FILE S1

Supporting Methods

Cross-linking Immunoprecipitation: 1 L of cells containing the *KHD1-TAP* allele were harvested at OD 2.5, washed twice with water and resuspended in 10X pellet volume. UV crosslinking was performed by irradiating shallow layers of this suspension three times at 400 mJ/cm^2. Cells were washed in calmodulin binding buffer (CBB) with .1% NP-40 (RIGAUT *et al.* 1999) and protease inhibitors (leupeptin, pepstatin, PMSF), resuspended in 10 mL and separated and into FastPrep tubes. 600 micron glass beads were added to ~1/3 volume and lysis performed three times, 45 seconds at maximum speed in a FastPrep 3000.

The lysate was collected by puncturing the bottom of the tube and spinning the sample into a 15 mL tube. Samples were spun at 3,000 rpm for 5 minutes and the supernatant was collected. The pellet was resuspended in 5 mL CBB with .1% NP-40 and protease inhibitors, spun again at 3,000 rpm for 5 minutes, and the supernatant collected. This process was repeated one more time. RNAse A (USB 70194Y) was added to the pooled supernatants at a dilution of 1:50,000 or 1:1,000 and incubated at 37° Celsius for 10 minutes. The sample was split into microcentrifuge tubes and spun at 9,500 rpm for 5 minutes. The supernatant was transferred to fresh tubes and spun at 12,000 rpm for 5 minutes. The supernatant was used for immunoprecipitation.

300 μL calmodulin-agarose beads (GE Healthcare 17-0529-01) were equilibrated for ten minutes in CBB with .1% NP-40 three times. The equilibrated beads were added to the supernatant and incubated for 2 hours at 4° Celsius on a rocking platform. The beads were collected through a column and washed twice in 5 mL CBB with .1% NP-40 and twice in 5 mL CBB with .02% NP-40. Protein was incubated in 3 mL calmodulin elution buffer (CEB) (RIGAUT *et al.* 1999) for 45 minutes at 4° Celsius on a rocking platform and then collected in a 15 mL tube. The beads were twice washed with 1 mL CEB which was pooled with the initial eluate.

800 μL Dynalbeads (Invitrogen 112-010) were equilibrated in CEB three times for ten minutes, added to the eluate, and incubated for 1 hour at 4° Celsius on a rocking platform. The beads were collected using a magnet and transferred to a microcentrifuge tube. They were washed with Nelson stringent buffer (5 mM Tris, pH 7.5, 5 mM EDTA, 2.5 mM EGTA, 1% Triton X-100, 1% Na-DOC, 0.1% SDS, 120 mM NaCl, 25 mM KCl) followed by Nelson high salt buffer (15 mM Tris, pH 7.5, 5 mM EDTA, 2.5 mM EGTA, 1% Triton X-100, 1% Na-DOC, 0.1% SDS, 1 M NaCl) for 10 minutes each at 4° Celsius on a rocking platform and transferred to a new tube where they were washed twice in Nelson low salt buffer (15 mM Tris, pH 7.5, 5 mM EDTA).

After this immunoprecipitation, the CLIP protocol was followed as previously described to obtain DNA molecules for sequencing (ULE *et al.* 2005), with the exception of the primers used for cDNA amplification as noted in the main text.

LITERATURE CITED

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ULE, J., K. JENSEN, A. MELE and R. B. DARNELL, 2005 CLIP: a method for identifying protein-RNA interaction sites in living cells. Methods **37:** 376-386.