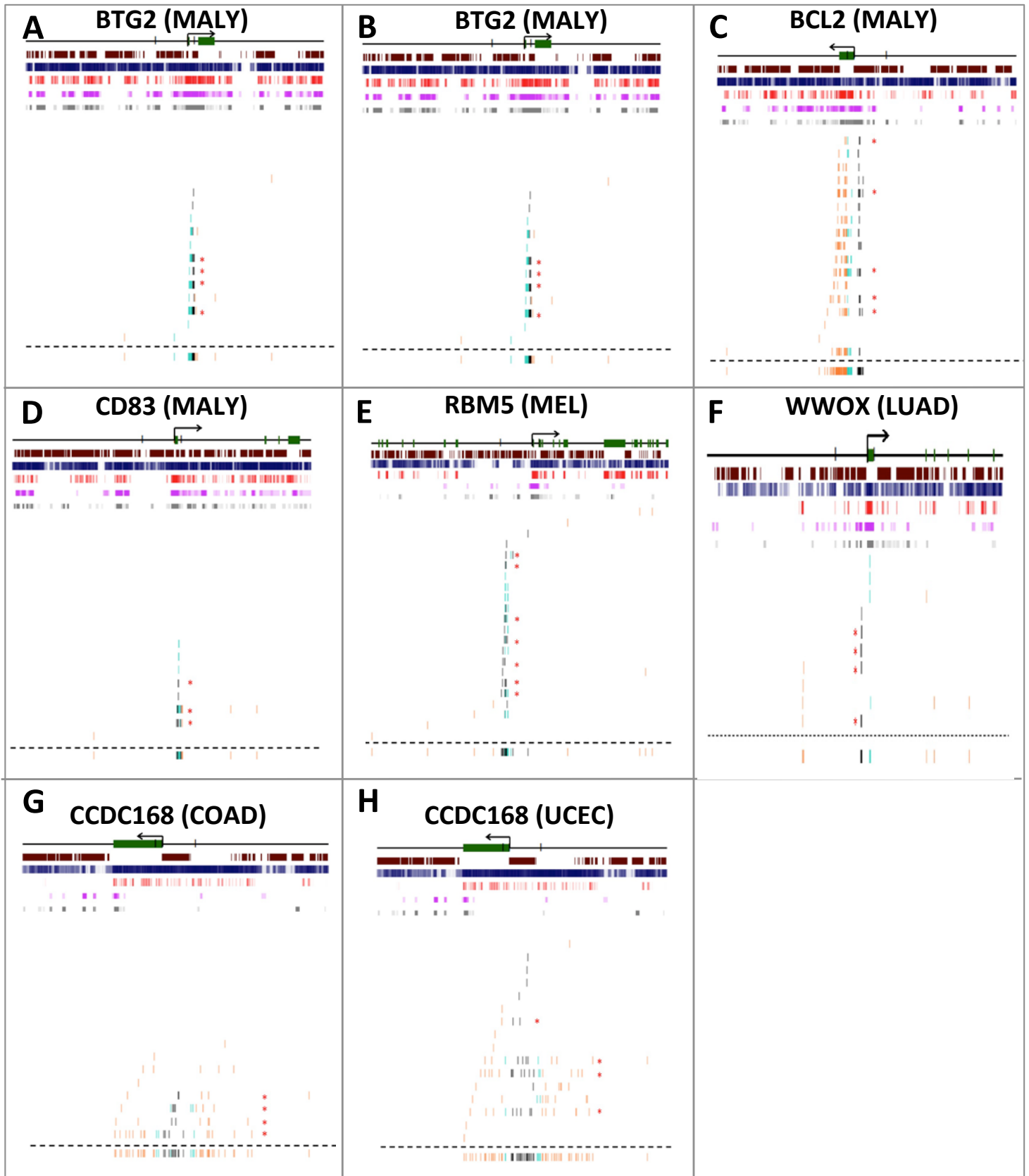


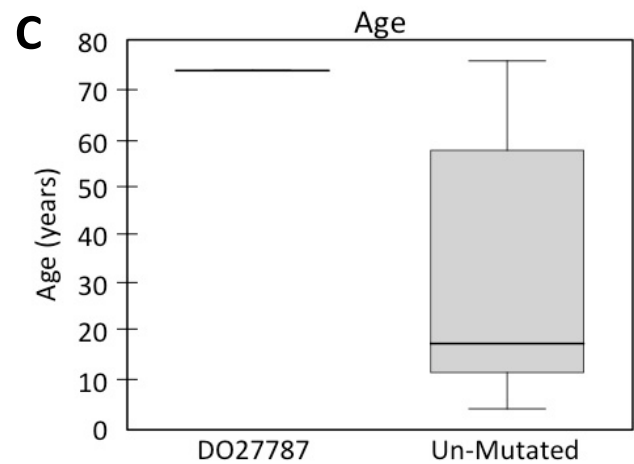
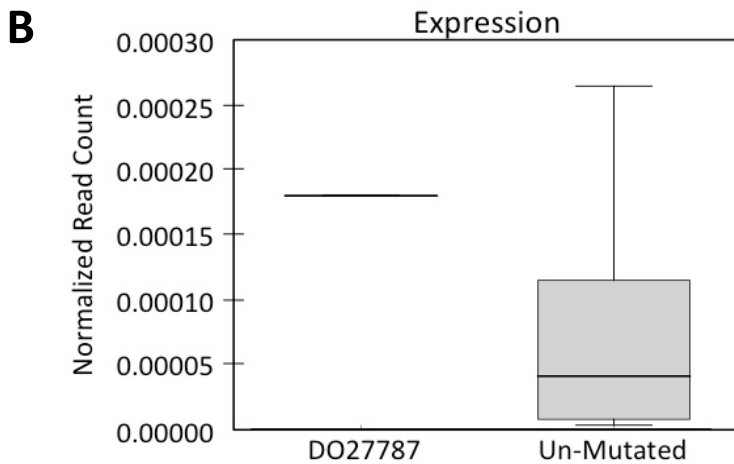
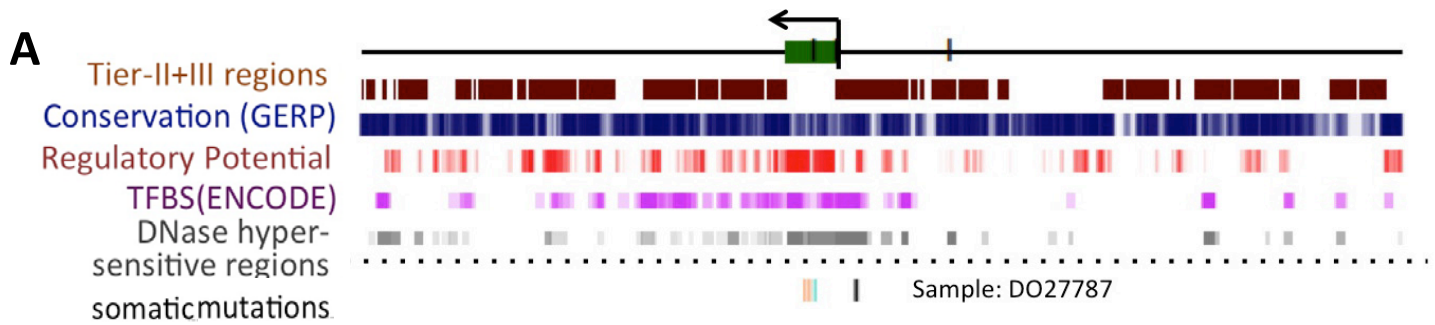
**Supplementary Information
for
Signatures of accelerated somatic evolution
in gene promoters in multiple cancer types**

