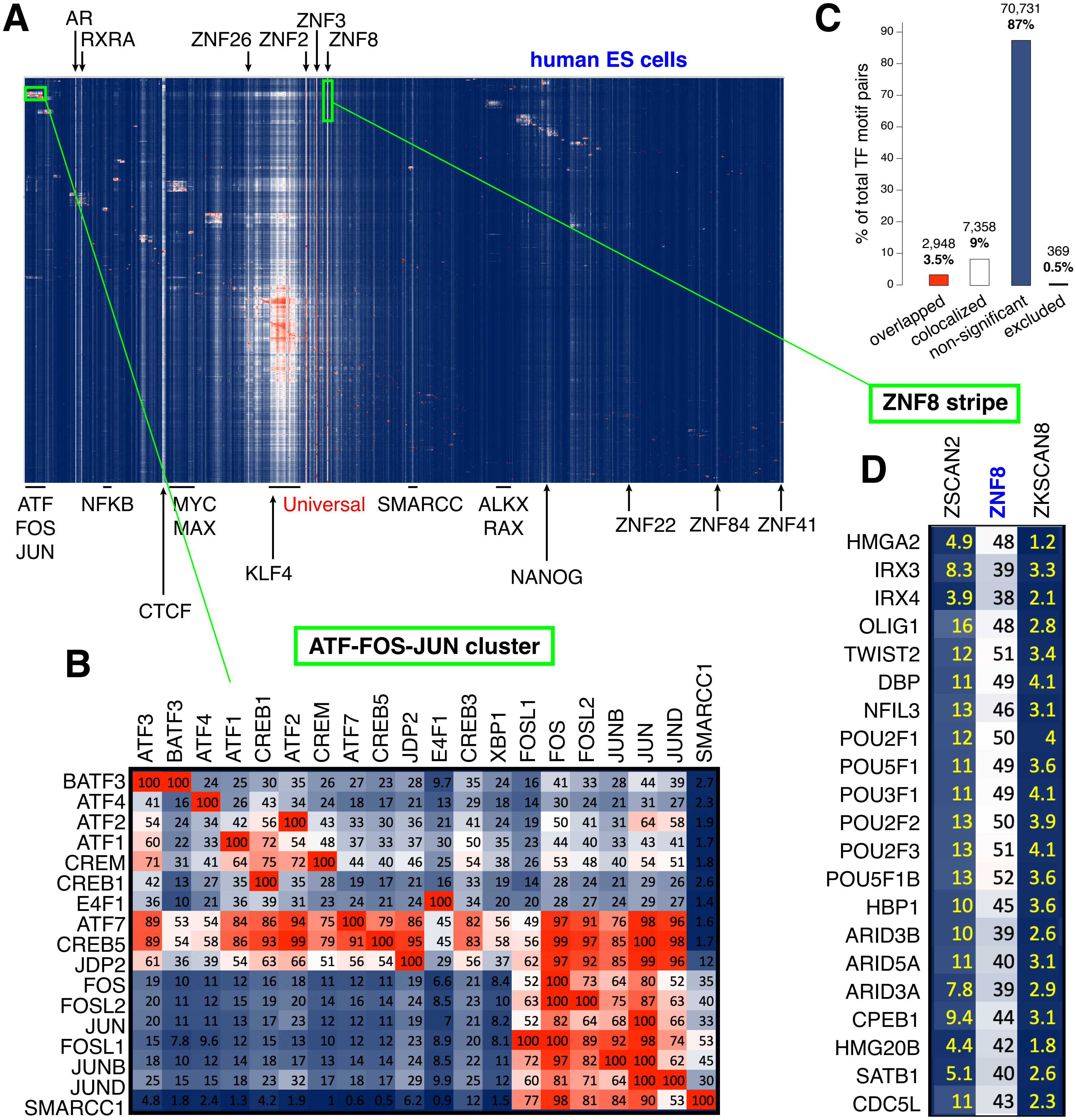
Supplementary Figure 1

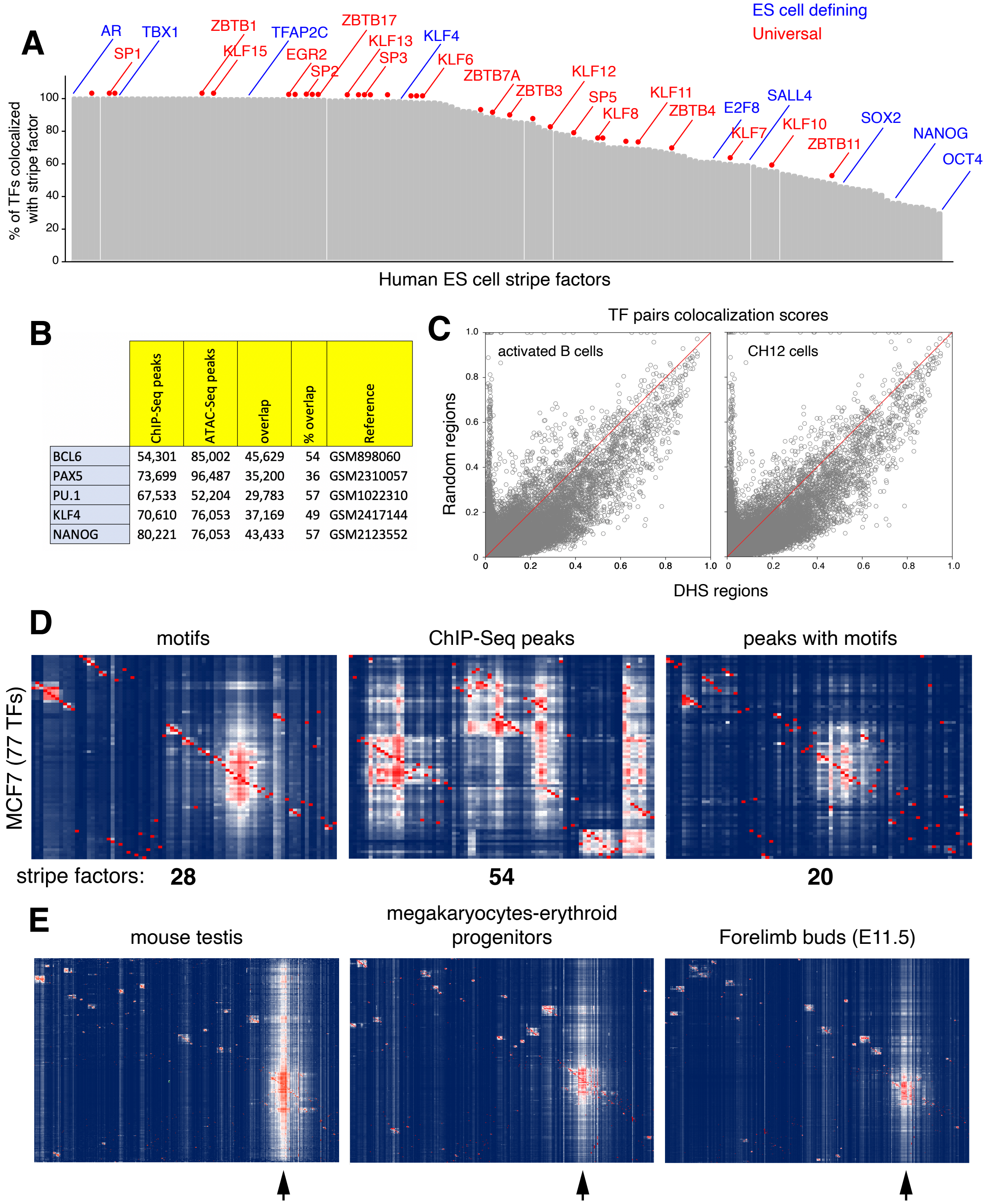


	ATF3	BATF3	ATF4	ATF1	CREB1	ATF2	CREM	ATF7	CREB5	JDP2	E4F1	CREB3	XBP1	FOSL1	FOS	FOSL2	JUNB	JUN	JUND	SMARCC1
BATF3	100	100	24	25	30	35	26	27	23	28	9.7	35	24	16	41	33	28	44	39	2.7
ATF4	41	16	100	26	43	34	24	18	17	21	13	29	18	14	30	24	21	31	27	2.3
ATF2	54	24	34	42	56	100	43	33	30	36	21	41	24	19	50	41	31	64	58	1.9
ATF1	60	22	33	100	72	54	48	37	33	37	30	50	35	23	44	40	33	43	41	1.7
CREM	71	31	41	64	75	72	100	44	40	46	25	54	38	26	53	48	40	54	51	1.8
CREB1	42	13	27	35	100	35	28	19	17	21	16	33	19	14	28	24	21	29	26	2.6
E4F1	36	10	21	36	39	31	23	24	21	24	100	34	20	20	28	27	24	29	27	1.4
ATF7	89	53	54	84	86	94	75	100	79	86	45	82	56	49	97	91	76	98	96	1.6
CREB5	89	54	58	86	93	99	79	91	100	95	45	83	58	56	99	97	85	100	98	1.7
