Figure S1. Pan-cancer analysis of *TBX15*. (A) Pan-cancer data for *TBX15*. (B) Forestplot was used to visualize the pan-cancer prognostic risk of *TBX15*. TBX15, T-box transcription factor 15; ACC, adrenocortical carcinoma; BLCA, bladder urothelial carcinoma; BRCA, breast invasive carcinoma; CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; CHOL, cholangiocarcinoma; COAD, colon adenocarcinoma; DLBC, lymphoid neoplasm diffuse large B-cell lymphoma; ESCA, esophageal carcinoma; GBM, glioblastoma multiforme; HNSC, head and neck squamous cell carcinoma; KICH, kidney chromophobe; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; LAML, acute myeloid leukemia; LGG, brain lower grade glioma; LIHC, liver hepatocellular carcinoma; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; MESO, mesothelioma; OV, ovarian serous cystadenocarcinoma, PAAD, pancreatic adenocarcinoma; PCPG, pheochromocytoma and paraganglioma; PRAD, prostate adenocarcinoma; READ, rectum adenocarcinoma; SARC, sarcoma; SKCM, skin cutaneous melanoma; STAD, stomach adenocarcinoma; TGCT, testicular germ cell tumors; THCA, thyroid carcinoma; THYM, thymoma; UCEC, uterine corpus endometrial carcinoma; UCS, uterine carcinosarcoma; UVM, uveal melanoma; OS, overall survival; DSS, disease-specific survival; DFI, disease-free interval; PFI, progression-free interval.

