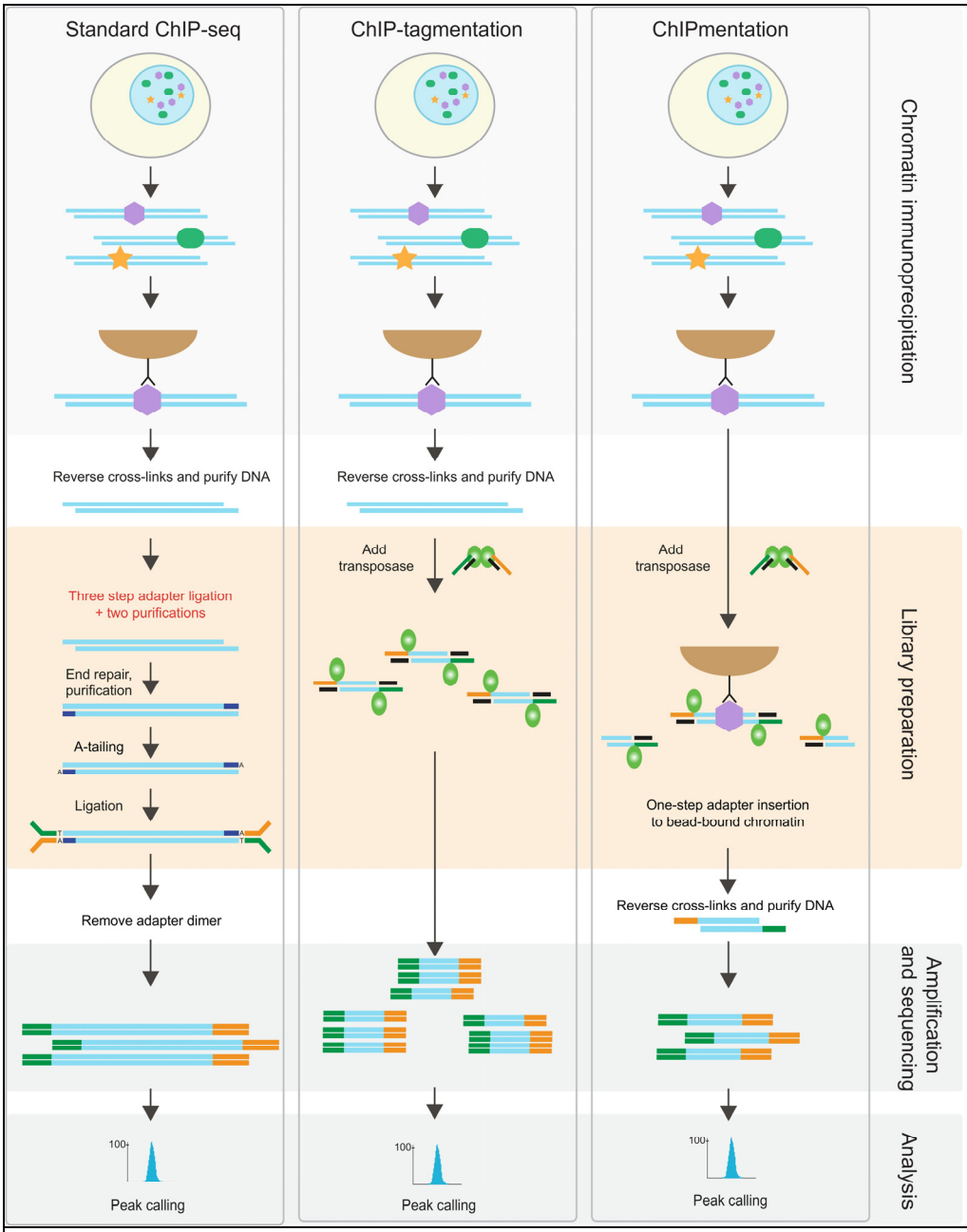
