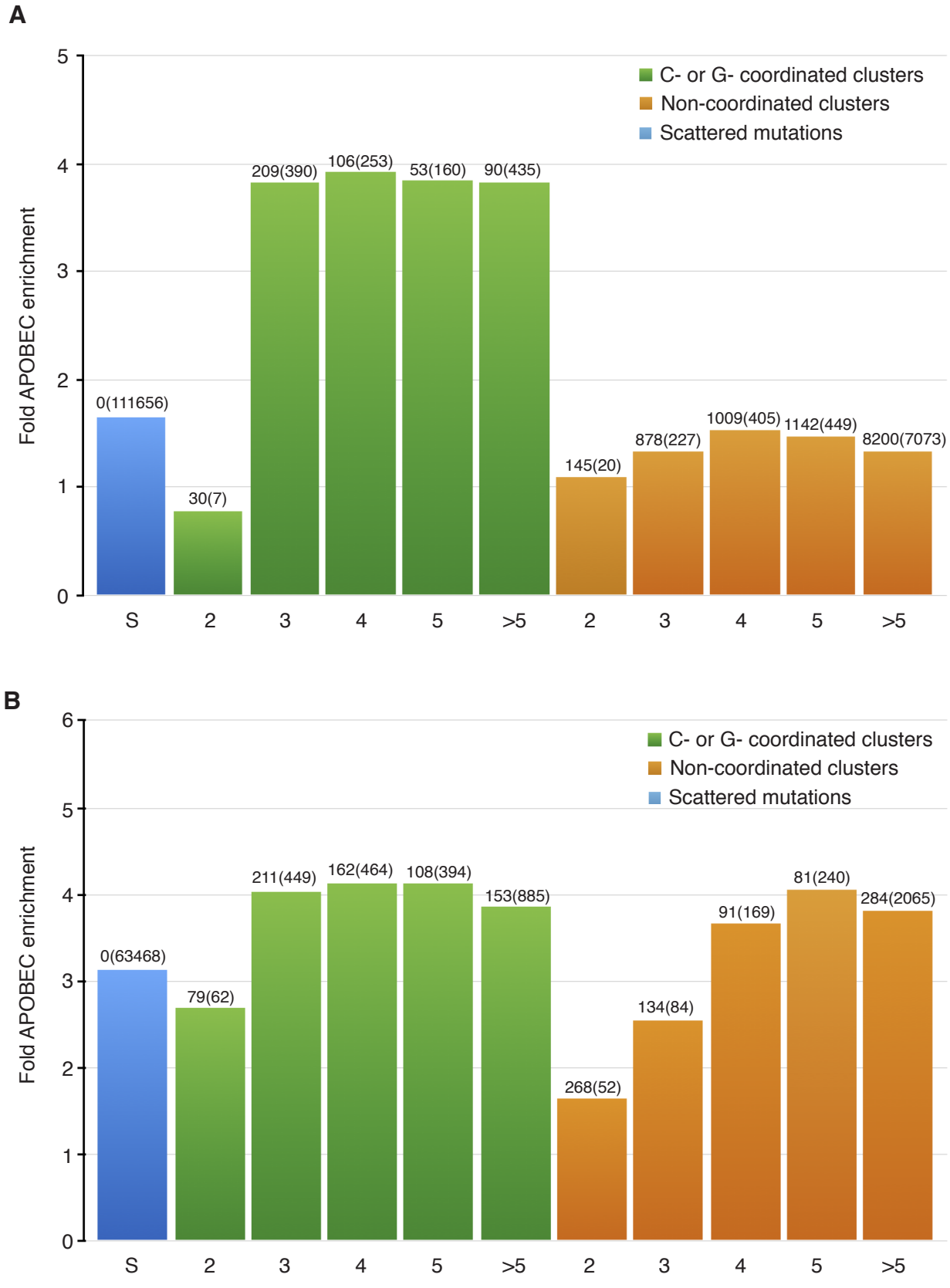

Figure S1, Related to Figure 1. Enrichment with APOBEC mutation signature was calculated for mutation clusters of different types (C- or G-coordinated, non-coordinated), sizes (number of mutations in a cluster shown under X-axis) as well as for scattered mutations in G:C pairs (S) as outlined in Methods and in ref. (Roberts et al. 2013). a. Lung cancers; b. Breast cancers. Since all C- or G- strand coordinated clusters of at least 3 mutations showed the maximum level of enrichment, these groups were taken for genome-wide distribution analysis.