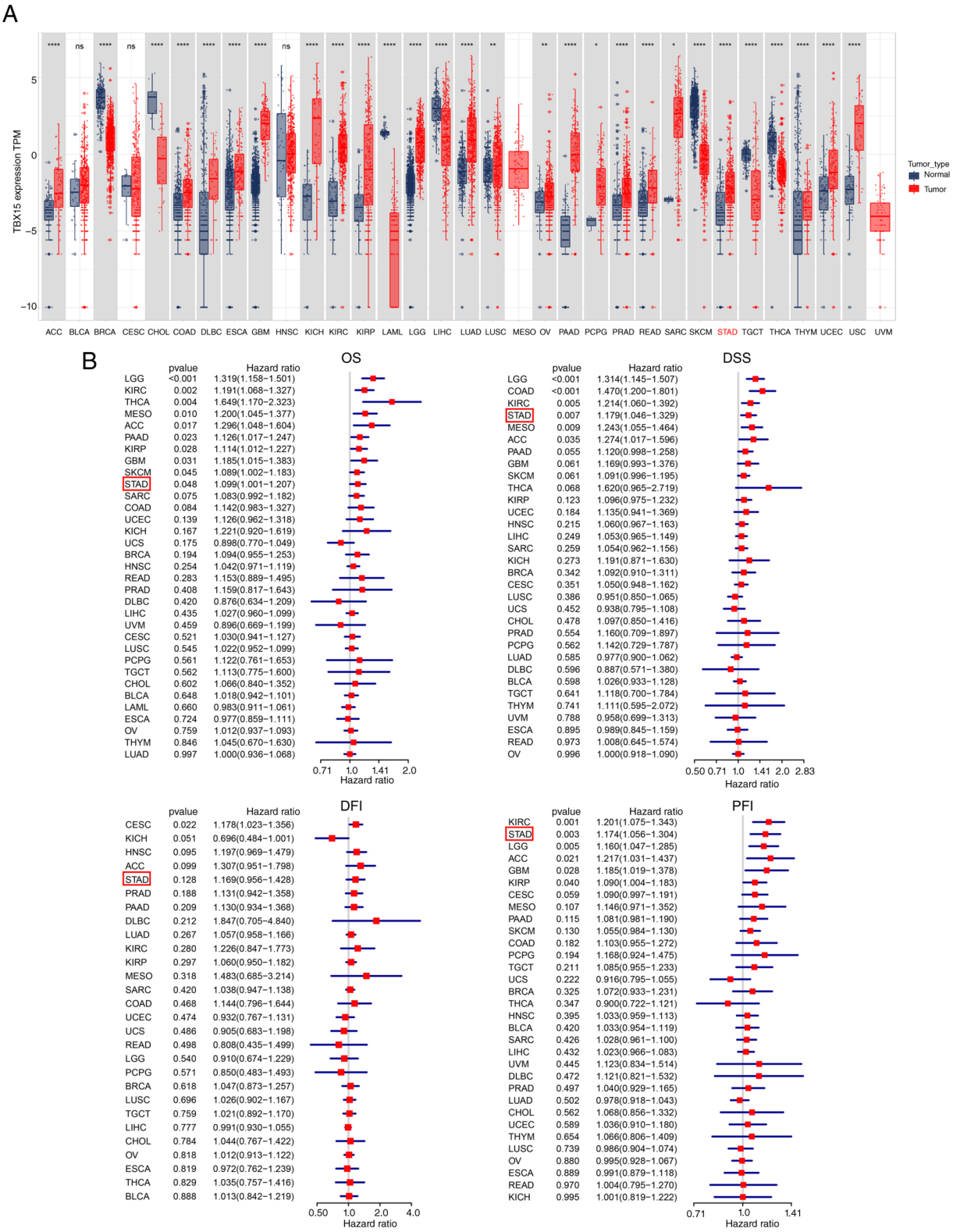


Figure S2. Silencing *TBX15* inhibits the proliferation, migration and invasion of MKN74 cells. (A) *TBX15* mRNA and protein levels were detected after silencing *TBX15* in MKN74. (B) Cell Counting Kit-8 assay. (C) EdU analysis. Scale bar, 50 μm. (D) Flow cytometric analysis of gastric cancer cell apoptosis levels. (E) Wound healing analysis. Scale bar, 100 μm. (F) Transwell assay was used to analyze cell invasion ability. Scale bar, 100 μm. **P<0.01 and ***P<0.001 vs. si-NC, one-way ANOVA and two-way ANOVA. TBX15, T-box transcription factor 15; si-, small interfering; NC, negative control.

