

Supplementary material

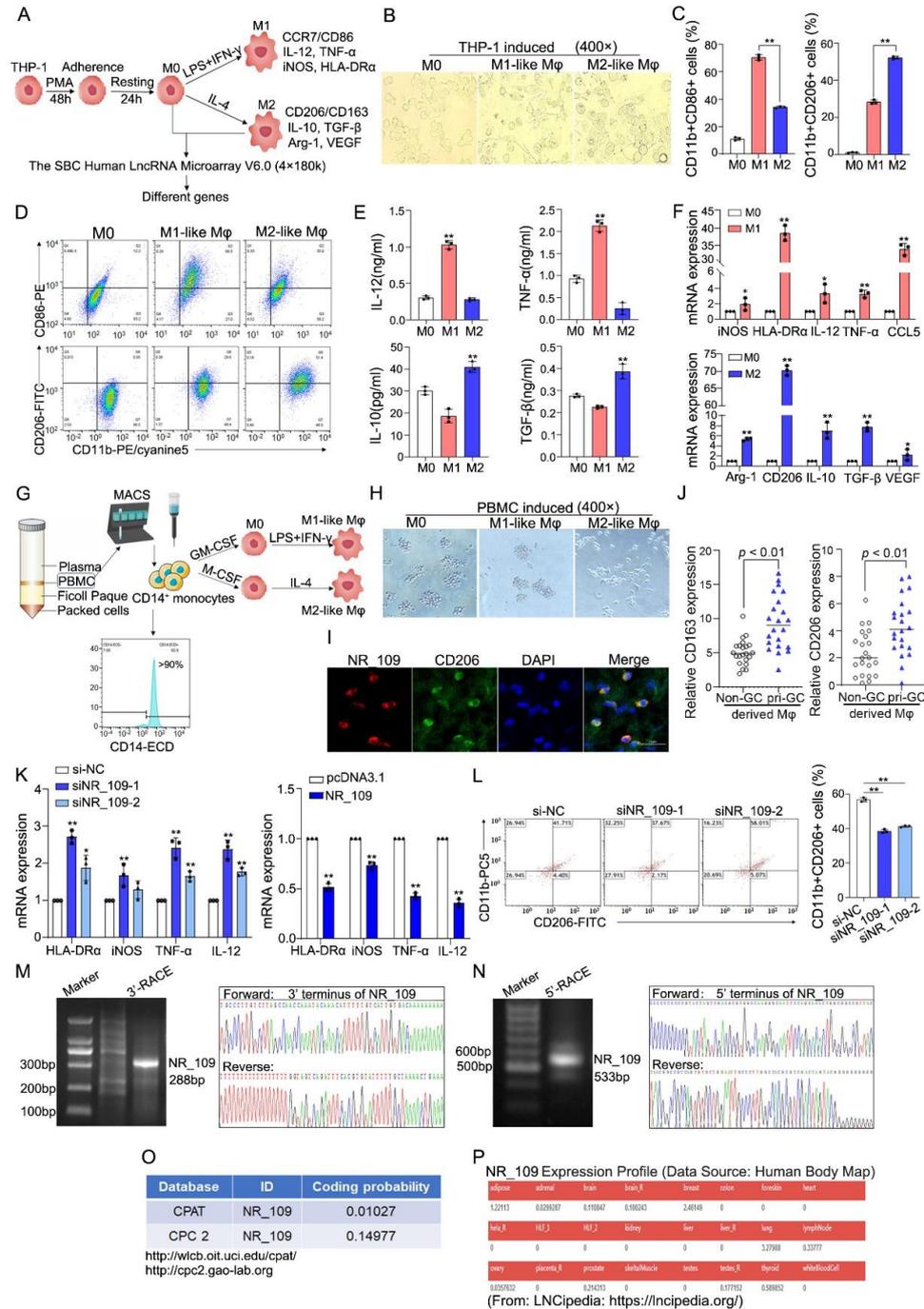


Figure. S1 The model of M0, M1-like and M2-like macrophages induced by THP-1 cells and PBMC.

