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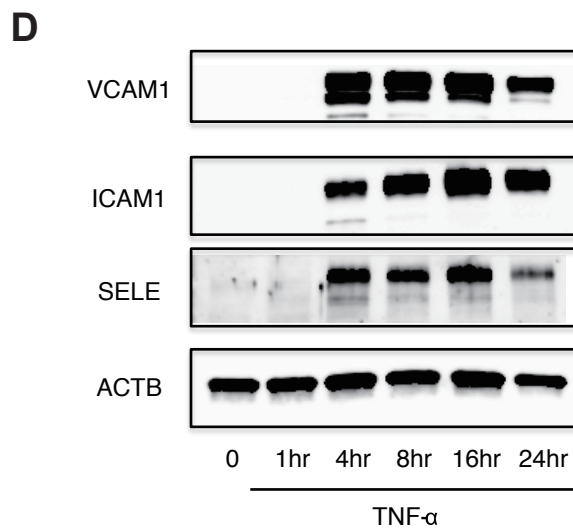
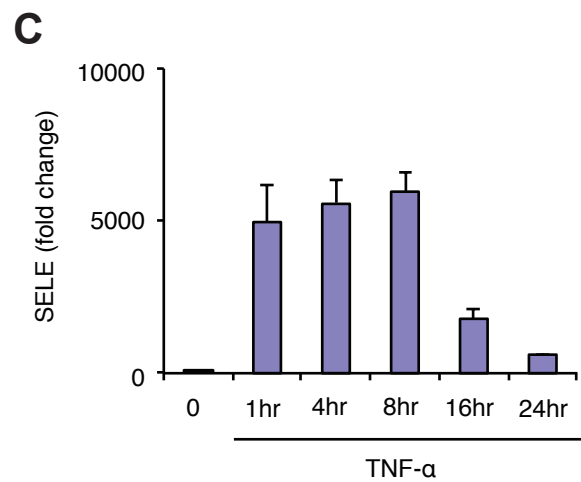
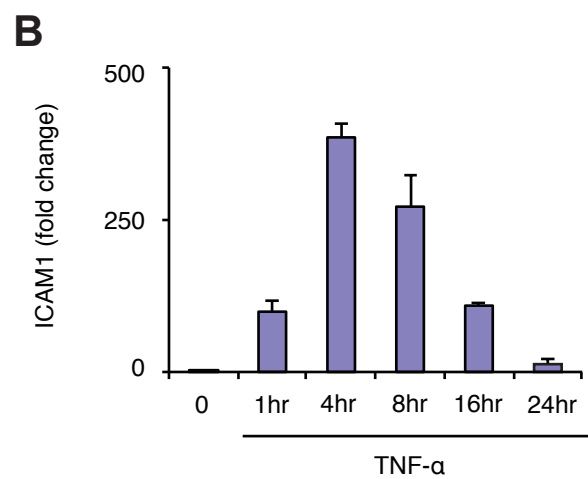
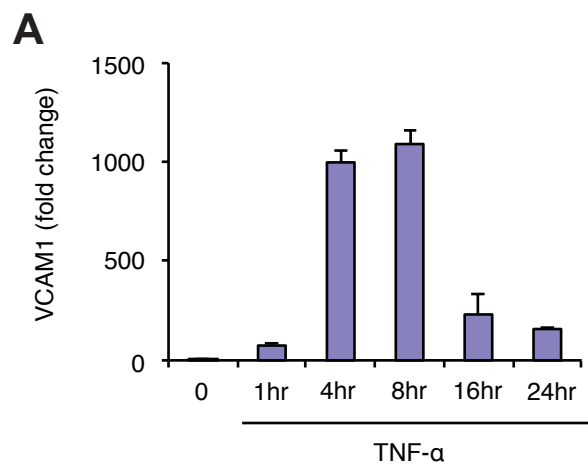
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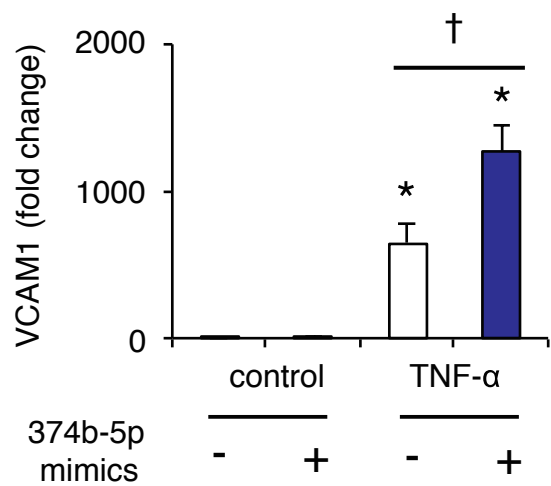
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Appendix Figure S1