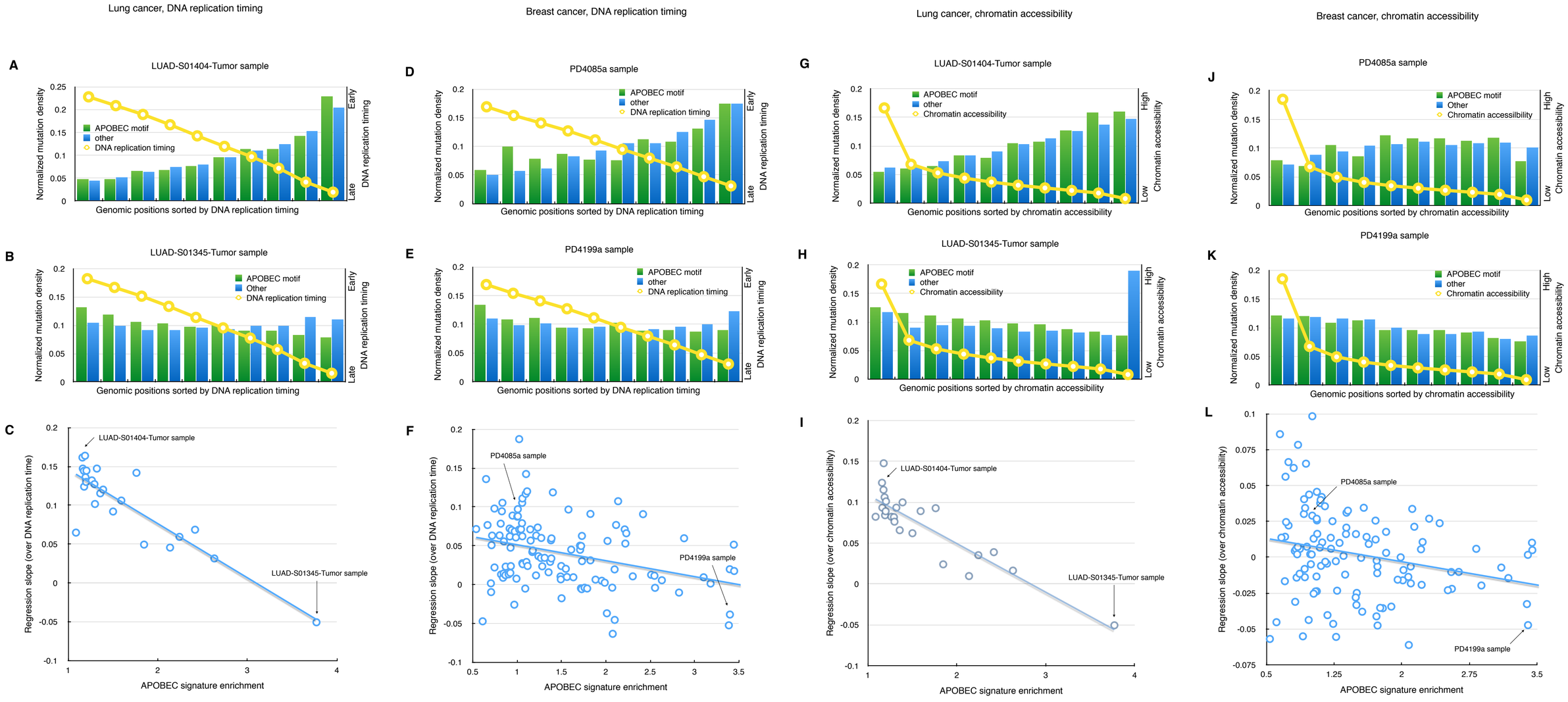

Figure S2, Related to Figure 2. (a) The distribution of the APOBEC-signature mutations with respect to DNA replication timing in a lung cancer sample with no enrichment of APOBEC signature. (b) The distribution of the APOBEC-signature mutations with respect to DNA replication timing in a lung cancer sample with high enrichment of APOBEC signature. (c) The dependency of regression slope on APOBEC-signature enrichment for lung cancer genomes. (d) The distribution of the APOBEC-signature mutations with respect to DNA replication timing in a breast cancer sample with no enrichment of APOBEC signature. (e) The distribution of the APOBEC-signature mutations with respect to DNA replication timing in a breast cancer sample with high enrichment of APOBEC signature. (f) The dependency of regression slope on APOBEC-signature enrichment for breast cancer genomes. (g) The distribution of the APOBEC-signature mutations with respect to DNA chromatin accessibility in a lung cancer sample with no enrichment of APOBEC signature. (h) The distribution of the APOBEC-signature mutations with respect to chromatin accessibility in a lung cancer sample with high enrichment of APOBEC signature. (i) The dependency of regression slope on APOBEC-signature enrichment for lung cancer genomes. (j) The distribution of the APOBEC-signature mutations with respect to DNA chromatin accessibility in a breast cancer sample with no enrichment of APOBEC signature. (k) The distribution of the APOBEC-signature mutations with respect to chromatin accessibility in a breast cancer sample with high enrichment of APOBEC signature. (l) The dependency of regression slope on APOBEC-signature enrichment for breast cancer genomes.