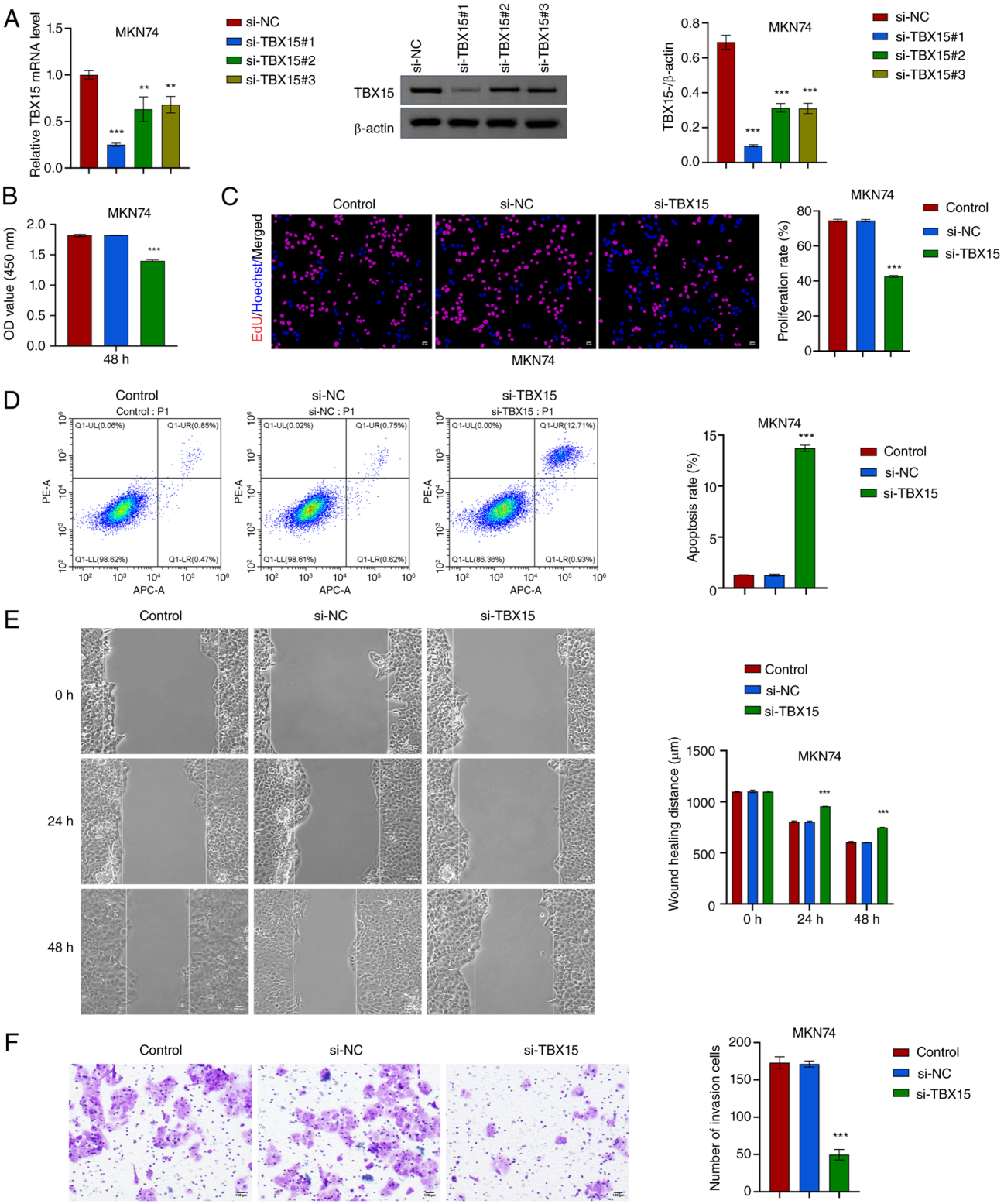


Figure S3. TBX15 and MMP14 participate in macrophage polarization. (A) *MMP14* mRNA levels in HGC27 and MKN74 cells. ***P<0.001 vs. oe-NC. (B) *TBX15* and *MMP14* mRNA levels in MKN74 cells. (C and D) Percentage of M1- and M2-type macrophages in the co-culture system of gastric cancer cell-TAMs. (E and F) Expression of *iNOS*, *IL-1β*, *TNF-α*, *Arg-1*, *IL-10* and *CD206*. *P<0.05 and ***P<0.001 vs. M0; $^{\#\#}$P<0.05 and $^{\#\#\#}$P<0.001 vs si-NC/TAM; $^{\&}$P<0.05, $^{\&\&}$P<0.01 and $^{\&\&\&}$P<0.001 vs. (si-*TBX15* + oe-NC)/TAM, one-way ANOVA and two-way ANOVA. TBX15, T-box transcription factor 15; MMP14, matrix metalloproteinase 14; oe-, overexpression; NC, negative control; TAM, tumor-associated macrophages; iNOS, inducible nitric oxide synthase; si-, small interfering.

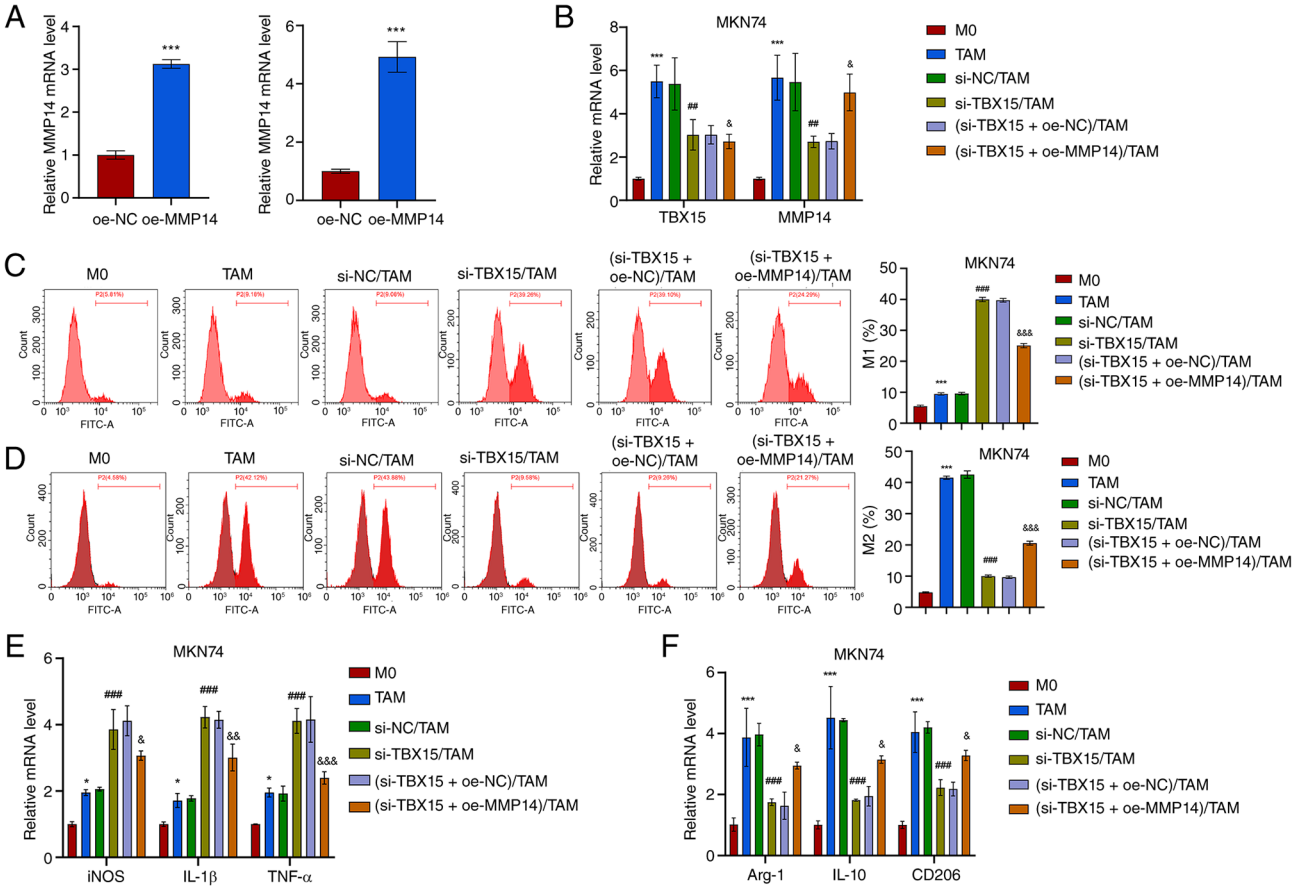


Figure S4. Gating strategies for macrophages in Fig. 5B and C and Fig. S3C and D. (A) Gating strategies for M1 macrophages in Figs. 5B and S3C. (B) Gating strategies for M2 macrophages in Figs. 5C and S3D. TAM, tumor-associated macrophages; si-, small interfering; NC, negative control; oe-, overexpression; TBX15, T-box transcription factor 15; MMP14, matrix metalloproteinase 14.

