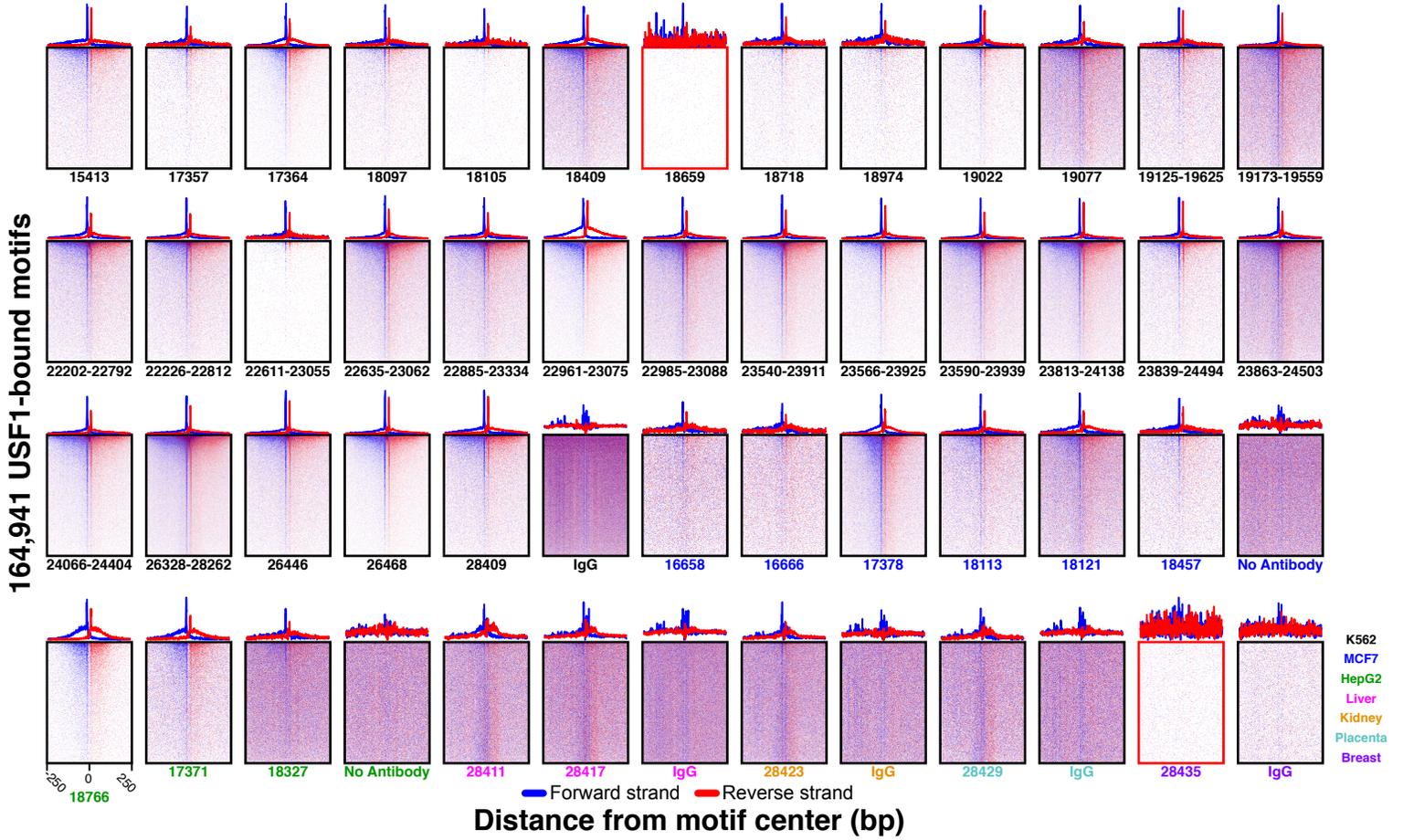
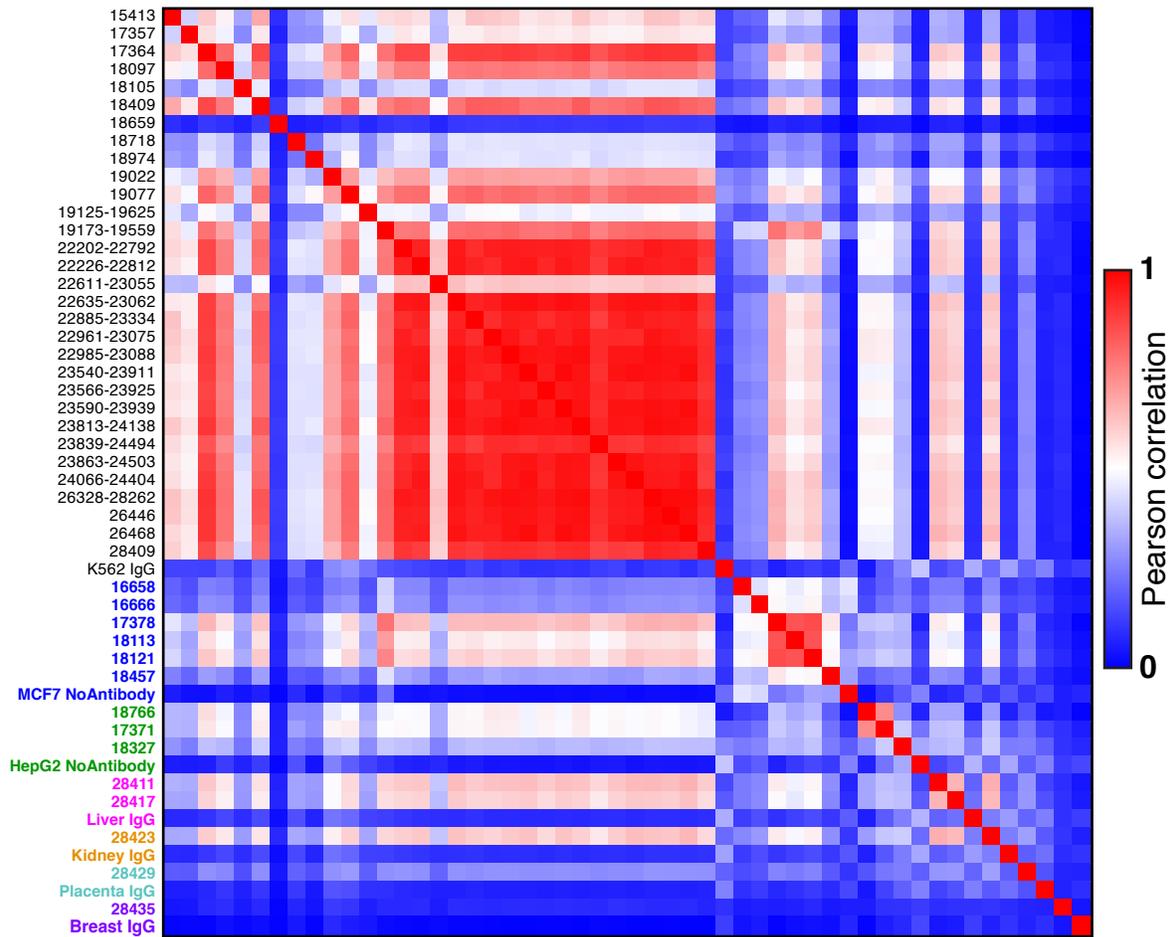