JDP2	61	36	39	54	63	66	51	56	54	100	29	56	37	62	97	92	85	99	96	12
FOS	19	10	11	12	16	18	11	12	11	19	6.6	21	8.4	52	100	73	64	80	52	35
FOSL2	20	11	12	15	19	20	14	16	14	24	8.5	23	10	63	100	100	75	87	63	40
JUN	20	11	11	13	17	23	12	12	11	19	7	21	8.2	52	82	64	68	100	66	33
FOSL1	15	7.8	9.6	12	15	13	10	12	12	23	8.9	20	8.1	100	100	89	92	98	74	53
JUNB	18	10	12	14	18	17	13	14	14	24	8.5	22	11	72	97	82	100	100	62	45
JUND	25	15	15	18	23	32	17	18	17	29	9.9	25	12	60	81	71	64	100	100	30
SMARCC1	4.8	1.8	2.4	1.3	4.2	1.9	1	0.6	0.5	6.2	0.9	12	1.5	77	98	81	84	90	53	100

	ZSCAN2	ZNF8	ZKSCAN8
HMGA2	4.9	48	1.2
IRX3	8.3	39	3.3
IRX4	3.9	38	2.1
OLIG1	16	48	2.8
TWIST2	12	51	3.4
DBP	11	49	4.1
NFIL3	13	46	3.1
POU2F1	12	50	4
POU5F1	11	49	3.6
POU3F1	11	49	4.1
POU2F2	13	50	3.9
POU2F3	13	51	4.1
POU5F1B	13	52	3.6
HBP1	10	45	3.6
ARID3B	10	39	2.6
ARID5A	11	40	3.1
ARID3A	7.8	39	2.9
CPEB1	9.4	44	3.1
HMG20B	4.4	42	1.8
SATB1	5.1	40	2.6
CDC5L	11	43	2.3

Supplementary Figure 1, related to Figure 2. TF combinatorial preferences. (**A**) Agglomerative hierarchical clustering analysis of TFs in human ES cells. Clusters of overlapped pairs are highlighted with bars below the graph while the location of stripe factors are shown with arrows. The universal stripe factor (USF) cluster is also highlighted (red). (**B**) Close up view of the ATF-FOS-JUN cluster (highlighted in panel A with a green rectangle). (**C**) Bar graph showing the percentage of human TF pairs classified as overlapping, colocalized, non-significant, or excluded. (**D**) Close up of the ZNF8 stripe (also highlighted in panel A with a green rectangle).