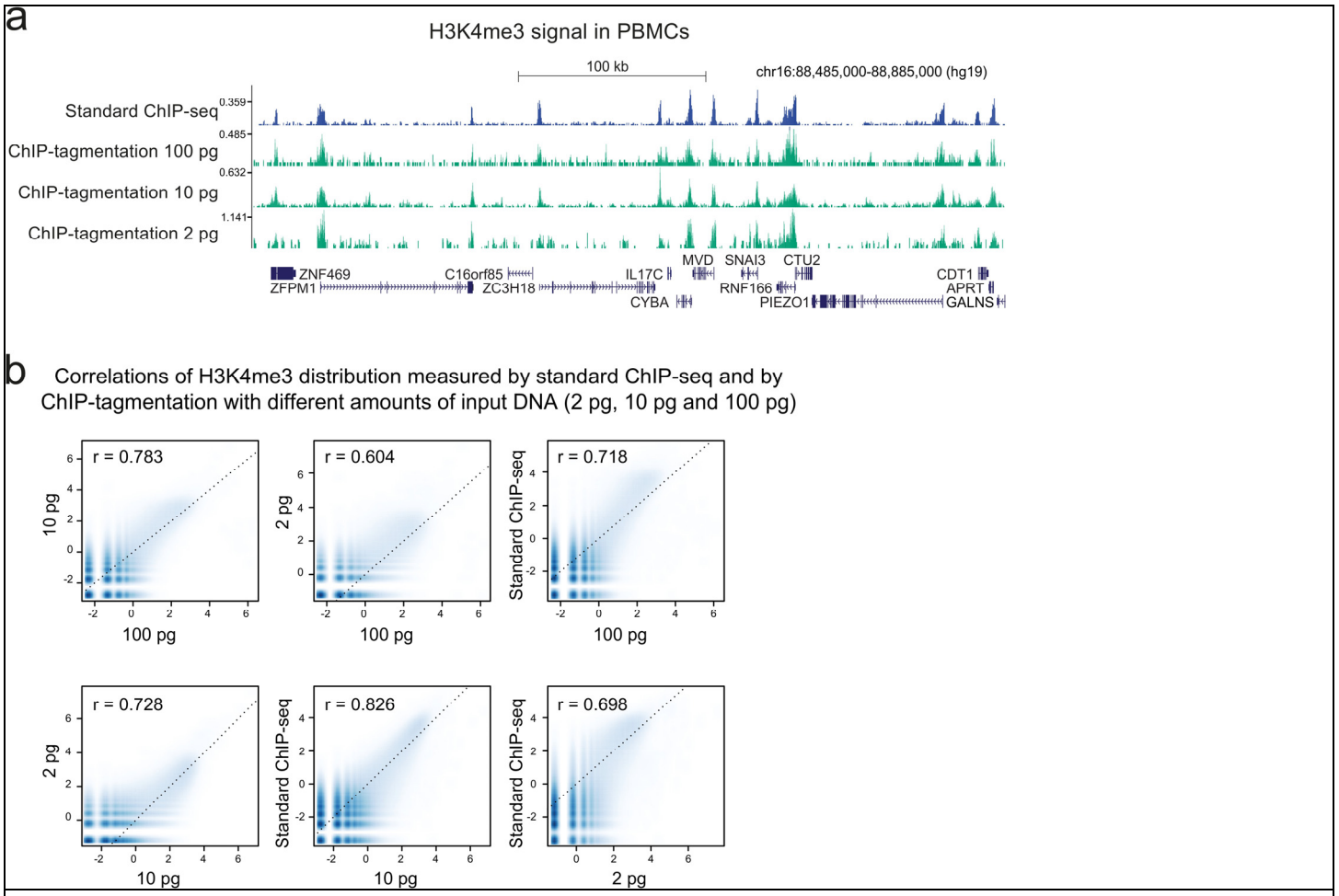