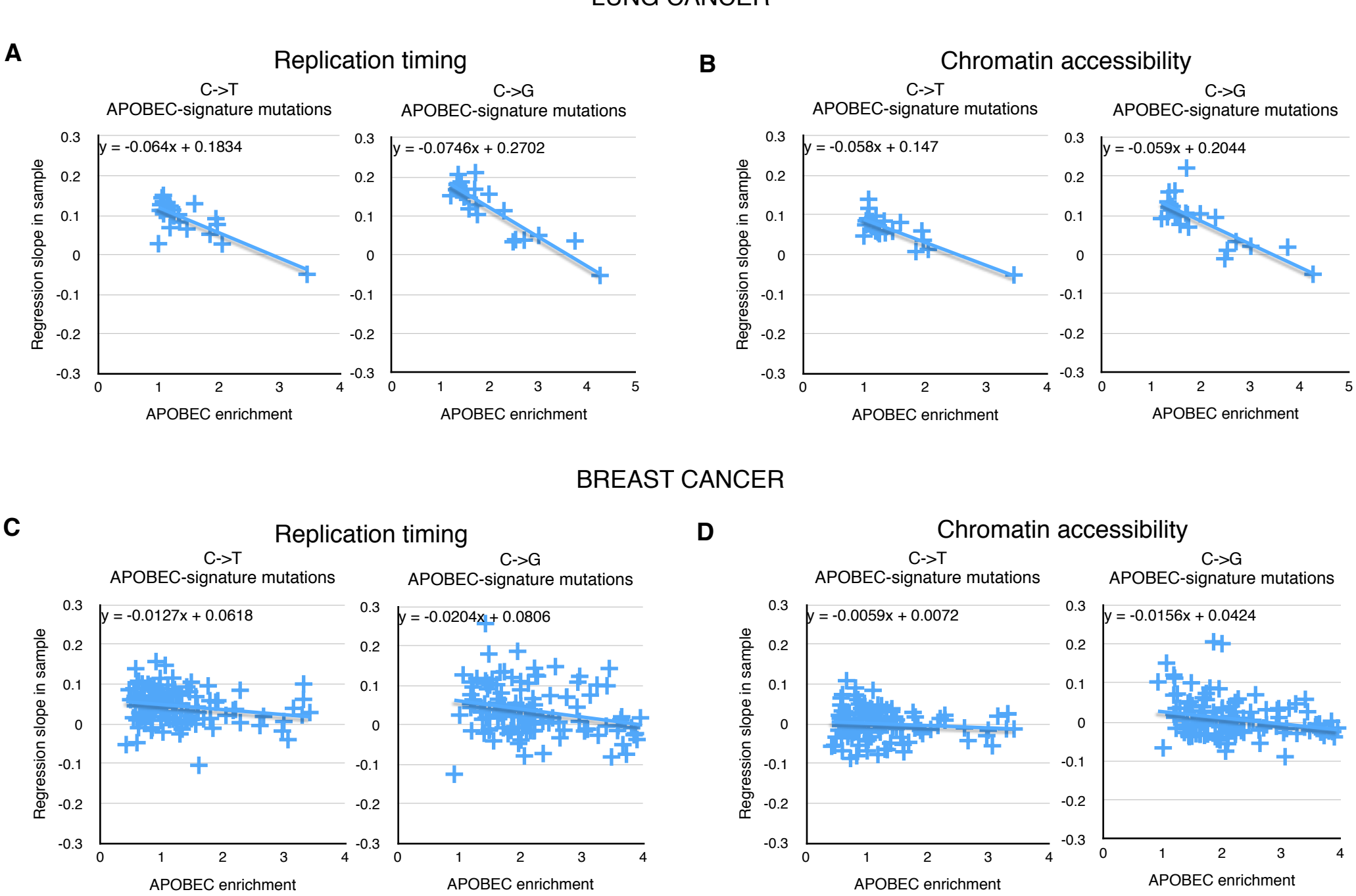

Figure S3, Related to Figure 2. The dependency of the sample-specific regression slopes, calculated for the distribution of C->T and C->G APOBEC-signature mutations relative to genomic features in cancer genomes, on APOBEC-signature enrichment in a sample: (a) lung cancer genome, replication timing, (b) lung cancer, chromatin accessibility, (c) breast cancer, replication timing, (d) breast cancer, chromatin accessibility.

Tables S2, Related to Figure 3. Parameters of the regression model (see Experimental Procedures) calculated for the replication timing and chromatin accessibility features using lung and cancer mutation data.

	Replication timing		Chromatin accessibility	
Regression parameters	**Lung cancer**	**Breast cancer**	**Lung cancer**	**Breast cancer**
β_{A0} (value)	0.13824	0.092625	0.14077	0.096673
β_{A0} (significance)	2.99E-102	6.84E-202	1.44E-51	8.63E-135
β_{A1} (value)	-0.078631	0.015037	-0.053432	0.004391
β_{A1} (significance)	6.93E-28	2.32E-24	7.61E-09	0.028
β_{N0} (value)	0.020467	0.075362	0.028799	0.10998
β_{N0} (significance)	3.93E-22	1.65E-56	1.78E-10	2.85E-75
β_{N1} (value)	0.16353	0.050229	0.093308	-0.013173
β_{N1} (significance)	6.67E-134	1.1E-16	1.48E-45	0.003
R-squared	0.917	0.998	0.892	0.995
p-value	5.41E-129	2.71E-284	1.84E-115	6.23E-239