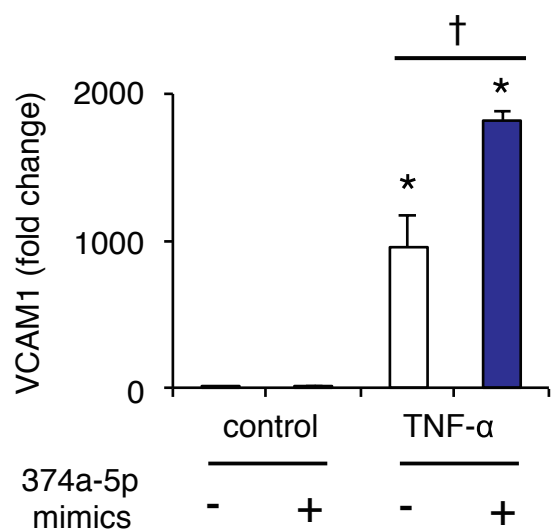


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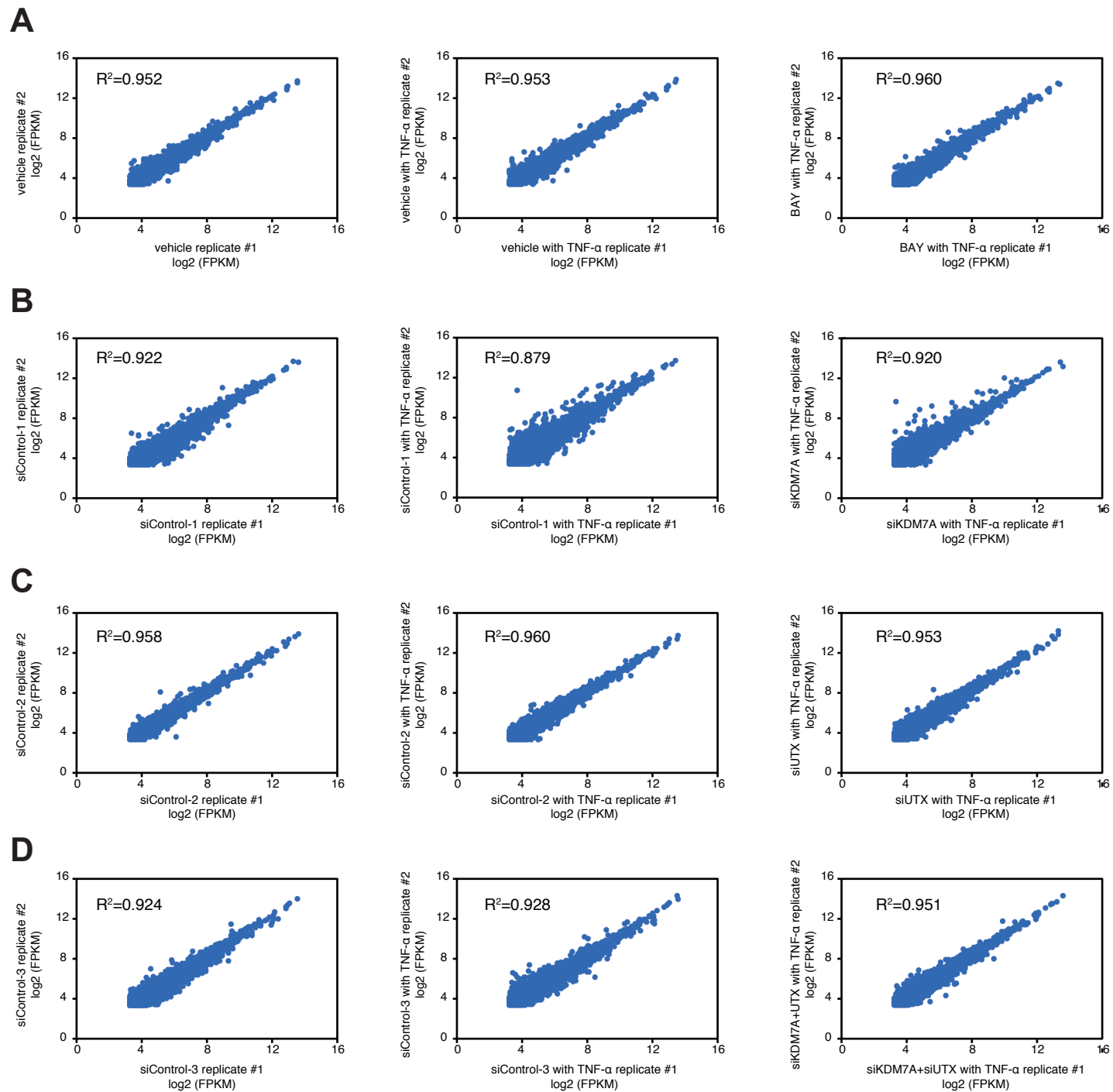
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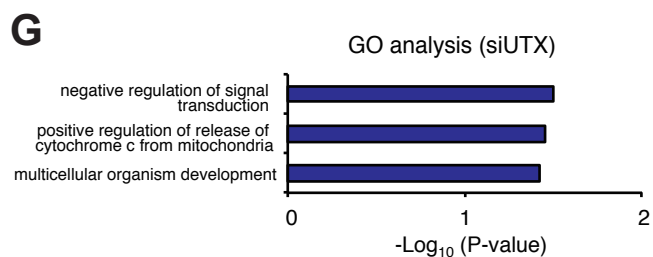
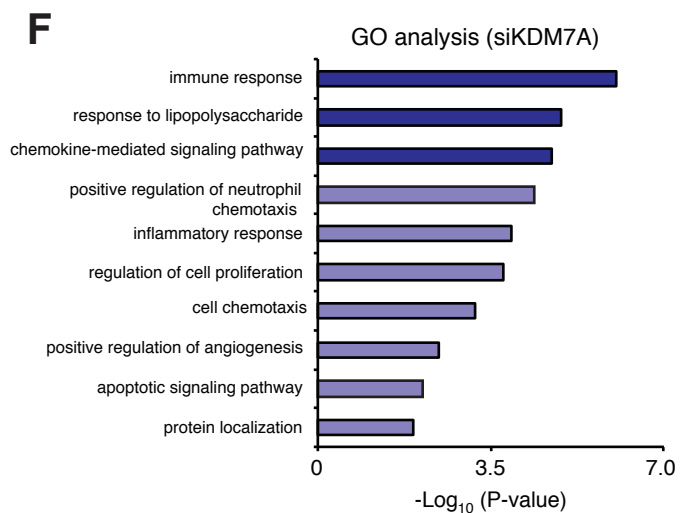
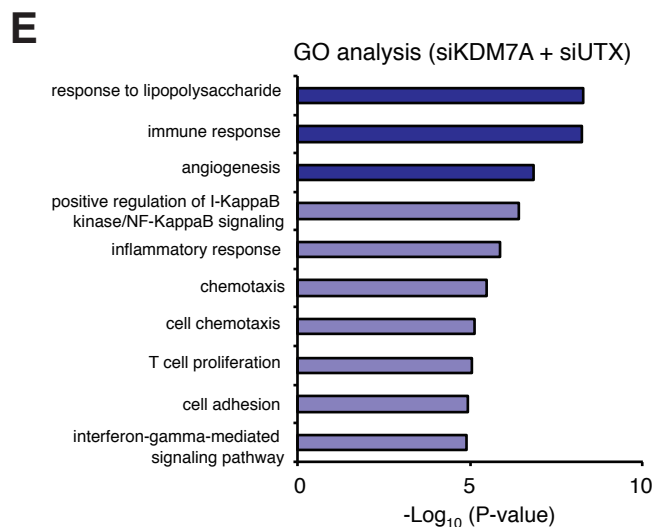
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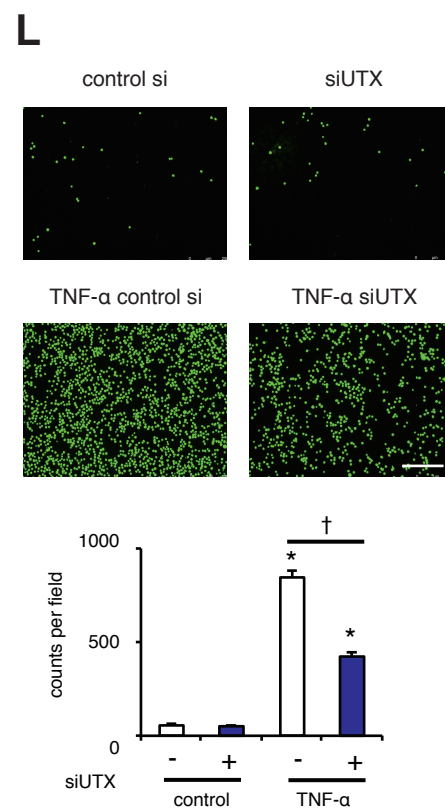
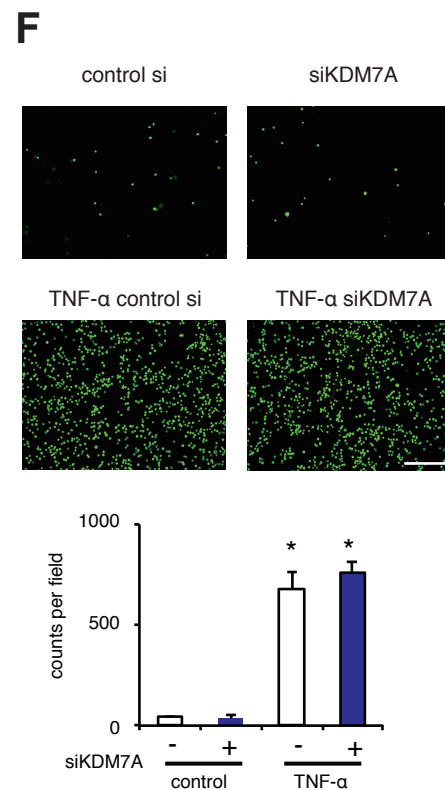
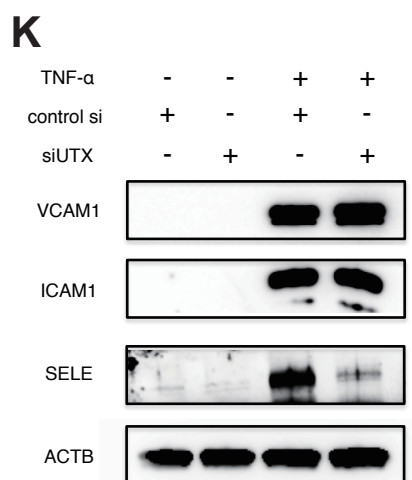
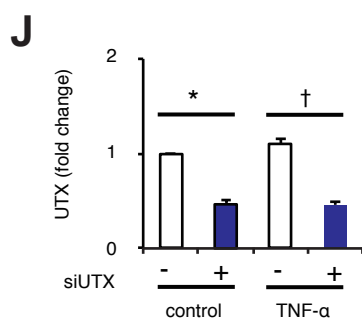
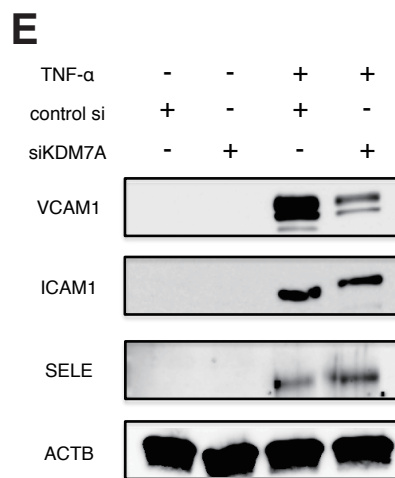
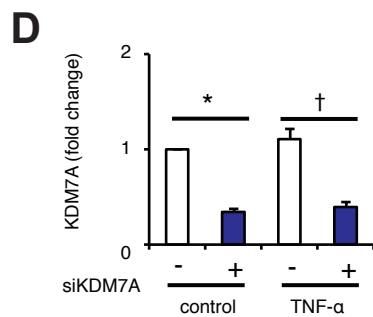
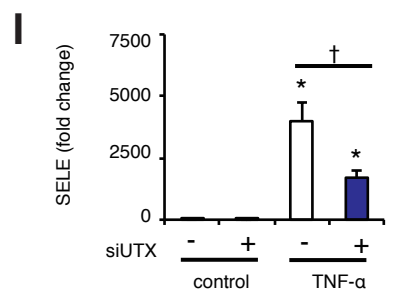
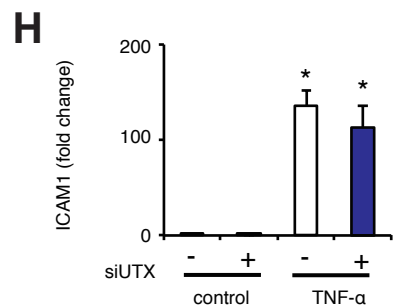
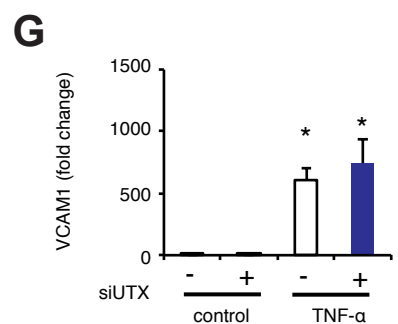
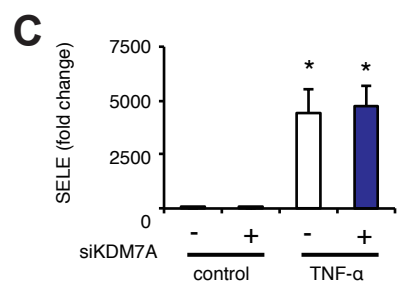
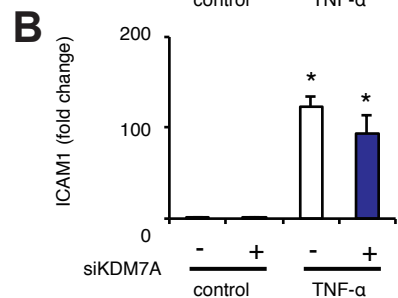
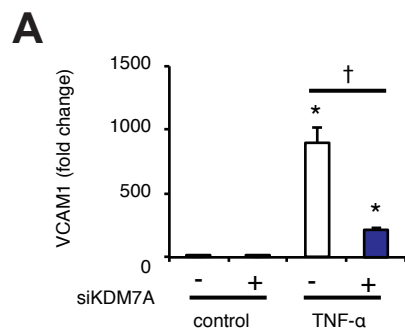
Appendix Figure S3