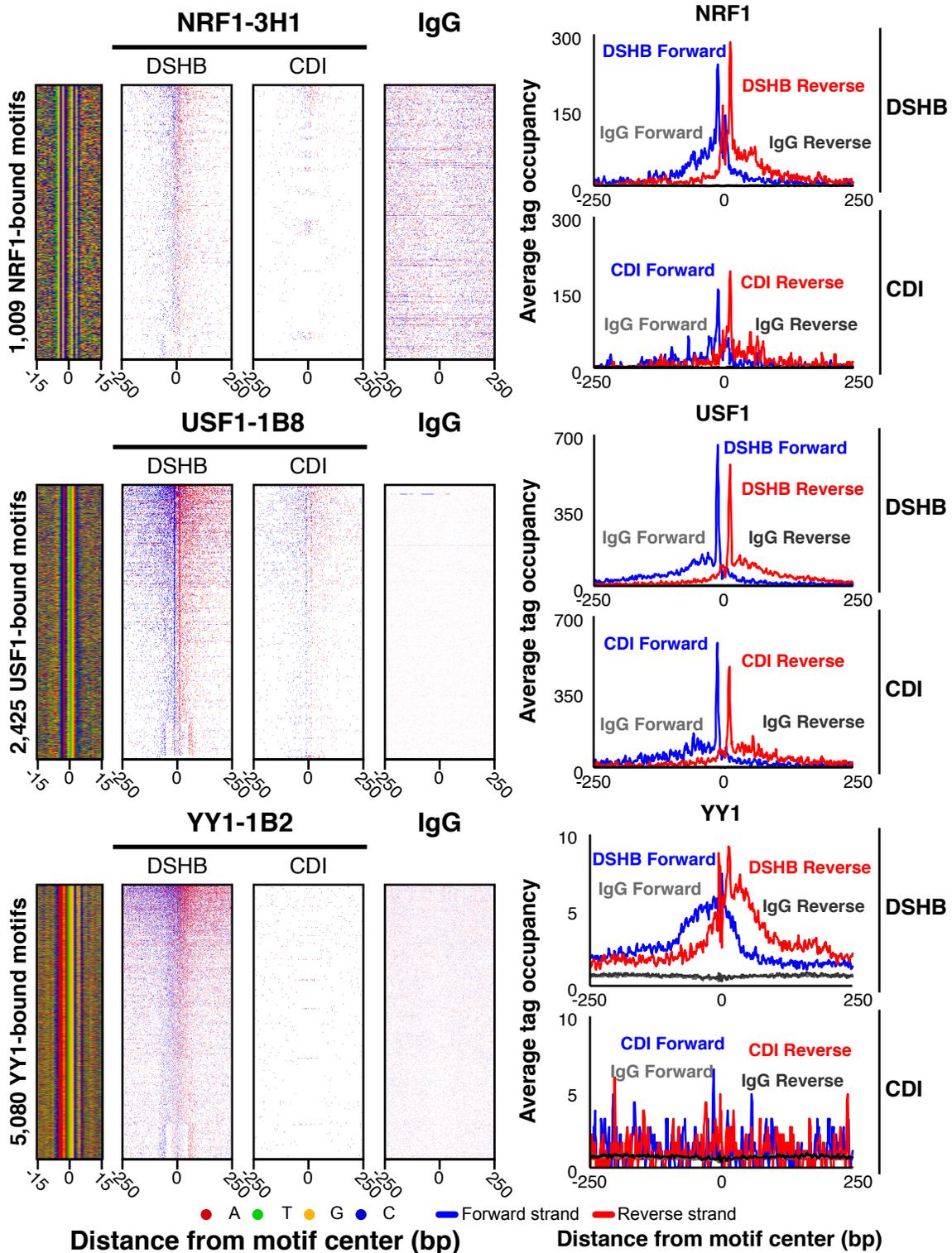
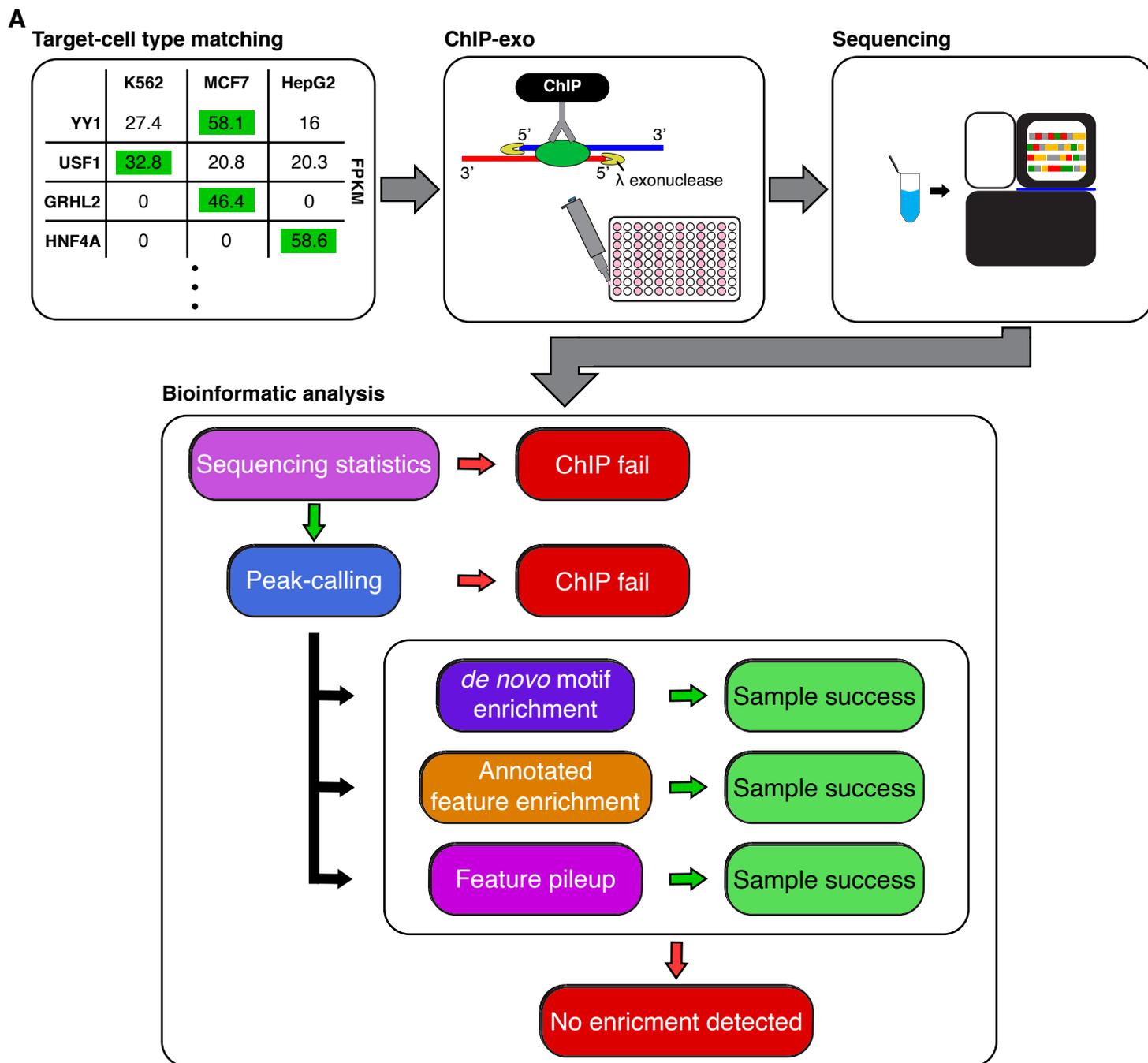


