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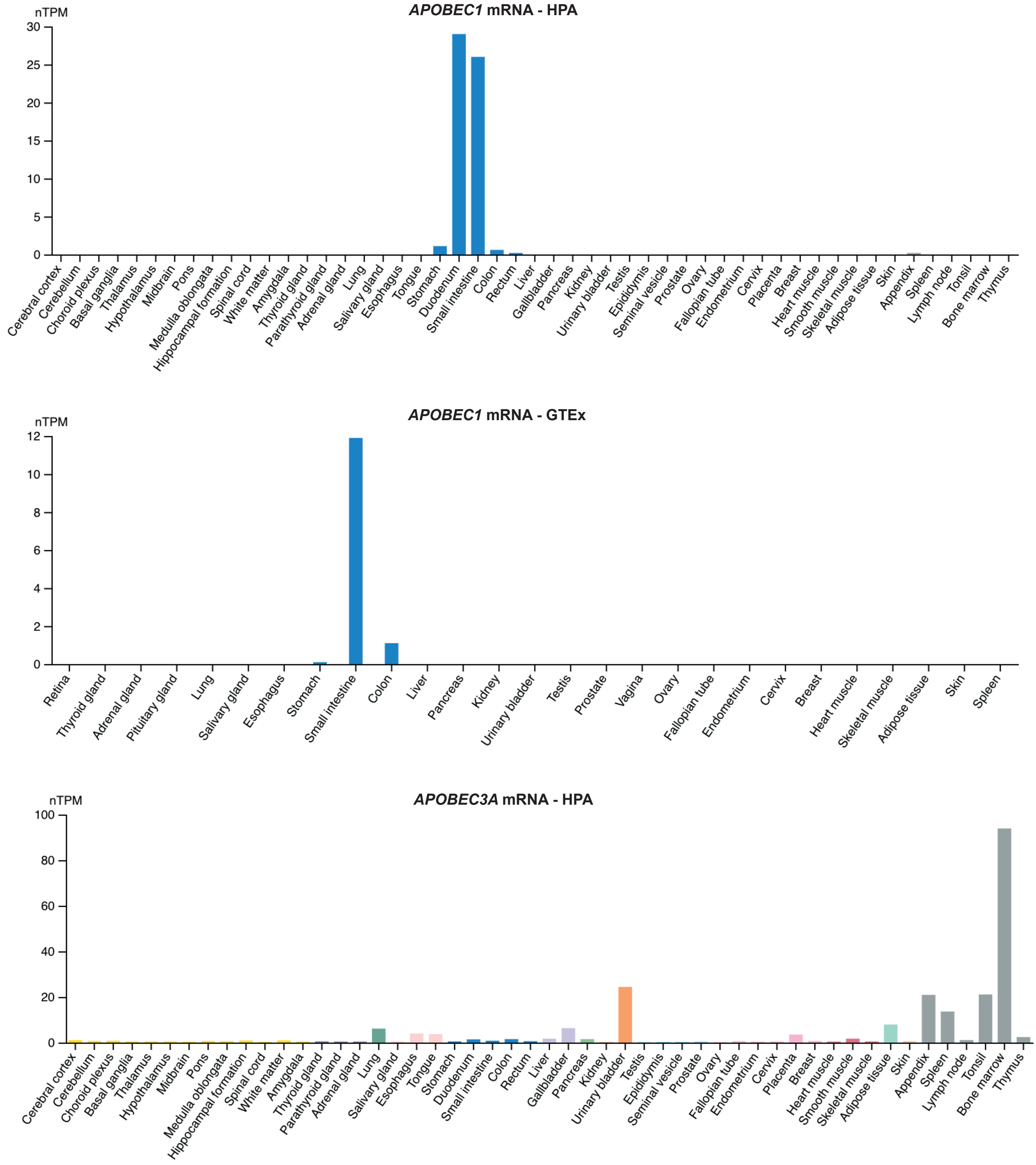
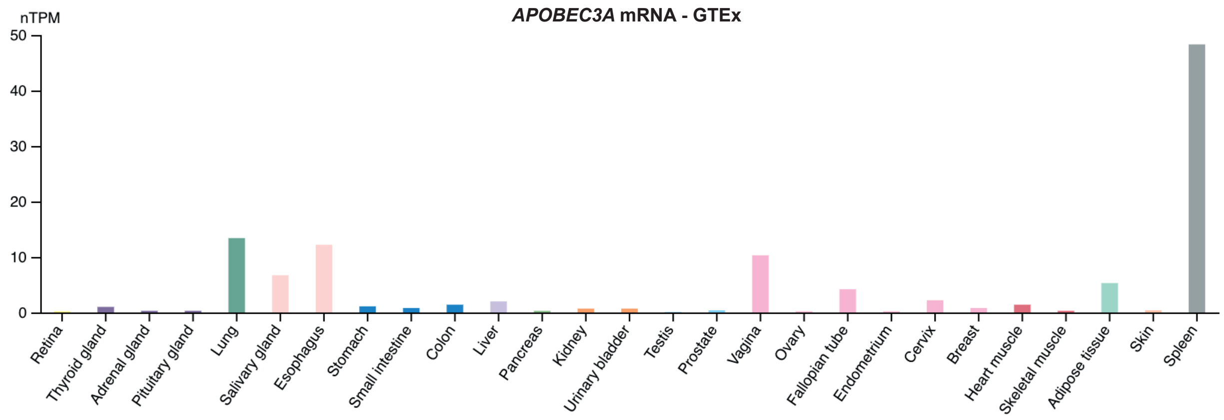
APOBEC mutagenesis is a common process in normal human small intestine