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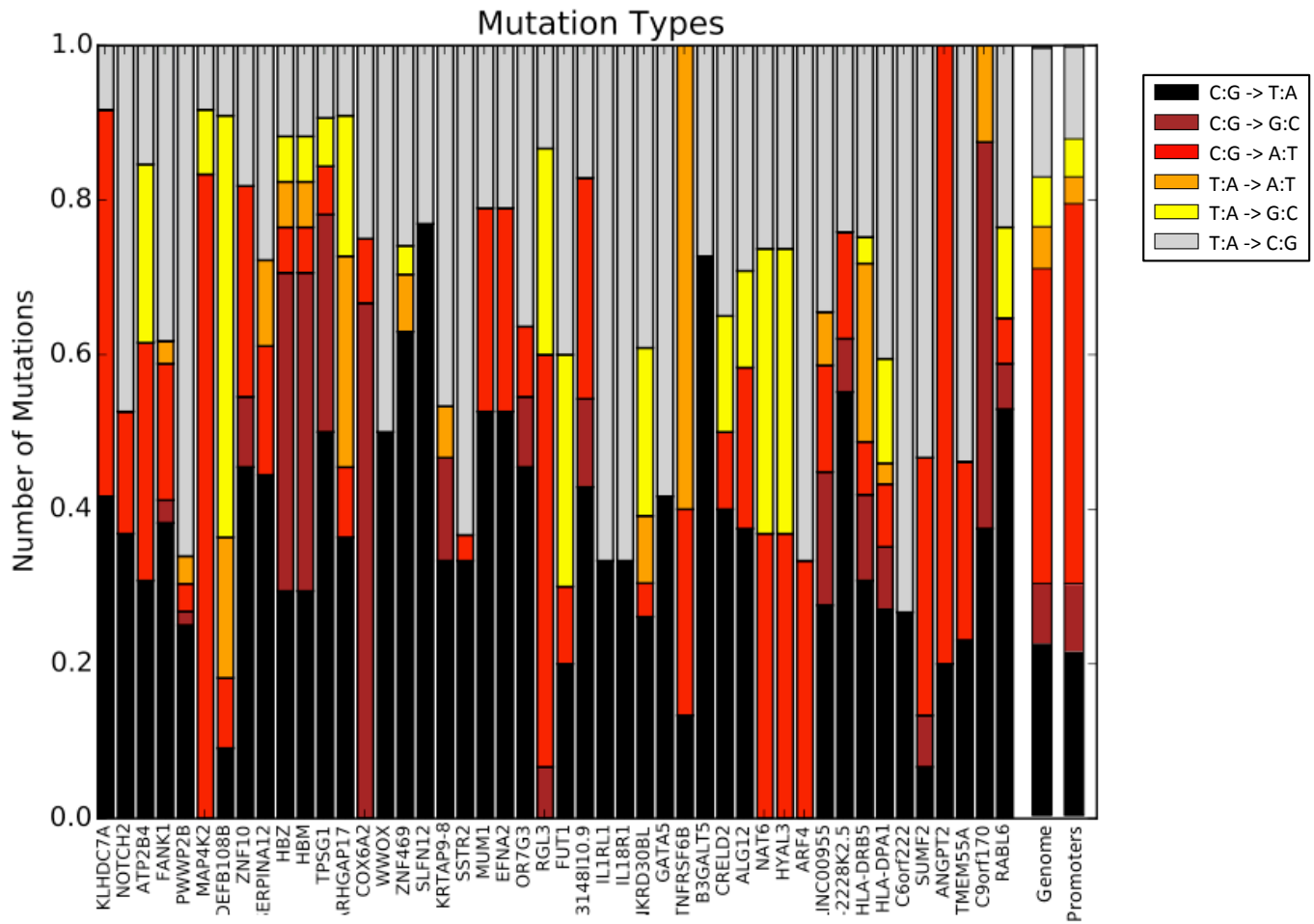
Supplementary Figure 1



Supplementary Figure 1: Signatures of accelerated somatic evolution in gene promoters in (A-D) malignant lymphoma, (E) melanoma, (F) lung adenocarcinoma, (G) UCEC and (H) COAD cohorts. Those cases that are found in multiple cancer types, show associated gene expression changes, or clinical attributes are listed. Mutations in Tier-II+III regions of predicted promoters (5kb upstream to 1kb downstream of transcription start site) are shown in grey, those in Tier-I+IV regions of predicted promoters are shown in cyan, as in Figure 1. Additional evolutionary and functional annotations are also shown, as in Figure 1. Significant promoters are shown with asterisk.



Supplementary Figure 2: Individual case study. A) We showcase a lymphoma sample DO27787 that shows signature of accelerated evolution in the promoter of BCL2. Sample DO27787 has a significant number of mutations in the promoter compared to the flanking regions. After masking the repetitive and coding regions there are 3 mutations in the promoter and 0 in the flanking regions (fisher's exact test p -value = 0.0036). The enrichment was maintained even when we considered alternate window sizes, applied filter for evolutionary conservation, or used permutation to assess statistical significance. The mutations in the BCL2 promoter mapped to DNase hypersensitive regions, and overlapped with multiple, predicted binding sites of transcription factor p65 also known as nuclear factor NF-kappa-B p65 subunit (RELA), insulator element CTCF, and several other transcription factors such as ZEB1, EGR1, FOXA1 etc. Sample DO27787 exemplifies **B)** the increased expression and **C)** advanced age shown to be associated with SASE in the BCL2 promoter.



Supplementary Figure 3: Nucleotide substitution patterns in the gene promoters that had signatures of accelerated somatic evolution, contrasted against that observed in all gene promoters and also in the completely sequenced genomes for lung adenocarcinoma samples.

Supplementary Table 1: Table showing FDR adjusted p-values for signatures of accelerated evolution in the promoters of the known protein-coding genes in different cancer cohorts. We repeated the analyses using alternative parameter-settings, as in Supplementary Table ST1-4, and found consistent results (exceptions: DNMT1, MAP4K2, GATA5).

