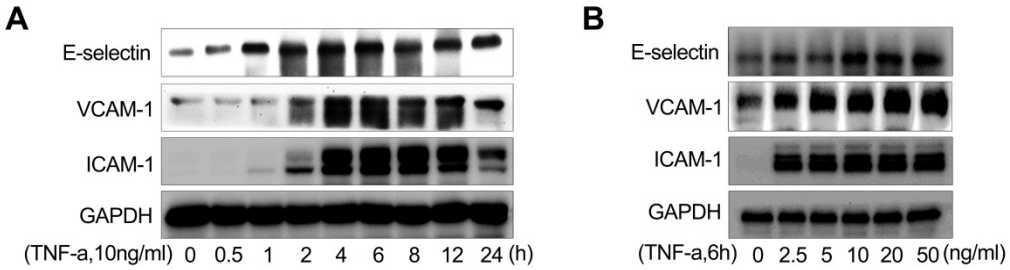
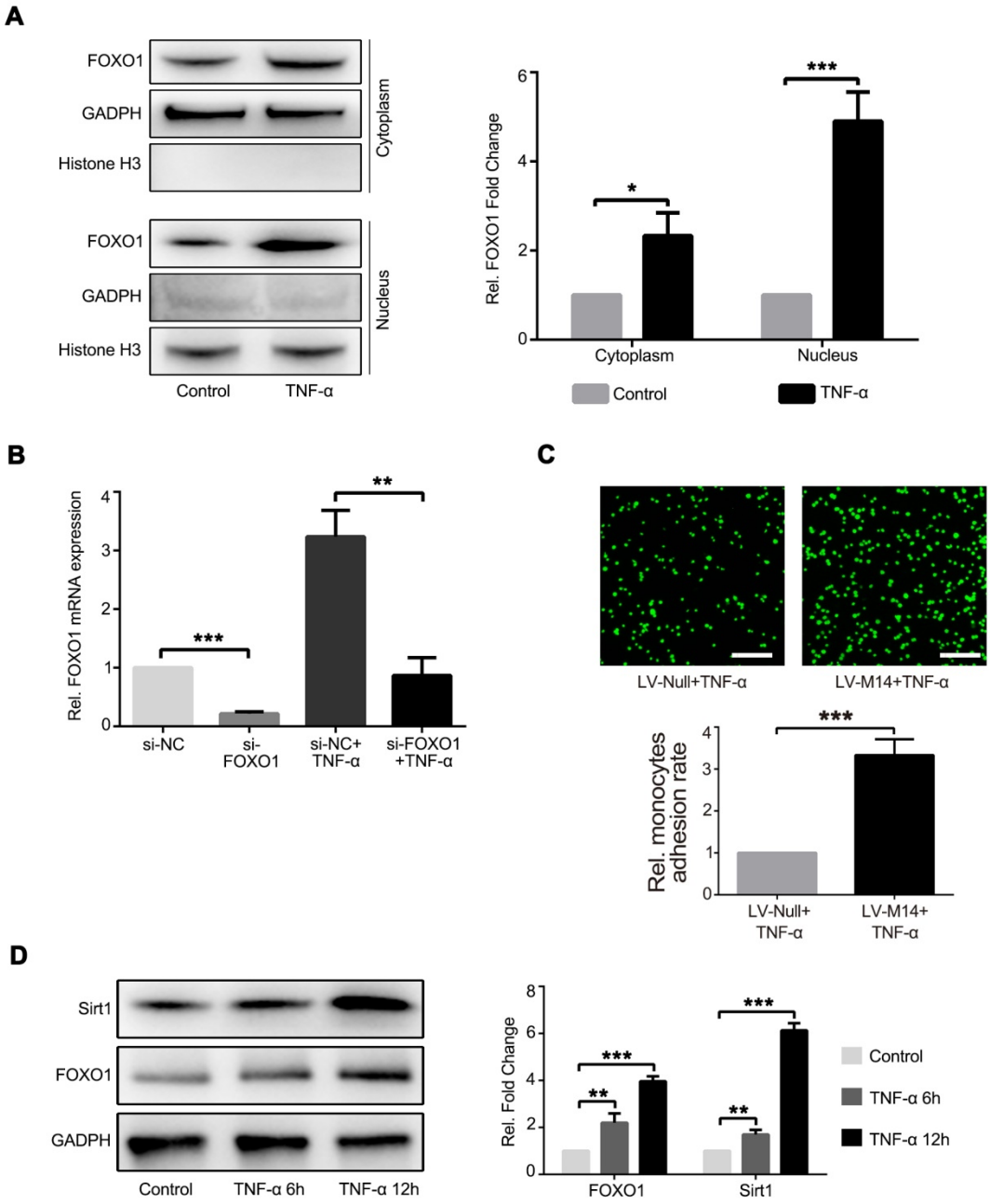
Supplement Figure 1: TNF-α-induced adhesion molecule expression in endothelial cells.