A**B****USF1 occupancy correlation matrix**

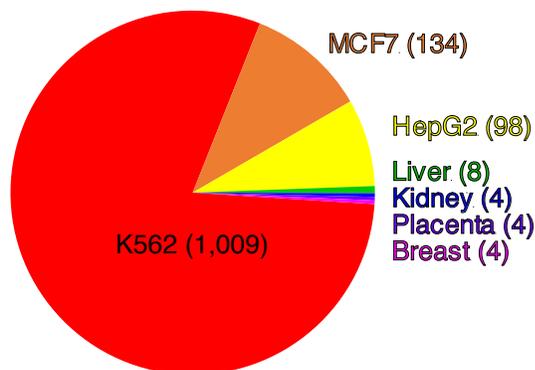
Supplementary Fig. 1 Technical robustness of the USF1 PCR mAb in the CHIP-exo assay. (A) Heatmap and row-averaged composite plots for 45 USF1 CHIP-exo experiments with the indicated project sample ID were performed in K562 (black), MCF7 (blue), HepG2 (green), human liver (pink), kidney (orange), placenta (cyan), and breast (purple). The 5' end of aligned sequence reads for each replicate were plotted against their distance from the nearest USF1 E-box motif. These motifs were present in the union of peak-pairs across all 45 USF1 datasets for a total of 164,941 peaks that intersected with an E-box motif. Reads are strand-separated (blue = motif strand, red = opposite strand). Rows are linked across samples and sorted based on their combined rank-order average in a 500 bp bin around each motif midpoint. Matching IgG or No-Antibody control experiments for each cell type are shown. Samples 18659 and 28435 are outlined in red and represent experiments that failed to show enrichment at USF1 peaks. (B) Correlation matrix of USF1 technical replicates. Pearson correlation was calculated between technical replicates and negative controls using the sum of tags in a 500 bp window centered around the motif midpoint for all potential USF1 binding events. Samples are labelled and colored as defined in panel B.



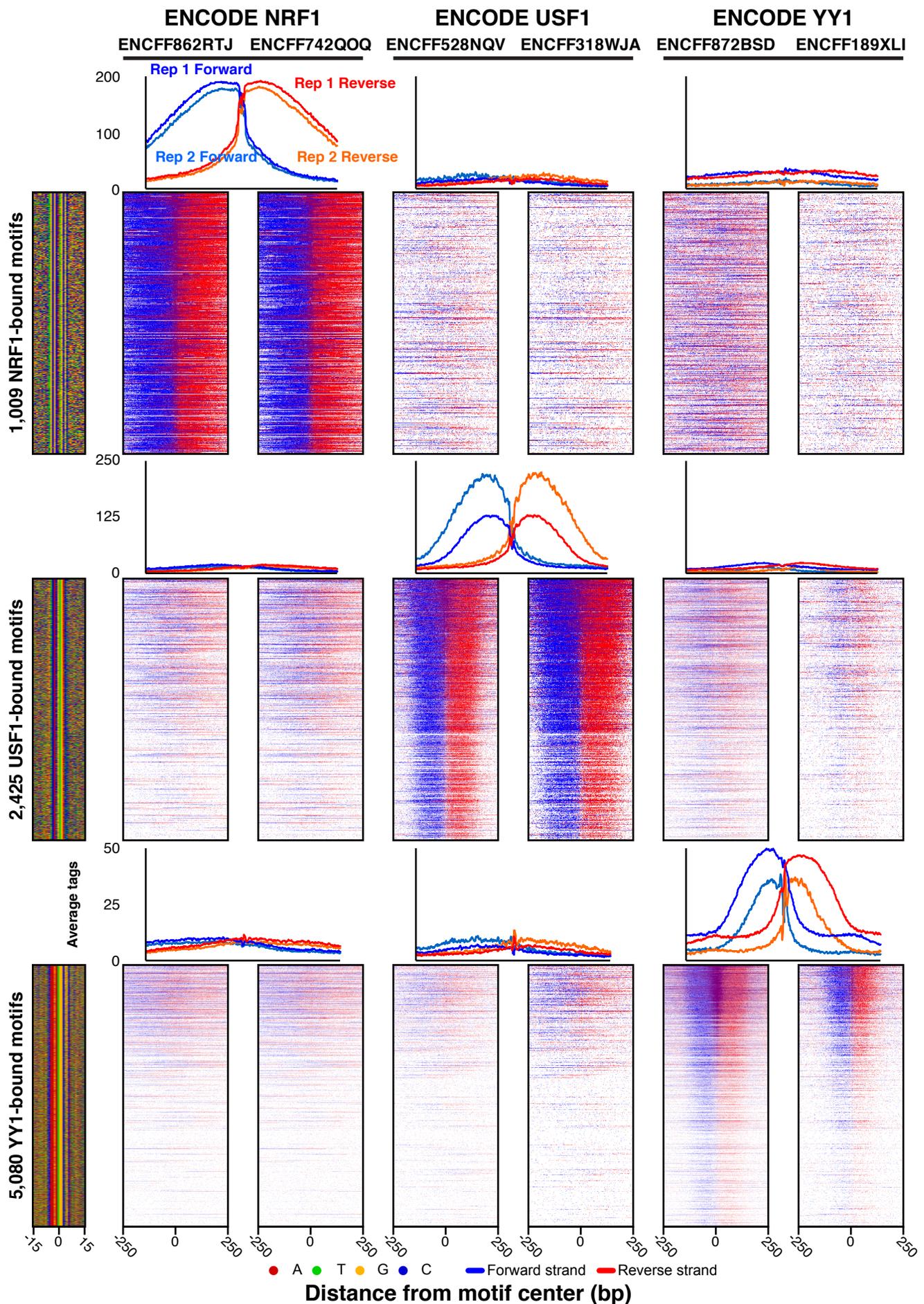
Supplementary Fig. 2 Assessment of antibody source (DSHB and CDI). DNA-sequence 4-color plots (left), heatmaps (middle), and composites (right) were generated for the indicated targets, number of bound motifs, and antibody source, tested in K562 cells. The 5' end of aligned sequence reads for each set of experiments were plotted against distance from cognate motif, present in the union of all called peaks between the datasets for each indicated target. Reads are strand-separated (blue = motif strand, red = reverse strand) and total-tag normalized across samples. Rows are linked across samples and sorted based on their combined average in a 100 bp bin around each motif midpoint. We note a jagged composite trace for CDI's YY1 ChIP-exo relative to the IgG negative control. This is likely due to the IgG negative control's significantly higher sequencing depth (due to it being a merger of multiple biological replicates). This generates a more linear (smoother) trace in a composite plot due to the deeper sequencing coverage producing a more uniform distribution. In comparison, the relatively lower sequencing depth of the CDI YY1 ChIP-exo displays more variability in a composite plot but lacks the distinct patterning of the DSHB sample. Smoothing of the CDI YY1 trace would produce the same linear pattern as IgG