Genes	Position	Cancer type	Cohort (total samples)	# samples with significant SASE	FDR adjusted p value
IGLL5	chr22:23229960:23238287:+1	Malignant Lymphoma	MALY-DE (44)	8	4.25E-11
BTG2	chr1:203274619:203278730:+1	Malignant Lymphoma	MALY-DE (44)	4	9.29E-10
BCL6	chr3:187439165:187463515:-1	Malignant Lymphoma	MALY-DE (44)	10	9.29E-10
TCL1A	chr14:96176304:96180533:-1	Malignant Lymphoma	MALY-DE (44)	4	7.88E-05
MYC	chr8:128747680:128753674:+1	Malignant Lymphoma	MALY-DE (44)	3	1.35E-04
BCL2	chr18:60790579:60987361:-1	Malignant Lymphoma	MALY-DE (44)	5	2.60E-04
CD83	chr6:14117872:14137149:+1	Malignant Lymphoma	MALY-DE (44)	3	1.07E-03
S1PR2	chr19:10334520:10341948:-1	Malignant Lymphoma	MALY-DE (44)	4	1.60E-03
BIRC3	chr11:102188215:102210134:+1	Malignant Lymphoma	MALY-DE (44)	4	5.30E-03
DNMT1	chr19:10244021:10341962:-1	Malignant Lymphoma	MALY-DE (44)	3	1.05E-02
RBM5	chr3:50126341:50156454:+1	Melanoma	Melanoma (25)	7	3.07E-07
MEAF6	chr1:37958176:37980375:-1	Melanoma	Melanoma (25)	3	1.54E-04
RNF223	chr1:1006346:1009687:-1	Melanoma	Melanoma (25)	6	4.09E-04
CCS	chr11:66360292:66373490:+1	Melanoma	Melanoma (25)	4	8.45E-03
KLHDC7A	chr1:18807424:18812478:1	Lung Adenocarcinoma	LUAD (32)	3	1.93E-03
NOTCH2	chr1:120454176:120612240:-1	Lung Adenocarcinoma	LUAD (32)	5	1.53E-02
ATP2B4	chr1:203595689:203713209:1	Lung Adenocarcinoma	LUAD (32)	3	6.35E-04
FANK1	chr10:127585108:127698161:1	Lung Adenocarcinoma	LUAD (32)	8	1.61E-09
PWWP2B	chr10:134210672:134231367:1	Lung Adenocarcinoma	LUAD (32)	15	2.21E-13
MAP4K2	chr11:64556290:64570713:-1	Lung Adenocarcinoma	LUAD (32)	3	6.71E-03
DEFB108B	chr11:71544246:71548756:1	Lung Adenocarcinoma	LUAD (32)	4	4.28E-03
ZNF10	chr12:133707161:133736051:1	Lung Adenocarcinoma	LUAD (32)	4	9.56E-03
SERPINA12	chr14:94953611:94984181:-1	Lung Adenocarcinoma	LUAD (32)	5	1.10E-04
HBZ	chr16:202686:204502:1	Lung Adenocarcinoma	LUAD (32)	5	1.65E-04
HBM	chr16:203891:216767:1	Lung Adenocarcinoma	LUAD (32)	5	1.10E-04
TPSG1	chr16:1271651:1275257:-1	Lung Adenocarcinoma	LUAD (32)	4	3.38E-02
ARHGAP17	chr16:24930706:25026987:-1	Lung Adenocarcinoma	LUAD (32)	3	6.35E-04
COX6A2	chr16:31439052:31439967:-1	Lung Adenocarcinoma	LUAD (32)	5	1.70E-11
WWOX	chr16:78133310:79246564:1	Lung Adenocarcinoma	LUAD (32)	4	7.30E-04
ZNF469	chr16:88493879:88507165:1	Lung Adenocarcinoma	LUAD (32)	7	2.22E-05
SLFN12	chr17:33738079:33760302:-1	Lung Adenocarcinoma	LUAD (32)	4	1.28E-04
KRTAP9-8	chr17:39394297:39395256:1	Lung Adenocarcinoma	LUAD (32)	3	2.57E-06
SSTR2	chr17:71161151:71167185:1	Lung Adenocarcinoma	LUAD (32)	9	1.25E-05
MUM1	chr19:1285890:1378430:1	Lung Adenocarcinoma	LUAD (32)	3	4.03E-03
EFNA2	chr19:1286153:1301430:1	Lung Adenocarcinoma	LUAD (32)	3	3.15E-03
OR7G3	chr19:9236688:9237626:-1	Lung Adenocarcinoma	LUAD (32)	3	5.82E-04
RGL3	chr19:11495017:11530018:-1	Lung Adenocarcinoma	LUAD (32)	3	7.58E-04
FUT1	chr19:49251268:49258647:-1	Lung Adenocarcinoma	LUAD (32)	4	3.20E-02
CTD-3148110.9	chr19:49966009:49989488:1	Lung Adenocarcinoma	LUAD (32)	7	3.03E-03
IL1RL1	chr2:102927962:102968497:1	Lung Adenocarcinoma	LUAD (32)	3	8.11E-04
IL18R1	chr2:102927989:103015218:1	Lung Adenocarcinoma	LUAD (32)	3	7.58E-04
ANKRD30BL	chr2:132905164:133015542:-1	Lung Adenocarcinoma	LUAD (32)	6	7.67E-05
GATA5	chr20:61038553:61051026:-1	Lung Adenocarcinoma	LUAD (32)	3	6.22E-04
TNFRSF6B	chr20:62328021:62330037:1	Lung Adenocarcinoma	LUAD (32)	7	4.97E-09
B3GALT5	chr21:40928369:41045064:1	Lung Adenocarcinoma	LUAD (32)	4	2.09E-02
ALG12	chr22:50293877:50312106:-1	Lung Adenocarcinoma	LUAD (32)	4	3.14E-05
CRELD2	chr22:50311815:50321188:1	Lung Adenocarcinoma	LUAD (32)	4	3.80E-02
HYAL3	chr3:50330262:50336899:-1	Lung Adenocarcinoma	LUAD (32)	3	1.32E-02
NAT6	chr3:50333833:50336852:-1	Lung Adenocarcinoma	LUAD (32)	3	1.23E-02
ARF4	chr3:57557090:57583947:-1	Lung Adenocarcinoma	LUAD (32)	3	3.79E-02
LINC00955	chr4:3578596:3592438:1	Lung Adenocarcinoma	LUAD (32)	9	5.67E-13
CTD-2228K2.5	chr5:466239:473213:-1	Lung Adenocarcinoma	LUAD (32)	6	9.56E-03
HLA-DRB5	chr6:32485120:32498064:-1	Lung Adenocarcinoma	LUAD (32)	12	3.39E-12
HLA-DPA1	chr6:33032346:33048552:-1	Lung Adenocarcinoma	LUAD (32)	5	5.36E-05
C6orf222	chr6:36283534:36304662:-1	Lung Adenocarcinoma	LUAD (32)	3	3.38E-02
SUMF2	chr7:56131695:56148363:1	Lung Adenocarcinoma	LUAD (32)	4	2.78E-03
ANGPT2	chr8:6357172:6420930:-1	Lung Adenocarcinoma	LUAD (32)	4	3.38E-02
TMEM55A	chr8:92006024:92053292:-1	Lung Adenocarcinoma	LUAD (32)	3	1.58E-02
C9orf170	chr9:89763559:89774471:1	Lung Adenocarcinoma	LUAD (32)	3	3.63E-03
RABL6	chr9:139702374:139735639:1	Lung Adenocarcinoma	LUAD (32)	3	6.35E-04
CCDC168	chr13:103381801:103389159:-1	Colon cancer	COAD-US (19)	4	1.04E-04
CCDC168	chr13:103381801:103389159:-1	Endometrial cancer	UCEC-US (131)	4	1.64E-08

Supplementary Table 2: Table showing FDR adjusted p-values for signatures of accelerated evolution when alternate window sizes for genomic neighborhood were considered. Our analysis shows that significant cases of SASE were not due to choice of window sizes, and typically became even more significant when larger window sizes for genomic neighborhood were considered. DNMT1, GATA5, and MAP4K2 are an exceptions, where the enrichment could be due to local increase in mutation rate, and may be false positives.

