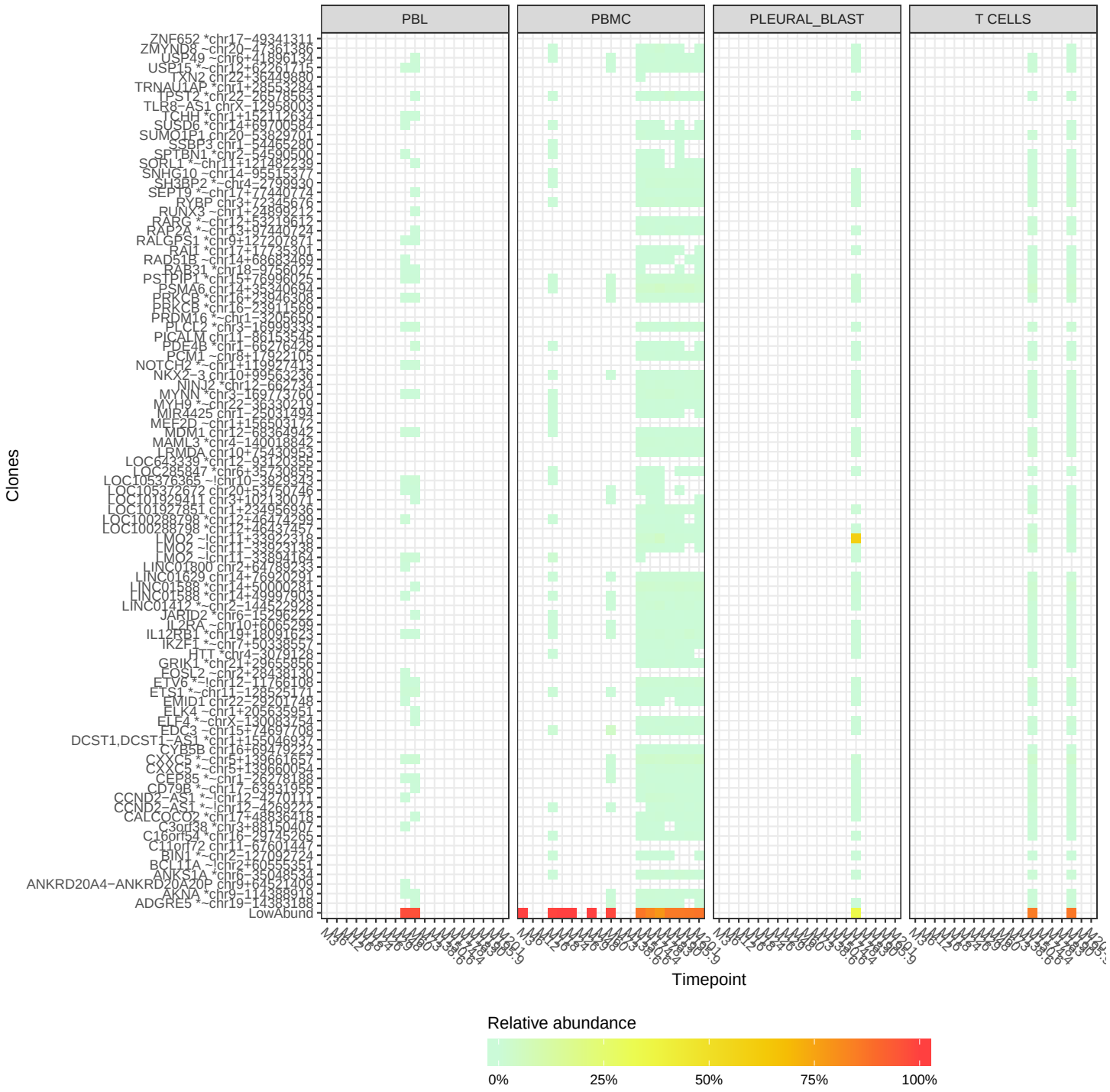
Alternatively, the relative abundances of the most abundant 10 clones from each cell sampled type can be visualized as a heat map.