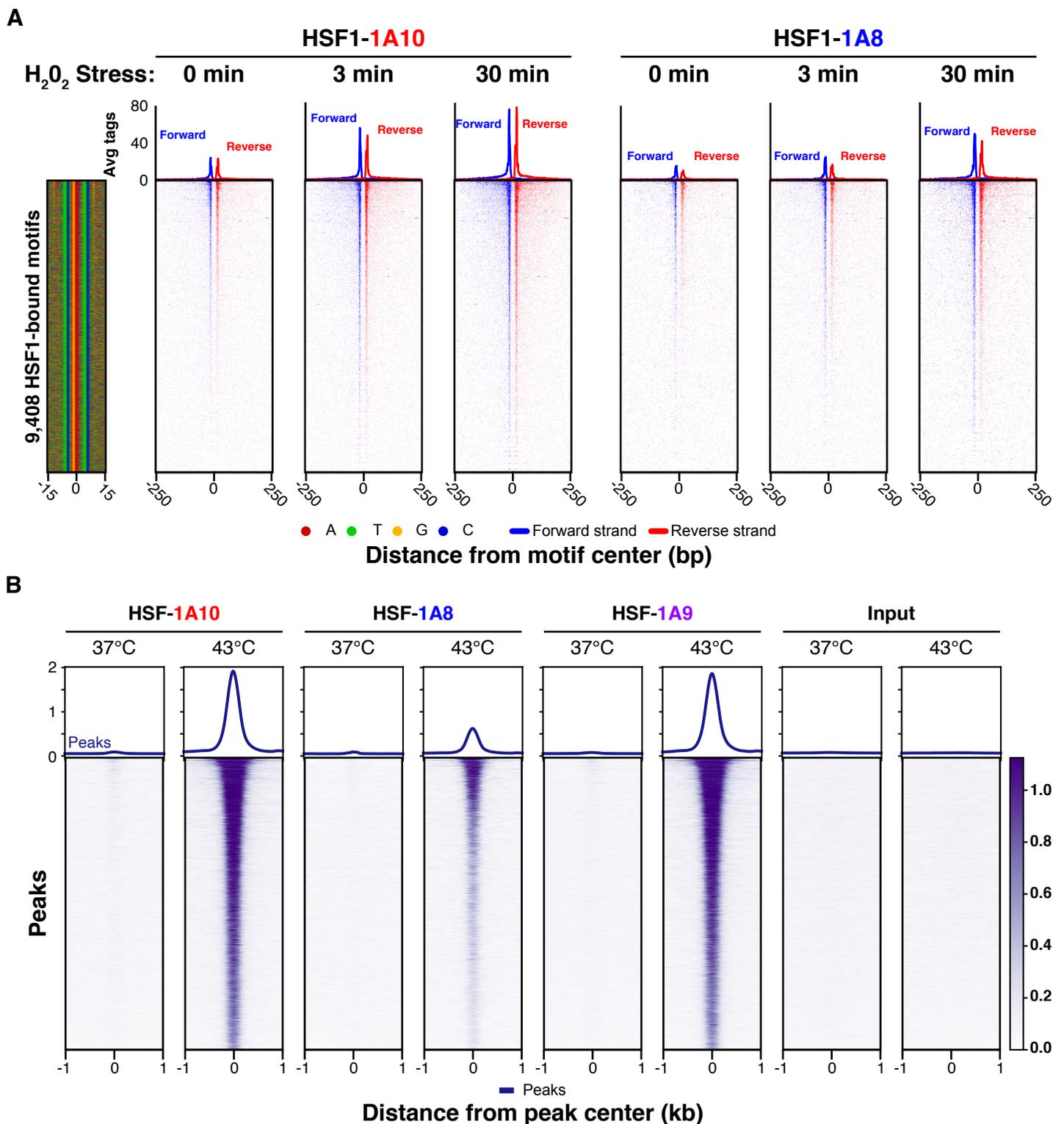
B 1,261 ChIP-exo datasets



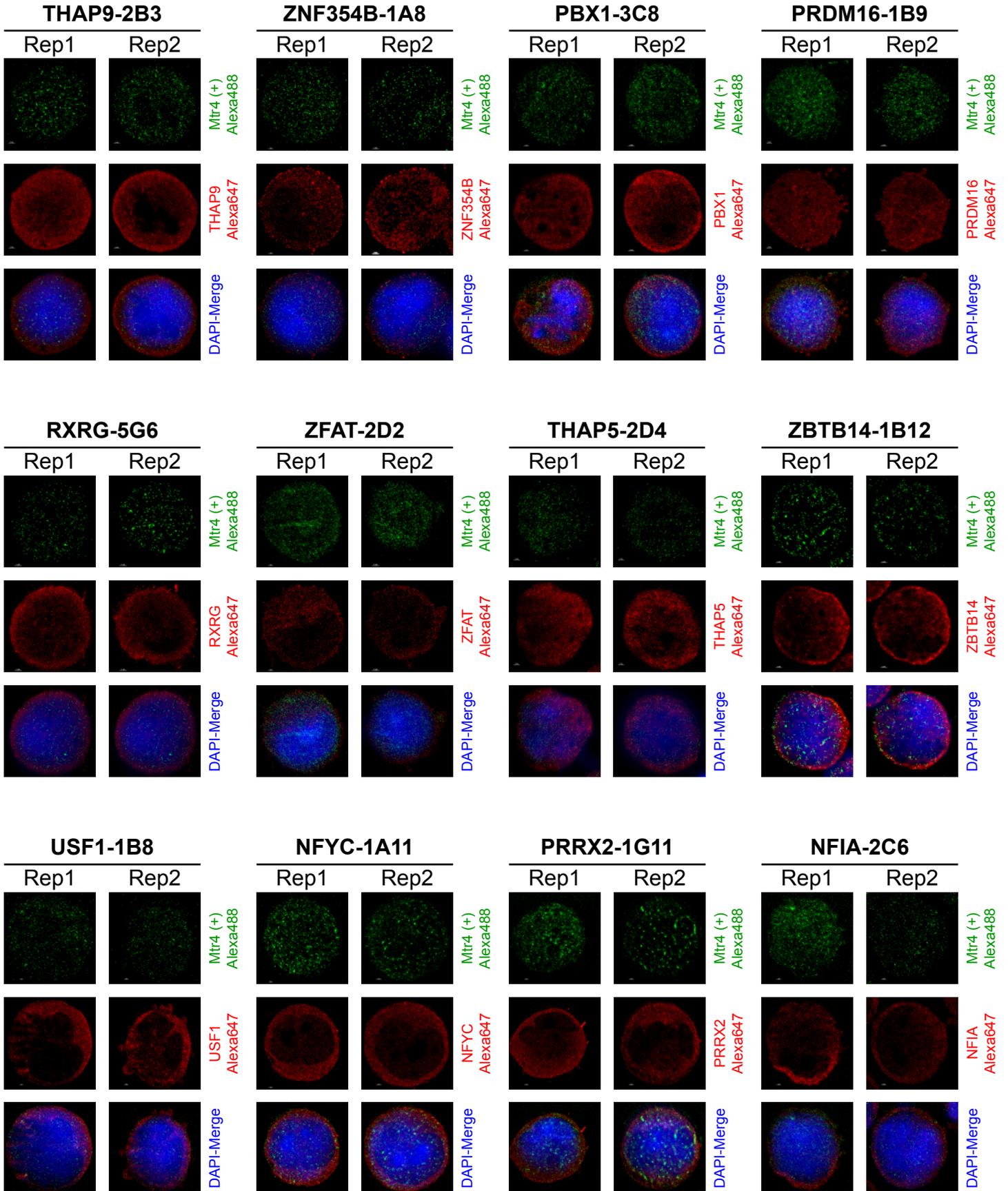
Supplementary Fig. 3 (A) Workflow schematic of bulk PCR^m mAb testing in the ChIP-exo assay. Targets having a strong RNA-seq (The Encode Project Consortium 2012) expression bias towards K562, MCF7, or HepG2 were assayed in that cell line. Otherwise, they were assayed in K562. Samples were processed in cohorts of 46 plus a USF1 positive control and an IgG or “No Antibody” negative control. After high-throughput sequencing, samples were automatically processed through a bioinformatics quality control pipeline. Samples were examined for sequencing depth, library complexity (% PCR duplication), and the ability to generate significant peaks. Peaks and raw tags were then examined to identify enriched sequence motifs, localization to annotated chromatin and sequence regions, and specific enrichment at genomic features such as transcription start sites. (B) Pie chart shows the cell/tissue type of biological material used for 1,261 ChIP-exo datasets.

