## **Supporting Information**

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Fig. S1. Enrichment due to high read coverage in the immunoprecipitate. Bar graphs show median number of reads for the input and immunoprecipitate (IP) samples genome-wide (black) and at Sir-enriched loci (gray) for Sir2, Sir3, and Sir4.



Fig. 52. Confirmation of ChIP enrichment at highly expressed genes by ChIP-qPCR. Sir4 ChIP-qPCR reproduces the ChIP-Seq enrichment at highly expressed CDC19, LSR1, and GCN4. No enrichment is seen at the uninduced MET3 negative control. The error bars show the SEM values from three biological replicates.



Fig. S3. Sir3 levels correlate with ChIP-Seq signals for Ste12 and Cse4. Boxplots show Cse4 and Ste12 ChIP-Seq levels, as a function of Sir3 enrichment.

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Fig. S4. Pol II levels correlate with ChIP-Seq signals for Sir2, Sir3, Sir4, and Cse4. Boxplots show Sir2, Sir3, Sir4, and Cse4 ChIP-Seq levels, as a function of Pol II enrichment.



Fig. S5. tRNA proximity correlates with ChIP-Seq signals for Sir2, Sir3, Sir4, Cse4, and Ste12. Sir2, Sir3, Sir4, Cse4, and Ste12 ChIP-Seq levels are shown as a function of the distance from *S. cerevisiae* annotated tRNAs. The red curve is a polynomial fit to the scatterplot.



Fig. S6. Sir proteins are enriched across the entire ORF. Sir2, Sir3, and Sir4 ChIP-Seq levels are shown as a function of the distance from the 5' starts of the 200 most highly expressed genes in the Saccharomyces cerevisiae genome.

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**Fig. 57.** Confirmation of GFP hyper-ChIPability. (A) Boxplots comparing the GFP ChIP-Seq levels genome-wide versus the 238 Sir-enriched euchromatic loci. Data are from the glucose condition. (*B*) GFP ChIP-qPCR in glucose reproduces the ChIP-Seq enrichment at highly expressed *CDC19, LSR1*, and *GCN4*. All values are shown as relative to the uninduced *MET3* negative control. The error bars show the SEM values from three biological replicates. (*C*) ChIP-qPCR values, normalized to *SEN1*, of an NLS-tagged GFP protein. Induction-dependent enrichment of the *GAL1* gene is shown; enrichment is seen only in the induced galactose condition. The error bars show the SEM values from three biological replicates.

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## **Other Supporting Information Files**

Table S1 (DOCX) Table S2 (DOCX) Table S3 (DOCX)

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