Supplementary Figure 1

Schematic overview of standard ChIP-seq, ChIP-tagmentation, and ChIPmentation

Workflow of ChIPmentation as compared to standard ChIP-seq and ChIP-tagmentation with purified ChIP DNA. All three protocols start by fixing cells with formaldehyde, followed by cell lysis, sonication of chromatin, and immunoprecipitation with a specific antibody bound to beads. For standard ChIP-seq (left), reverse-crosslinking is followed by purification of ChIP DNA, which is then subjected to library preparation in a multi-step procedure comprising end repair, purification, A-tailing, adapter ligation, and size selection. ChIP-tagmentation (center) uses purified ChIP DNA for tagmentation-based library preparation. In ChIPmentation (right), the sequencing adapters are introduced in a single step by tagmentation of bead-bound chromatin.

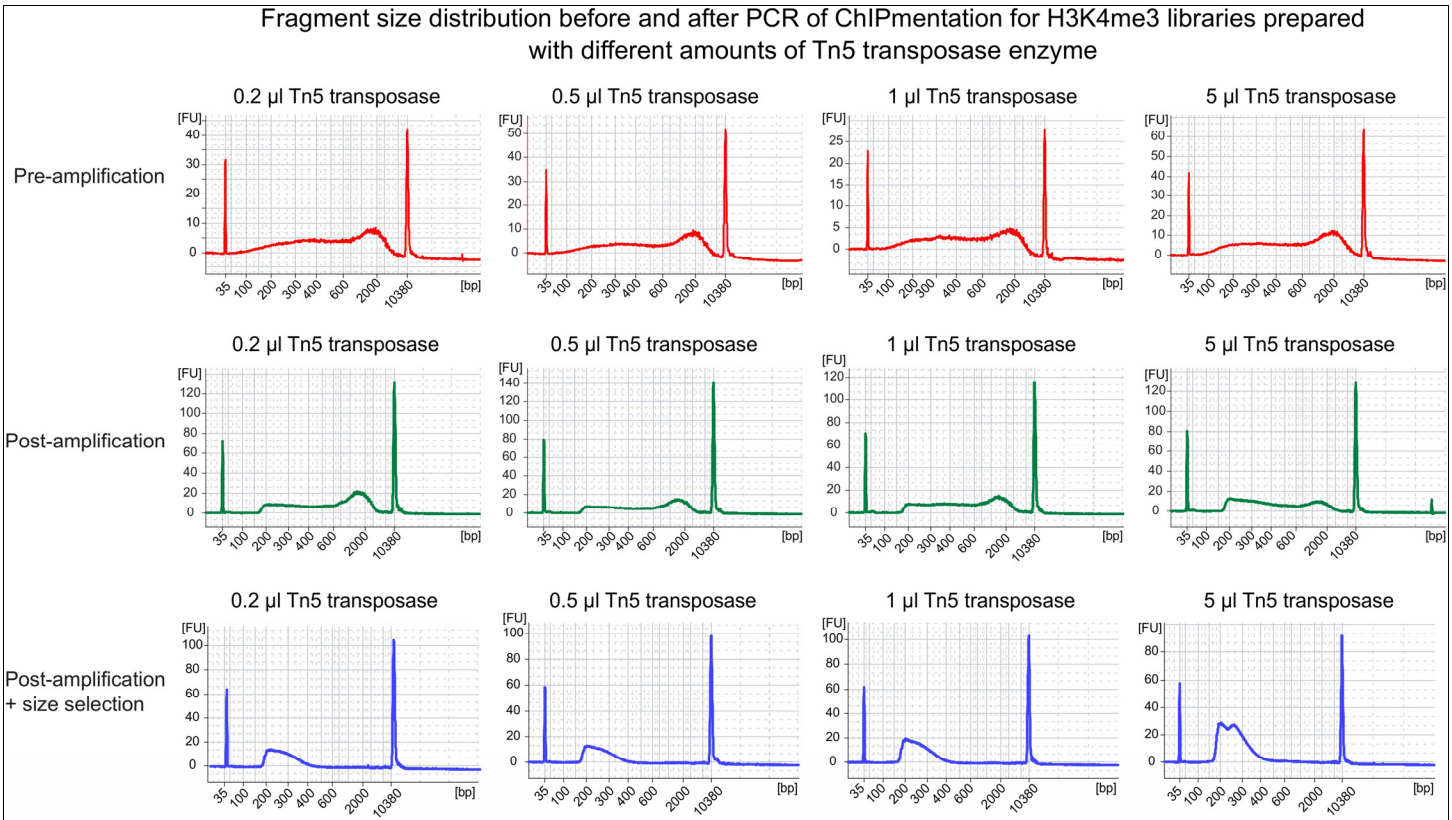


Supplementary Figure 2

Sequencing results for libraries prepared by ChIP-tagmentation starting from purified ChIP DNA as compared to standard ChIP-seq

(a) Representative UCSC Genome Browser screenshot of ChIP-tagmentation profiles for H3K4me3 in peripheral blood mononuclear cells (PBMCs) using different amounts of purified ChIP DNA as starting material. Data obtained by standard ChIP-seq for the same cell type are also included as reference.