(A) Representative images and quantification of expression of endothelial adhesion molecules (VCAM-1, ICAM-1, and E-selectin) after treatment of HUVECs with 10 ng/ml of TNF-α at different time points.

(B) Representative images and quantification of expression of endothelial adhesion molecules (VCAM-1, ICAM-1, and E-selectin) in HUVECs treated with different concentrations of TNF-α for 6 h.

Supplement Figure 2: TNF-α-induced FOXO1 expression in endothelial cells.



(A) Representative images and quantification of FOXO1 expression in the cytoplasm and nucleus after treatment of HUVECs with TNF-α (10 ng/ml, 12 h).

(B) The effect of FOXO1 knockdown on FOXO1 mRNA expression with or without TNF-α stimulation (10 ng/ml, 12 h).

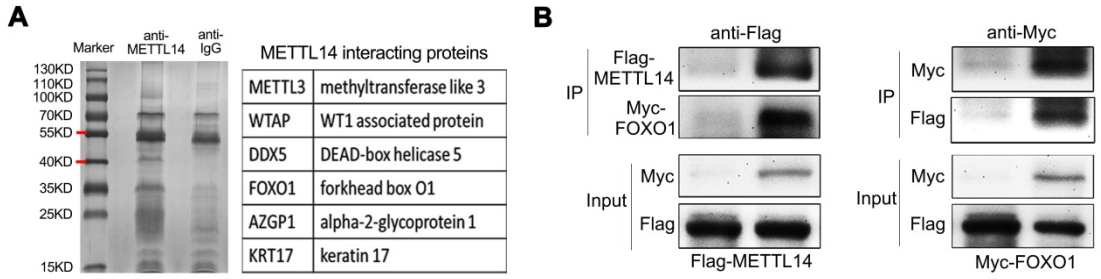
(C) The effect of overexpression of METTL14 on TNF-α-induced monocyte-endothelial cell adhesion.

(D) Representative images and quantification of FOXO1 and Sirt1 expression after

treatment of HUVECs with TNF-α (10 ng/ml, 6/12 h).

(A, B, and C) Data are presented as mean ± SEM. Two-tailed unpaired Student's *t*-test was applied to compare the indicated two groups. (D) One-way ANOVA with Bonferroni's post-hoc test was applied to compare the indicated groups. **P*<0.05, ***P*<0.01, and ****P*<0.001.