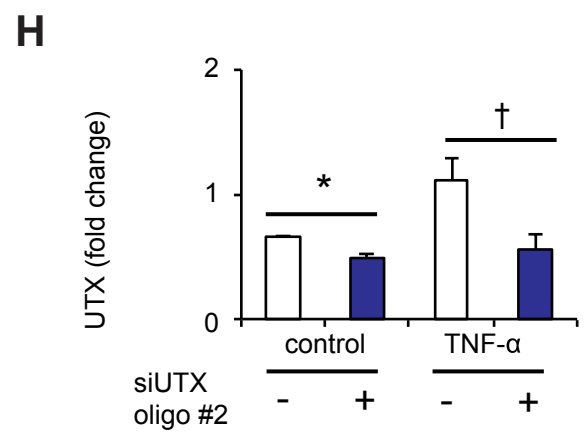
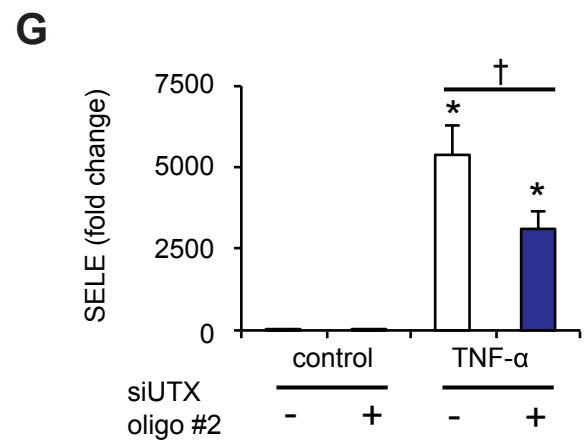
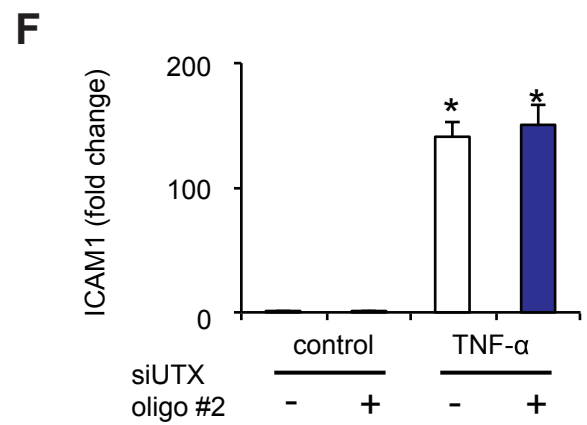
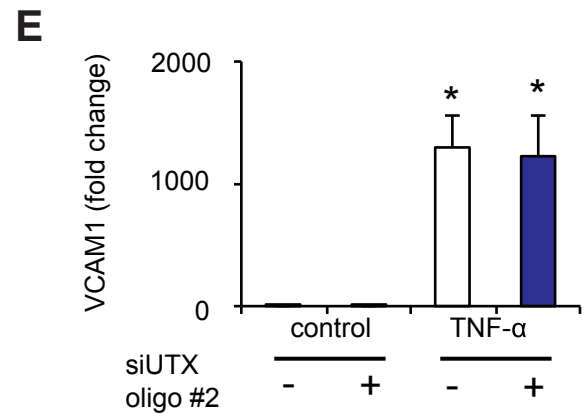
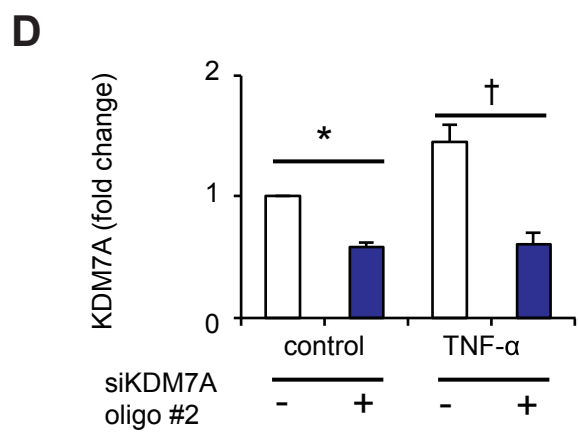
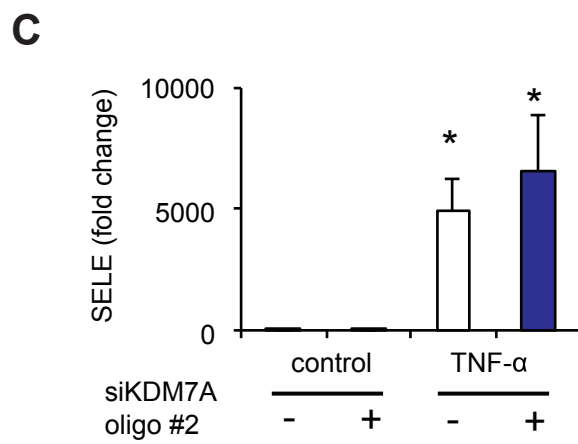
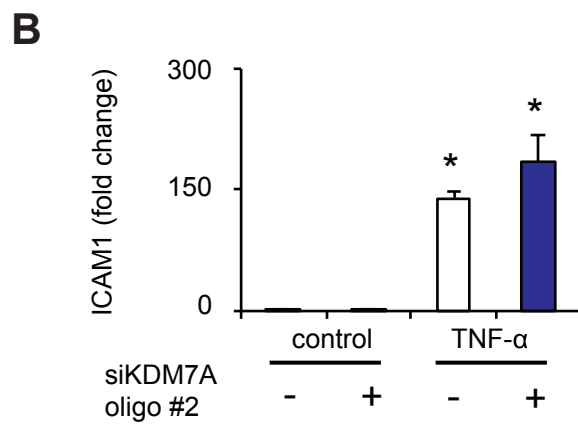
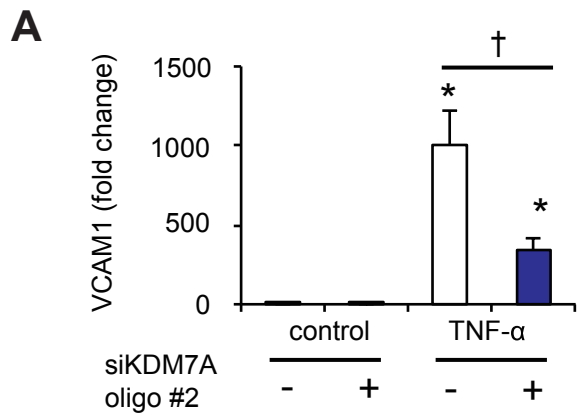
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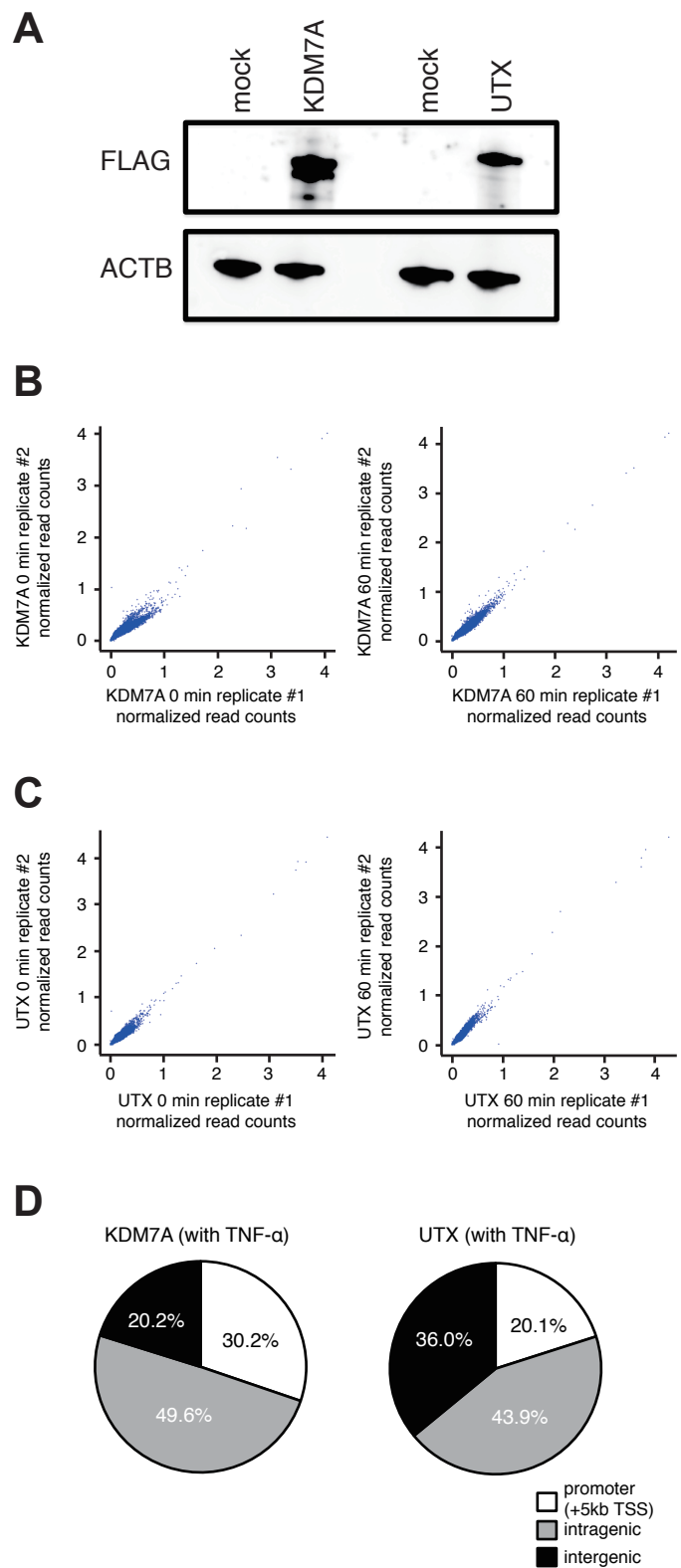
Appendix Figure S5



