



## Supplemental Figure 2

**(A)** Distributions of sequencing coverage of CpG sites of the three whole-genome 5mC sequencing libraries made by APOBEC(5mC), BS kit 1 and BS kit 2. All the libraries were down sampled to 118 million reads with an average sequencing depth of 5X for this analysis. **(B)** Read coverage at different genomic regions of the three whole-genome 5mC sequencing libraries made by APOBEC(5mC) (left), BS kit 1 (middle) and BS kit 2 (right). At an equal number of reads, the enzymatic deamination method yields notably higher coverage in cytosine-rich regions such as promoter and CpG islands leading to a more even coverage across features compared to both bisulfite conversion methods. **(C)** Relationship between read coverage and cytosine density: colored lines represent the normalized proportions of read coverage at various cytosine content bins (normalized coverage is calculated as proportion of reads at a specific C % bin divided by fraction of the 100-bp windows across the reference genome, which is illustrated by the histogram in grey). The enzymatic deamination method APOBEC(5mC) (green) shows the least coverage bias relative to cytosine content and covers notably more cytosine rich regions compared to the WGBS libraries. **(D)** Relationship between read coverage and density of converted cytosines: colored lines represent the normalized proportions of read coverage at various densities of converted cytosines (normalized coverage is calculated as proportion of reads at a specific bin of converted cytosine density divided by fraction of the 100-bp windows across the reference genome, which is illustrated by the histogram in grey). The library by enzymatic deamination method (green) has the least biased sequencing coverage in terms of converted cytosine content.