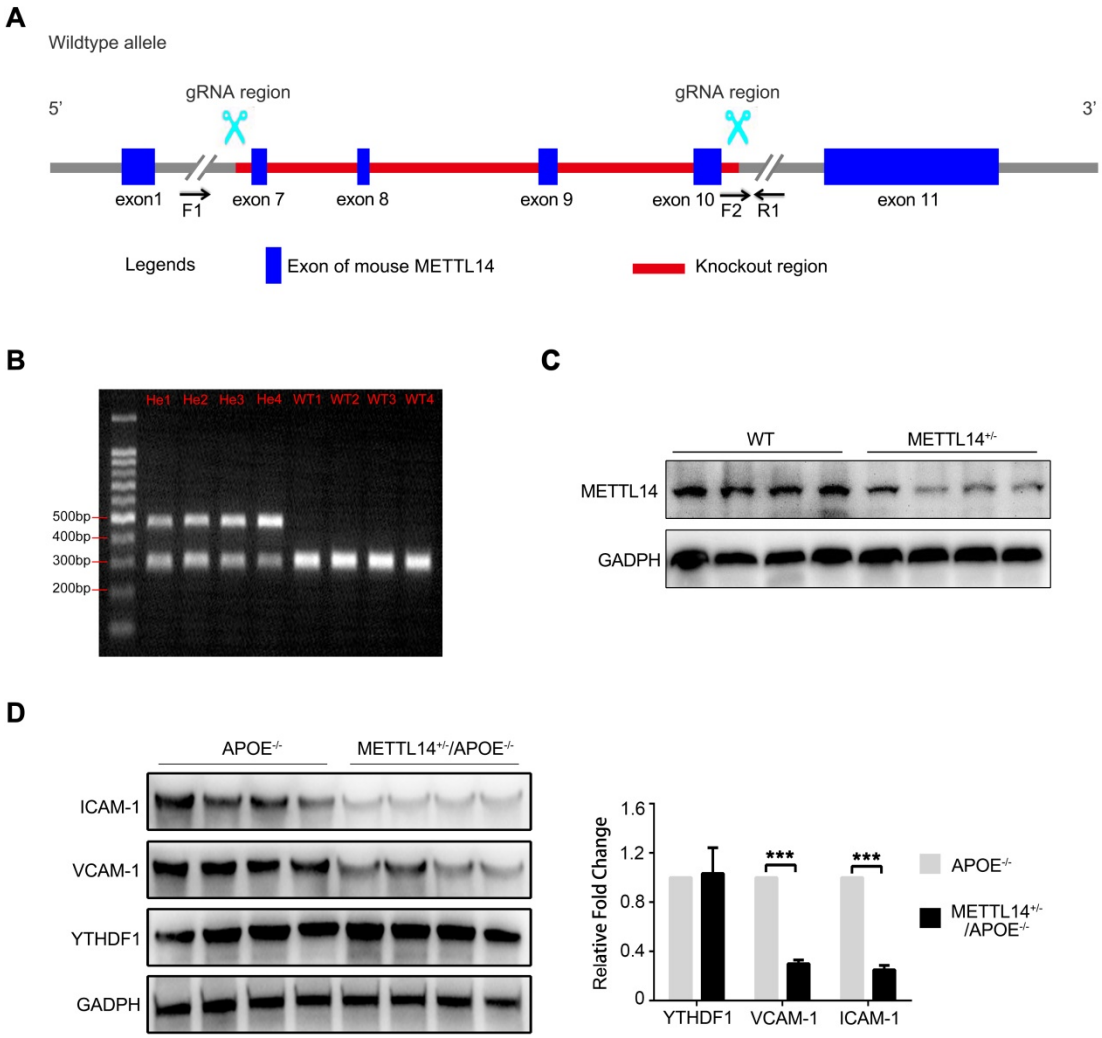
Supplement Figure 3: METTL14 cooperates with FOXO1 to promote VCAM-1 and ICAM-1 transcription.



(A) The protein complex was precipitated with anti-METTL14 antibody using IgG as an endogenous control. The METTL14-interacting proteins are listed in the Table.

(B) 293T cells were transfected with flag-METTL14 and myc-FOXO1 and co-IP was performed using anti-flag or anti-myc antibody, followed by immunoblot analysis with indicated antibodies.

Supplement Figure 4: Genotype and knockdown verification of METTL14 knockout mice and related gene expression profile.