Genes	Position	Cohort (total samples)	# samples with significant SASE	FDR adjusted p-value	
				Neighborhood: 40kb	Neighborhood: 100kb
IGLL5	chr22:23229960:23238287:+1	MALY-DE (44)	8	9.70E-30	2.25E-60
BTG2	chr1:203274619:203278730:+1	MALY-DE (44)	4	1.02E-17	5.79E-28
BCL6	chr3:187439165:187463515:-1	MALY-DE (44)	10	2.82E-18	1.24E-31
TCL1A	chr14:96176304:96180533:-1	MALY-DE (44)	4	1.19E-06	7.12E-10
MYC	chr8:128747680:128753674:+1	MALY-DE (44)	3	4.77E-06	1.01E-07
BCL2	chr18:60790579:60987361:-1	MALY-DE (44)	5	1.41E-09	1.45E-18
CD83	chr6:14117872:14137149:+1	MALY-DE (44)	3	2.24E-05	2.31E-08
S1PR2	chr19:10334520:10341948:-1	MALY-DE (44)	4	1.16E-03	9.36E-08
BIRC3	chr11:102188215:102210134:+1	MALY-DE (44)	4	3.55E-04	2.05E-08
DNMT1	chr19:10244021:10341962:-1	MALY-DE (44)	3	3.69E-01	4.38E-01
RBM5	chr3:50126341:50156454:+1	Melanoma (25)	7	1.77E-09	1.53E-13
MEAF6	chr1:37958176:37980375:-1	Melanoma (25)	3	4.43E-03	1.07E-02
RNF223	chr1:1006346:1009687:-1	Melanoma (25)	6	3.82E-06	3.43E-06
CCS	chr11:66360292:66373490:+1	Melanoma (25)	4	1.68E-03	1.90E-04
KLHDC7A	chr1:18807424:18812478:-1	LUAD (32)	3	5.80E-05	2.21E-06
NOTCH2	chr1:120454176:120612240:-1	LUAD (32)	5	3.79E-05	4.18E-08
ATP2B4	chr1:203595689:203713209:1	LUAD (32)	3	4.52E-05	1.93E-05
FANK1	chr10:127585108:127698161:-1	LUAD (32)	8	4.44E-13	1.88E-20
PWWP2B	chr10:134210672:134231367:1	LUAD (32)	15	4.71E-24	6.28E-32
MAP4K2	chr11:64556290:64570713:-1	LUAD (32)	15	9.42E-03	8.52E-02
DEFB108B	chr11:71544246:71548756:1	LUAD (32)	4	4.28E-03	2.95E-02
ZNF10	chr12:133707161:133736051:1	LUAD (32)	4	4.06E-04	1.51E-06
SERPINA12	chr14:94953611:94984181:-1	LUAD (32)	5	4.98E-06	3.68E-09
HBZ	chr16:202686:204502:1	LUAD (32)	5	4.98E-06	3.99E-08
HBM	chr16:203891:216767:1	LUAD (32)	5	3.03E-06	2.00E-08
TPSG1	chr16:1271651:1275257:-1	LUAD (32)	4	4.06E-04	1.20E-09
ARHGAP17	chr16:24930706:25026987:-1	LUAD (32)	3	2.25E-05	9.16E-08
COX6A2	chr16:31439052:31439967:-1	LUAD (32)	5	1.93E-13	1.47E-16
WWOX	chr16:78133310:79246564:1	LUAD (32)	4	5.88E-06	5.03E-07
ZNF469	chr16:88493879:88507165:1	LUAD (32)	7	3.75E-10	2.80E-11
SLFN12	chr17:33738079:33760302:-1	LUAD (32)	4	4.54E-03	6.91E-04
KRTAP9-8	chr17:39394297:39395256:1	LUAD (32)	3	4.29E-09	6.01E-09
SSTR2	chr17:71161151:71167185:1	LUAD (32)	9	5.01E-10	3.67E-11
MUM1	chr19:1285890:1378430:1	LUAD (32)	3	3.98E-04	9.35E-05
EFNA2	chr19:1286153:1301430:1	LUAD (32)	3	2.82E-04	6.92E-05
OR7G3	chr19:9236688:9237626:-1	LUAD (32)	3	8.67E-05	2.66E-09
RGL3	chr19:11495017:11530018:-1	LUAD (32)	3	3.09E-05	2.20E-07
FUT1	chr19:49251268:49258647:-1	LUAD (32)	4	2.03E-02	3.07E-03
TD-314810	chr19:49966009:49989488:1	LUAD (32)	7	1.11E-04	1.58E-08
IL1RL1	chr2:102927962:102968497:1	LUAD (32)	3	1.70E-04	8.76E-06
IL18R1	chr2:102927989:103015218:1	LUAD (32)	3	1.60E-04	8.23E-06
ANKRD30BL	chr2:132905164:133015542:-1	LUAD (32)	6	2.44E-07	2.01E-11
GATA5	chr20:61038553:61051026:-1	LUAD (32)	6	5.51E-02	1.01E-01
TNFRSF6B	chr20:62328021:62330037:1	LUAD (32)	7	4.44E-13	4.22E-18
B3GALT5	chr21:40928369:41045064:1	LUAD (32)	4	9.95E-04	1.00E-03
ALG12	chr22:50293877:50312106:-1	LUAD (32)	4	3.36E-07	3.68E-09
CRELD2	chr22:50311815:50321188:1	LUAD (32)	4	3.99E-04	6.13E-05
HYAL3	chr3:50330262:50336899:-1	LUAD (32)	3	1.63E-03	1.00E-04
NAT6	chr3:50333833:50336852:-1	LUAD (32)	3	1.47E-03	9.11E-05
ARF4	chr3:57557090:57583947:-1	LUAD (32)	3	1.74E-02	3.03E-04
LINC00955	chr4:3578596:3592438:1	LUAD (32)	9	6.65E-05	9.06E-08
TD-2228K2	chr5:466239:473213:-1	LUAD (32)	6	2.89E-06	1.37E-09
HLA-DRB5	chr6:32485120:32498064:-1	LUAD (32)	12	1.34E-24	1.29E-35
HLA-DPA1	chr6:33032346:33048552:-1	LUAD (32)	5	1.19E-08	6.79E-11
C6orf222	chr6:36283534:36304662:-1	LUAD (32)	3	3.22E-03	2.54E-04
SUMF2	chr7:56131695:56148363:1	LUAD (32)	4	2.14E-05	6.24E-08
ANGPT2	chr8:6357172:6420930:-1	LUAD (32)	4	5.52E-03	3.40E-02
TMEM55A	chr8:92006024:92053292:-1	LUAD (32)	3	8.24E-04	5.76E-05
C9orf170	chr9:89763559:89774471:1	LUAD (32)	3	2.56E-04	1.61E-06
RABL6	chr9:139702374:139735639:1	LUAD (32)	3	2.60E-05	1.71E-06
CCDC168	chr13:103381801:103389159:-1	COAD-US (19)	4	1.34E-07	8.50E-11
CCDC168	chr13:103381801:103389159:-1	UCEC-US (131)	4	1.64E-08	6.33E-19

Supplementary Table 3: Table showing FDR adjusted p-values for signatures of accelerated evolution when only highly conserved base positions were considered (GERP score <5, <3, and <1). Our analysis shows that significant cases of SASE were not due to accumulation of excess of mutations at lowly conserved base positions, and those remain statistically significant even when only high conserved base positions were considered.