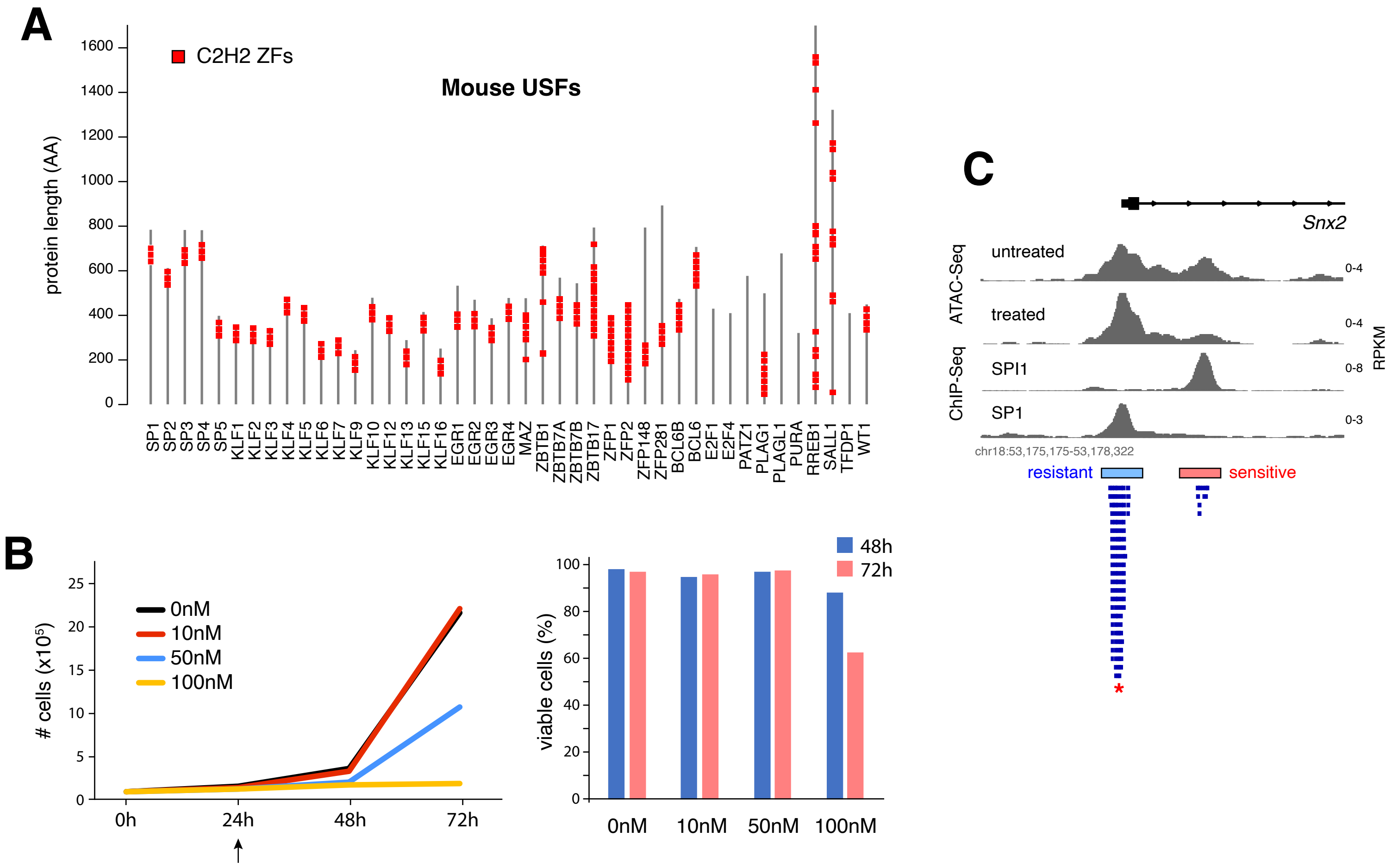
Supplementary Figure 2



	ChIP-Seq peaks	ATAC-Seq peaks	overlap	% overlap	Reference
BCL6	54,301	85,002	45,629	54	GSM898060
PAX5	73,699	96,487	35,200	36	GSM2310057
PU.1	67,533	52,204	29,783	57	GSM1022310
KLF4	70,610	76,053	37,169	49	GSM2417144
NANOG	80,221	76,053	43,433	57	GSM2123552