SUPPLEMENTARY INFORMATION CONTENTS

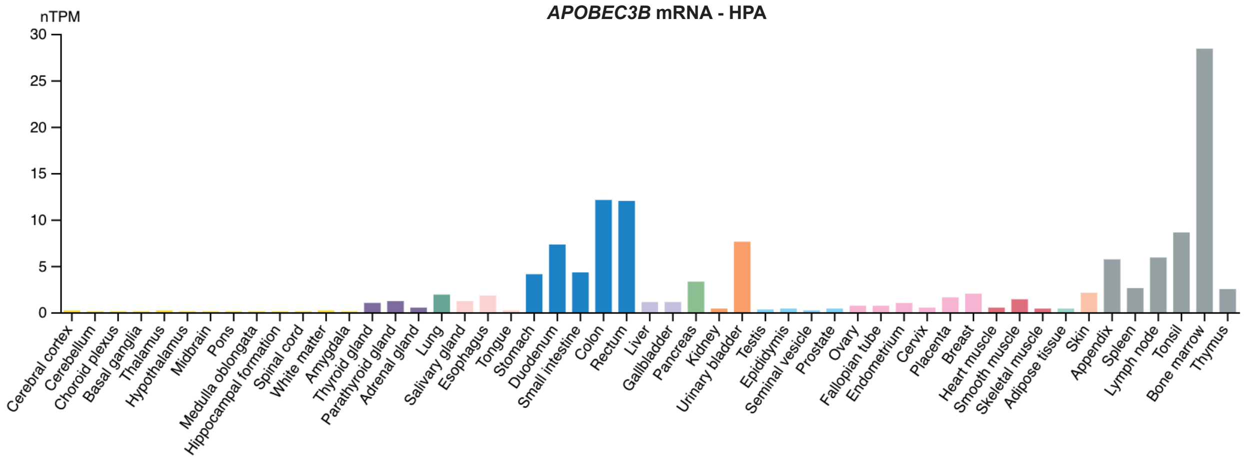
Supplementary Information Figure 1 | APOBEC1/APOBEC3A/APOBEC3B mRNA expression across normal tissues.