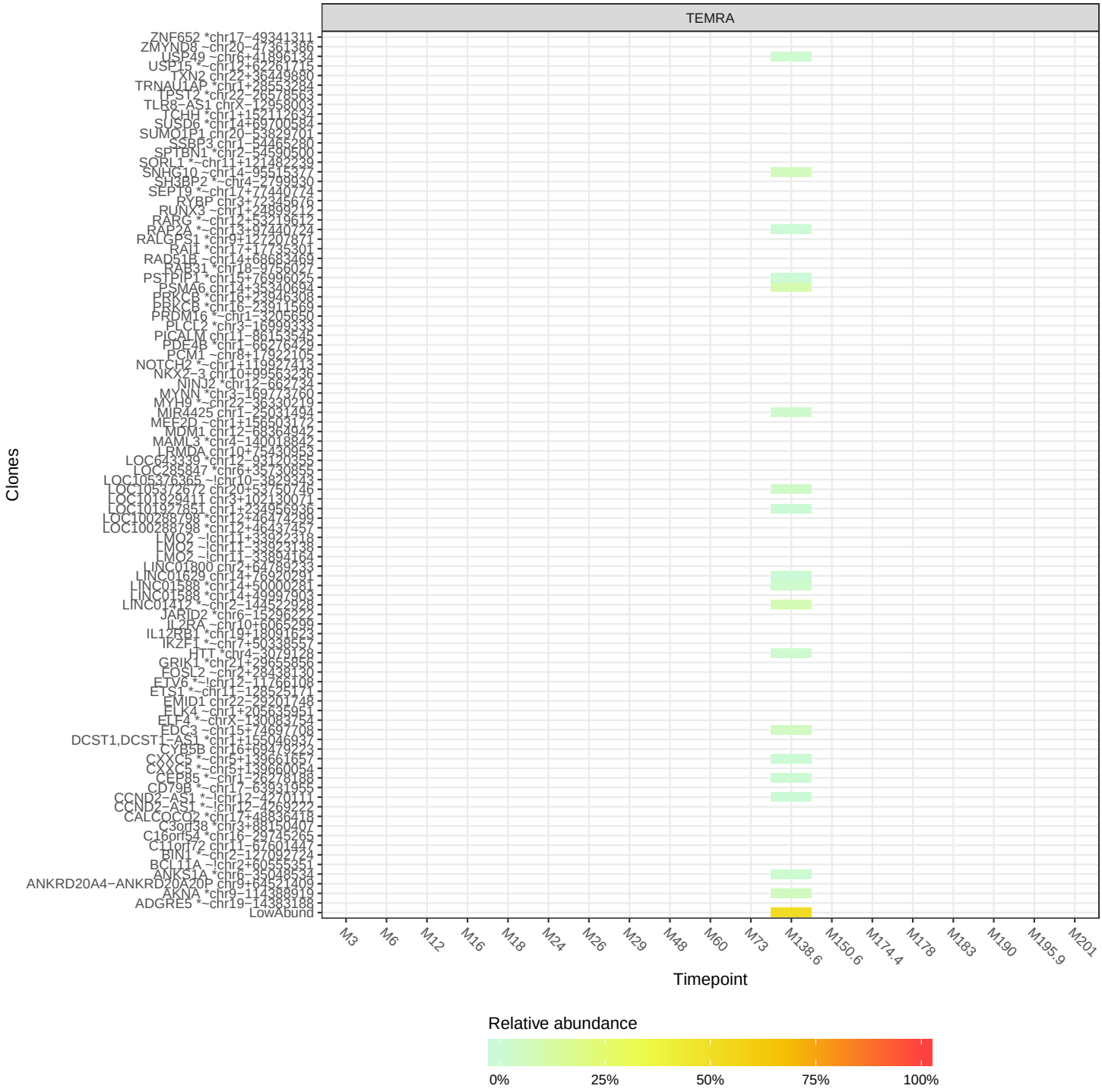



CD4MEMORY
CD4NAIVE
CD4POSCD45RAPOS
CD4POSCD45ROPOS
Clones
Timepoint
Relative abundance
0%
25%
50%
75%
100%


CD8MEMORY
CD8NAIVE
CD8POSCD45RAPOS
CD8POSCD45ROPOS
Clones
Timepoint
Relative abundance
0%
25%
50%
75%
100%


LN_BLAST
MEMORY
MNC
NAIVE
Clones
Timepoint
Relative abundance
0%
25%
50%
75%
100%