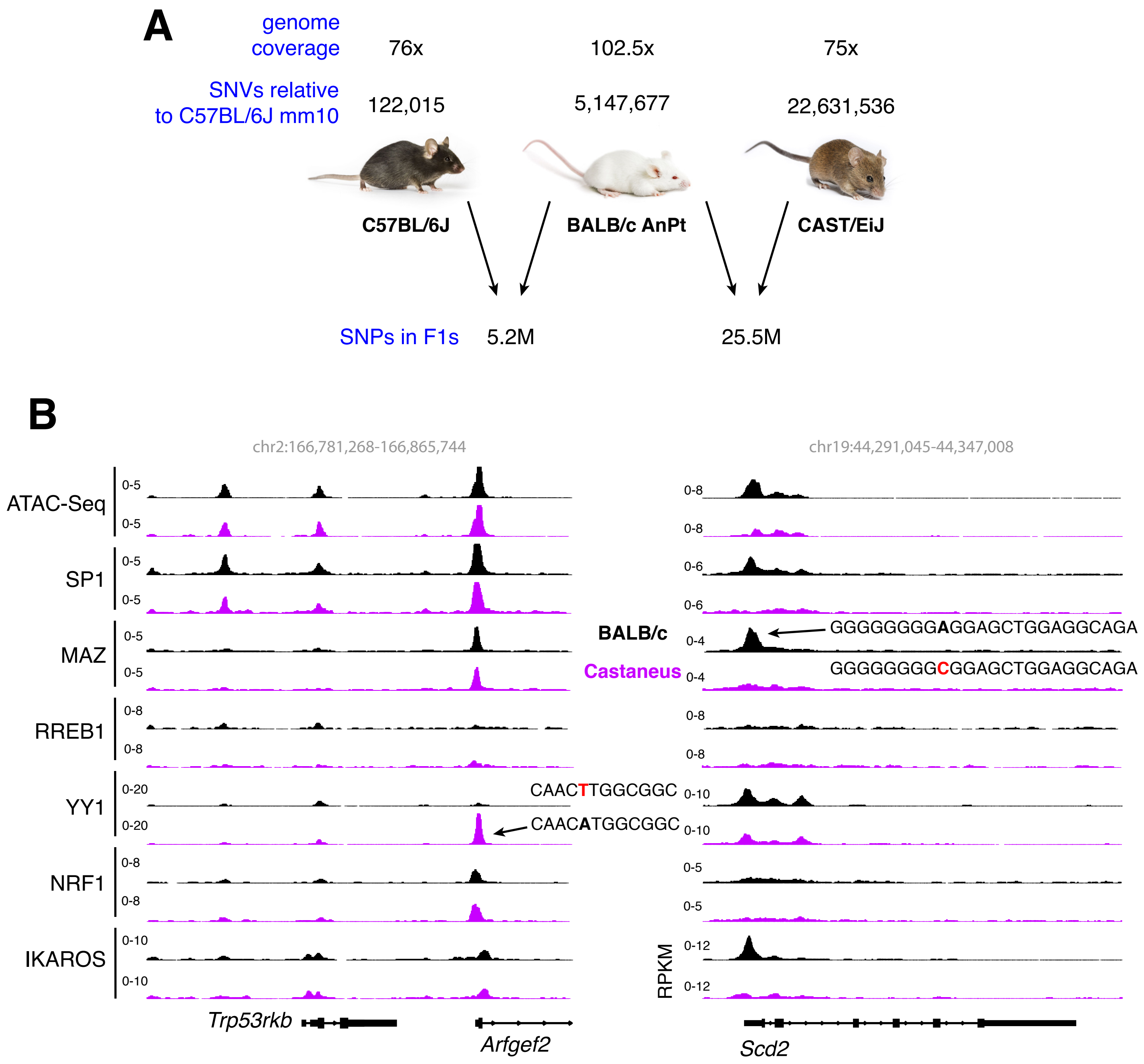
Supplementary Figure 2, related to Figures 2 and 3. Stripe and Universal Stripe Factors. (**A**) Bar graph showing the percentage of TFs colocalized with stripe factors in human ES cells. ES cell-defining factors are highlighted in blue while USFs are highlighted in red. (**B**) Table showing the overlap between TF ChIP-Seq peaks and accessible elements (ATAC-Seq peaks) as obtained from the literature (references). (**C**) Scatter plots showing TF pairs colocalization scores in 201bp random genomic regions versus DHS summits in activated B cells (left) or CH12 B cells (right). For a detailed explanation see Statistical analysis of TF motif colocalization in the Methods section. (**D**) Agglomerative hierarchical clustering of 77 TFs expressed in MCF7 cells based on TF motifs (left), ChIP-Seq peaks (middle), or ChIP-Seq peaks with cognate motifs (right). The number of stripe factors are included below each graph. (**E**) Additional examples of USF clustering (indicated with arrows) in diverse mouse cells and tissues (testis, megakaryocytes-erythroid progenitors, and forelimb buds (E11.5).