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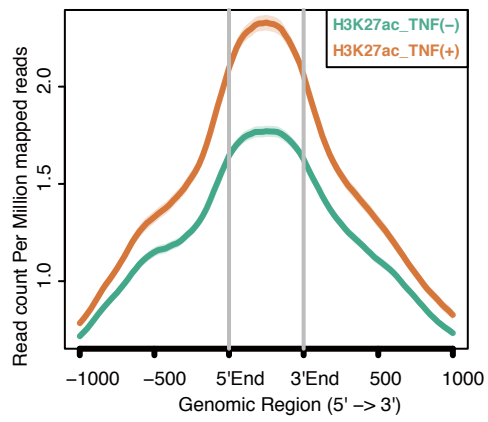
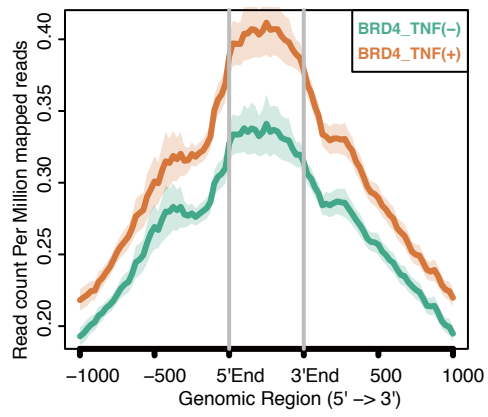