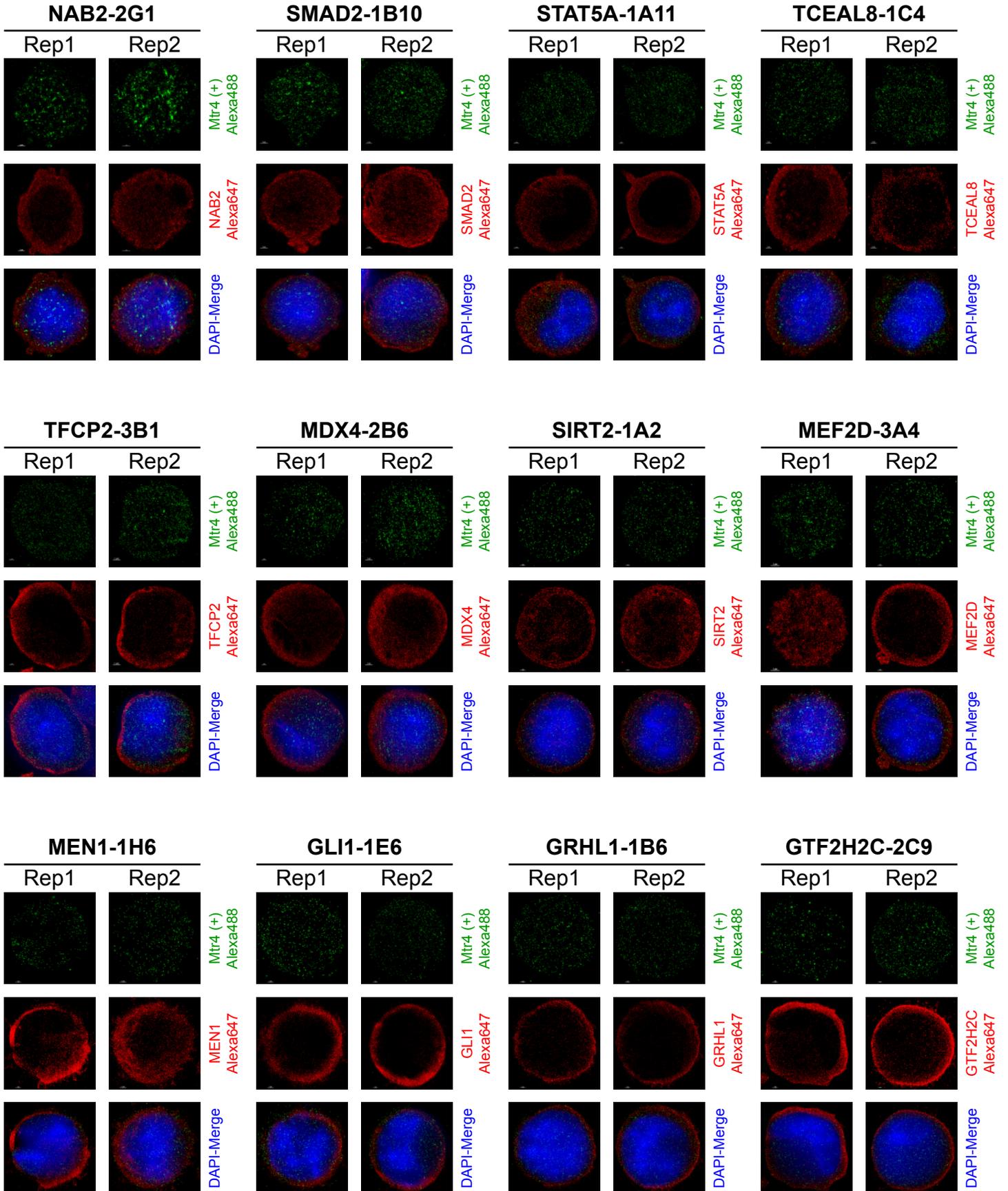


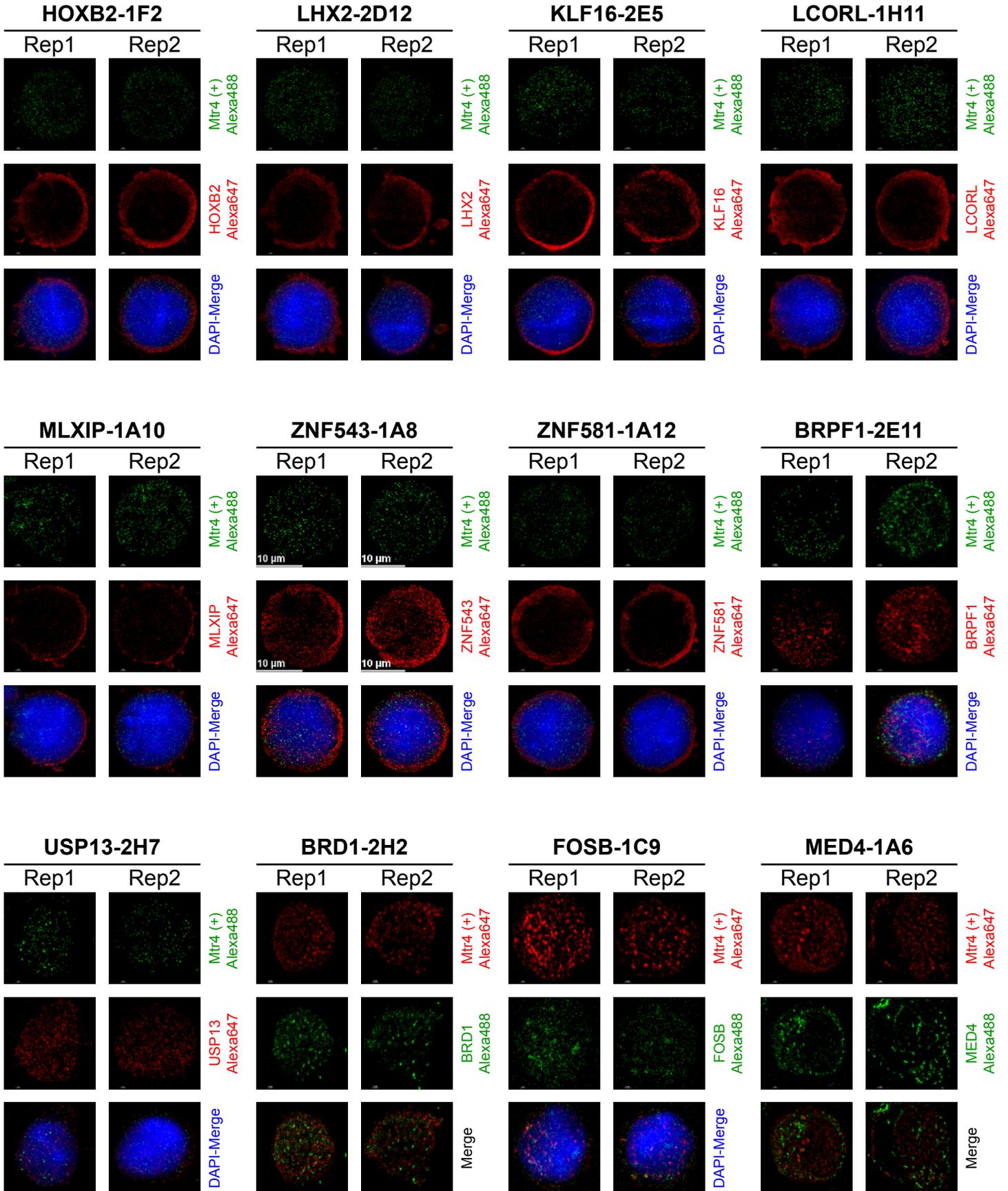
Supplementary Fig. 4. Overlay of ENCODE data at motifs defined by PCRp mAbs using CHIP-exo. CHIP-seq heatmap, composite, and DNA-sequence 4-color plots at the bound motifs defined in Figure 1 for the indicated targets in K562. The 5' end of aligned sequence reads for each set of experiments were plotted against distance from cognate motif of target. Reads are strand-separated (blue = motif strand, red = opposite strand) and total-tag normalized across samples. Rows are linked across samples and sorted as in Supplementary Fig. 2.

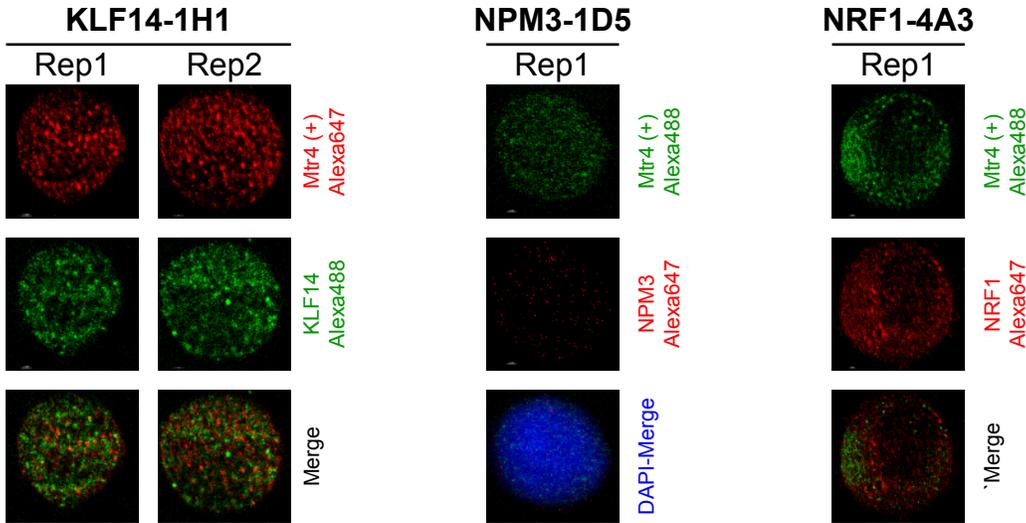


Supplementary Fig. 5. Validation of HSF1 mAb in a cell state change (stress). (a) ChIP-exo heatmap, composite, and DNA-sequence 4-color plots are shown for the indicated number of bound motifs for the indicated mAb in response to hydrogen peroxide treatment (0.3mM); where binding increases with treatment time) in K562 cells. The 5' end of aligned sequence reads for each set of experiments were plotted against distance from cognate motif, present in the union of all called peaks between the datasets for each indicated target. Reads are strand-separated (blue = motif strand, red = opposite strand) and total-tag normalized across samples. Rows are linked across samples and sorted based on their combined average in a 100 bp bin around each motif midpoint. (b) ChIP-seq heatmap and composite plot are shown for the indicated number of bound loci for the indicated antibody hybridoma clone and input in HCT116 cells in response to 1 hr. of heat shock (42°C) or mock (37°C). Rows are linked across samples and sorted in descending order by mean score per region.