Supplementary Figure 3



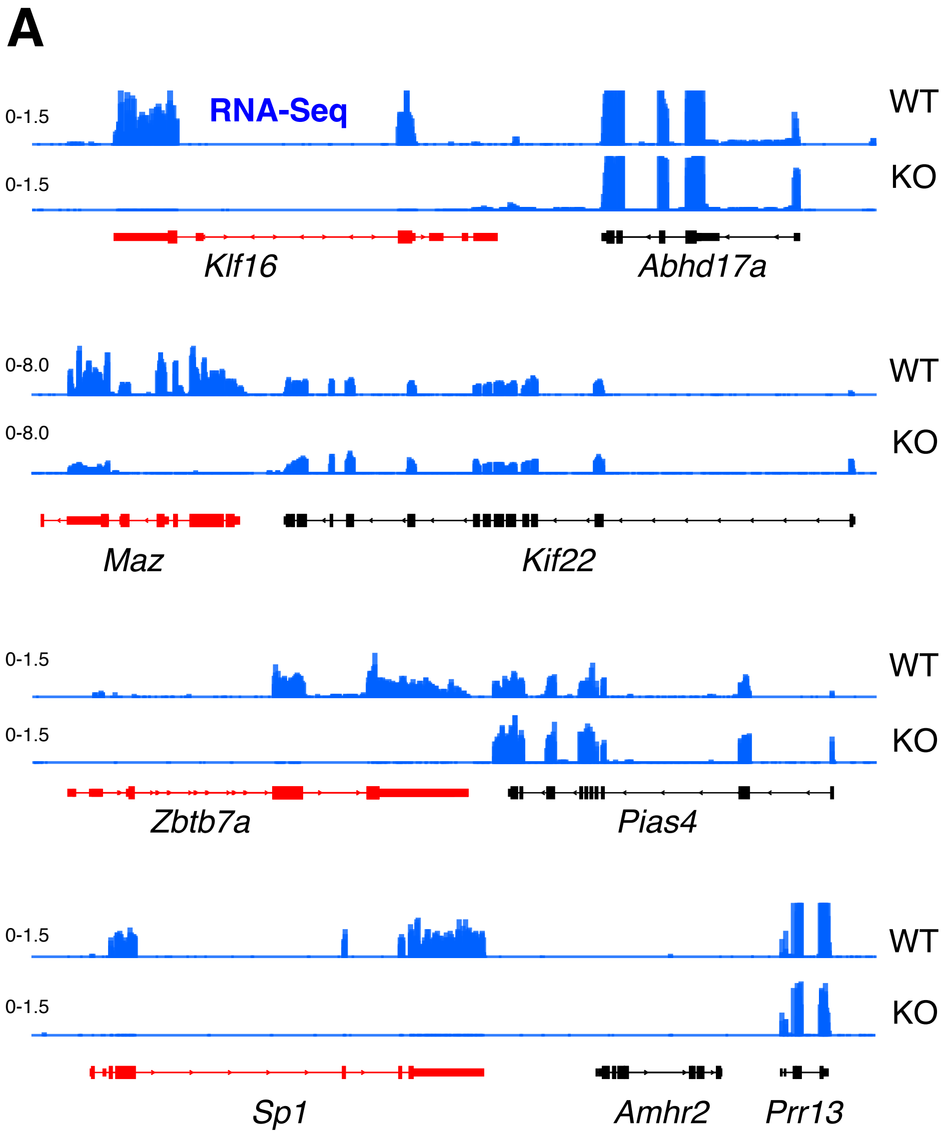
Supplementary Figure 3, related to Figure 4. Mouse USFs and MTM treatment. (**A**) Location of C2H2 ZFs (red squares) in mouse USFs. (**B**) Left line graph shows cell division of mouse B cells activated with LPS+IL-4 in the absence or presence of 10, 50 or 100nM of MTM. Right bar graph shows the percentage of viable cells in those cultures at 48h or 72h. (**C**) Example of MTM-resistant and sensitive elements at the Snx2 locus in mouse B cells. Binding of SP1 (USF) and SPI1 (based on ChIP-Seq) and predicted TF motifs are included. Red asterisk below denotes overlapping USF motifs.

Supplementary Figure 4



Supplementary Figure 4, related to Figure 5. Disruption of USF binding in hybrid mouse B cells. (**A**) Schematics showing sequencing coverage and number of SNPs in C57BL/6J, BALB/c AnPt, and CAST/EiJ genomes. SNPs in F1 progeny highlighted below. (**B**) Examples of ATAC-Seq peaks carrying single SNPs targeting YY1 (left) or MAZ (right) binding motifs. BALB/c and Castaneus alleles are depicted in black and purple respectively.