Genes	Position	Cohort (total samples)	# samples with significant SASE	FDR adjusted p-value		
				GERP score < 5	GERP score < 3	GERP score < 1
IGLL5	chr22:23229960:23238287:+1	MALY-DE (44)	8	4.25E-11	4.12E-11	4.20E-12
BTG2	chr1:203274619:203278730:+1	MALY-DE (44)	4	8.75E-10	1.56E-09	7.15E-09
BCL2	chr18:60790579:60987361:-1	MALY-DE (44)	5	2.80E-04	3.95E-04	2.12E-04
CD83	chr6:14117872:14137149:+1	MALY-DE (44)	3	1.07E-03	4.78E-03	5.29E-03
BCL6	chr3:187439165:187463515:-1	MALY-DE (44)	10	7.40E-10	2.98E-09	6.20E-04
TCL1A	chr14:96176304:96180533:-1	MALY-DE (44)	4	7.88E-05	7.81E-05	6.26E-05
DNMT1	chr19:10244021:10341962:-1	MALY-DE (44)	3	1.06E-02	9.42E-03	8.39E-03
MYC	chr8:128747680:128753674:+1	MALY-DE (44)	3	1.37E-04	1.32E-04	1.12E-04
S1PR2	chr19:10334520:10341948:-1	MALY-DE (44)	4	1.60E-03	8.20E-04	1.12E-04
BIRC3	chr11:102188215:102210134:+1	MALY-DE (44)	4	5.30E-03	5.01E-03	3.62E-03
RNF223	chr1:1006346:1009687:-1	Melanoma (25)	6	4.98E-04	5.04E-04	5.16E-04
MEAF6	chr1:37958176:37980375:-1	Melanoma (25)	3	1.58E-04	1.72E-04	2.85E-04
CCS	chr11:66360292:66373490:+1	Melanoma (25)	4	8.45E-03	8.64E-03	1.18E-02
RBM5	chr3:50126341:50156454:+1	Melanoma (25)	7	3.11E-07	3.19E-07	6.27E-07
KLHDC7A	chr1:18807424-18812478:1	LUAD (32)	3	1.94E-03	1.95E-03	2.10E-03
NOTCH2	chr1:120454176-120612240:-1	LUAD (32)	5	1.53E-02	1.72E-02	3.73E-02
ATP2B4	chr1:203595689-203713209:1	LUAD (32)	3	6.32E-04	6.22E-04	2.47E-04
FANK1	chr10:127585108-127698161:1	LUAD (32)	8	1.60E-09	1.64E-09	1.70E-06
PWWP2B	chr10:134210672-134231367:1	LUAD (32)	15	2.20E-13	2.23E-13	7.17E-14
MAP4K2	chr11:64556290-64570713:-1	LUAD (32)	3	6.89E-03	6.64E-03	2.28E-03
DEFB108B	chr11:71544246-71548756:1	LUAD (32)	4	4.38E-03	4.34E-03	3.13E-03
ZNF10	chr12:133707161-133736051:1	LUAD (32)	4	9.74E-03	9.89E-03	1.00E-02
SERPINA12	chr14:94953611-94984181:-1	LUAD (32)	5	1.10E-04	1.10E-04	1.19E-04
HBZ	chr16:202686-204502:1	LUAD (32)	5	1.64E-04	1.63E-04	1.73E-04
HBM	chr16:203891-216767:1	LUAD (32)	5	1.10E-04	1.10E-04	1.17E-04
TPSG1	chr16:1271651-1275257:-1	LUAD (32)	4	3.37E-02	3.08E-02	2.22E-02
ARHGAP17	chr16:24930706-25026987:-1	LUAD (32)	3	6.32E-04	6.22E-04	5.99E-04
COX6A2	chr16:31439052-31439967:-1	LUAD (32)	5	1.69E-11	1.60E-11	6.17E-12
WWOX	chr16:78133310-79246564:1	LUAD (32)	4	7.28E-04	7.30E-04	7.22E-04
ZNF469	chr16:88493879-88507165:1	LUAD (32)	7	2.21E-05	2.27E-05	2.14E-05
SLFN12	chr17:33738079-33760302:-1	LUAD (32)	4	1.27E-04	1.26E-04	1.23E-04
KRTAP9-8	chr17:39394297-39395256:1	LUAD (32)	3	2.56E-06	2.54E-06	2.21E-06
SSTR2	chr17:71161151-71167185:1	LUAD (32)	9	1.22E-05	9.77E-06	4.61E-06
MUM1	chr19:1285890-1378430:1	LUAD (32)	3	4.13E-03	4.16E-03	3.65E-03
EFNA2	chr19:1286153-1301430:1	LUAD (32)	3	3.14E-03	3.20E-03	2.77E-03
OR7G3	chr19:9236688-9237626:-1	LUAD (32)	3	5.79E-04	5.73E-04	4.36E-04
RGL3	chr19:11495017-11530018:-1	LUAD (32)	3	7.54E-04	7.38E-04	2.55E-03
FUT1	chr19:49251268-49258647:-1	LUAD (32)	4	3.19E-02	3.17E-02	2.36E-02
CTD-3148110.5	chr19:49966009-49989488:1	LUAD (32)	7	2.94E-03	3.20E-03	2.86E-03
IL1RL1	chr2:102927962-102968497:1	LUAD (32)	3	8.07E-04	7.89E-04	7.22E-04
IL18R1	chr2:102927989-103015218:1	LUAD (32)	3	7.54E-04	7.38E-04	7.03E-04
ANKRD30BL	chr2:132905164-133015542:-1	LUAD (32)	6	7.64E-05	7.56E-05	7.15E-05
GATA5	chr20:61038553-61051026:-1	LUAD (32)	3	6.20E-04	6.04E-04	5.12E-04
TNFRSF6B	chr20:62328021-62330037:1	LUAD (32)	7	4.94E-09	3.98E-09	3.58E-09
B3GALT5	chr21:40928369-41045064:1	LUAD (32)	4	2.08E-02	2.13E-02	1.75E-02
ALG12	chr22:50293877-50312106:-1	LUAD (32)	4	3.13E-05	2.91E-05	2.87E-05
CRELD2	chr22:50311815-50321188:1	LUAD (32)	4	3.79E-02	3.79E-02	3.73E-02
HYAL3	chr3:50330262-50336899:-1	LUAD (32)	3	1.31E-02	1.25E-02	9.66E-02
NAT6	chr3:50333833-50336852:-1	LUAD (32)	3	1.25E-02	1.17E-02	9.19E-03
ARF4	chr3:57557090-57583947:-1	LUAD (32)	3	3.71E-02	3.65E-02	3.30E-02
LINC00955	chr4:3578596-3592438:1	LUAD (32)	9	5.64E-13	5.59E-13	2.94E-13
CTD-2228K2.5	chr5:466239-473213:-1	LUAD (32)	6	9.74E-03	9.55E-03	9.32E-03
HLA-DRB5	chr6:32485120-32498064:-1	LUAD (32)	12	3.37E-12	3.10E-12	6.10E-12
HLA-DPA1	chr6:33032346-33048552:-1	LUAD (32)	5	5.33E-05	5.29E-05	4.35E-05
C6orf222	chr6:36283534-36304662:-1	LUAD (32)	3	3.37E-02	3.43E-02	3.30E-02
SUMF2	chr7:56131695-56148363:1	LUAD (32)	4	2.79E-03	2.77E-03	2.28E-03
ANGPT2	chr8:6357172-6420930:-1	LUAD (32)	4	3.37E-02	3.34E-02	3.47E-02
TMEM55A	chr8:92006024-92053292:-1	LUAD (32)	3	1.54E-02	1.50E-02	1.03E-02
C9orf170	chr9:89763559-89774471:1	LUAD (32)	3	3.72E-03	3.51E-03	2.55E-03
RABL6	chr9:139702374-139735639:1	LUAD (32)	3	6.32E-04	6.22E-04	5.27E-04
CCDC168	chr13:103381801:103389159:-1	COAD-US (19)	4	2.11E-05	2.14E-05	1.56E-05
CCDC168	chr13:103381801:103389159:-1	UCEC-US (131)	4	1.24E-08	8.47E-09	9.34E-08

Supplementary Table 4: Table showing FDR adjusted p-values for signatures of accelerated evolution when all the samples in a cohort were pooled. This analysis includes all the samples including those that were deemed 'significant' and also those deemed 'not significant' in the cohort in the original analysis.

Genes	Position	Cohort (total samples)	FDR pvalue
BCL6	chr3:187439165:187463515:-1	MALY-DE (44)	1.41E-15
IGLL5	chr22:23229960:23238287:+1	MALY-DE (44)	1.30E-13
BTG2	chr1:203274619:203278730:+1	MALY-DE (44)	5.97E-13
TCL1A	chr14:96176304:96180533:-1	MALY-DE (44)	1.09E-09
BCL2	chr18:60790579:60987361:-1	MALY-DE (44)	4.78E-07
BIRC3	chr11:102188215:102210134:+1	MALY-DE (44)	1.60E-06
MYC	chr8:128747680:128753674:+1	MALY-DE (44)	2.03E-06
S1PR2	chr19:10334520:10341948:-1	MALY-DE (44)	3.26E-06
CD83	chr6:14117872:14137149:+1	MALY-DE (44)	4.04E-05
DNMT1	chr19:10244021:10341962:-1	MALY-DE (44)	5.88E-03
RBM5	chr3:50126341:50156454:+1	Melanoma (25)	9.88E-18
RNF223	chr1:1006346:1009687:-1	Melanoma (25)	1.71E-07
CCS	chr11:66360292:66373490:+1	Melanoma (25)	1.45E-06
MEAF6	chr1:37958176:37980375:-1	Melanoma (25)	7.31E-04
KLHDC7A	chr1:18807424:18812478:1	LUAD (32)	4.63E-05
NOTCH2	chr1:120454176:120612240:-1	LUAD (32)	3.10E-11
ATP2B4	chr1:203595689:203713209:1	LUAD (32)	1.08E-06
FANK1	chr10:127585108:127698161:1	LUAD (32)	3.34E-21
PWWP2B	chr10:134210672:134231367:1	LUAD (32)	5.45E-28
MAP4K2	chr11:64556290:64570713:-1	LUAD (32)	7.05E-04
DEFB108B	chr11:71544246:71548756:1	LUAD (32)	2.46E-07
ZNF10	chr12:133707161:133736051:1	LUAD (32)	3.59E-07
SERPINA12	chr14:94953611:94984181:-1	LUAD (32)	5.09E-14
HBZ	chr16:202686:204502:1	LUAD (32)	6.27E-09
HBM	chr16:203891:216767:1	LUAD (32)	1.05E-08
TPSG1	chr16:1271651:1275257:-1	LUAD (32)	2.37E-06
ARHGAP17	chr16:24930706:25026987:-1	LUAD (32)	1.41E-10
COX6A2	chr16:31439052:31439967:-1	LUAD (32)	1.36E-15
WWOX	chr16:78133310:79246564:1	LUAD (32)	6.29E-07
ZNF469	chr16:88493879:88507165:1	LUAD (32)	2.81E-15
SLFN12	chr17:33738079:33760302:-1	LUAD (32)	6.28E-11
KRTAP9-8	chr17:39394297:39395256:1	LUAD (32)	1.25E-10
SSTR2	chr17:71161151:71167185:1	LUAD (32)	2.97E-13
MUM1	chr19:1285890:1378430:1	LUAD (32)	1.91E-08
EFNA2	chr19:1286153:1301430:1	LUAD (32)	1.00E-08
OR7G3	chr19:9236688:9237626:-1	LUAD (32)	7.88E-06
RGL3	chr19:11495017:11530018:-1	LUAD (32)	5.78E-10
FUT1	chr19:49251268:49258647:-1	LUAD (32)	3.35E-04
CTD-3148I10.9	chr19:49966009:49989488:1	LUAD (32)	1.15E-10
IL1RL1	chr2:102927962:102968497:1	LUAD (32)	1.30E-07
IL18R1	chr2:102927989:103015218:1	LUAD (32)	1.19E-07
ANKRD30BL	chr2:132905164:133015542:-1	LUAD (32)	3.37E-12
GATA5	chr20:61038553:61051026:-1	LUAD (32)	6.91E-05
TNFRSF6B	chr20:62328021:62330037:1	LUAD (32)	3.78E-14
B3GALT5	chr21:40928369:41045064:1	LUAD (32)	1.22E-06
ALG12	chr22:50293877:50312106:-1	LUAD (32)	1.30E-13
CRELD2	chr22:50311815:50321188:1	LUAD (32)	8.08E-07
HYAL3	chr3:50330262:50336899:-1	LUAD (32)	1.00E-11
NAT6	chr3:50333833:50336852:-1	LUAD (32)	8.56E-12
ARF4	chr3:57557090:57583947:-1	LUAD (32)	3.34E-04
LINC00955	chr4:3578596:3592438:1	LUAD (32)	1.18E-18
CTD-2228K2.5	chr5:466239:473213:-1	LUAD (32)	3.20E-08
HLA-DRB5	chr6:32485120:32498064:-1	LUAD (32)	2.81E-15
HLA-DPA1	chr6:33032346:33048552:-1	LUAD (32)	1.25E-07
C6orf222	chr6:36283534:36304662:-1	LUAD (32)	8.51E-06
SUMF2	chr7:56131695:56148363:1	LUAD (32)	5.45E-06
ANGPT2	chr8:6357172:6420930:-1	LUAD (32)	7.75E-05
TMEM55A	chr8:92006024:92053292:-1	LUAD (32)	6.19E-09
C9orf170	chr9:89763559:89774471:1	LUAD (32)	1.77E-05
RABL6	chr9:139702374:139735639:1	LUAD (32)	8.34E-11
CCDC168	chr13:103381801:103389159:-1	COAD-US (19)	8.90E-07
CCDC168	chr13:103381801:103389159:-1	UCEC-US (131)	2.20E-13