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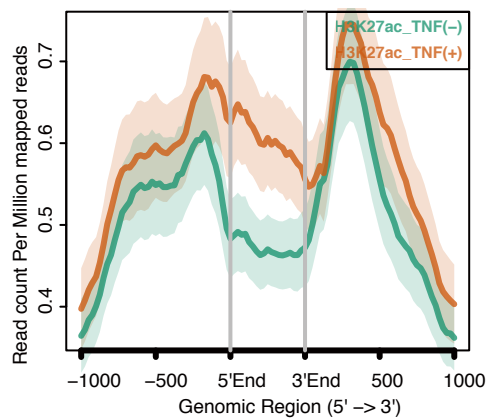
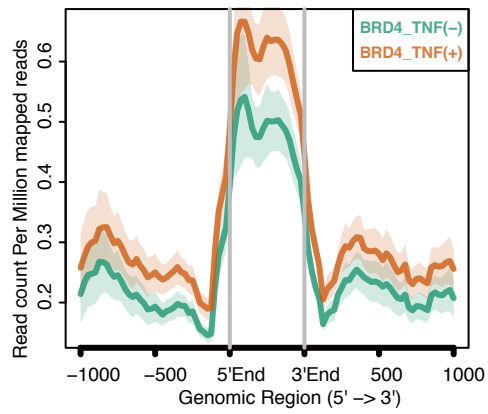