a-b. APOBEC1 bulk tissue gene expression data. Image credit: Human Protein Atlas (v21.proteinatlas.org. a-b: https://v21.proteinatlas.org/ENSG00000111701-APOBEC1/tissue, c-d: https://v21.proteinatlas.org/ENSG00000128383-APOBEC3A/tissue, e-f: https://v21.proteinatlas.org/ENSG00000179750-APOBEC3B/tissue). (a) APOBEC1 expression levels from the Human Protein Atlas project. Duodenum nTPM = 29, small intestine nTPM = 26, colon nTPM = 0.6. (b) APOBEC1 expression levels from GTEx. Small intestine nTPM = 11.9, colon nTPM = 1.1. c-d. APOBEC3A bulk tissue gene expression data. (c) APOBEC3A expression levels from The Human Protein Atlas project. Duodenum nTPM = 1.4, small intestine nTPM = 0.8, colon nTPM = 1.5. (d) APOBEC3A expression levels from GTEx. Small intestine nTPM = 0.8, colon nTPM = 1.4. e-f. APOBEC3B bulk tissue gene expression data. (e) APOBEC3B expression levels from The Human Protein Atlas project. Duodenum nTPM = 7.3, small intestine nTPM = 4.3, colon nTPM = 12.1. (f) APOBEC3B expression levels from GTEx. Small intestine nTPM = 2.1, colon nTPM = 6.0.