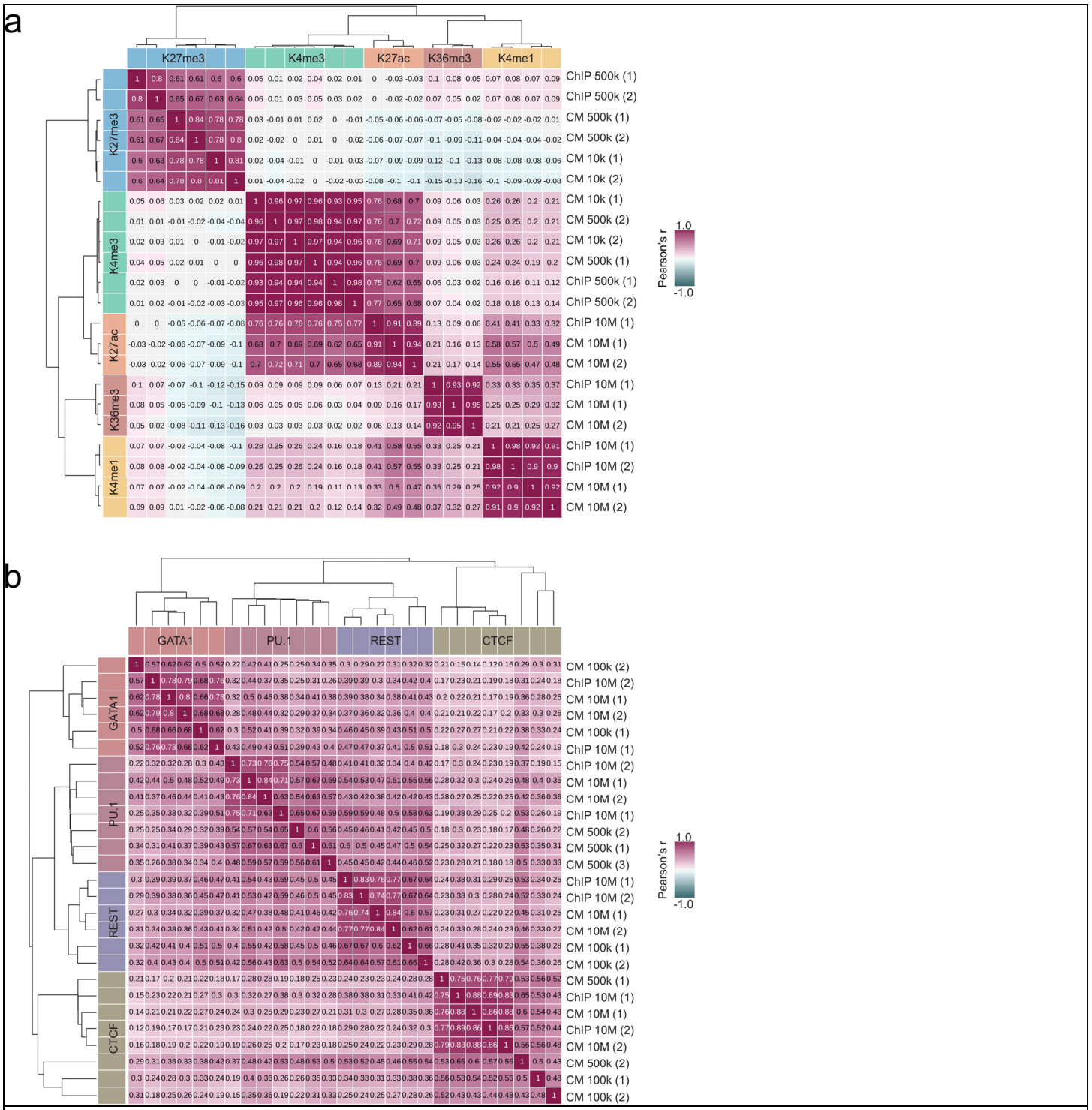
(b) Pairwise scatterplots comparing H3K4me3 signal in peripheral blood mononuclear cells (PBMCs) between standard ChIP-seq obtained from 10 million cells and ChIP-tagmentation using different amounts of purified DNA as starting material.