Supplementary Figure 5



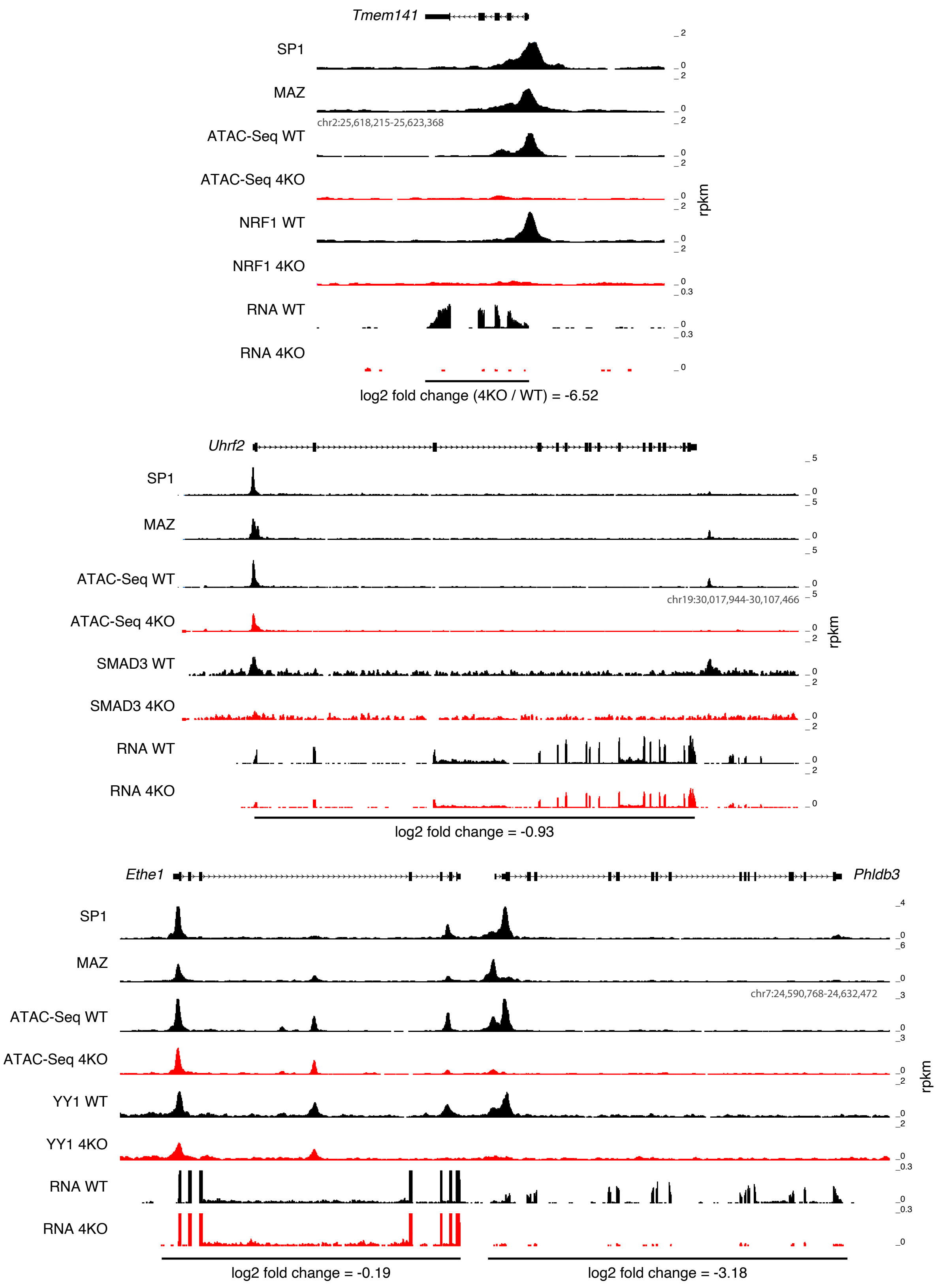
B

Expression (TPM)

	WT	4KO
Nrf1	32.1	29.0
	33.8	30.2
	33.8	30.1
	33.3	**29.8**
Nfyb	30.7	21.3
	30.6	22.4
	32.0	21.4
	31.1	**21.7**
Yy1	101.3	96.3
	102.5	93.5
	100.9	93.1
	101.6	**94.3**
Smad3	4.6	5.0
	4.3	4.8
	4.4	**4.9**
Smad7	20.8	21.9
	18.9	21.6
	19.9	**21.8**