PBL
PBMC
PLEURAL_BLAST
T CELLS
Clones
Timepoint
Relative abundance
0%
25%
50%
75%
100%


TEMRA
Clones
ZNF652 *chr17−49341311
ZMYND8 ~chr20−47861386
USP49 ~chr5+41896134
USP15 *~chr12+62261715
TXN2 chr22+36449880
TRNAU1AP *chr1+28553284
TPST2 *chr22−26578563
TLR8−AS1 chrX−12958003
TCHH *chr1+152112634
SUSD6 *chr14+69700584
SUMO1P1 chr20−53829701
SSBP3 chr1−54465280
SPTBN1 *chr2−54590590
SQRLD1 *~chr11+121482239
SNHG10 ~chr14−95515477
SH3BP2 *~chr4−2799930
SEPT9 *~chr17+77440774
RYBP chr3+72345676
RUNX3 ~chr1+24899212
RARG *~chr12+53219612
RAP2A *~chr13+97440724
RALGPS1 *chr9+127207871
RAI1 *chr17+17735301
RAD51B ~chr14+68683469
PPP3R1 *chr2−86560027
PSTPIP1 *chr15+76996025
PSMA6 chr14+35340654
PRKCB *chr16+23946308
PRKCB *chr16−23911569
PRDM16 *~chr1−3205650
PLCL2 *chr3−16999333
PICALM chr11−86153545
PDE4B *chr1−66276429
PCM1 ~chr8+17922105
NOTCH2 *~chr1+119827413
NKX2−3 chr10+99563236
NINJ2 *chr12−662734
MYNN *chr3−169773760
MYH9 *~chr22−36330219
MIR4425 chr1−25031494
MEF2D ~chr1+156503172
MDM1 chr12−68364942
MAML3 *chr4−140018842
LRMDA chr10−7543053
LOC643338 *chr12−93720355
LOC285847 *chr6+35730855
LOC105376365 ~!chr10−3829343
LOC105372672 chr20+53750746
LOC101929411 chr3+102130071
LOC101927851 chr1+234956936
LOC100288798 *chr12+46474299
LOC100288798 *chr12+46437457
LMO2 ~!chr11+33922318
LMO2 ~!chr11−33921789
LMO2 ~!chr11−33864164
LINC01800 chr2+64789233
LINC01629 chr14+76920291
LINC01588 *chr14+50000281
LINC01588 *chr14+49997903
LINC01412 *~chr2−144522928
JARID2 *chr6−15296222
IL2RA ~chr10+6065299
IL12RB1 *chr19+18091623
IKZF1 *~chr7+50338557
HTT *chr4−3071128
GRIK1 *chr21+29655956
EOSL2 ~chr2+28438130
ETV6 *~!chr12−11766108
ETS1 *~chr11−128525171
EMID1 chr22−29201748
ELK4 ~chr1+205635951
ELF4 *~chrX−130083754
EDC3 ~chr15+74697708
DCST1,DCST1−AS1 *chr1+155046937
CYB5B chr16+69479773
CXXC5 *~chr5+138661657
CXXC5 *~chr5+138660054
CEP85 *~chr1−28278188
CD79B *~chr17−63931955
CCND2−AS1 *~!chr12−4270111
CCND2−AS1 *~!chr12−4269222
CALCOCO2 *chr17+48836418
C3orf38 *chr3+88150407
C16orf54 *chr16−29745265
C11orf72 chr11−67601447
BIN1 *~chr2−127092724
BCL11A ~!chr2+60555551
ANKS1A *chr6−35048534
ANKRD20A4−ANKRD20A2P chr9+64521409
AKNA *chr9−114388919
ADGRE5 *~chr19−14383188
LowAbund
M3
M6
M12
M16
M18
M24
M26
M29
M48
M60
M73
M138.6
M150.6
M174.4
M178
M183
M190
M195.9
M201
Timepoint
Relative abundance
0%
25%
50%
75%
100%

What are the most frequently occuring gene types in the subject?

The word clouds below illustrate the nearest genes of the most abundant clones from each sample where the numeric ranges represent the upper and lower clonal abundances.