Supplementary Figure 3

Effect of tagmentation enzyme concentration on ChIPmentation library size distributions

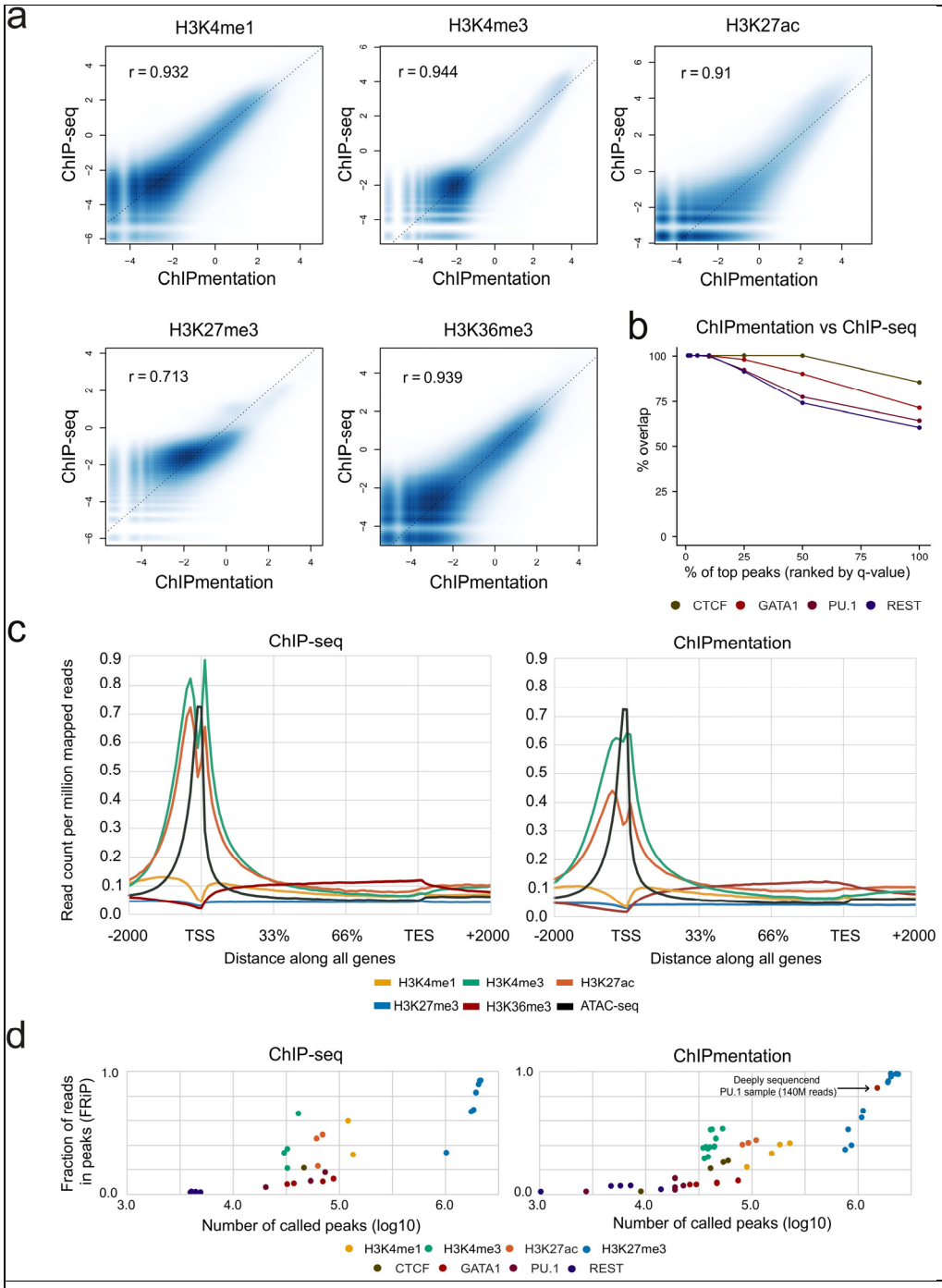
DNA fragment size distribution of ChIPmentation libraries for H3K4me3 that were prepared with different amounts of Tn5 transposase (0.2 μl to 5 μl enzyme from the Illumina Nextera DNA library preparation kit). Fragment size distributions after reverse-crosslinking but before library enrichment are shown in red, fragment size distributions after enrichment PCR are shown in green, and fragment size distributions of the size-selected final libraries are shown in blue.



