

Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: Series of in-house patients with newly generated sequencing data.

File Name: Supplementary Data 2

Description: Correspondence of disease, study name, study abbreviation and organ used for signature fitting in the series of Genomics England patients.

File Name: Supplementary Data 3

Description: Single base substitution catalogues on the complete series of samples.

File Name: Supplementary Data 4

Description: List of common and rare SBS mutational signatures per tissue.

File Name: Supplementary Data 5

Description: Substitution frequencies of SBS mutational signatures used for data fitting.

File Name: Supplementary Data 6

Description: Absolute exposures to SBS mutational signatures in selected tumor samples.

File Name: Supplementary Data 7

Description: Substitution frequencies of SBSnovel.

File Name: Supplementary Data 8

Description: Signature exposure and cosine similarity statistics in samples with SBS96 as a candidate rare signature.

File Name: Supplementary Data 9

Description: Number of variants with a high probability of originating from individual SBS mutational signatures per lineage.

File Name: Supplementary Data 10

Description: List of publicly available human epigenomic datasets used.

File Name: Supplementary Data 11

Description: Transcription strand asymmetry analysis statistics.

File Name: Supplementary Data 12

Description: Replication strand asymmetry analysis statistics.

File Name: Supplementary Data 13

Description: Methylation blocks differential methylation analysis and mutation rates per tumor type.

File Name: Supplementary Data 14

Description: Mapping statistics of CUT&RUN experiments.