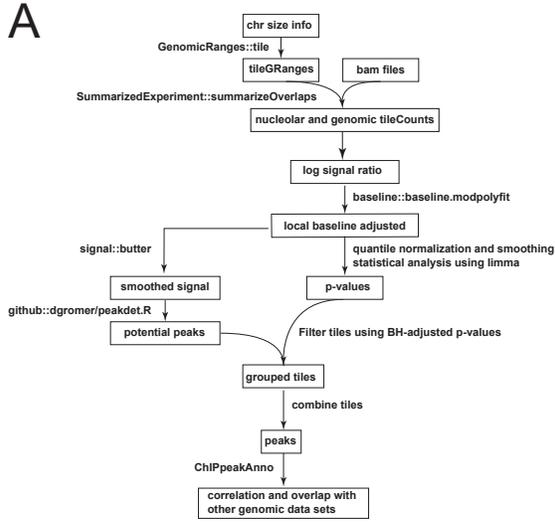
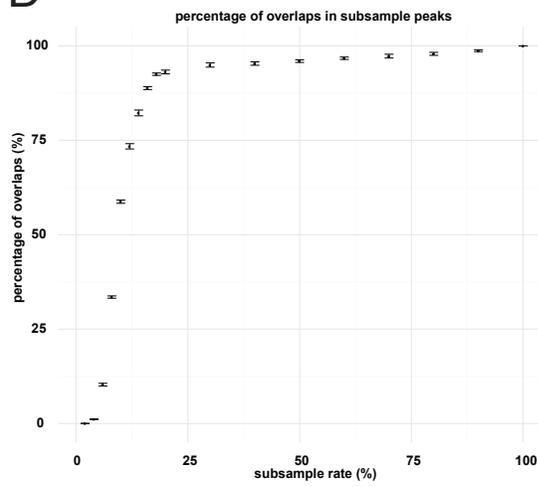