Supplementary Figure 4

Genome-wide correlations for all ChIPmentation and ChIP-seq samples

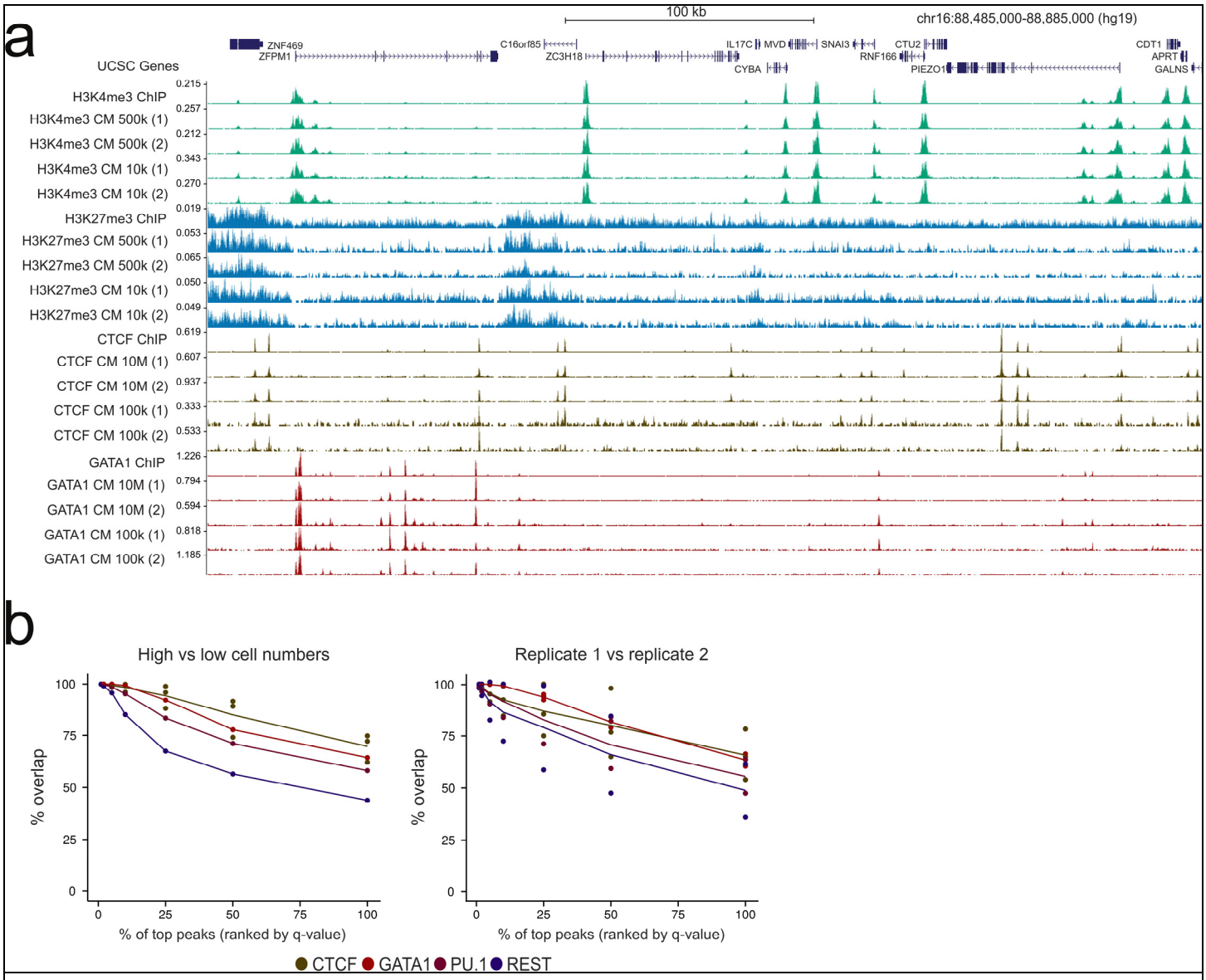
(a) Genome-wide correlations (1,000 bp windows) for standard ChIP-seq ("ChIP") and ChIPmentation ("CM") data across different histone marks and different cell input amounts. (b) Genome-wide correlations (1,000 bp windows) for standard ChIP-seq and ChIPmentation data across different transcription factors and different cell input amounts.