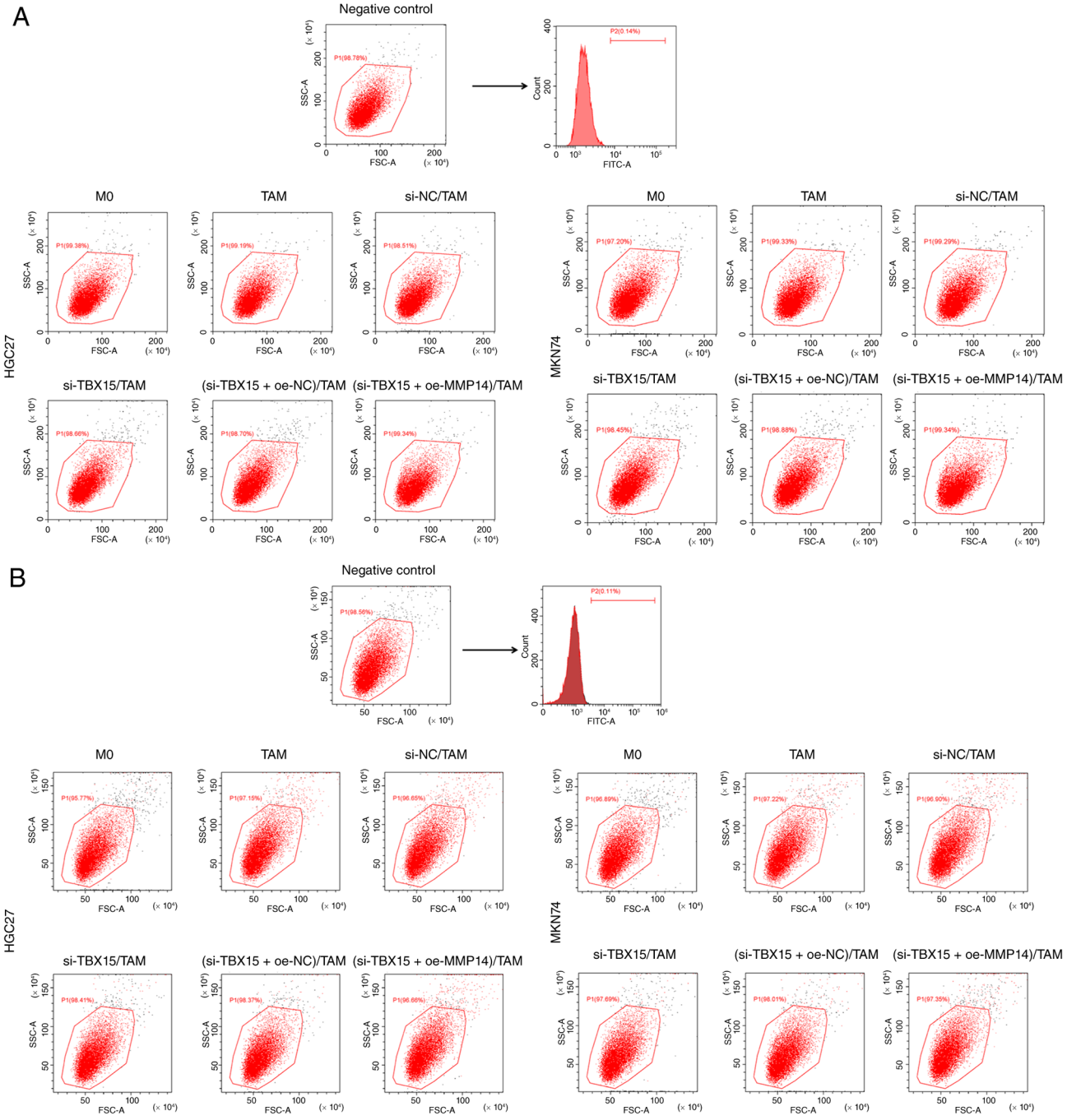
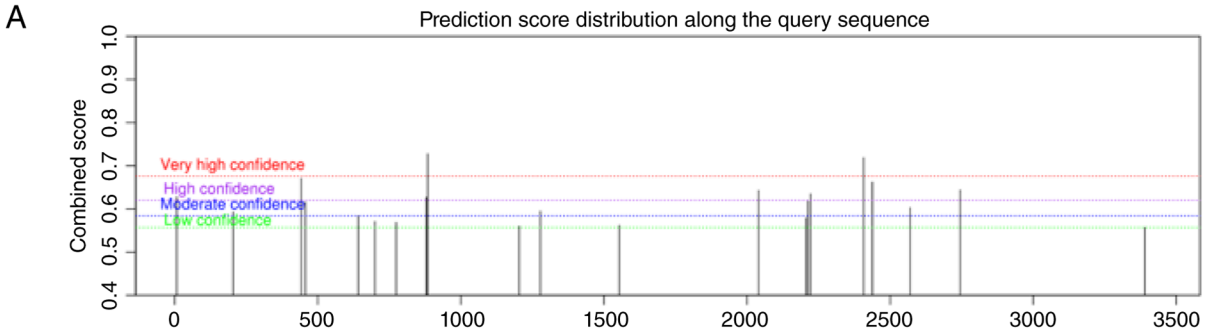