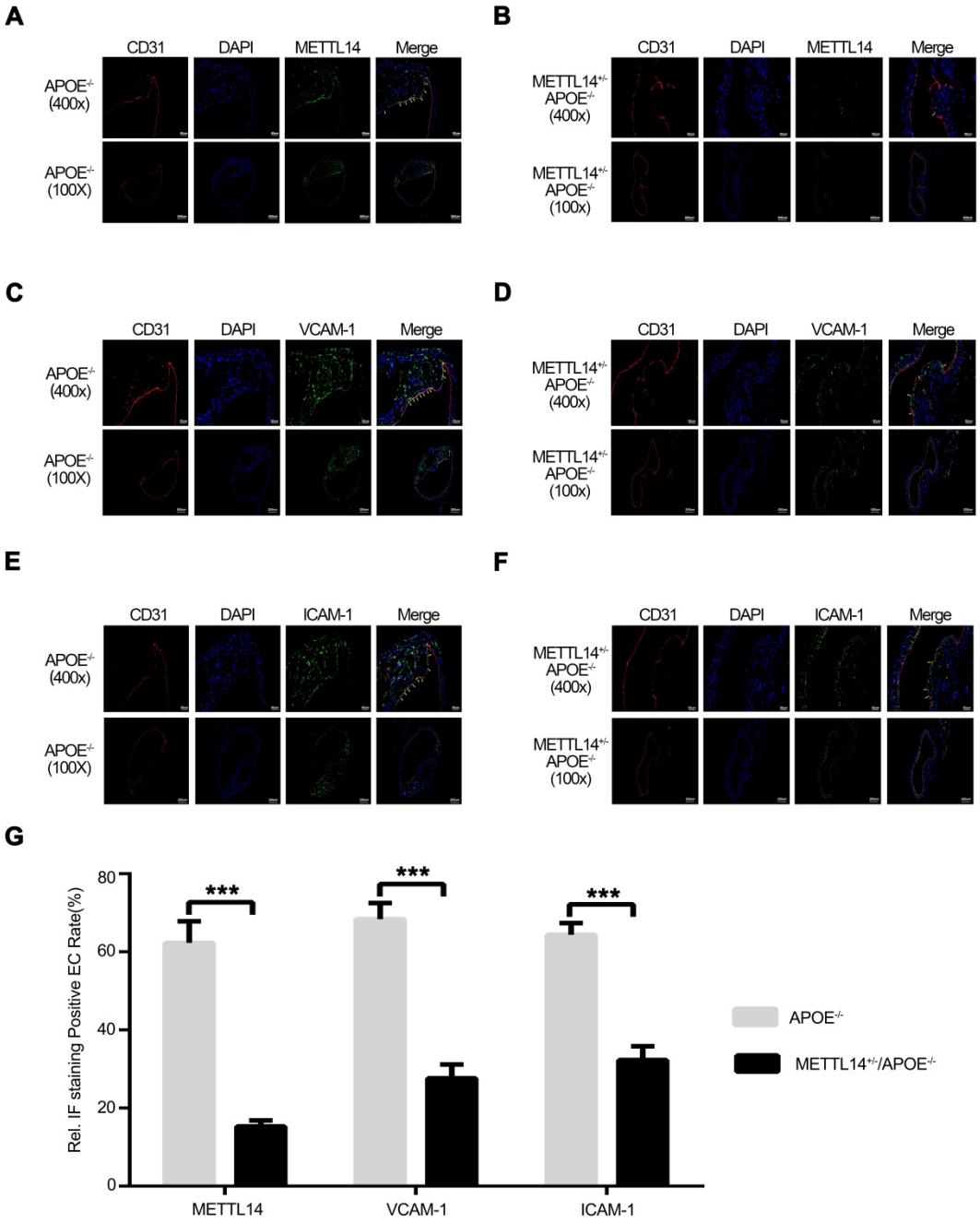
(A) An overview of the targeting strategy used to construct the METTL14 knockout mouse model. METTL14 knockout was performed using CRISPR/Cas9-based targeting strategy. Two gRNAs were designed between the 7th and 10th exon, and the sequence was deleted. Two pairs of PCR primers were used to identify whether the mice were heterozygous: the F1/R1 primer can amplify a 474 bp sequence and the F2/R1 primer can amplify a 247 bp sequence, thus confirming heterozygous status.

(B) Genotype verification of METTL14 knockout mice. Two bands of 437 and 274 bp appeared in METTL14 knockout heterozygous mice (He 1-4), while only one band of 274 bp was seen in METTL14 wild-type mice (WT 1-4).

(C) METTL14 expression in the vascular tissues of METTL14$^{+/-}$ and C57BL/6 mice.

