Chromatin Immunoprecipitation protocol (Ram *et al.,* Cell, 2011)

- Cells were crosslinked in formaldehyde (1%, 37_C for 10 min), and then quenched with glycine (5 min at 37_C).
- Fixed cells were lysed in 1% SDS, 10mM EDTA and 50mM Tris-HCl pH 8.1 supplemented with protease inhibitor (Roche, 04693159001), fragmented with a Branson Sonifier (model S-450D) at 4_C to a size range between 200 and 800 bp, and precipitated by centrifugation.
- 5 to 10 ug of antibody were pre-bound by incubating with a mix of Protein-A and Protein-G Dynabeads (Invitrogen, 100-02D and100-07D, respectively) in blocking buffer (PBS supplemented with 0.5% TWEEN and 0.5% BSA) for 2 hr.
- Washed beads were added to the chromatin lysate, and then incubated overnight. Samples were washed 6 times with RIPA buffer, twice with RIPA buffer supplemented with 500 mM NaCl, twice with LiCl buffer (10 mM TE, 250mM LiCl, 0.5% NP-40, 0.5% DOC), twice with TE (10Mm Tris-HCl pH 8.0, 1mM EDTA), and then eluted in 0.5% SDS, 300 mM NaCl, 5 mM EDTA, 10 mM Tris Hcl pH 8.0 at 65_C. Eluate was incubated in 65_C over-night, and then treated sequentially with RNaseA (Roche, 11119915001) for 30 min and Proteinase K (NEB, P8102S) for two hours.
- DNA was purified using a DNA purification kit (QIAGEN, 28004).

ChIP-Seq Library Preparation and Sequencing

- Libraries of CR ChIP samples were prepared according to a modified version of the Illumina Genomic DNA protocol, as described previously (Mikkelsen et al., 2007).
- Briefly, ChIP DNA was ligated to Illumina adaptors and subjected to 22 cycles of PCR amplification.
- Amplified products between 200 and 800 bp were purified on a 2% agarose gel. Roughly 5 picomoles of DNA library was then applied to each lane of the flow cell and sequenced on Illumina GAII sequencers according to standard Illumina protocols.