A. The procedure and **B.** the morphology of M0, M1-like and M2-like macrophages induced from THP-1 cells. **C-D.** Expression of CD86 and CD206 in M0, M1-like and

M2-like macrophages was measured by FCM. **E.** The level of IL-12, TNF- α , IL-10 and TGF- β in the supernatant of M0, M1, and M2-like macrophages was examined by ELISA assays. **F.** Expression of M1-related markers in M1-like macrophages and M2-related markers in M2-like macrophages were analyzed by qPCR. **G.** The procedure and **H.** the morphology of M0, M1-like and M2-like macrophages induced from PBMC. **I.** IF combined with FISH assays showed that NR_109 was expressed in CD206⁺ TAMs of GC tissues. **J.** Expression of CD163 and CD206 in TAMs isolated from the primary GC tissues (pri-GC) and the matched adjacent non neoplastic tissues (non-GC) was measured using qPCR. **K.** Expression of M1-related markers in M2-NR_109^{low} cells and M2-NR_109^{high} cells was tested by qPCR. **L.** Expression of CD206 in THP-1 induced M2-NR_109^{low} cells was measured using FCM. **M.** The 3' and **N.** 5' RACE assays of NR_109 in THP-1 induced M2-like macrophages. **O.** The CPAT and CPC 2 database showed that NR_109 has barely any coding probability. **P.** The NONCODE database showed the distribution of NR_109 in human body. The statistical data are from three independent experiments and the bar indicates the SD values (* $p < 0.05$, ** $p < 0.01$).

assays. **F.** The schematic diagram showed the coculture system of tumor cells and macrophages. **G.** The migration of tumor cells was reduced when cocultured with M2-NR_109^{low} cells. **H.** The construction of HSC-NPG mice. **I.** The proportion of human CD45⁺ cells in HSC-NPG mice was analyzed by FCM. **J.** The CD3⁺ T cells, CD14⁺ cells, CD19⁺ B cells and CD56⁺ NK cells derived from human were detected in the peripheral blood of HSC-NPG mice. **K.** The M2shNR_109 cells in which NR_109 were stably knocked down in M2-like macrophages were established. **L.** The tumor size of different groups in HSC-NPG mice was analyzed by *in vivo* imaging. **M.** IF combined with FISH assays showed that the MFI of NR_109 and CD206 in tumor tissues were also decreased in M2shNR_109 group. **N-P.** The percentage of M2-like macrophages (CD163⁺CD206⁺) in spleen and peritoneum macrophages, and the percentage of CD4⁺ T cells and NK cells (CD3⁻CD16⁺CD56⁺) in the PBMC and spleen were measured by FCM assays. The statistical data are from three independent experiments and the bar indicates the SD values (**p* < 0.05, ***p* < 0.01).