(D) Representative images and quantification of ICAM-1, VCAM-1, and YTHDF1 expression in the vascular tissues of $APOE^{-/-}$ and $METTL14^{+/-}/APOE^{-/-}$ mice. Data are presented as mean ± SEM. Two-tailed unpaired Student's *t*-test was applied to compare the indicated two groups. ***$P<0.001$.

Supplement Figure 5: Immunofluorescence staining of METTL14, VCAM-1 and ICAM-1 positive cells in the atherosclerotic plaque regions of METTL14$^{+/-}$/APOE$^{-/-}$ and APOE$^{-/-}$ mice.



(A to G) Immunofluorescence staining showing the expression of METTL14-, VCAM-1-, and ICAM-1-positive cells in the atherosclerotic plaque regions of METTL14$^{+/-}$/APOE$^{-/-}$ and APOE$^{-/-}$ mice (n=10 per group). All representative images are from mice fed WD. Data are presented as mean ± SEM. Two-tailed unpaired Student's *t*-test was applied to compare the indicated two groups. ***P<0.001.

Supplement Table 1: Full-length sequence of FOXO1 mRNA and GGACT site regions.

5′-1 gatcccgtaa gtcgggcggc ctggtagtcg cagcagccgc tgccgcagcc gccacattca
61 acaggcagca gcgcagcggg cgcgccgctg gggagagcaa gcggcccgcg gcgtccgtcc
121 gtccttccgt ccgcggccct gtcagctgga gcgcggcgca ggctctgccc cggcccggcg
181 gctctggccg gccgtccagt ccgtgcggcg gaccccgagg agcctcgatg tggatggccc
241 cgcgaagtta agttctgggc tcgcgcttcc actccgccgc gccttcctcc cagtttccgt
301 ccgctcgccg caccggcttc gttcccccaa atctcggacc gtcccttcgc gccccctccc
361 cgtccgcccc cagtgctgcg ttctcccccc cttggctctc ctgcggctgg gggaggggcg
421 ggggtcacca tggccgaggc gcctcaggtg gtggagatcg acccggactt cgagccgctg
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541 gccacctcca gcccggcgcc gtcgggcagc gcggctgcca accccgacgc cgcggcgggc
601 ctgccctcgg cctcggctgc cgctgtcagc gccgacttca tgagcaacct gagcttgctg
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901 aacgcgtggg gcaacctgtc ctacgccgac ctcatcacca aggccatcga gagctcggcg
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1021 aaggataagg gtgacagcaa cagctcggcg ggctggaaga attcaattcg tcataatctg
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1141 atgctcaatc cagagggtgg caagagcggg aaatctccta ggagaagagc tgcatccatg
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5221 gaaatcattc tccaacgata tacaaattgg acttgttcaa ctgctggata tatgctacca
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5581 ccgatactct gagaagtgcc tgatgttgat gtacttacag acacaagaac aatctttgct
5641 ataattgtat aaagccataa atgtacataa attatgttta aatggcttgg tgtctttctt
5701 ttctaattat gcagaataag ctctttatta ggaatttttt gtgaagctat taaatacttg
5761 agttaagtct tgtcagcca-3’

The red font indicates the CDS area, and the yellow background font indicates the GGACT area.

Table S2: Weight gain and plasma lipid profiles between $APOE^{-/-}$ and $METTL14^{+/-}/APOE^{-/-}$ mice.

	$APOE^{-/-}$	$METTL14^{+/-}/APOE^{-/-}$	*P* Value
Body Weight (g)	23.71±1.88	23.21±1.54	0.527
LDL (mg/dL)	355.73±17.74	343.84±13.81	0.113
HDL (mg/dL)	83.61±6.55	85.60±5.68	0.475
TG (mg/dL)	138.80±6.09	133.90±7.32	0.122

Table S2. $APOE^{-/-}$ and $METTL14^{+/-}/APOE^{-/-}$ mice were fed with WD for 12 weeks and the body weight (n=12-15 for each group) and plasma lipid profiles (LDL, HDL, and TG) was measured by Elisa (n=10). All data are mean ± SEM. Significance was determined using a 2-tailed unpaired Student *t* test.