Supplementary Table 5: Table showing FDR adjusted p-values for signatures of accelerated evolution when all the alternative transcripts were included. When a gene has multiple transcripts with significant SASE in the promoters, only the most significant one is shown below.

Genes	Position	Cohort (total samples)	# samples with significant SASE	FDR p-value
IGLL5	chr22:23229960-23238287:1	MALY-DE (44)	10	9.88E-17
RHOH	chr4:40192673-40248587:1	MALY-DE (44)	6	5.71E-14
BCL2	chr18:60790579-60987361:-1	MALY-DE (44)	11	1.05E-13
BCL6	chr3:187439165-187463515:-1	MALY-DE (44)	10	2.14E-11
BTG2	chr1:203274619-203278730:1	MALY-DE (44)	4	1.62E-09
BCL2L11	chr2:111876955-111926024:1	MALY-DE (44)	4	5.33E-08
TCL1A	chr14:96176304-96180533:-1	MALY-DE (44)	5	1.25E-06
MYC	chr8:128747680-128753674:1	MALY-DE (44)	3	1.26E-04
CD83	chr6:14117872-14137149:1	MALY-DE (44)	3	1.14E-03
DNMT1	chr19:10244021-10341962:-1	MALY-DE (44)	4	1.82E-03
S1PR2	chr19:10334520-10341948	MALY-DE (44)	4	1.82E-03
CIITA	chr16:10971055-11026079:1	MALY-DE (44)	3	2.34E-03
BIRC3	chr11:102188215-102210134:1	MALY-DE (44)	4	6.24E-03
CCDC168	chr13:103381801-103389159:-1	COAD-US (19)	4	8.81E-04
CCDC168	chr13:103381801-103389159:-1	UCEC-US (131)	4	1.23E-07
F7	chr13:113760105-113774995:1	Melanoma (25)	8	8.70E-10
FAM210A	chr18:13663346-13726662:-1	Melanoma (25)	14	3.47E-09
PXMP2	chr12:133264192-133297276:1	Melanoma (25)	4	1.74E-07
RBM5	chr3:50126341-50156454:1	Melanoma (25)	7	1.74E-07
ERICH1	chr8:564746-688106:-1	Melanoma (25)	8	1.37E-05
CCDC146	chr7:76751751-76958850:1	Melanoma (25)	5	2.71E-05
MEAF6	chr1:37958176-37980375:-1	Melanoma (25)	3	1.57E-04
FRG1	chr4:190861943-190884359:1	Melanoma (25)	8	2.44E-04
RNF223	chr1:1006346-1009687:-1	Melanoma (25)	6	5.77E-04
ABR	chr17:906758-1132315:-1	Melanoma (25)	3	1.76E-03
GPR176	chr15:40091233-40213093:-1	Melanoma (25)	6	3.96E-03
SCFD1	chr14:31091318-31205018:1	Melanoma (25)	5	9.19E-03
CCS	chr11:66360292-66373490:1	Melanoma (25)	4	1.14E-02
SMAP1	chr6:71377479-71571718:1	Melanoma (25)	4	1.31E-02
POM121C	chr7:75046066-75115548:-1	Melanoma (25)	4	1.44E-02
PLEKHG4B	chr5:140373-190085:1	Melanoma (25)	8	1.73E-02
CCDC65	chr12:49297893-49325623:1	Melanoma (25)	3	3.78E-02
NCAPD3	chr11:134020014-134095348:-1	Melanoma (25)	5	3.85E-02
OSBPL8	chr12:76745577-76953589:-1	Melanoma (25)	5	4.02E-02
RNASE10	chr14:20973696-20979328:1	Melanoma (25)	4	4.95E-02
MTA1	chr14:105886159-105937066:1	Melanoma (25)	3	4.95E-02
AGRN	chr1:955503-991496:1	LUAD (32)	3	1.58E-02
PRAMEF1	chr1:12851546-12856777:1	LUAD (32)	12	2.71E-15
NBPF1	chr1:16888814-16940057:-1	LUAD (32)	8	1.44E-02
KLHDC7A	chr1:18807424-18812478:1	LUAD (32)	3	1.90E-03
INPP5B	chr1:38326369-38412729:-1	LUAD (32)	3	1.14E-02
PLK3	chr1:45265897-45271662:1	LUAD (32)	3	8.74E-03
GBP1	chr1:89518002-89531043:-1	LUAD (32)	3	3.05E-03
NOTCH2	chr1:120454176-120612240:-1	LUAD (32)	5	1.37E-02
PDE4DIP	chr1:144836157-145076186:-1	LUAD (32)	5	4.35E-03
FCGR2A	chr1:161475220-161493803:1	LUAD (32)	6	1.88E-03
ATP2B4	chr1:203595689-203713209:1	LUAD (32)	3	7.41E-04
BTRC	chr10:103113820-103317078:1	LUAD (32)	3	1.25E-02
TRIM8	chr10:104404253-104418164:1	LUAD (32)	3	9.40E-04