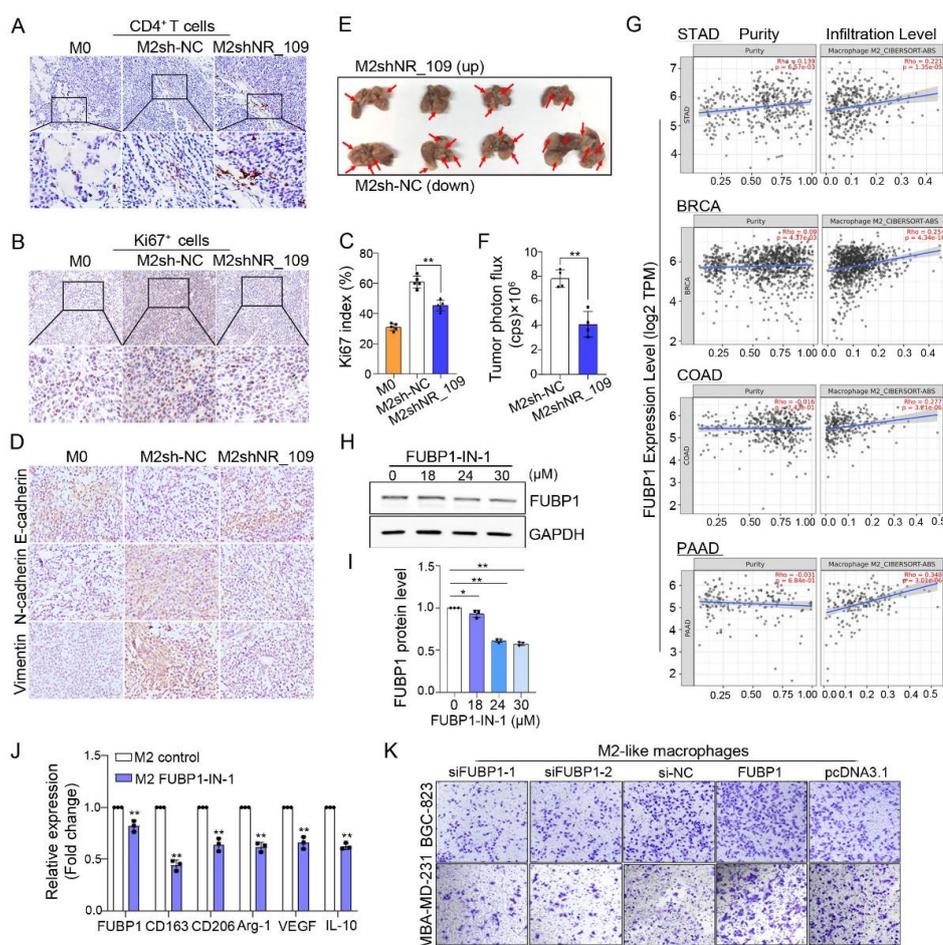


Figure. S3 Knockdown NR₁₀₉ reduced the activity of M2-like macrophages to promote growth and metastasis of tumor cells *in vivo*.

A. The infiltration of CD4⁺ T cells, **B-C.** Ki67 index and **D.** EMT-related markers in tumor tissues of different groups in HSC-NPG mice were analyzed by IHC. **E.** The number of lung metastasis nodules and **F.** the statistical graph of photon flux which presented the tumor size of distinct groups in lung metastasis model were exhibited. **G.** TIMER2.0 database revealed a significant positive correlation between the expression of FUBP1 and the infiltration of M2-like macrophages in many cancer types. **H.** Western-blot and **I.** qPCR assays showed the expression of FUBP1 was significantly attenuated in M2-like macrophages treated with the FUBP1 inhibitor, FUBP1-IN-1. **J.** Expression of M2-related markers in M2-like macrophages treated with FUBP1-IN-1 was measured by qPCR. **K.** The migration of tumor cells was examined when cocultured with M2-FUBP1^{low} cells or M2-FUBP1^{high} cells. The statistical data are from three independent experiments and the bar indicates the SD values (**p* < 0.05, ***p* < 0.01).

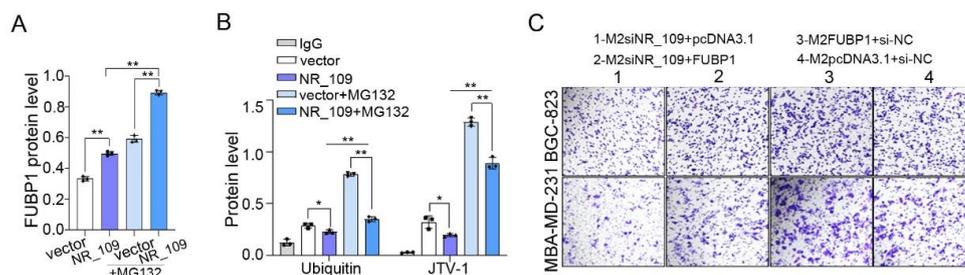


Figure. S4 NR₁₀₉ hindered the ubiquitin-mediated degradation of FUBP1.

A. The statistical chart showed that the expression of FUBP1 was further increased in M2-NR₁₀₉^{high} cells treated with MG132 (25μM). **B.** The statistical chart of the co-IP assays exhibited that ectopic NR₁₀₉ expression decreased the density of ubiquitin and JTV-1, and the MG132 further enhanced the effect. **C.** The migration of cocultured tumor cells was partially reversed when co-transfected with FUBP1 and siNR₁₀₉ in M2-like macrophages. The statistical data are from three independent experiments and the bar indicates the SD values (**p* < 0.05, ***p* < 0.01).