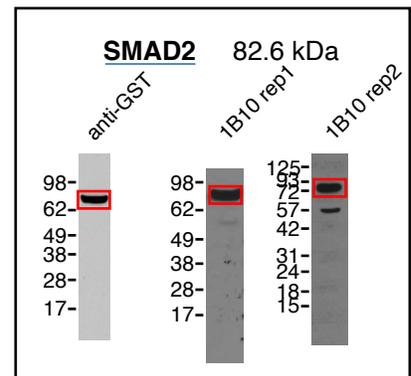
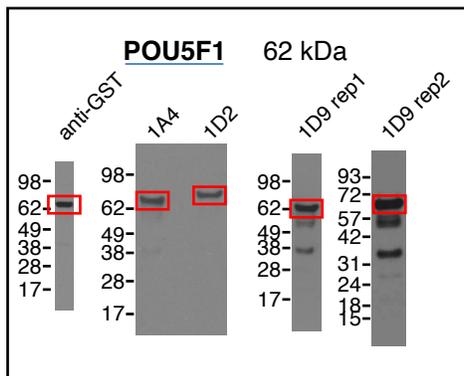
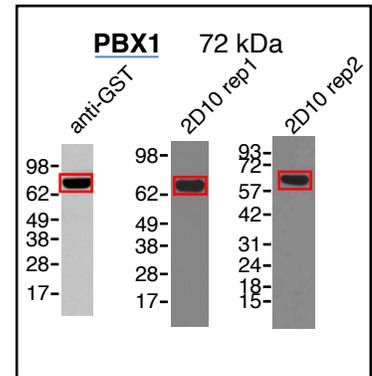
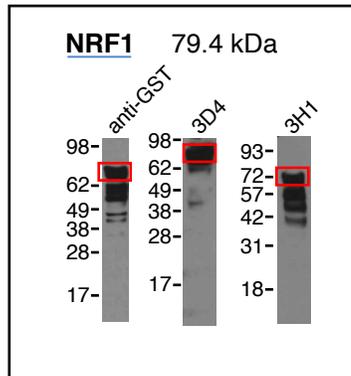
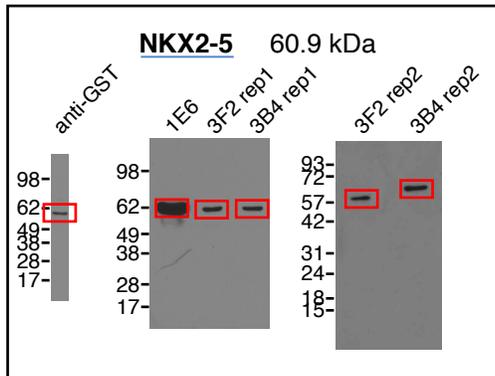
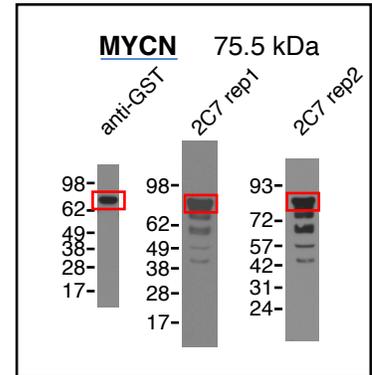
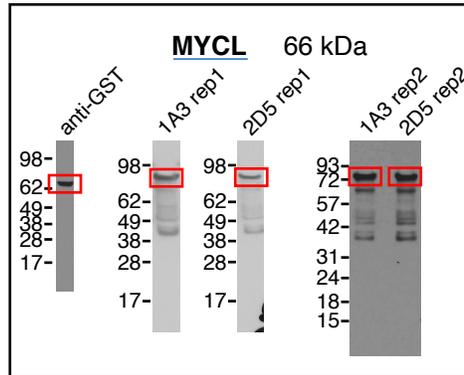
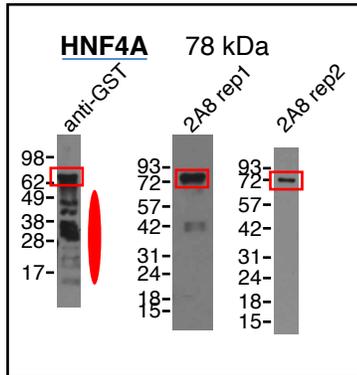
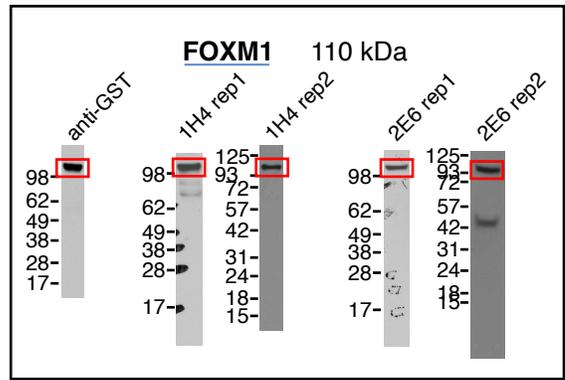
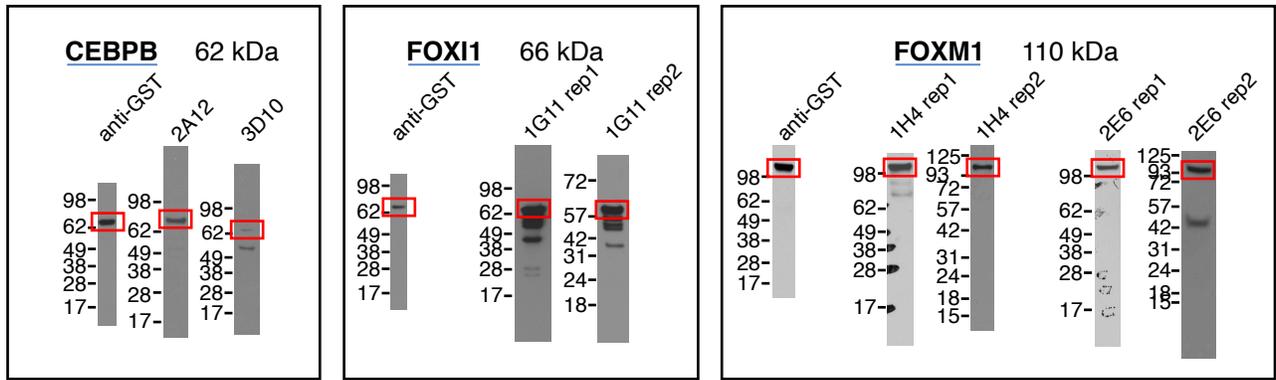