DHX32	chr10:127524906-127585005:-1	LUAD (32)	8	6.60E-09
FANK1	chr10:127585108-127698161:1	LUAD (32)	8	2.09E-09
PWWP2B	chr10:134210672-134231367:1	LUAD (32)	15	1.54E-13
TUBGCP2	chr10:135093135-135125841:-1	LUAD (32)	8	5.30E-10
BRSK2	chr11:1411129-1483919:1	LUAD (32)	5	2.12E-02
TCP11L1	chr11:33060963-33127489:1	LUAD (32)	4	2.32E-02
ACCS	chr11:44087475-44105772:1	LUAD (32)	7	5.86E-07
NXF1	chr11:62559595-62573774:-1	LUAD (32)	3	2.78E-02
MAP4K2	chr11:64556290-64570713:-1	LUAD (32)	3	8.75E-04
CDC42BPG	chr11:64590859-64612041:-1	LUAD (32)	3	4.85E-02
DEFB108B	chr11:71544246-71548756:1	LUAD (32)	4	6.18E-05
GDPD5	chr11:75145685-75236948:-1	LUAD (32)	4	4.48E-05
CWF19L2	chr11:107197071-107328572:-1	LUAD (32)	5	2.53E-08
NXPE1	chr11:114392437-114430617:-1	LUAD (32)	7	5.72E-11
ITFG2	chr12:2921788-2968957:1	LUAD (32)	4	2.41E-02
A2ML1	chr12:8975068-9039597:1	LUAD (32)	5	5.77E-04
PRR4	chr12:10977559-11324212:-1	LUAD (32)	6	3.41E-07
DDX11	chr12:31226779-31257725:1	LUAD (32)	6	4.36E-04
TMBIM6	chr12:50101508-50158717:1	LUAD (32)	3	3.26E-02
SLC11A2	chr12:51373184-51422349:-1	LUAD (32)	3	2.40E-04
TBK1	chr12:64845660-64895888:1	LUAD (32)	3	1.53E-02
HSP90B1	chr12:104323885-104347423:1	LUAD (32)	3	2.24E-02
TDG	chr12:104359582-104382652:1	LUAD (32)	6	7.36E-09
ULK1	chr12:132379196-132407712:1	LUAD (32)	8	1.32E-12
ZNF891	chr12:133694740-133707059:-1	LUAD (32)	4	2.06E-03
ZNF10	chr12:133707161-133736051:1	LUAD (32)	4	8.86E-03
FARP1	chr13:98794816-99102027:1	LUAD (32)	4	4.39E-02
GAS6	chr13:114523522-114567046:-1	LUAD (32)	4	1.63E-02
GEMIN2	chr14:39583427-39606177:1	LUAD (32)	5	1.44E-02
PPP1R36	chr14:65016620-65056098:1	LUAD (32)	4	3.05E-03
PLEKHH1	chr14:68000018-68056329:1	LUAD (32)	4	1.41E-02
RGS6	chr14:72399156-73030654:1	LUAD (32)	3	2.61E-02
DPF3	chr14:73086004-73360809:-1	LUAD (32)	3	5.00E-02
CCDC88C	chr14:91737667-91884188:-1	LUAD (32)	4	1.96E-03
SERPINA12	chr14:94953611-94984181:-1	LUAD (32)	5	1.21E-04
EVL	chr14:100437786-100610573:1	LUAD (32)	4	2.72E-06
TNFAIP2	chr14:103589779-103603776:1	LUAD (32)	3	2.64E-02
MARK3	chr14:103851729-103970168:1	LUAD (32)	3	3.76E-02
JAG2	chr14:105607318-105635161:-1	LUAD (32)	8	2.09E-06
HERC2	chr15:28356186-28567298:-1	LUAD (32)	11	7.97E-17
PLCB2	chr15:40570377-40600136:-1	LUAD (32)	6	1.99E-03
HDC	chr15:50534144-50558223:-1	LUAD (32)	4	5.69E-03
GOLGA6A	chr15:74362198-74374891:-1	LUAD (32)	5	7.89E-05
CHRNB4	chr15:78916461-79020096:-1	LUAD (32)	4	1.10E-02
KIF7	chr15:90152020-90198682:-1	LUAD (32)	4	1.67E-03
VPS33B	chr15:91541646-91565833:-1	LUAD (32)	3	4.85E-02
HBZ	chr16:202686-204502:1	LUAD (32)	5	1.89E-04
HBM	chr16:203891-216767:1	LUAD (32)	5	1.21E-04
TMEM8A	chr16:420773-437113:-1	LUAD (32)	3	1.18E-02
DECR2	chr16:451826-462487:1	LUAD (32)	3	2.12E-02
CAPN15	chr16:577717-604636:1	LUAD (32)	21	2.84E-58
TPSG1	chr16:1271651-1275257:-1	LUAD (32)	4	2.77E-02
BAIAP3	chr16:1383602-1399439:1	LUAD (32)	4	1.27E-02
IL32	chr16:3115298-3131908:1	LUAD (32)	4	3.09E-02
NPIPA1	chr16:15016659-15045915:1	LUAD (32)	6	8.08E-04
RRN3	chr16:15153879-15188174:-1	LUAD (32)	3	2.00E-06
ARHGAP17	chr16:24930706-25026987:-1	LUAD (32)	3	3.21E-04
COX6A2	chr16:31439052-31439967:-1	LUAD (32)	5	2.74E-11
EDC4	chr16:67906926-67918406:1	LUAD (32)	3	2.45E-03

CALB2	chr16:71392616-71424341:1	LUAD (32)	24	2.43E-55
WVVOX	chr16:78133310-79246564:1	LUAD (32)	4	6.45E-04
PLCG2	chr16:81772702-81991899:1	LUAD (32)	3	1.59E-02
ZNF469	chr16:88493879-88507165:1	LUAD (32)	7	1.81E-05
CTU2	chr16:88772871-88781794:1	LUAD (32)	5	2.56E-02
MYO1C	chr17:1367392-1396106:-1	LUAD (32)	3	2.44E-03
TP53	chr17:7565097-7590856:-1	LUAD (32)	8	1.65E-12
PER1	chr17:8043790-8059824:-1	LUAD (32)	6	6.71E-08
FBXW10	chr17:18647326-18682662:1	LUAD (32)	5	3.90E-02
LRRC37B	chr17:30334891-30380523:1	LUAD (32)	3	6.02E-04
SLFN12	chr17:33738079-33760302:-1	LUAD (32)	4	1.45E-04
KRTAP9-8	chr17:39394297-39395256:1	LUAD (32)	3	2.00E-06
BRCA1	chr17:41196312-41277500:-1	LUAD (32)	4	2.99E-04
SLC25A39	chr17:42396993-42402238:-1	LUAD (32)	3	1.28E-03
ITGA2B	chr17:42449548-42466873:-1	LUAD (32)	3	7.96E-03
ADAM11	chr17:42836399-42859214:1	LUAD (32)	3	2.17E-04
ITGB3	chr17:45331212-45421658:1	LUAD (32)	4	2.45E-03
ITGB3	chr17:45331263-45421658:1	LUAD (32)	4	2.45E-03
CACNA1G	chr17:48638429-48704835:1	LUAD (32)	3	2.50E-02
SSTR2	chr17:71161151-71167185:1	LUAD (32)	9	9.34E-06
9-Sep	chr17:75276651-75496678:1	LUAD (32)	4	3.20E-03
TMC6	chr17:76106539-76128488:-1	LUAD (32)	4	4.85E-02
SLC38A10	chr17:79218800-79269347:-1	LUAD (32)	3	8.90E-03
FSCN2	chr17:79495422-79504156:1	LUAD (32)	4	1.04E-02
FN3KRP	chr17:80674559-80688204:1	LUAD (32)	7	2.06E-07
PQLC1	chr18:77662420-77711664:-1	LUAD (32)	4	1.01E-04
PALM	chr19:708953-748329:1	LUAD (32)	4	4.31E-04
MUM1	chr19:1285890-1378430:1	LUAD (32)	3	4.05E-03
EFNA2	chr19:1286153-1301430:1	LUAD (32)	3	3.06E-03
UBXN6	chr19:4444996-4457819:-1	LUAD (32)	3	3.26E-05
OR7G3	chr19:9236688-9237626:-1	LUAD (32)	3	6.11E-04
RGL3	chr19:11495017-11530018:-1	LUAD (32)	3	8.77E-04
DDX39A	chr19:14519631-14530192:-1	LUAD (32)	3	8.74E-03
SUPT5H	chr19:39926796-39967310:1	LUAD (32)	3	2.66E-02
GLTSCR1	chr19:48111453-48206533:1	LUAD (32)	4	2.38E-02
GRWD1	chr19:48949030-48960279:1	LUAD (32)	4	4.36E-04
FUT1	chr19:49251268-49258647:-1	LUAD (32)	4	1.53E-02
FGF21	chr19:49258816-49261587:1	LUAD (32)	3	3.64E-02
RUVBL2	chr19:49496705-49519252:1	LUAD (32)	3	5.75E-03
ALDH16A1	chr19:49956426-49974305:1	LUAD (32)	8	6.21E-06
CTD-314810.1	chr19:49966009-49989488:1	LUAD (32)	7	2.91E-03
SYT3	chr19:51124564-51171651:-1	LUAD (32)	6	9.48E-04
PXDN	chr2:1635659-1748624:-1	LUAD (32)	3	3.06E-02
CAD	chr2:27440258-27466811:1	LUAD (32)	5	3.66E-02
RASGRP3	chr2:33661391-33789817:1	LUAD (32)	3	3.31E-02
ANKRD36C	chr2:96514587-96657541:-1	LUAD (32)	6	9.41E-05
IL1RL1	chr2:102927962-102968497:1	LUAD (32)	3	8.32E-04
IL18R1	chr2:102927989-103015218:1	LUAD (32)	3	8.77E-04
ANKRD30BL	chr2:132905164-133015542:-1	LUAD (32)	6	7.73E-05
TANC1	chr2:159825146-160089170:1	LUAD (32)	3	7.41E-04
MFSO6	chr2:191273081-191373931:1	LUAD (32)	4	2.94E-02
C2orf80	chr2:209030067-209054797:-1	LUAD (32)	3	3.67E-02
KIF1A	chr2:241653181-241759725:-1	LUAD (32)	3	3.24E-03
TSHZ2	chr20:51588946-52111869:1	LUAD (32)	3	4.31E-04
GATA5	chr20:61038553-61051026:-1	LUAD (32)	3	6.78E-04
BIRC7	chr20:61867235-61871859:1	LUAD (32)	5	9.40E-04
TNFRSF6B	chr20:62328021-62330037:1	LUAD (32)	7	5.22E-09
ZNF512B	chr20:62588055-62680113:-1	LUAD (32)	4	1.12E-03
B3GALT5	chr21:40928369-41045064:1	LUAD (32)	4	1.81E-02

