

**S3 Table.** Calculation of tumor mutational burden (TMB)

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$$\text{TMB} = \frac{\text{Total eligible variants (N)}}{\text{Total coding region } \geq 50\text{X coverage (N)}}$$

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**TruSight Oncology 500 and Whole-exome sequencing**

**Eligible variants**

SNVs and indels

In coding regions

In high-confidence regions<sup>a)</sup>

With  $\geq 50$ x coverage

With  $\geq 5\%$  VAF

**Non-eligible variants**

In non-coding regions

In low-confidence regions

With high COSMIC counts ( $\geq 50$ )

Multinucleotide variants

**Filtered germline variants**

Found in germline variant databases<sup>b)</sup>

**Additional variants flagged based on VAF**

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SNV, single nucleotide variant; indel, insertion and deletion; VAF, variant allele frequency. <sup>a)</sup>High-confidence regions defined as more than 50x coverage, <sup>b)</sup>Germline variant databases include gnomAD, ExAC, and dbSNP.