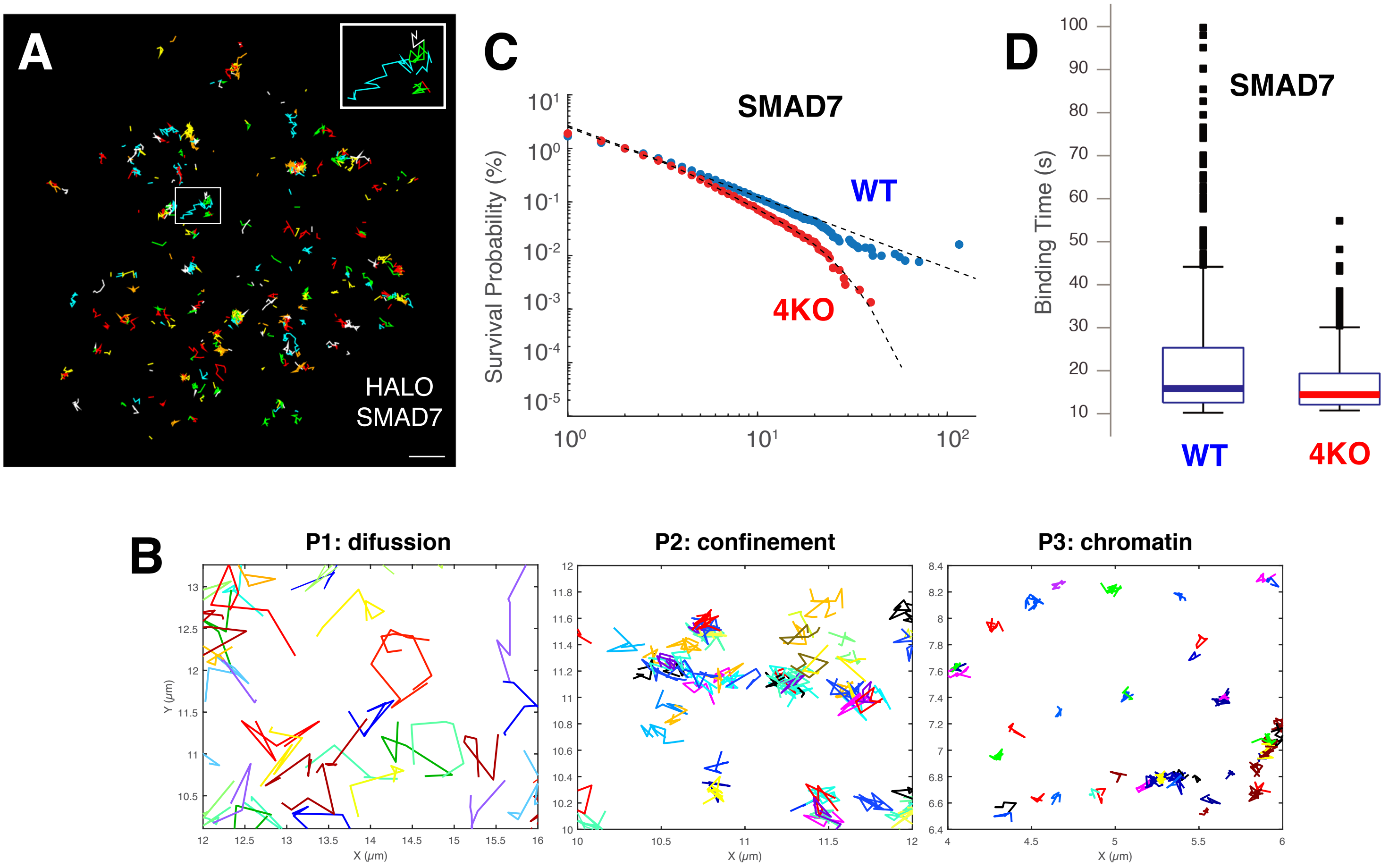
Supplementary Figure 5, related to Figure 6. Characterization of 4KO cells. (**A**) Browser tracks showing RNA-Seq analysis of WT and 4KO CH12 B cells at Klf16, Zbtb7a, Maz, and Sp1 loci. (**B**) Expression of Nrf1, Nfyb, Yy1, Smad3 and Smad7 genes in WT and 4KO Ch12 B cells.

Supplementary Figure 6



Supplementary Figure 6, related to Figure 6. Transcriptional impact of USF deletion. Examples of NRF1 (upper), SMAD3 (middle) and YY1 targets (lower, Phldb3 gene) affected in 4KO cells. The log2 fold change for total number of reads sequenced for each gene in the two cell types is included.

Supplementary Figure 7



diffusion coefficient ($\mu m^2/s$)

	WT	4KO
SMAD3	2.72	2.60
SMAD7	2.1	2.37

Supplementary Figure 7, related to Figure 7. SMT analysis. (**A**) Micrograph showing particle trajectories of HALO-SMAD7 in WT CH12 B cells. Colors represent different tracks. Bar = 1 um. (**B**) Representative examples of particle trajectories of diffusion, confinement, or chromatin-associated populations (P1, P2, and P3) as classified by SMT. Diffusion coefficients for SMAD3 and SMAD7 P1 in WT or 4KO cells are provided. (**C**) Survival probability (%) of HALO-SMAD7 molecules in WT (blue) or 4KO (red) CH12 B cells. The data was fitted to power-law or bi-exponential curves respectively. (**D**) Binding time distribution (in seconds) of HALO-SMAD7 molecules expressed in WT or 4KO cells.