PRDM15	chr21:43218385-43299591:-1	LUAD (32)	6	1.85E-04
CARD10	chr22:37886400-37915549:-1	LUAD (32)	5	1.88E-03
CELSR1	chr22:46756731-46933067:-1	LUAD (32)	4	2.79E-02
ALG12	chr22:50293877-50312106:-1	LUAD (32)	4	2.81E-05
CRELD2	chr22:50311815-50321188:1	LUAD (32)	4	1.49E-06
NCAPH2	chr22:50946645-50961901:1	LUAD (32)	3	7.41E-04
FANCD2	chr3:10068098-10143614:1	LUAD (32)	5	1.08E-03
HYAL3	chr3:50330262-50336899:-1	LUAD (32)	3	7.50E-03
NAT6	chr3:50333833-50336852:-1	LUAD (32)	3	8.94E-03
CACNA1D	chr3:53528683-53847760:1	LUAD (32)	3	3.25E-02
ARF4	chr3:57557090-57583947:-1	LUAD (32)	3	2.99E-02
SIDT1	chr3:113251143-113348425:1	LUAD (32)	3	1.04E-02
LINC00955	chr4:3578596-3592438:1	LUAD (32)	9	3.62E-13
WFS1	chr4:6271576-6304992:1	LUAD (32)	3	8.08E-05
RAPGEF2	chr4:160025330-160281321:1	LUAD (32)	6	1.97E-10
CTD-2228K2.5	chr5:466239-473213:-1	LUAD (32)	6	5.78E-03
ADAMTS16	chr5:5140443-5320417:1	LUAD (32)	5	6.55E-03
BRD8	chr5:137475455-137514675:-1	LUAD (32)	4	2.57E-08
UIMC1	chr5:176332006-176449634:-1	LUAD (32)	3	1.15E-04
RASGEF1C	chr5:179527795-179636153:-1	LUAD (32)	5	4.39E-02
FLT4	chr5:180028506-180076624:-1	LUAD (32)	4	4.73E-02
HLA-C	chr6:31236526-31239907:-1	LUAD (32)	11	5.37E-21
HLA-B	chr6:31321649-31324965:-1	LUAD (32)	4	2.00E-06
HLA-DRB5	chr6:32485120-32498064:-1	LUAD (32)	12	4.55E-12
HLA-DQB1	chr6:32627244-32636160:-1	LUAD (32)	9	4.22E-13
HLA-DPA1	chr6:33032346-33048552:-1	LUAD (32)	5	5.11E-05
C6orf222	chr6:36283534-36304662:-1	LUAD (32)	3	2.77E-02
PRIM2	chr6:57179603-57513375:1	LUAD (32)	6	6.55E-03
MTHFD1L	chr6:151186685-151423023:1	LUAD (32)	4	8.29E-09
FRMD1	chr6:168456425-168482237:-1	LUAD (32)	4	2.07E-02
INTS1	chr7:1509913-1545489:-1	LUAD (32)	9	1.17E-05
TMEM106B	chr7:12250867-12282993:1	LUAD (32)	4	3.33E-02
CAMK2B	chr7:44256749-44374176:-1	LUAD (32)	6	2.69E-10
SUMF2	chr7:56131695-56148363:1	LUAD (32)	3	1.75E-03
ZP3	chr7:76026835-76071388:1	LUAD (32)	7	4.42E-04
IMPDH1	chr7:128032331-128050306:-1	LUAD (32)	3	3.33E-02
KMT2C	chr7:151832010-152133090:-1	LUAD (32)	7	4.88E-04
ARHGEF10	chr8:1772142-1906807:1	LUAD (32)	8	3.80E-09
MYOM2	chr8:1993155-2113475:1	LUAD (32)	8	1.63E-02
CSMD1	chr8:2792875-4852494:-1	LUAD (32)	3	4.88E-02
ANGPT2	chr8:6357172-6420930:-1	LUAD (32)	4	2.66E-02
DPYSL2	chr8:26371791-26515694:1	LUAD (32)	4	2.60E-02
HGSNAT	chr8:42995556-43057998:1	LUAD (32)	3	6.32E-03
TMEM55A	chr8:92006024-92053292:-1	LUAD (32)	3	1.44E-02
DPY19L4	chr8:95731931-95806064:1	LUAD (32)	3	6.21E-03
SCRIB	chr8:144873090-144897549:-1	LUAD (32)	4	4.26E-02
AQP7	chr9:33384765-33402643:-1	LUAD (32)	3	1.18E-02
PRSS3	chr9:33750515-33799230:1	LUAD (32)	16	2.54E-81
CNTNAP3B	chr9:43684902-43924049:1	LUAD (32)	6	2.39E-03
C9orf170	chr9:89763559-89774471:1	LUAD (32)	3	3.56E-03
SH3GLB2	chr9:131769315-131790582:-1	LUAD (32)	3	3.45E-04
CCDC183	chr9:139690802-139702193:1	LUAD (32)	3	1.67E-03
RABL6	chr9:139702374-139735639:1	LUAD (32)	3	6.02E-04
ABCA2	chr9:139901686-139923367:-1	LUAD (32)	3	1.81E-02
ENTPD2	chr9:139942550-139948497:-1	LUAD (32)	6	9.67E-05
GTPBP6	chrX:220025-230886:-1	LUAD (32)	3	7.53E-08
NROB1	chrX:30322323-30327715:-1	LUAD (32)	4	4.85E-02
MAMLD1	chrX:149529689-149682448:1	LUAD (32)	5	2.90E-04

Supplementary Table 6: Table showing cancer genes with somatic mutations in promoters and no somatic mutations in corresponding flanking regions in the second lymphoma cohort (Morin et al. Blood. 2013). The genes that had somatic mutations in the promoter of the major transcript are shown with asterisk.

gene	cohort	n_samples (40)	Major transcript
NCAPD3	melanoma	7	
MTA1	melanoma	6	
OSBPL8	melanoma	5	
FAM210A	melanoma	3	
ABR	melanoma	2	
ERICH1	melanoma	2	
CCDC168	AD-US, UCEC	1	*
BCL2	MALY-DE	1	*
CD83	MALY-DE	1	*
DNMT1	MALY-DE	1	
RHOH	MALY-DE	1	
TCL1A	MALY-DE	1	*
CCDC146	melanoma	1	
CCS	melanoma	1	*
SMAP1	melanoma	1	