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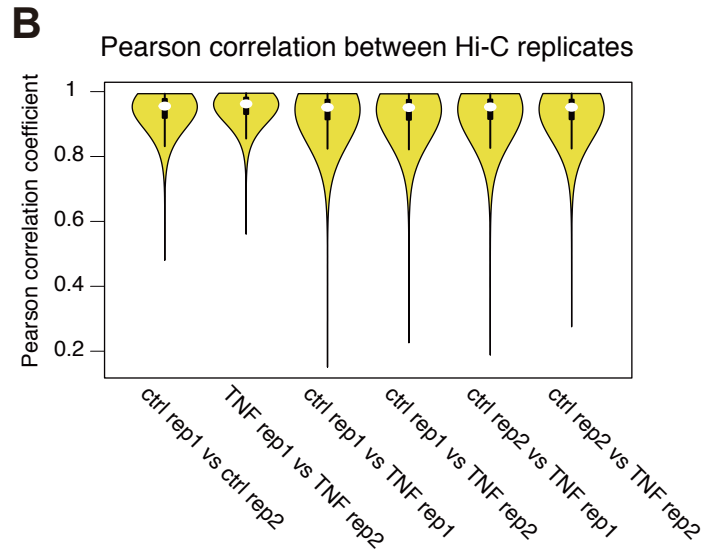
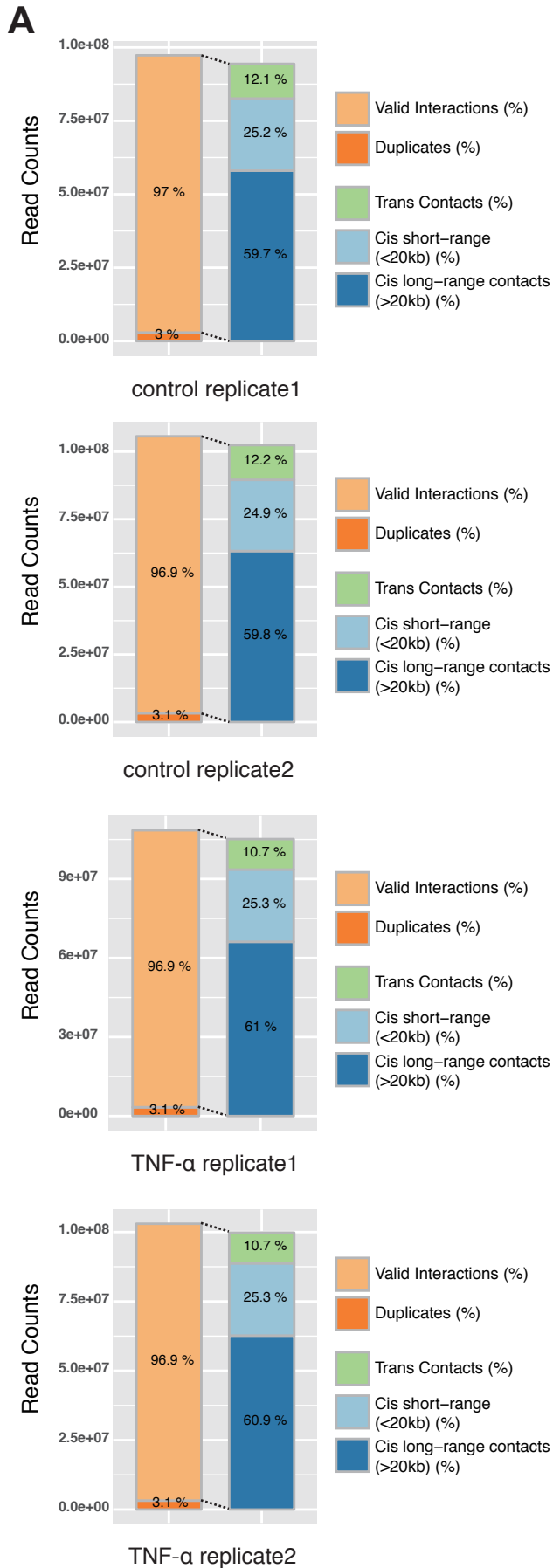
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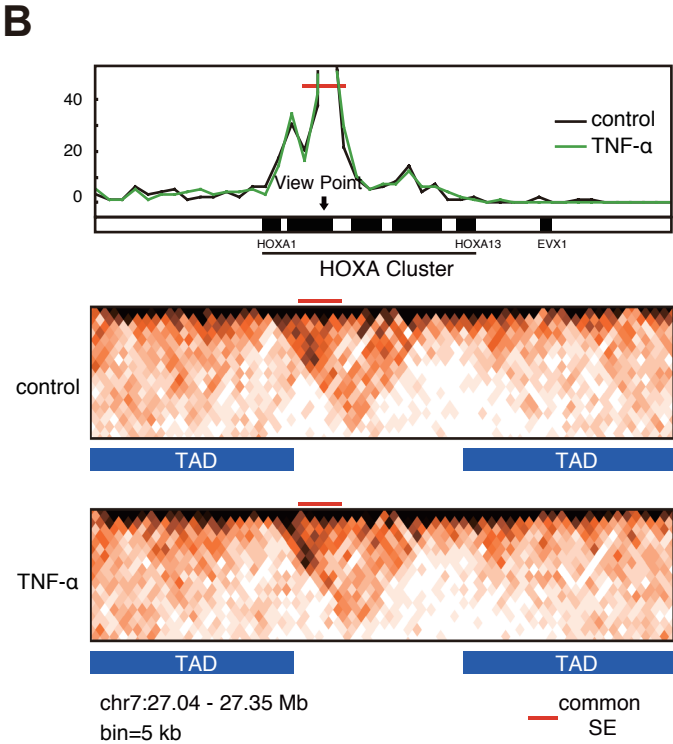
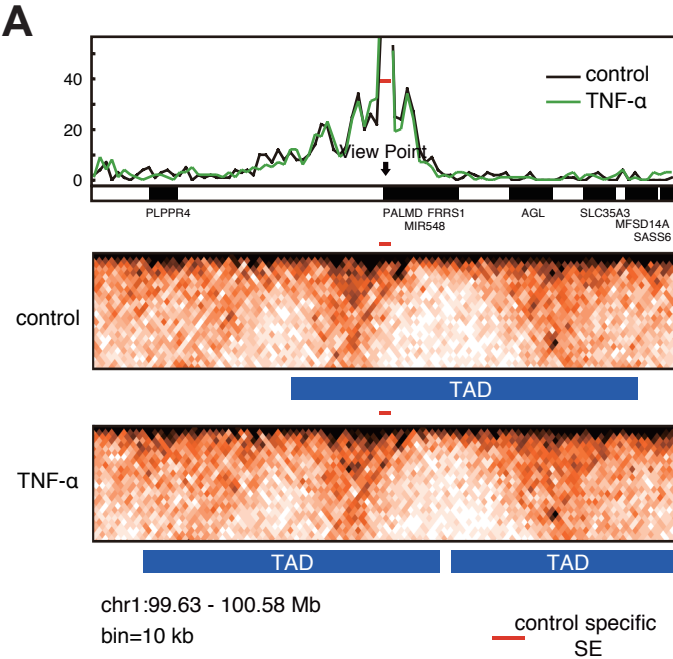
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Appendix Figure S9