Figure S5. Silencing *METTL3* inhibits the m6A level of *TBX15*. (A) The m6A modification of *TBX15*. (B) RM2Target database predicted the binding of METTL3 to *TBX15*. (C) METTL3 levels were detected after silencing *METTL3* in MKN74. (D) The m6A level of *TBX15*. (E) RNA Pull-down assay. (F) The stability of *TBX15* mRNA. *P<0.05, **P<0.01 and ***P<0.001 vs. si-NC, one-way ANOVA and two-way ANOVA. METTL3, methyltransferase-like 3; m6A, N6-methyladenosine; TBX15, T-box transcription factor 15; si-, small interfering; NC, negative control.



B

RM2Target ID	WERs Name	WERs Type	Target Gene	Modification	Organism
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RM2Target_1497137	Mettl3	Writer	Tbx15	m6A	Mus musculus
RM2Target_368352	METTL3	Writer	TBX15	m6A	Homo sapiens
RM2Target_368354	METTL3	Writer	TBX15	m6A	Homo sapiens
RM2Target_368351	METTL3	Writer	TBX15	m6A	Homo sapiens
RM2Target_368353	METTL3	Writer	TBX15	m6A	Homo sapiens
RM2Target_1497134	Mettl3	Writer	Tbx15	m6A	Mus musculus
RM2Target_1497135	Mettl3	Writer	Tbx15	m6A	Mus musculus