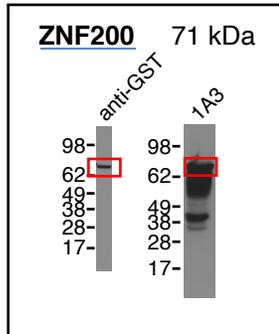
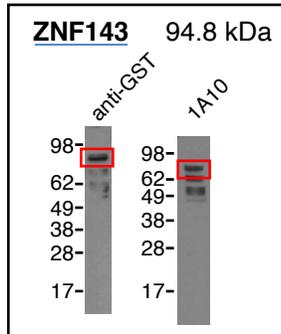
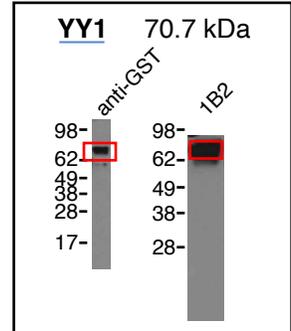
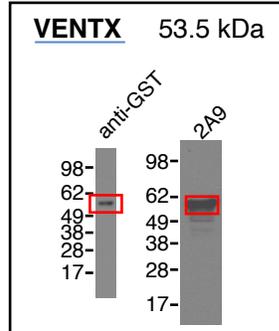
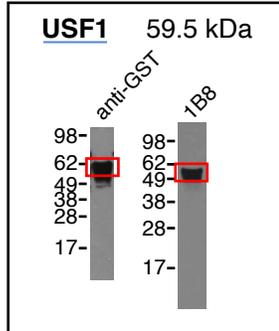
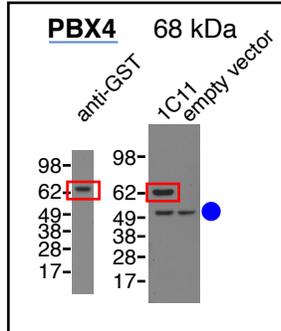
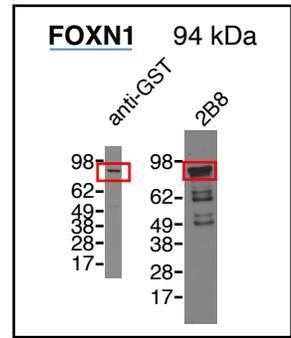
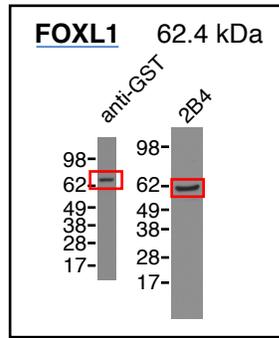
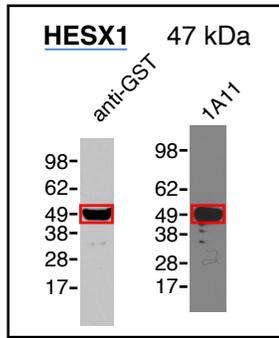
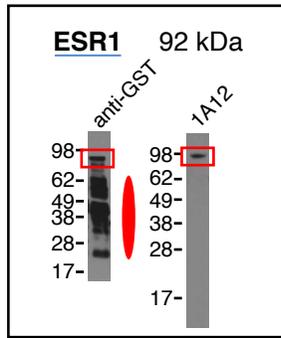


Supplementary Fig. 6. Example of STORM capabilities employing three different fluorescence channels displaying one K562 cell for nuclear localization. The STORM positive control was performed by staining the cell with commercial anti-Mtr4 (a helicase expected to be found in the nucleus and cytoplasm³⁷) followed by incubation with secondary anti-rabbit conjugated to Alexa-488 (green) or Alexa-647 (red). Cells were stained with concentrated PCR supernatant and then incubated with secondary antibody conjugated to Alexa-488 (green) or Alexa-647 (red) as labelled. DAPI nuclear staining was performed where indicated to contrast the location of the nucleus relative to sample and Mtr4 positive control staining. Note that for many of the PCR antibodies, the antibody staining forms a ring at the periphery of the nucleus, possibly indicating non-specific binding.

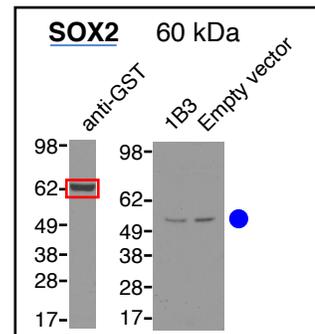
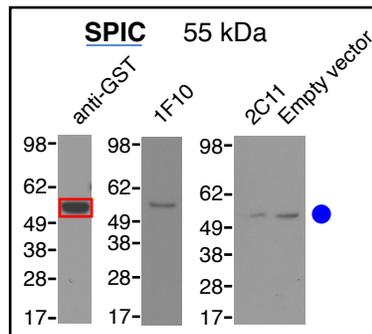
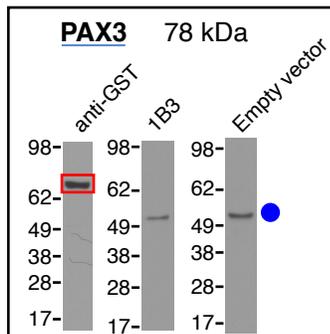
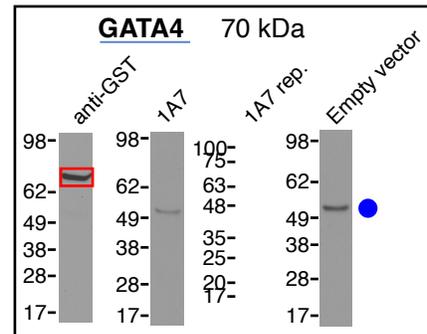
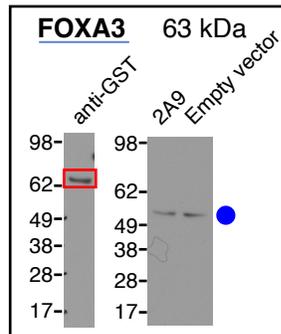
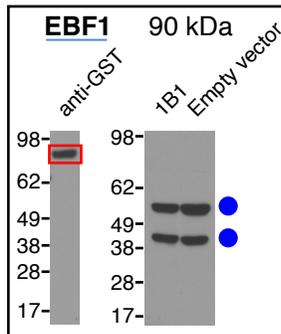
Replicated



Single replicate



Failed



Supplementary Fig. 7. Immunoblots were conducted to assay whether PCRPs can detect the full-length TF. Anti-GST immunoblots are shown for comparison. The red box indicates the correct band, corresponding to the full-length TF. An IVT negative control empty vector was assayed with PCRPs and blue dot indicates cross-reactivity with the 1-Step Human Coupled IVT Kit. The red oval alongside the anti-GST Western blot lanes for HNF4A and ESR1 GST-fusion proteins likely represents incomplete synthesis and/or N-terminal degradation products. Replicated immunoblots (left) are composed of twelve targets that were biologically replicated with the same antibody and nine targets that were technically replicated with distinct hybridoma clones against the same target. Ten targets were assayed as a single replicate (right). The following PCRPs resulted in no bands on Western blots: 1F8 (anti-FOXO1); 2C4 (anti-KLF1); 1B3 (anti-PAX3); 1C12 (anti-SMAD2); 1A7(anti-GATA4); 1A2(anti-SMAD3).