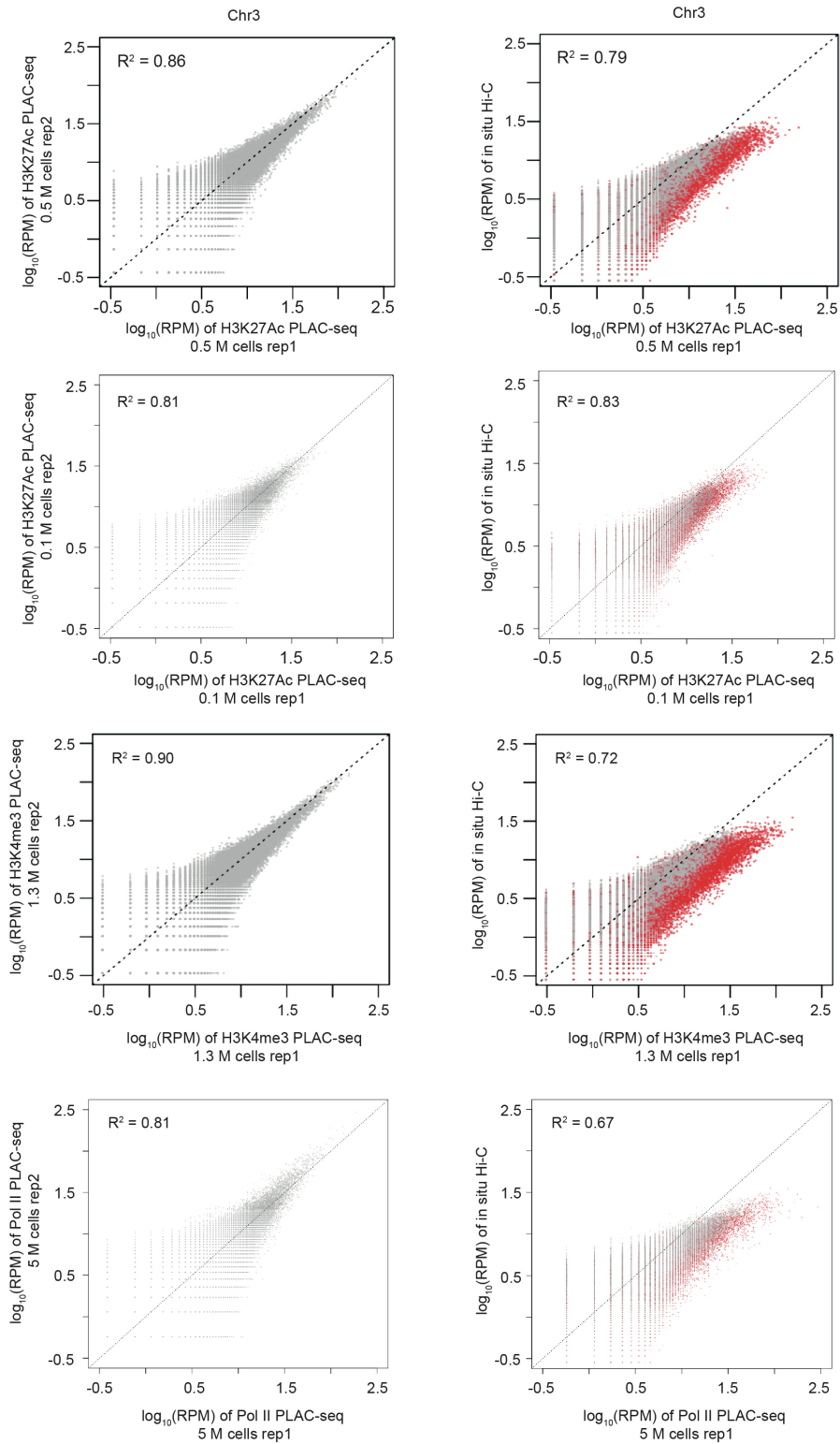


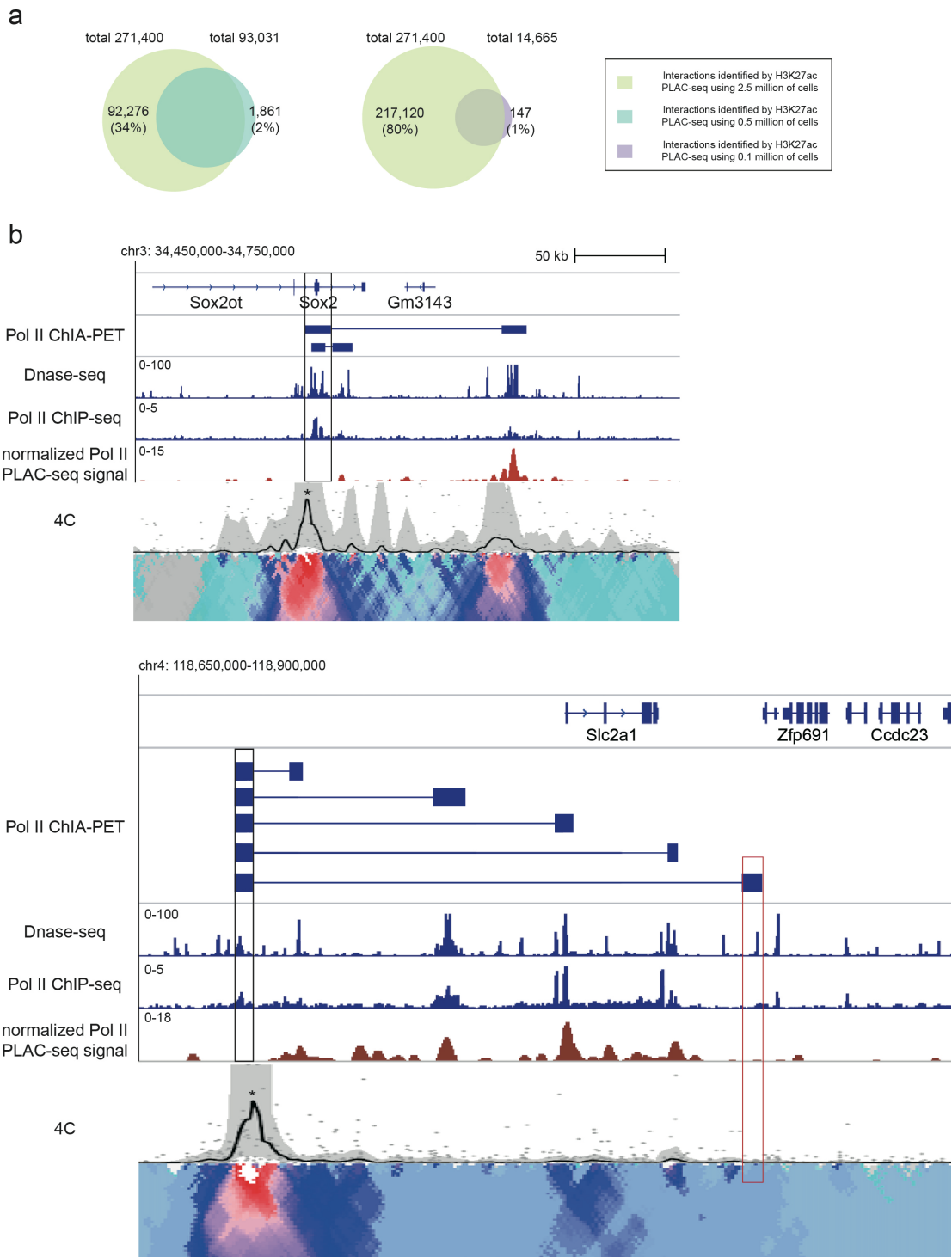
Supplementary Figure 1 Development and validation of PLAC-seq.