Supplementary Figure 5

Global comparison of standard ChIP-seq and ChIPmentation data

(a) Pairwise scatterplots comparing standard ChIP-seq and ChIPmentation for H3K4me1, H3K4me3, H3K27ac, H3K27me3, and H3K36me3. (b) Peak overlap calculated as the percentage of top-X% peaks in one method that overlap with peaks in the other method. (c) Composite plot for the distribution of histone marks along all genes, shown separately for standard ChIP-seq (left) and ChIPmentation (right). Chromatin accessibility obtained by ATAC-seq is shown in black. (d) Fraction of reads in peaks (FRiP) and number of peaks called from standard ChIP-seq (left) and ChIPmentation (right) data for all sequenced libraries. Note that the sequencing depth varies between replicates (**Supplementary Table 1**).

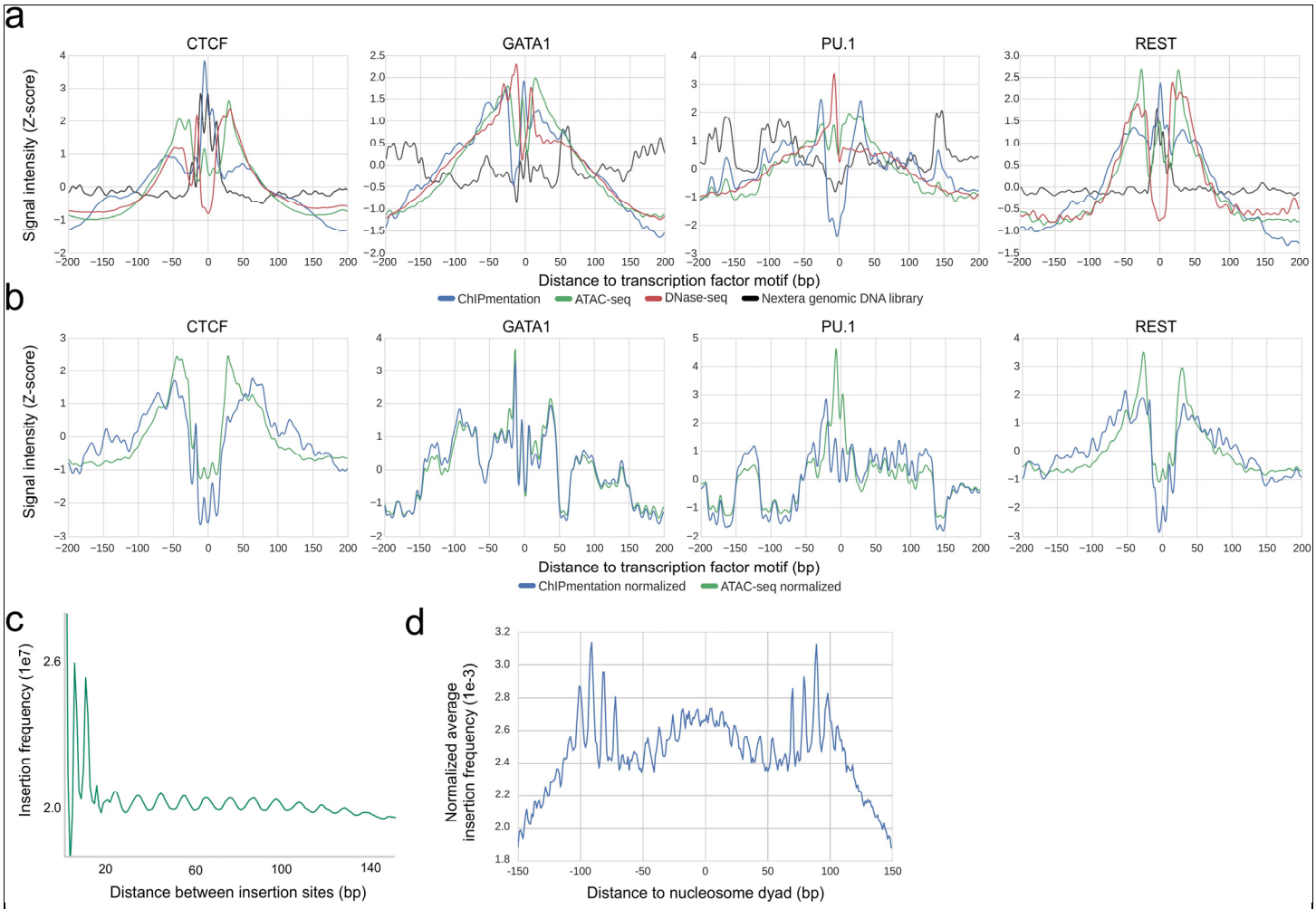


Supplementary Figure 6

Performance of ChIPmentation for low-input samples

(a) Genome browser screenshot showing ChIPmentation ("CM") data for individual biological replicates and different cell input amounts (i.e., 10M, 500k, 100k, and 10k cells). Standard ChIP-seq ("ChIP") data obtained from 500k (H3K4me3, H3K27me3) or 10 million cells (CTCF, GATA1) are shown as a reference.

(b) Peak overlap (fraction of top-X% peaks in one condition that overlap peaks in the other condition) between ChIPmentation samples obtained for different cell numbers (left) and between biological replicates with the same cell number (right). Lines represent the mean of all points of one factor at one x-axis position.



Supplementary Figure 7

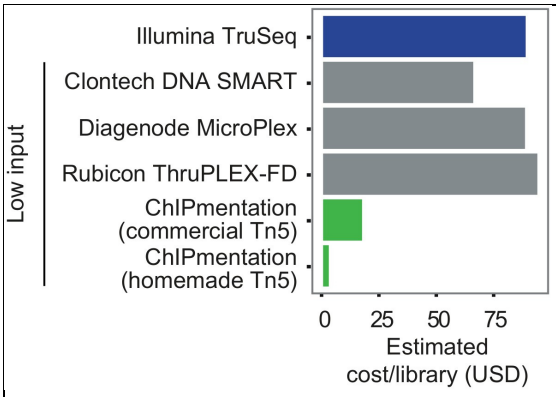
Evidence of high-resolution patterns in ChIPmentation data