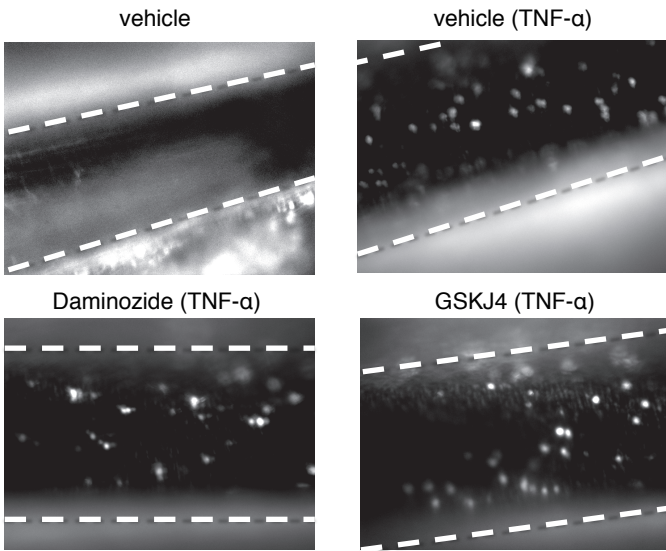


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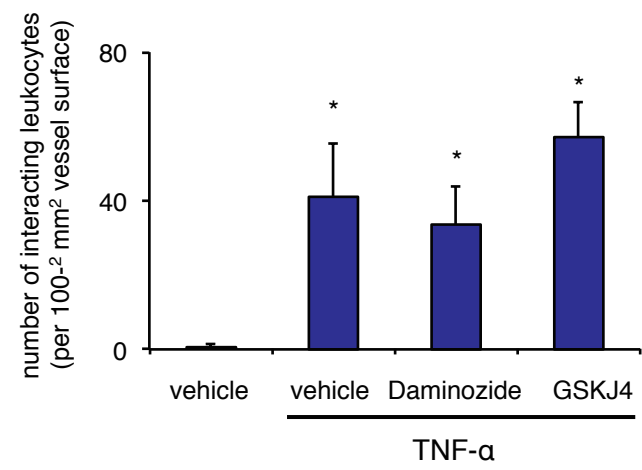


Appendix Figure S11

A



B



Appendix Table S1. List of synthetic oligos and primers.

	Sequence
miR-374b-5p	AUAUAAUACAACCUGCUAAGUG
miR-374a-5p	UUAUAAUACAACCUGAUAAAGUG
miR-3679-5p	UGAGGAUAUGGCAGGGAAGGGGA
Negative control	Ambion MirVana™ miRNA mimic Negative Control #1 Confidential Sequence

Gene symbol		Sequence
KDM7A	oligo1	sense; GUAUCGCUAUGAUAAACCATT antisense; UGGUUUAUCAUAGCGAUACAA
KDM7A	oligo2	sense; CAGAAAUGGCCAUGCACGUTT, antisense; ACGUGCAUGGCCAUUUCUGTT
UTX	oligo1	sense; GCAUUGUGAAAGUAAUAGATT antisense; UCUAUUACUUUCACAAUGCCA,
UTX	oligo2	sense; GACAACAAGGCAUUACCUUTT, antisense; AAGGUA AUGCCUUGUUGUCTT
Negative control	oligo1	Ambion Silencer Select Negative control #1 Confidential sequence
Negative control	oligo2	Sigma Mission siRNA Universal Negative Control #1 Confidential sequence

Target gene	Species	Strand	Sequence (5' end)
VCAM-1	human	Forward	TTCCCTAGAGATCCAGAAATCGAG
		Reverse	CTTGCAGCTTACAGTGACAGAGC
ICAM-1	human	Forward	AGCTGTTTGAGAACACCTCGGCC
		Reverse	AGACTGGGAACAGCCCGTCCA
E-selectin	human	Forward	TACAAGTCCTCTTGTGCCTTCAG
		Reverse	CATTTTACCACTTGGCAGGAAGG
KDM7A	human	Forward	GGAAAACGGCAAACCAGTTA
		Reverse	TCATCTTTCTTCGGGAATGG
UTX	human	Forward	AAGCTGAAGGAAAAGTGGAGTCT
		Reverse	AAAGGCAGCATTCTTCCAGTAGT
ACTB	human	Forward	CACCTTCTACAATGAGCTGCGTGTG
		Reverse	ATAGCACAGCCTGGATAGCAACGTAC

Target 3'UTR	Location	Strand	Sequence (5' end)
KDM7A	6469-6815	Forward	CGGAGCTCGCCCAGGGCATGCTACTTTA
		Reverse	CGTCTAGAGTACCCAACCCAGAGCTGTC
UTX	5445-5925	Forward	TTCCAGATTTACCTGCCATTG
		Reverse	GCAGCAATTGTTTATTGGTCTG

	Location	Strand	Sequence (5' end)
KDM7A	Primer 1 (1-382)	Forward	caagcttgccggccgcCATGGCCGGAGCGGCGGCGG
		Reverse	CTCGAGAGCGTAATTCCTTAATGAAAG
	Primer 2 (382-2816)	Forward	AATTACGCTCTCGAGTCTTCCCAAGTG
		Reverse	tcctctagatgcacTCACACAAAGAAACGTGCATG
UTX	Primer 1 (1(-28)-4465)	Forward	GTTGGAGTTGTGAATTCGCTGCGTT
		Reverse	CTATCTCGTAAGGCTGCTGGCTGAA

	Strand	Sequence (5' end)
VCAM-1 (-15kb)	Forward	AACCTTTTGTGGGAAGGCCA
	Reverse	GTCCCCTTCTGCCTGGTAAC
VCAM-1 (-11kb)	Forward	AACAGGGCAATGAATTTTAAGTATGATT
	Reverse	GTATCATCAATGCAAACCTATTTTTACCAT
VCAM-1 (TSS)	Forward	GAATACCCTCCCAGGCACAC
	Reverse	CGACCATCTTCCCAGGCATT
SELE (-12kb)	Forward	CTCATATCGGAGAAAGTGTTTCATT
	Reverse	TTATCTCATAGAAAGATGCCTCCAG
SELE (-6kb)	Forward	CCAATCATTTCCAAATATCAAAGAC
	Reverse	TTTTGGAGAAGTAGGAGAAAAACCT
SELE (TSS)	Forward	TGGACAAAGGTGAAGTAGCTTCA
	Reverse	TAAAGAGGAAATCCCCAATGGCA

APPENDIX FIGURE LEGENDS

Appendix Figure S1. Temporal expression of adhesion molecules during TNF- α -signaling in human ECs

(A-C) Bar plots showing temporal changes of mRNA levels of vascular cell adhesion molecule-1 (VCAM1) (A), intracellular cell adhesion molecule-1 (ICAM1) (B), and E-selectin (SELE) (C) after stimulation of human endothelial cells (ECs) with TNF- α . Data are shown as means \pm SD. (D) Time-course western blot analyses for VCAM1, ICAM1, SELE, and β -actin (ACTB) in lysates from ECs treated with TNF- α .

Appendix Figure S2. Validation of TNF- α -responsive miRNA, miR-374b-5p and miR-374a-5p (A and B) Bar plots showing mean mRNA levels of VCAM1 measured 4 hrs after stimulation of ECs with or without TNF- α \pm miR-374b-5p (A) and miR-374a-5p (B). Data are shown as means \pm SE. * P < 0.05 compared to TNF- α (-) mimics (-). † P < 0.05 compared to TNF- α (+) mimics (-).