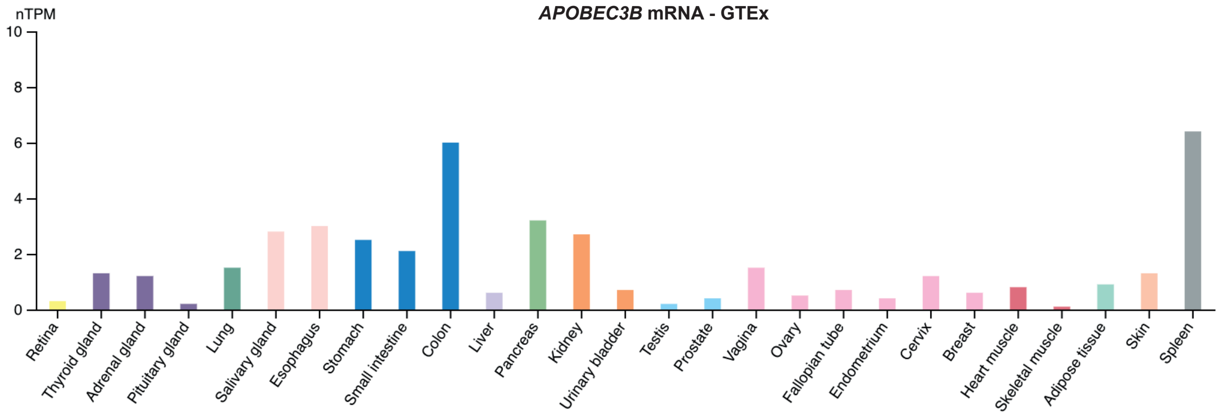




***APOBEC3A* mRNA - GTEx**

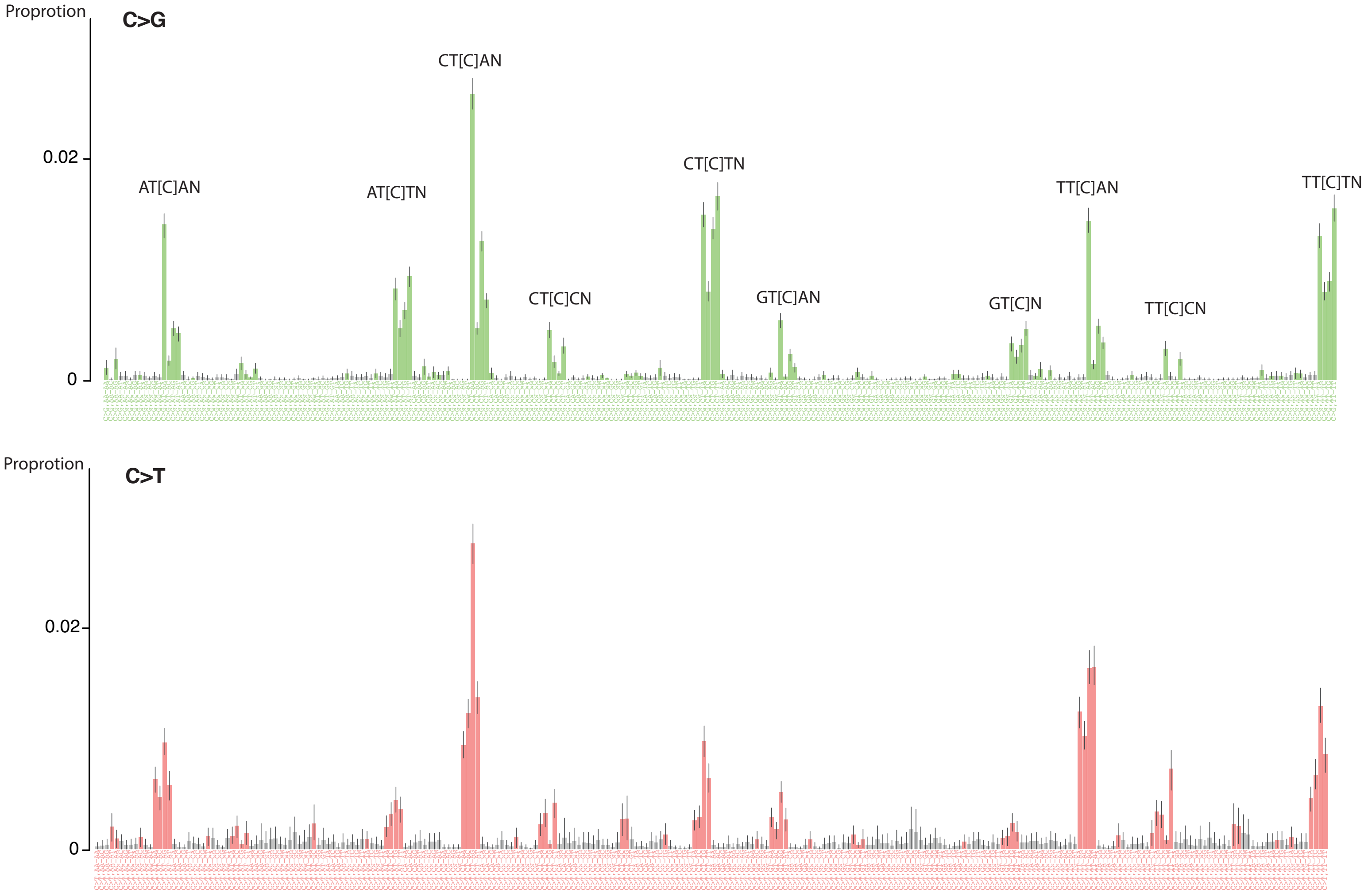


***APOBEC3B* mRNA - HPA**

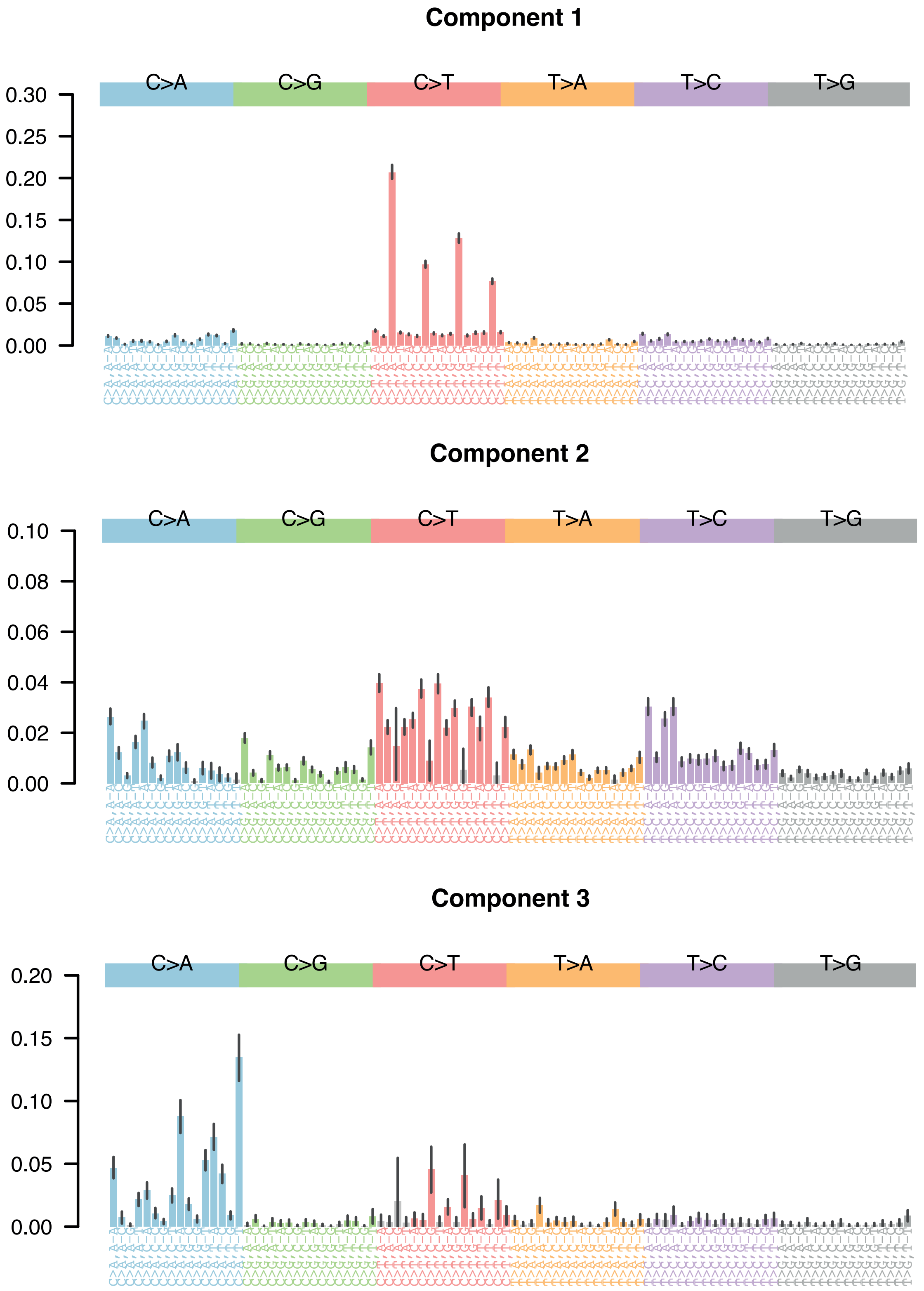


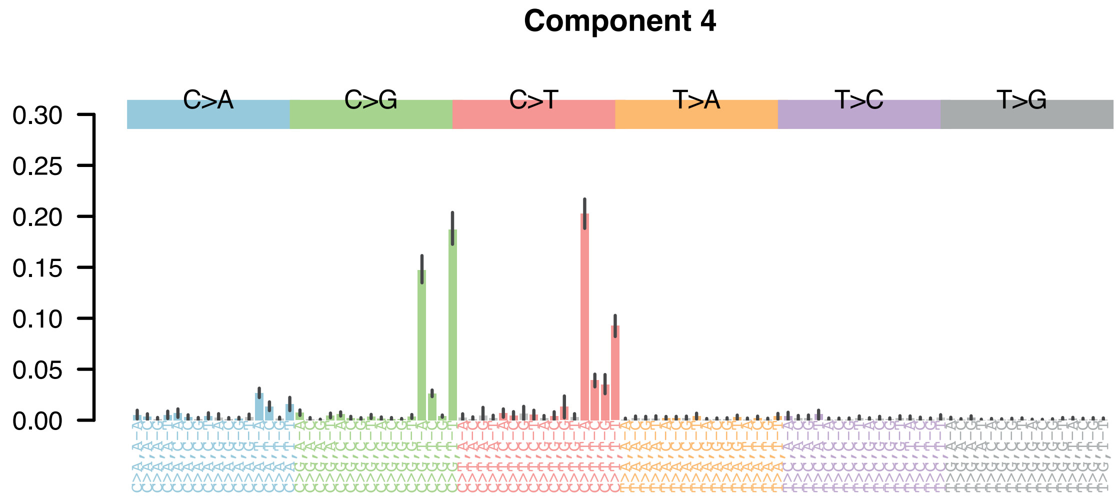
***APOBEC3B* mRNA - GTEx**

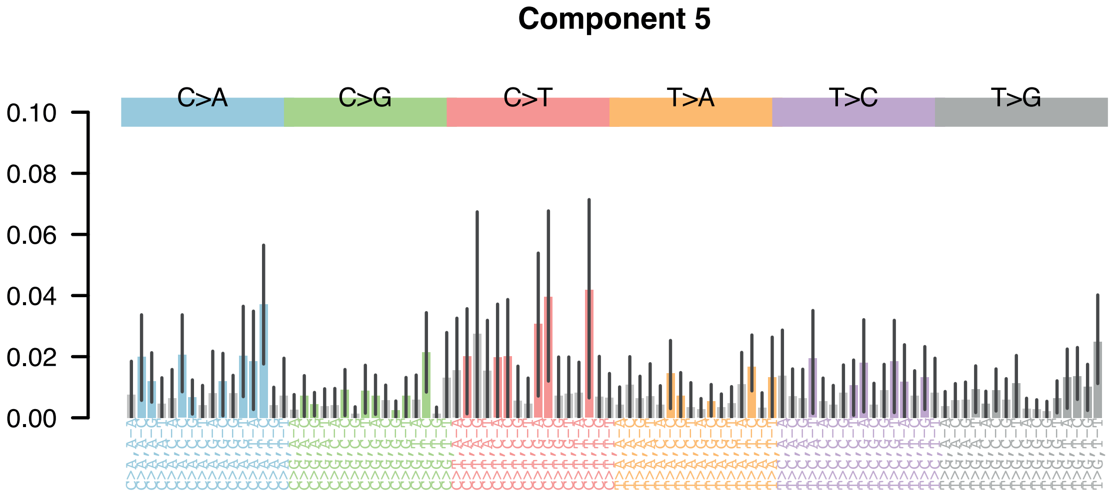
Supplementary Information Figure 2 | Extended contexts of APOBEC signatures.
5bp context of the C>G/T part of the APOBEC signature from HDP *de novo* extraction. X axis represents 96 categories of trinucleotide context and y axis represents the proportion. The black lines indicate 95% confidence intervals. Trinucleotide contexts that are not statistically significant are shown in light grey. The peaks show C/T at the -2 position are favoured compared to A/G. Enrichment of pyrimidines instead of purines at -2 position indicate APOBEC3B is unlikely to be the major contributing enzyme, while APOBEC1/3A could not be excluded.