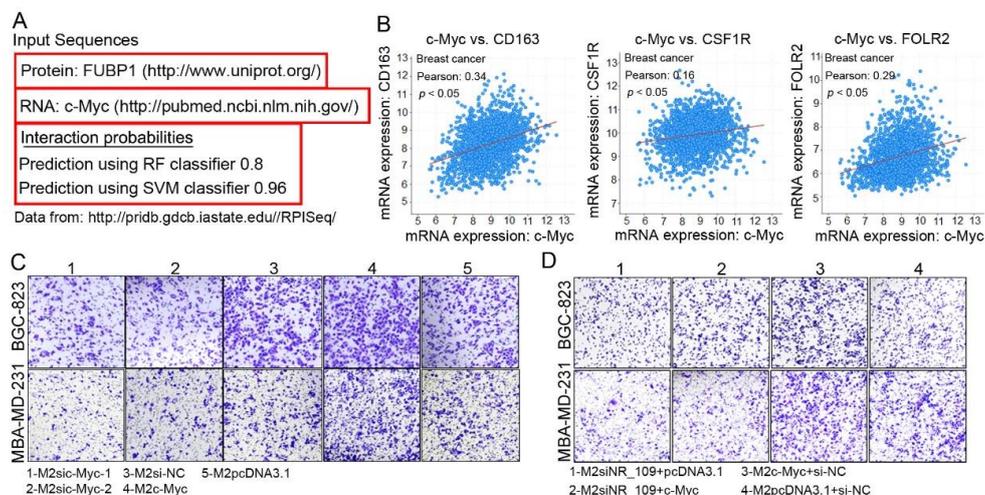


Figure. S5 c-Myc was participated in M2-like macrophage polarization.

A. The RNA-Protein Interaction Prediction (RPISeq) website showed an obvious interaction probability score between FUBP1 protein and the c-Myc RNA sequence. **B.** The cBioPortal database showed that c-Myc was significant associated with TAM-related markers including CD163, CSF1R and FOLR2 in BC. **C.** The migration of tumor cells was measured when cocultured with M2-c-Myc^{low} cells or M2-c-Myc^{high} cells. **D.** The migration of cocultured tumor cells was partially reversed when co-transfected with c-Myc and siNR_109 in M2-like macrophages.

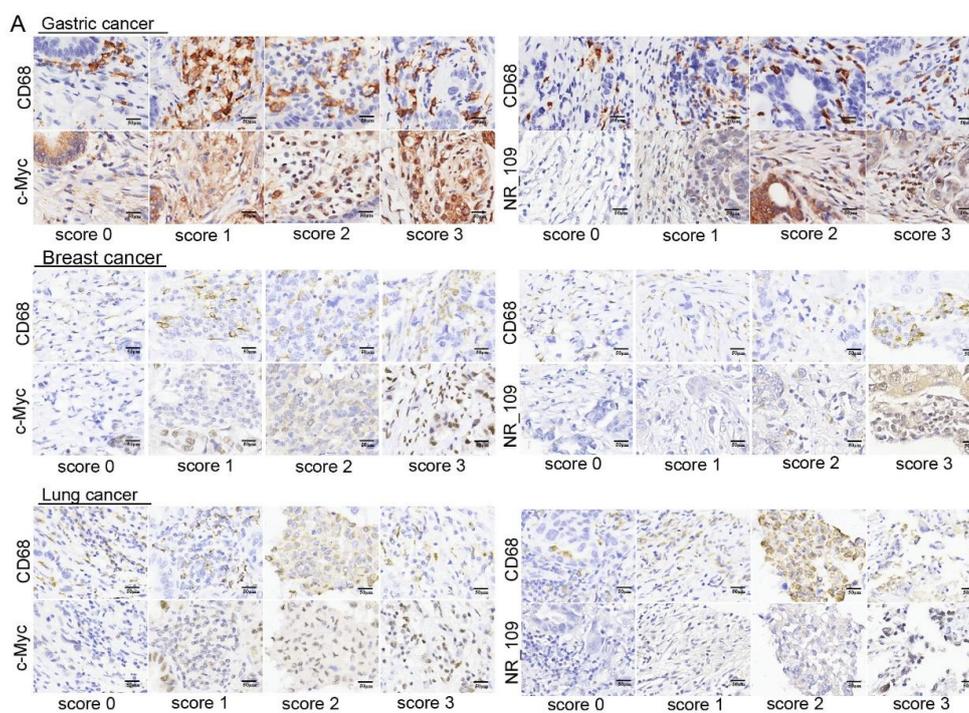


Figure. S6 A. The representative regions and scores of IHC staining for CD68 and ISH staining for NR_109 in GC, BC and LC tissues.