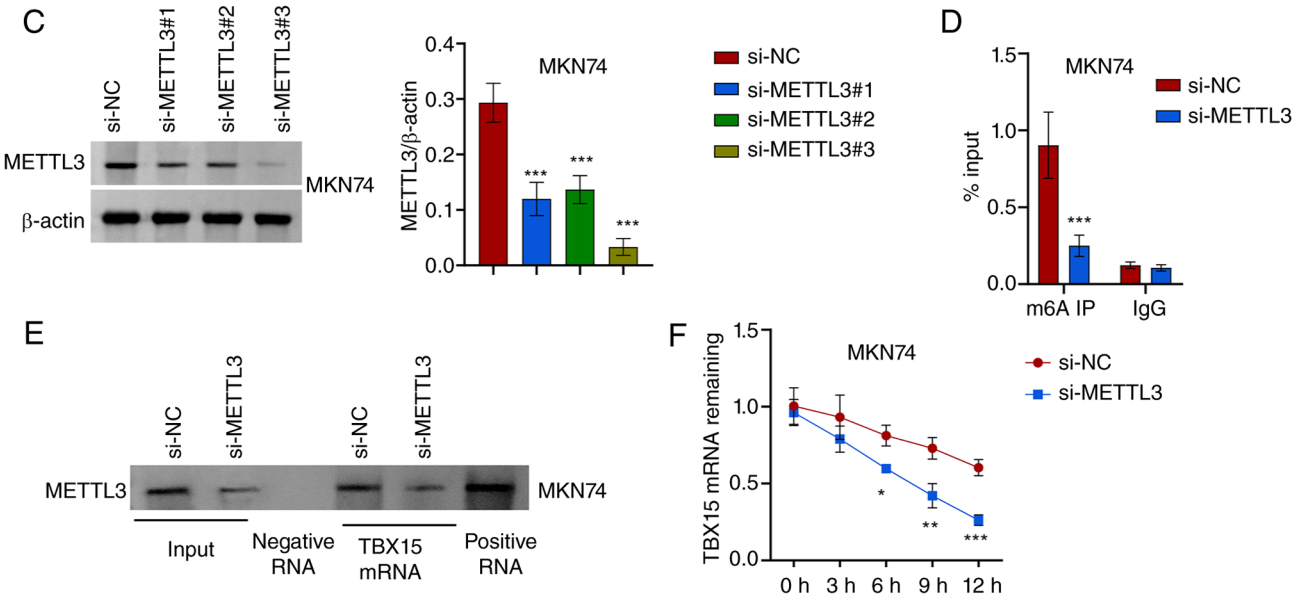

Figure S6. METTL3 regulates GC cell function and development through the TBX15/MMP14 signaling axis. (A) The expression of METTL3, TBX15 and MMP14 was identified after *METTL3* silencing and *TBX15* overexpression. (B and C) Analysis of GC cell proliferation activity. Scale bar, 50 μm. (D) Flow cytometric analysis of GC cell apoptosis. (E and F) Migration and invasion assays. Scale bar, 100 μm. ***P<0.001 vs. si-NC; $^{\#\#}$P<0.01 and $^{\#\#\#}$P<0.001 vs. si-*METTL3* + oe-NC, one-way ANOVA and two-way ANOVA. (G and H) In the co-culture system of GC cell-macrophages, the proportion of M1 and M2 macrophages was analyzed after *METTL3* silencing and *TBX15* overexpression intervention. (I and J) Levels of *iNOS*, *IL-1β*, *TNF-α*, *Arg-1*, *IL-10* and *CD206*. $^{\&}$P<0.05 and $^{\&\&\&}$P<0.001 vs. M0; *P<0.05 and ***P<0.001 vs. si-NC/TAM; $^{\#}$P<0.05 and $^{\#\#\#}$P<0.001 vs. (si-*METTL3* + oe-NC)/TAM, one-way ANOVA and two-way ANOVA. METTL3, methyltransferase-like 3; GC, gastric cancer; TBX15, T-box transcription factor 15; MMP14, matrix metalloproteinase 14; si-, small interfering; NC, negative control; oe-, overexpression; iNOS, inducible nitric oxide synthase.