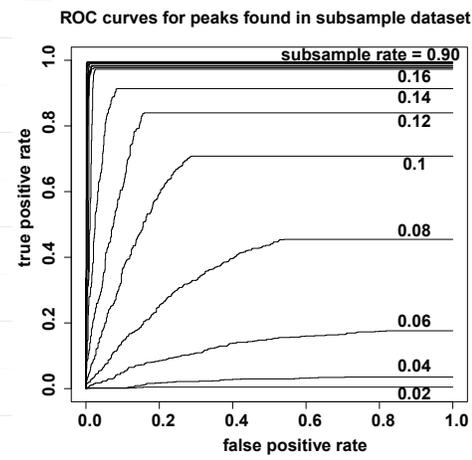
A



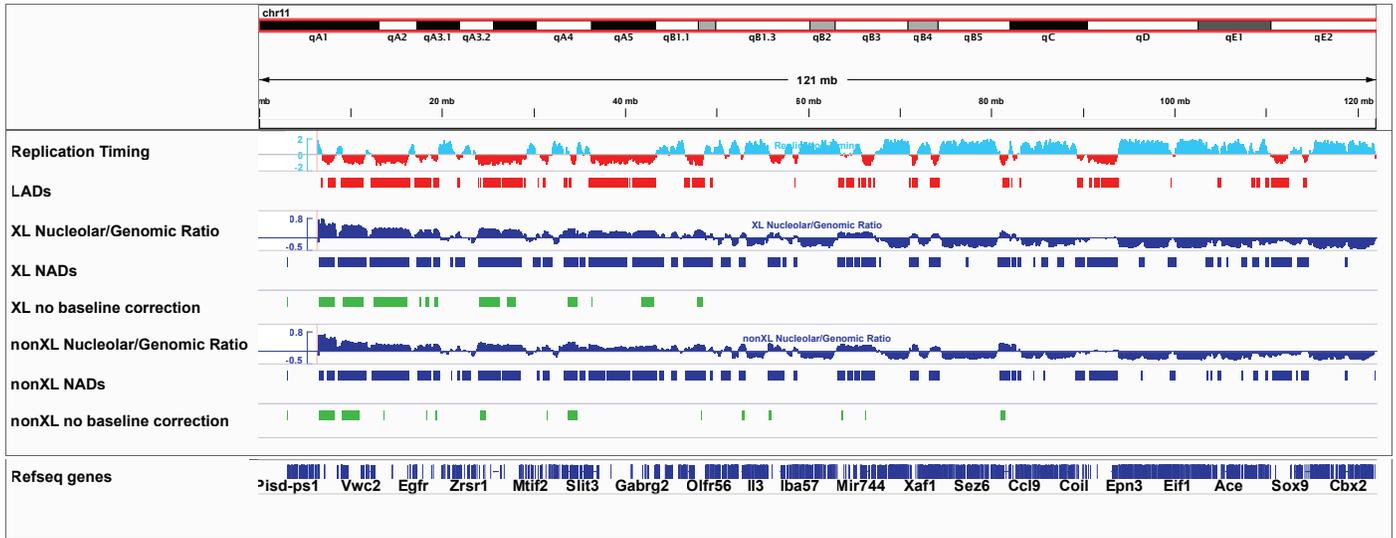
D



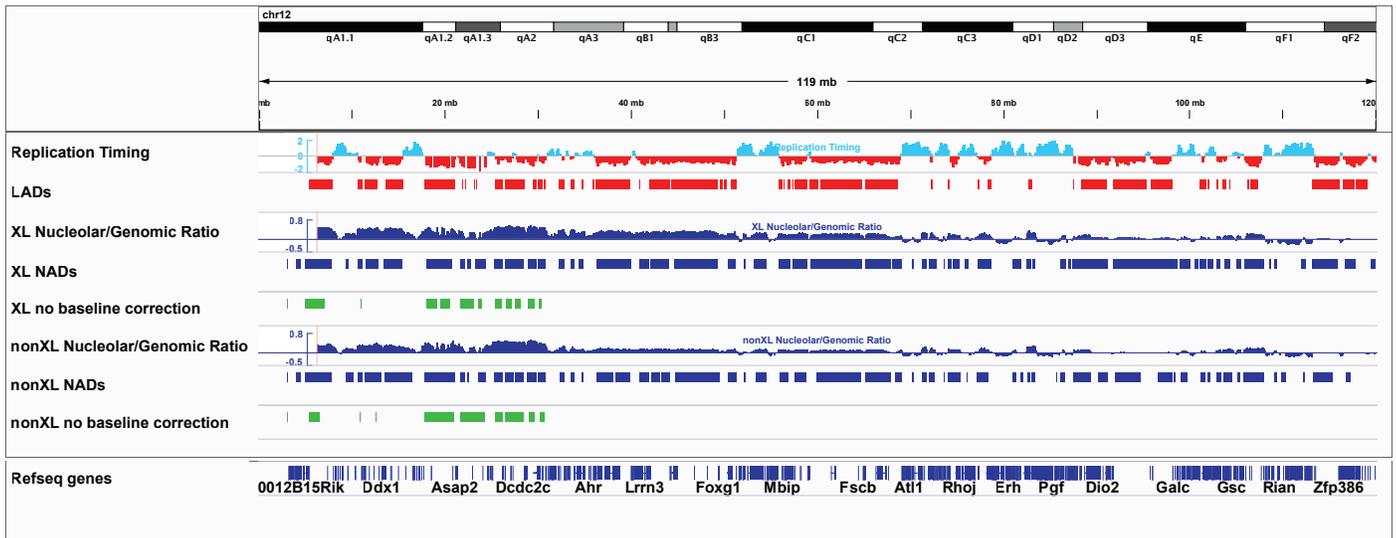
E



B



C



### Supplemental Figure S4. Testing baseline correction and sequencing depth requirements for NADfinder.

A. Workflow of NAD-seq analysis using NADfinder and ChIPpeakAnno.

B. Chromosome-level baseline correction is necessary for optimal peak calling by NADfinder, shown for Chr11.

Without baseline correction, peaks at the distal region of the Chr11 are missed. Replication timing and LAD peak data from MEFs are shown as in Fig. 1. Blue tracks show nucleolar/genomic ratios from crosslinked (XL) and non-crosslinked (nonXL) preparations, with NADfinder peaks also in blue. Green tracks show peaks called by NADfinder without baseline correction.

C. As in panel B, Chr12 is shown. Same as Chr11, without baseline correction, peaks at the distal region of the Chr12 are missed.

D. Subsampling analysis with peak calling at 5% false discovery rate. In this experiment, about 200 million reads per library were obtained for 2 pairs of genomic and nucleolar samples. This analysis suggests that 25% of subsampling rate resulting in about 50 million reads, would identify similar sets of peaks at 5% discovery rate as the whole dataset, i.e. 200 million reads.

E. Receiver operating characteristic curves (ROC) show that a 20% subsampling rate results in similar ROC as observed using the entire 200 million read dataset in panel D.