(a) Tn5 transposase insertion frequencies for ChIPmentation (blue), ATAC-seq signal (green), and DNase-seq signal (red) at ChIP-seq peaks for CTCF, GATA1, PU.1, and REST, centered on the corresponding binding motifs. Signal from tagmented genomic DNA (Nextera genomic DNA library) is displayed in black, indicating inherent sequence bias of the tagmentation enzyme. Signals were averaged over all peaks, smoothed with a 20 bp Hanning window, and Z score transformed for better comparability.

(b) Normalized ChIPmentation (blue) and ATAC-seq (green) signal at ChIP-seq peaks for CTCF, GATA1, PU.1, and REST, centered on the corresponding binding motif. ChIPmentation and ATAC-seq signals were normalized against the signal observed for tagmentation of genomic DNA (Nextera genomic DNA library), in order to correct for the sequence bias of the tagmentation enzyme. Signals were averaged over all peaks, smoothed with a 20 bp Hanning window, and Z score transformed for better comparability.

(c) Frequency of pairwise distances between insertion events (5' position of reads) in ChIPmentation data for H3K4me3.

(d) Average signal intensity (insertion frequencies) for H3K4me1 ChIPmentation data around centers of nucleosomes (dyads) positioned using the NucleoATAC software (https://github.com/GreenleafLab/NucleoATAC) with ATAC-seq data from GM12878 cells. Note the structured pattern with higher and periodical insertions at the nucleosome borders.



Supplementary Figure 8

Comparison of reagent costs for standard ChIP-seq and ChIPmentation

Comparison of reagent costs for standard ChIP-seq (dark blue), commercially available low-input library preparation kits (grey), and ChIPmentation (green). Cost estimates were calculated for library preparation including amplification and indexing, but excluding reagents for size selection, reaction purifications, and the final quality control step prior to sequencing.