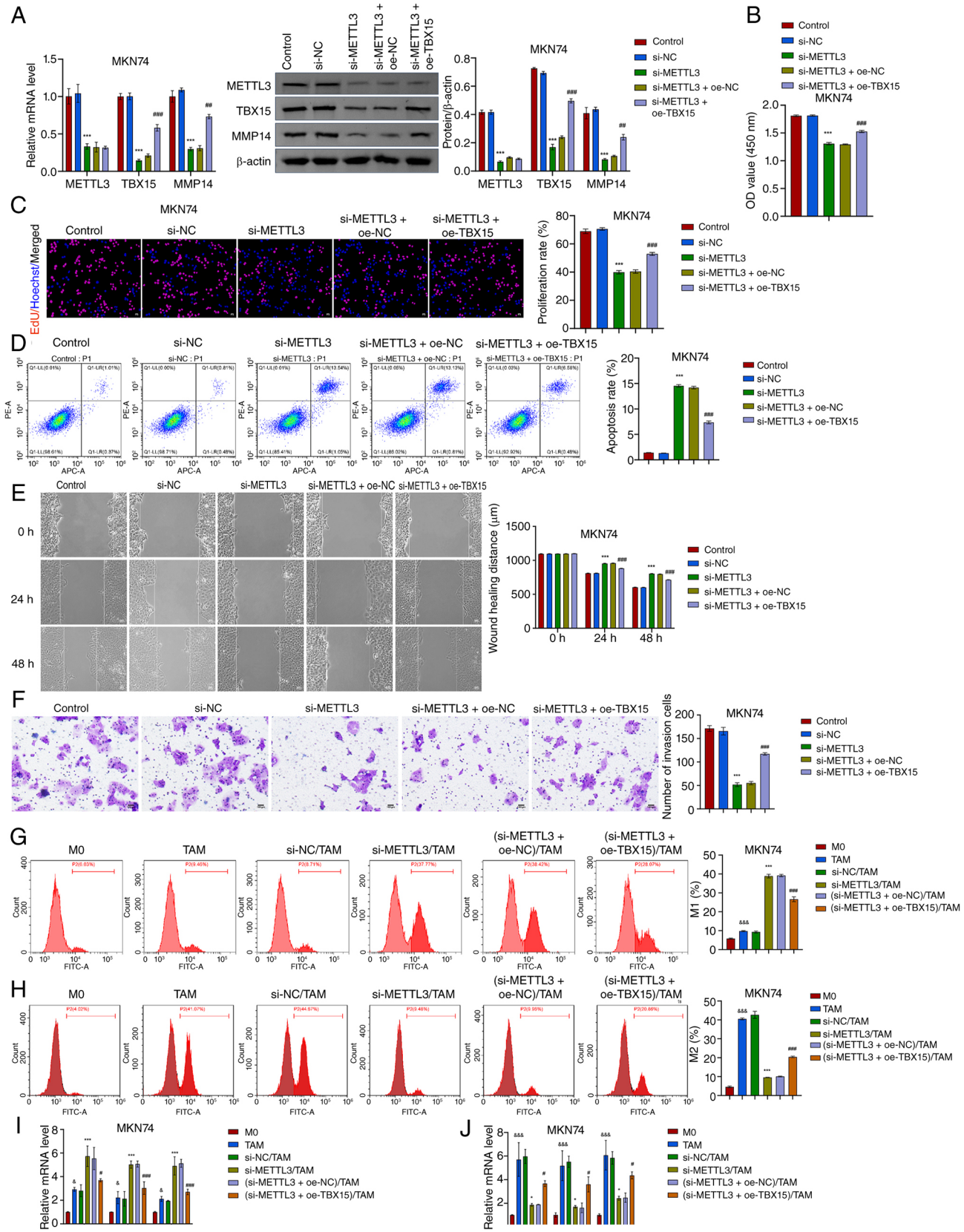

Figure S7. Gating strategies for macrophages in Fig. S3G and H. (A) Gating strategies for M1 macrophages in Figs. 7G and S6G. (B) Gating strategies for M2 macrophages in Figs. 7H and S6H. METTL3, methyltransferase-like 3; TAM, tumor associated macrophage; TBX15, T-box transcription factor 15; si-, small interfering; NC, negative control; oe-, overexpression.

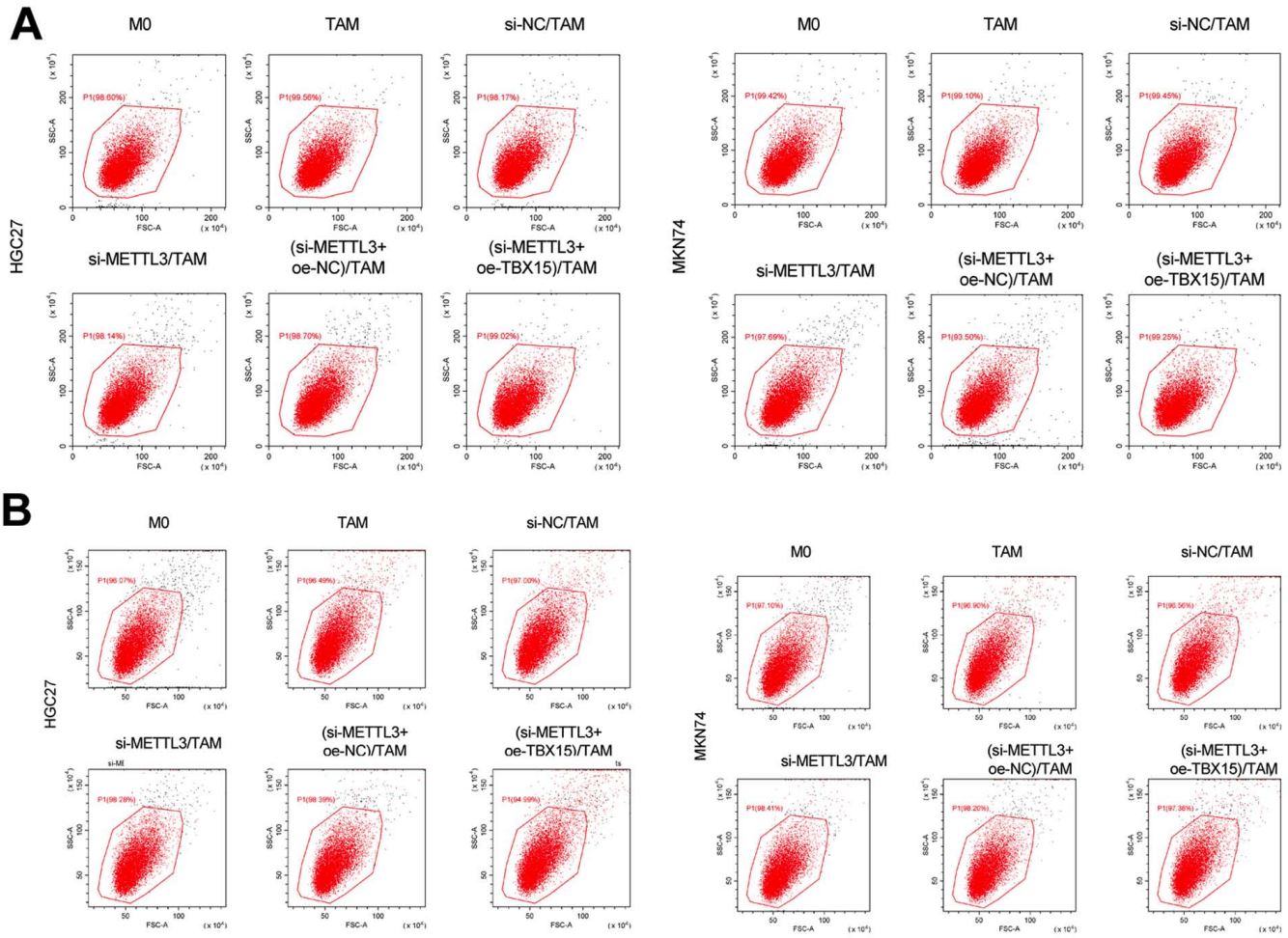

Figure S8. IHC results for PD-L1, CD100, IFN-γ and TNF-α in Fig. 8I. Images of IHC representative results for PD-L1, CD100, IFN-γ and TNF-α. Scale bars, 100 and 25 μm. IHC, immunohistochemistry; PD-L1, programmed death-ligand 1; IFN, interferon; NC, negative control; oe-, overexpression; sh-, short hairpin.