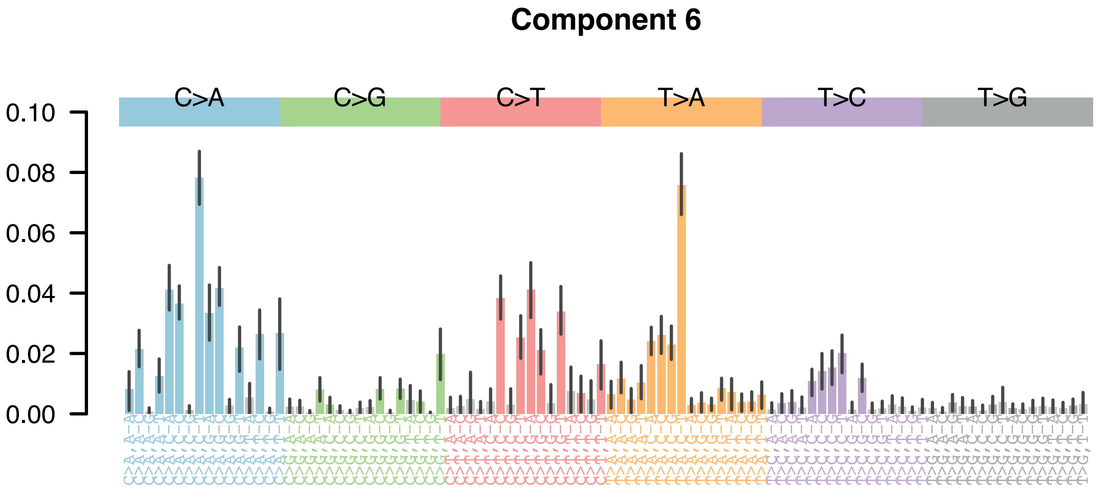


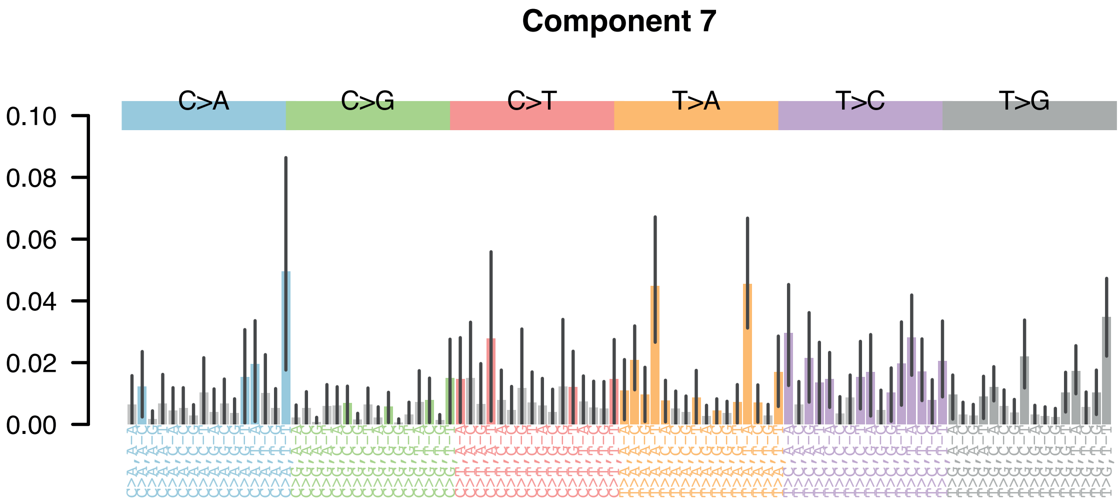
Extended Data Fig. 9 | HDP signatures from *de novo* extraction.
Mutational spectrum of nine HDP components from *de novo* extraction. X axis represents 96 categories of trinucleotide context and y axis represents the proportion. The black lines indicate 95% confidence intervals. Trinucleotide contexts that are not statistically significant are shown in light grey.