Appendix Figure S3. Reproducibility of RNA-seq between biological replicates.

(A-D) Scatter plots showing reproducibility of RNA-seq signals between the two biological replicates in Figure 3A. The R_2 correlation coefficient is shown in each graph.

Appendix Figure S4. KDM7A and UTX participate in TNF- α -induced NF- κ B-p65 signaling pathways.

(A-C) Venn diagrams showing overlap of the genes downregulated by BAY and siKDM7A+siUTX (A), siKDM7A (B), or siUTX (C) treatments of TNF- α -responsive genes (KDM7A: lysine demethylase 7A, UTX: lysine demethylase 6A). The overlapping area shows the number of overlapping genes. (D-G) GO analysis of TNF- α -responsive genes downregulated by BAY (D), siKDM7A+siUTX (E), siKDM7A (F), or siUTX (G) treatments, as determined in Appendix Figure S4A-C. The P -values of each category analyzed by DAVID are shown in the bar graphs.

Appendix Figure S5. KDM7A and UTX control TNF- α -induced expression of adhesion molecules in human ECs

(A-D) Bar plots showing mean mRNA levels of VCAM1 (A), ICAM1 (B), SELE (C), and KDM7A (D) measured 4 hrs after stimulation of ECs with or without TNF- α \pm siKDM7A. Data are shown as means \pm SE. * P < 0.05 compared to TNF- α (-) siKDM7A (-). † P < 0.05 compared to TNF- α (+) siKDM7A (-). (E) Western blots for VCAM1, ICAM, SELE, and ACTB in lysates from ECs treated with or without TNF- α (4 hrs) \pm siKDM7A. (F) Representative images (top)

and bar plot quantification (bottom) showing adhesion of calcein-labeled U937 monocytes to ECs treated with or without TNF- α \pm siKDM7A. Scale bar represents 250 μ m. Data are shown as means \pm SD. * P < 0.05 compared to TNF- α (-) siKDM7A (-). † P < 0.05 compared to TNF- α (+) siKDM7A (-). (G-J) Bar plots showing mean mRNA levels of VCAM1 (G), ICAM1 (H), SELE (I), and UTX (J) measured 4 hrs after stimulation of ECs with or without TNF- α \pm siUTX. Data are shown as means \pm SE. * P < 0.05 compared to TNF- α (-) siUTX (-). † P < 0.05 compared to TNF- α (+) siUTX (-). (K) Western blots for VCAM1, ICAM, SELE, and ACTB in lysates from ECs treated with or without TNF- α (4 hrs) \pm siUTX. (L) Representative images (top) and bar plot quantification (bottom) showing adhesion of calcein-labeled U937 monocytes to ECs treated with or without TNF- α \pm siUTX. Scale bar represents 250 μ m. Data are shown as means \pm SD. * P < 0.05 compared to TNF- α (-) siUTX (-). † P < 0.05 compared to TNF- α (+) siUTX (-).

Appendix Figure S6. Validation of KDM7A- and UTX- knockdown experiments

(A-D) Bar plots showing mean mRNA levels of VCAM-1 (A), ICAM-1 (B), E-selectin (C), and KDM7A (D), measured 4 hrs after stimulation of ECs with or without TNF- α \pm siKDM7A-2. Data are expressed as means \pm SE. * P < 0.05 compared with TNF- α (-) siKDM7A-2 (-). † P < 0.05 compared with TNF- α (+) siKDM7A-2 (-). (E-H) Bar plots showing mean mRNA levels of VCAM-1 (E), ICAM-1 (F), E-selectin (G), and UTX (H), measured 4 hrs after stimulation of ECs with or without TNF- α \pm siUTX-2. Data are expressed as means \pm SE. * P < 0.05 compared with TNF- α (-) siUTX-2 (-). † P < 0.05 compared with TNF- α (+) siUTX-2 (-).

Appendix Figure S7. Characterization of KDM7A- and UTX-recruited elements

(A) Western hybridization detection of exogenous KDM7A and UTX in human ECs 1 day after adenoviral infection. (B and C) Scatter plots showing reproducibility of ChIP-seq signals for KDM7A (B) and UTX (C) between the two biological replicates. The R_2 correlation coefficient is shown in each graph. (D) Pie charts of KDM7A (left) and UTX (right) binding site distributions in ECs with TNF- α (+).

Appendix Figure S8. Enhancer marks distribution around the KDM7A- and UTX-binding sites

(A and B) The average profiles of enrichment of ChIP-seq experiments for bromodomain-containing protein 4 (BRD4; top) and H3K27ac (bottom) under TNF- α treatment (TNF+) and control (TNF-) around broad peaks of the KDM7A (A) or UTX (B) ChIP-seq experiment.

Appendix Figure S9. Characterization of Hi-C data

(A) Fractions of intra- and inter- chromosomal interactions identified by Hi-C that connect regions within valid interactions. Valid interactions or duplicates, and intra- or inter-chromosomal interactions were calculated by HiC-Pro (<https://github.com/nservant/HiC-Pro>).
(B) Violin plots showing reproducibility between all Hi-C replicates. The Y axis indicates Pearson's correlation coefficient.

Appendix Figure S10. Hi-C contact matrix of the *PALMD* and *HOXA* gene loci

(A and B) Virtual 4C views and heat maps of Hi-C data around the *PALMD* locus (A) and the *HOXA* cluster (B). Virtual 4C calculated from Hi-C datasets, using bins covering the indicated viewpoints. The Y axis in the virtual 4C view indicates the number of reads that interact with the viewpoint bin. Control reads are raw reads and TNF- α reads were normalized to control reads. Topologically associating domains (TADs) were calculated by TADtool (<https://github.com/vaquerizaslab/tadtool>) and indicated as blue bars. Red lines indicate SEs.

Appendix Figure S11. Single drug effect of the KDM7A or UTX enzymatic inhibitor against monocyte adhesion in mice

Male, 10 week old C57BL/6 mice (n=3/group) were pretreated with vehicle, Daminiozed (50 mg/kg), or GSKJ4 (50 mg/kg) at 16 hrs and 1 hr prior to TNF- α treatment. Inflammation was induced by an intraperitoneal injection of TNF- α (5 μ g/mouse) and IVM was performed 4 hrs later. (A) Representative snapshot from IVM analysis of leukocyte adhesive interactions in the femoral arteries. Margins of vessels are indicated with dashed lines. White spots represent fluorescently labeled leukocytes visualized by an intravenous injection of rhodamine 6G. (B) Quantitative analyses of leukocyte adhesive interactions in the femoral arteries. Data are shown as means \pm SE. * $P < 0.05$ compared to the vehicle group.