(a) Comparison of input material requirement of PLAC-seq and ChIA-PET. (b) Principal component analysis (PCA) of short-range reads in different PLAC-seq experiments highlights the reproducibility between biological replicates. (c) Box plots of Reads Per Kilobase per Million reads (RPKM) calculated using PLAC-seq short-range *cis* pairs (distance < 1kb) suggest that PLAC-seq signals are significantly enriched in ChIP-seq peaks compared to randomly chosen regions (***)Wilcoxon tests, $P < 2.2e-16$). (d) The signals of short-range reads (< 1kb) from PLAC-seq were similar to those of ChIP-seq. (e) Box plots of reads per million (RPM) at ChIP-enriched regions for PLAC-seq and *in situ* Hi-C. Only long-range (>10kb) *cis* reads were considered (***)Wilcoxon tests, $P < 2.2e-16$). (f) Scatter plots of pair-wise interaction frequency on chromosome 3. Left, PLAC-seq biological replicates were highly reproducible ($R^2=0.90$); right, interaction intensity is skewed towards PLAC-seq for fragments with H3K27ac ChIP-seq peaks comparing to *in situ* Hi-C ($R^2=0.76$). (Red dots represent fragment pairs with at least one end bound by H3K27ac) (g) Example of long-range *cis* reads enrichment in H3K27ac, H3K4me and Pol II PLAC-seq compared to *in situ* Hi-C (visualized by Juicebox).



Supplementary Figure 2

Scatter plots of interaction intensity between PLAC-seq biological replicates (left panels) and between PLAC-seq and *in situ* Hi-C (right panels) on chromosome 3. (Red dots represent fragment pairs bound by corresponding ChIP-seq peaks)



Supplementary Figure 3. Validation of PLAC-seq data by 4C-seq.

(a) Long-range interactions identified by H3K27ac PLAC-seq are reproducible using different number of cells. (b) Comparison of 4C, PLAC-seq, ChIA-PET results on the selected locus. (4C anchor points are marked by asterisk while PLAC-seq and ChIA-PET anchor regions are marked by black rectangle; red rectangle highlights chromatin interaction uniquely detected by ChIA-PET but not observed from 4C-seq).

Supplementary Table 1. Summary of 4C experiments

Sample No.	Anchor point	1st digestion enzyme	2nd digestion enzyme	PCR primer (forward)	PCR primer (reverse)	Figure related
4C_1	Chr3: 34,545,849-34,546,065	Csp6I	NlaIII	TCCCTACACGACGCTC TTCCGATCTATTGCCTC TGATAAGTAC	GTGACTGGAGTTCAGACG TGTGCTCTTCCGATCTATG ACAGCCCCAGCCCAT	Supplementary Fig. 2 upper panel
4C_2	Chr1: 72,261,052-72,261,738	DpnII	Csp6I	TCCCTACACGACGCTC TTCCGATCTAGACAAGC CTCAGTTGGATC	GTGACTGGAGTTCAGACG TGTGCTCTTCCGATCTATC CCAAGGCTACATCATA	Fig. 1j, left
4C_3	Chr5: 110,901,207-110,901,593	DpnII	Csp6I	TCCCTACACGACGCTC TTCCGATCTGGGAGTC ATGGAAACTGATC	GTGACTGGAGTTCAGACG TGTGCTCTTCCGATCTTIG ATAGTAACAAGGCCCC	Fig. 1j, right
4C_4	Chr4: 118,684,035-118,684,927	DpnII	Csp6I	TCCCTACACGACGCTC TTCCGATCTATTCTTCT TCTGAAAGGATC	GTGACTGGAGTTCAGACG TGTGCTCTTCCGATCTATT TTAGCGGAAGACTCACA	Supplementary Fig. 2 lower panel