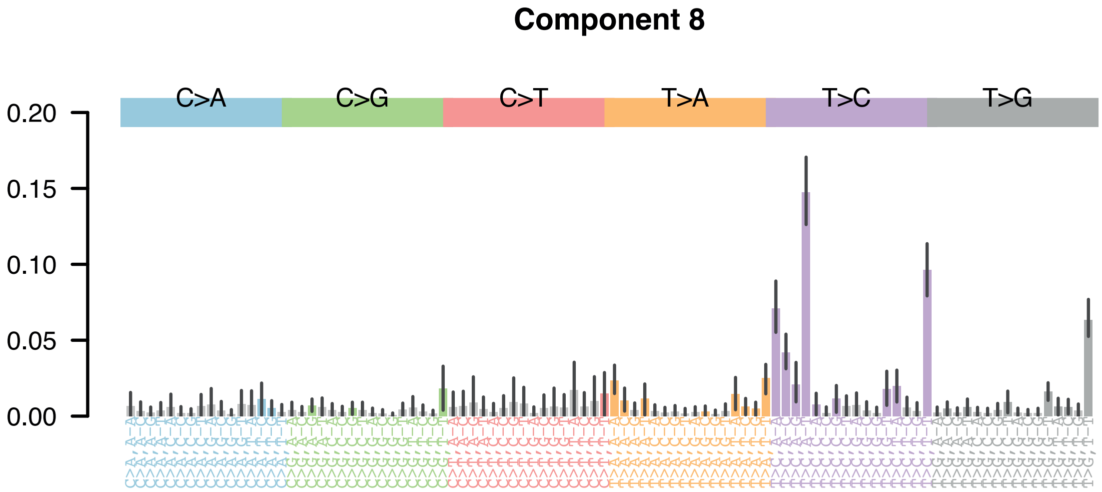


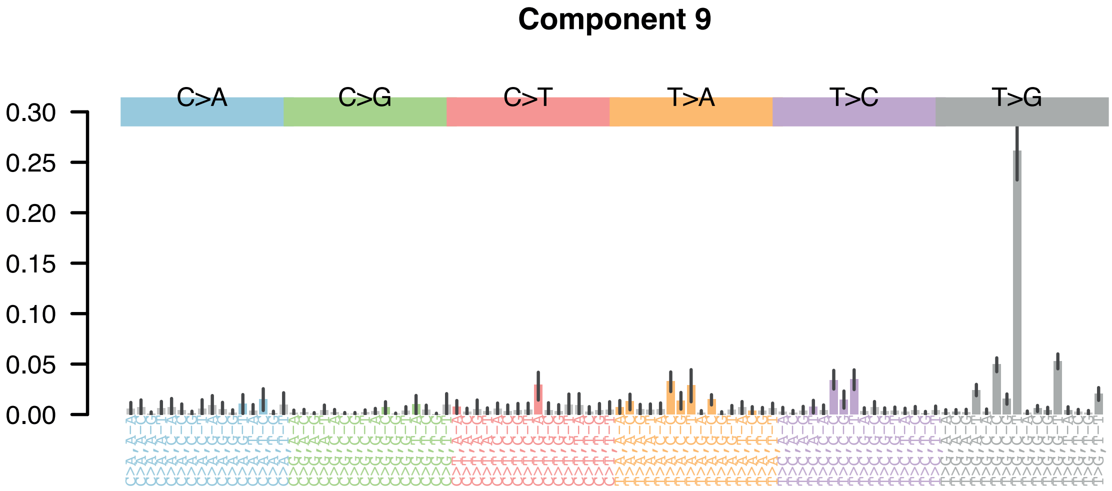

Component 4
C>A
C>G
C>T
T>A
T>C
T>G
0.30
0.25
0.20
0.15
0.10
0.05
0.00


Component 5
C>A
C>G
C>T
T>A
T>C
T>G
0.10
0.08
0.06
0.04
0.02
0.00


Component 6
C>A
C>G
C>T
T>A
T>C
T>G
0.10
0.08
0.06
0.04
0.02
0.00


Component 7
C>A
C>G
C>T
T>A
T>C
T>G
0.10
0.08
0.06
0.04
0.02
0.00


Component 8
C>A
C>G
C>T
T>A
T>C
T>G
0.20
0.15
0.10
0.05
0.00


Component 9
C>A
C>G
C>T
T>A
T>C
T>G
0.30
0.25
0.20
0.15
0.10
0.05
0.00

Supplementary Information Figure 4 | Cosine similarity plot for HDP components and shortlisted PCAWG reference signatures.
The APOBEC reference was made from the average spectrum of SBS2 and SBS13.