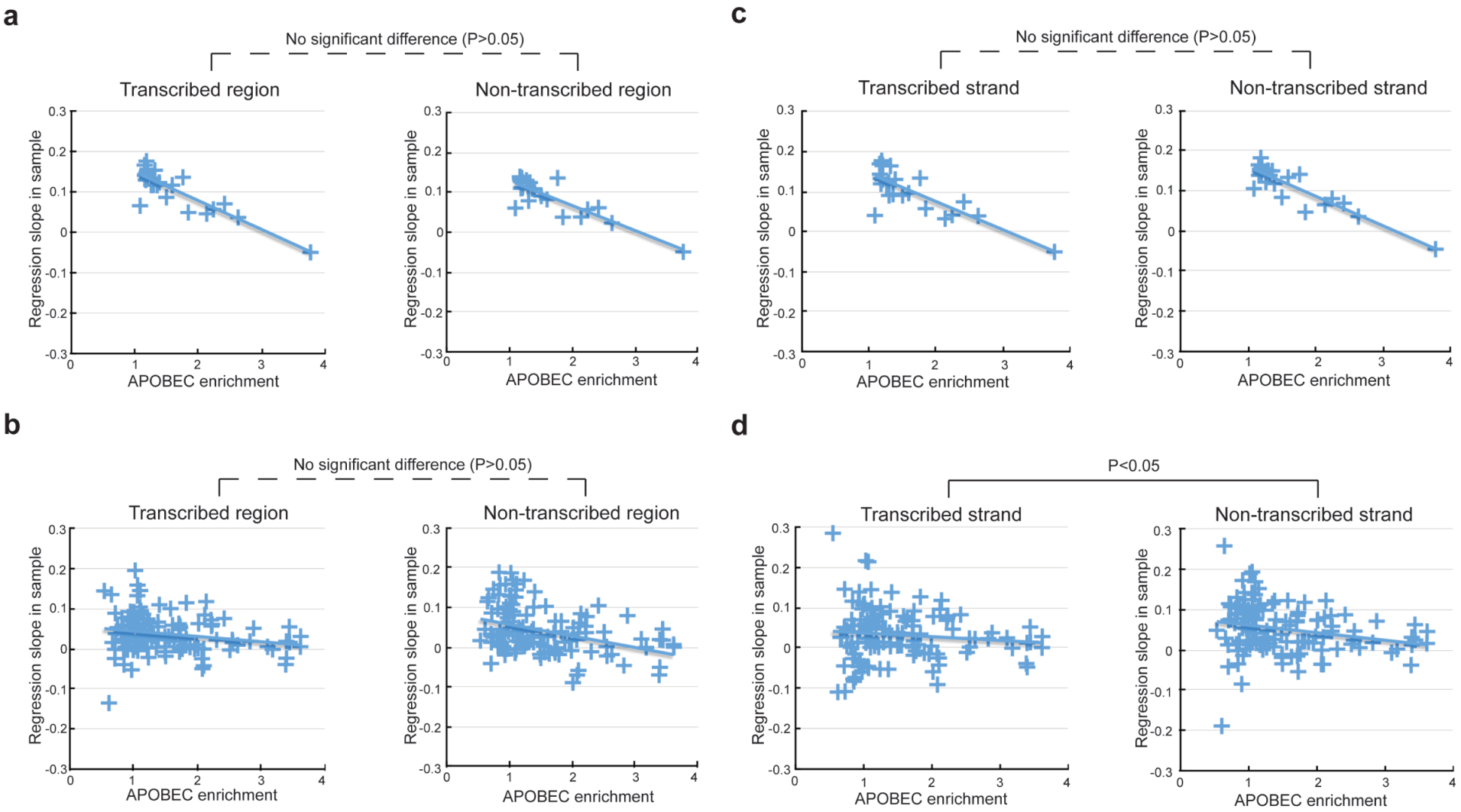

Figure S4, Related to Figure 4. Comparison of the degree of anticorrelation of regression slopes with APOBEC-signature enrichment between transcribed and non-transcribed strands of the lung (a,c) and breast (b,d) cancer genomes for all samples regardless of statistically significant enrichment with APOBEC mutation signature. Exact P-values: (a) 0.0055, (b) 0.52, (c) 0.14, (d) 0.015.