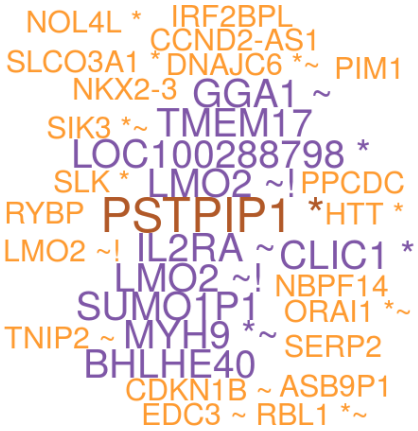
PBMC
M3 1:1

CD3
M6 1:1

CD19
M6 1:1

CD3
M12 1:1

PBMC
M16 2:5



CD3
M18 1:1

PBMC
M18 1:1

PBMC
M24 1:1

CD3
M26 1:3

PBMC
M29 1:1

PBL
M48 1:3

PBL
M60 1:4

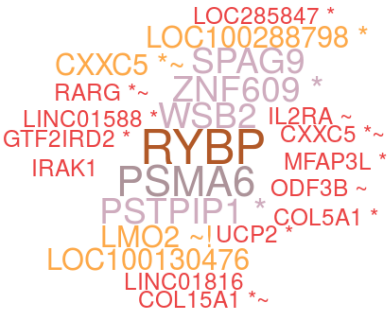
PBMC
M60 1:3

MEMORY
M73 2:5

NAIVE
M73 2:4

CD4POSCD45RAPOS
M138.6 1:3

CD4POSCD45ROPOS
M138.6 1:7



CD8POSCD45RAPOS
M138.6 1:3

CD8POSCD45ROPOS
M138.6 1:8

TEMRA
M138.6 1:23

CD4POSCD45RAPOS
M150.6 3:43

CD4POSCD45ROPOS
M150.6 2:23

CD8POSCD45RAPOS
M150.6 2:49

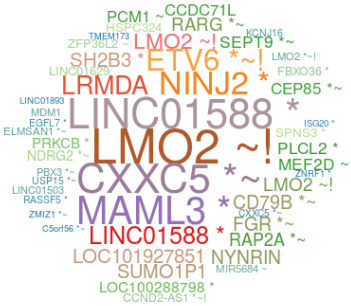
CD8POSCD45ROPOS
M150.6 2:62

PBMC
M150.6 10:152

T CELLS
M150.6 7:106

CD4MEMORY
M174.4 21:309

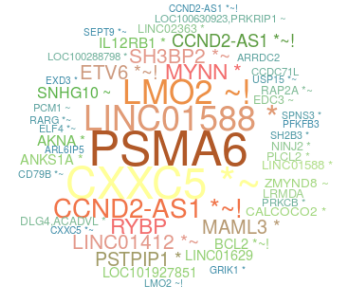
CD4NAIVE
M174.4 20:375



CD8MEMORY
M174.4 11:449

CD8NAIVE
M174.4 12:217

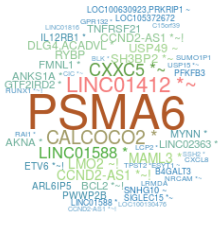
PBMC
M174.4 12:205



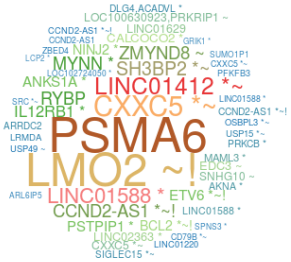
BM BLAST
M178 3:578

LN BLAST
M178 1:1527

MNC
M178 2:62



PBMC
M178 6:145



PLEURAL BLAST
M178 2:1446

PBMC
M183 3:49

T CELLS
M190 19:244

PBMC
M195.9 3:69

PBMC
M201 7:136

Methods

All coordinates are on human genome draft hg38.

Detailed methods can be found these publications:
- Bioinformatics. 2012 Mar 15; 28(6): 755–762.
- Mol Ther Methods Clin Dev. 2017 Mar 17; 4: 17–26.
- Mol Ther Methods Clin Dev. 2017 Mar 17; 4: 39–49.

Analysis software:
- INSPIIRED v1.1 (http://github.com/BushmanLab/INSPIIRED)

Report generation software:
- subjectReport v0.1 (http://github.com/everettJK/geneTherapySubjectReport)