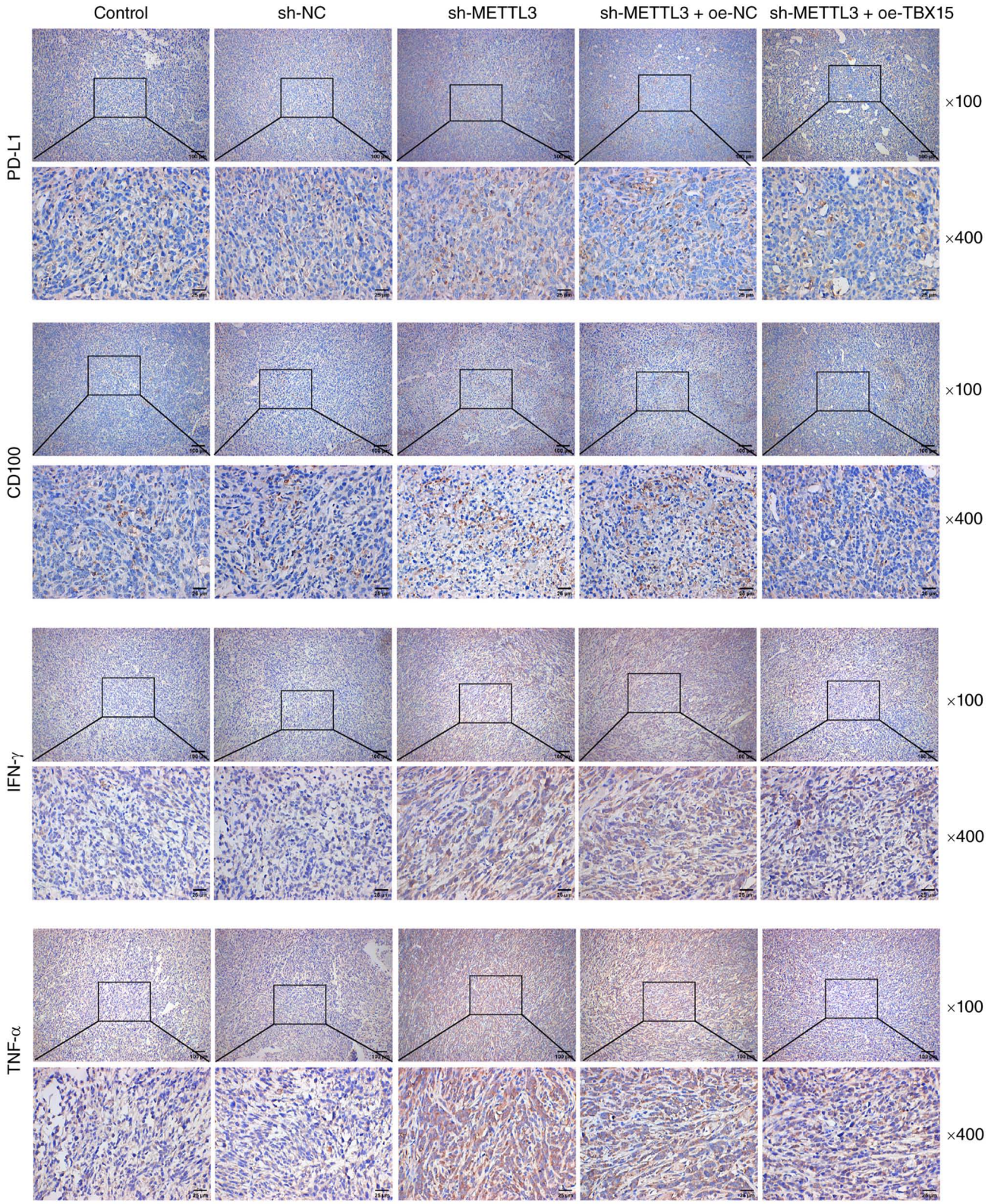

Figure S9. Experimental design diagram of the present study. TCGA, The Cancer Genome Atlas; GTEx, Genotype-Tissue Expression; GC, gastric cancer; m6A, N6-methyladenosine; CCK-8, Cell Counting Kit-8; IHC, immunohistochemistry; TAMs, tumor-associated macrophages.