Table S1 Correlation between the number of CD163⁺ TAMs and clinicopathologic characteristics in GC and BC

Parameters	Number of CD163 ⁺ TAMs				P-value
	TS		TN		
GC	Low (%)	High (%)	Low (%)	High (%)	P-value
Age/year					0.705
< 60	5 (50)	5 (50)	7 (70)	3 (30)	
≥ 60	8 (40)	12 (60)	12 (60)	8 (40)	
Gender					0.427
Male	11 (48)	12 (52)	16 (70)	7 (30)	
Female	2 (29)	5 (71)	3 (43)	4 (57)	
Grade					0.419
I-II	10 (45)	12 (55)	16 (73)	6 (27)	
III	2 (25)	6 (75)	2 (25)	6 (75)	
Tumor size					0.721
≤ 5cm	5 (38)	8 (62)	8 (62)	5 (38)	
> 5cm	8 (47)	9 (53)	11 (65)	6 (35)	
Lymph node					0.045*
No	7 (70)	3 (30)	7 (70)	3 (30)	
Yes	5 (25)	15 (75)	12 (60)	8 (40)	
TNM Stage					1.000
I-II	7 (47)	8 (53)	10 (67)	5 (33)	
III-IV	6 (40)	9 (60)	9 (60)	6 (40)	
BC					
Age/year					0.022*
< 70	16 (36)	28 (64)	25 (57)	19 (43)	
≥ 70	10 (71)	4 (29)	8 (57)	6 (43)	
Grade					0.771
I-II	14 (47)	16 (53)	18 (60)	12 (40)	
III	12 (43)	16 (57)	15 (54)	13 (46)	
Tumor size					1.000
≤ 4cm	23 (45)	28 (55)	29 (57)	22 (43)	
> 4cm	3 (43)	4 (57)	4 (57)	3 (43)	
Lymph node					0.506
No	14 (41)	20 (59)	23 (68)	11 (32)	
Yes	12 (50)	12 (50)	10 (42)	14 (58)	
TNM Stage					0.020*
I-II	22 (55)	18 (45)	24 (60)	16 (40)	
III-IV	4 (22)	14 (78)	9 (50)	9 (50)	

The χ^2 -tests were used. *Statistically significant values.

TN: tumor nest, TS: tumor stroma, GC: gastric cancer, BC: breast cancer

Table S2 Correlation between the expression of NR_109 and the number of CD163⁺ TAMs in TS and TN of GC and BC

Protein	Expression	NR_109		r	P-value
		Low	High		
TS (GC)	Low	8	7	0.424	0.019*
	High	2	13		
TN (GC)	Low	7	11	0.144	0.447
	High	3	9		
TS (BC)	Low	17	9	0.309	0.018*
	High	11	21		
TN (BC)	Low	16	17	0.005	0.971
	High	12	13		

The Spearman correlation analysis were used. *Statistically significant values. TN: tumor nest, TS: tumor stroma, GC: gastric cancer, BC: breast cancer.

Table. S3 Primers for quantifying gene expression

Gene	Primer Sequence (5'->3')
Arg-1	Forward: GCAAGGTGATGGAAGAAA Reverse: CTGGTGTGAAAGATGGGT
IL-10	Forward: GGAGAACCTGAAGACCCT Reverse: GGCTTTGTAGATGCCTTC
TGF- β	Forward: GGCCAGATCCTGTCCAAGC Reverse: GTGGGTTTCCACCATTAGCAC
CCL5	Forward: CCTCATTGCTACTGCCCTCT Reverse: GTTCAGCCGGGAGTCATAACA
CD206	Forward: CGTGTGCACCTACCTCAAGA Reverse: AAGGACAGACCAGTACAATTCAGTA
CD163	Forward: TTTGTCAACTTGAGTCCCTTCAC Reverse: TCCCGCTACACTTGTTTTAC
VEGF	Forward: CTTGCCTTGCTGCTCTACCT Reverse: TCTCTCCTATGTGCTGGCCT
TNF- α	Forward: TTTCCGTGAAAACGGAGCTG Reverse: CACCCACAAGAAGAGGCAGAT
HLA-DRA	Forward: GGCGGCTTGAAGAATTTGGAC Reverse: CATTGGTGATCGGAGTATAGTTGGA
IL-12	Forward: CCTTGCACTTCTGAAGAGATTGA Reverse: ACAGGGCCATCATAAAAGAGGT
iNOS	Forward: CCATCATGGACCACCACACA Reverse: TCCGCATTAGCACAGAAGCA
GAPDH	Forward: CGCTGAGTACGTCGTGGAGTC Reverse: GCTGATGATCTTGAGGCTGTTGTC
NR_109	Forward: TTGAGATGTCGAGAGCGAGC Reverse: CTTGGGCTGTGCTGAGACTA
c-Myc	Forward: CCACCAGCAGCGACTCTGA Reverse: GCAGAAGGTGATCCAGACTC

FUBP1	Forward: AGGATTACCAGCCTGAACT Reverse: GACAACACCCGAAAGGATAGC
siRNA Oligos	
Target gene	Sequence (5'→3')
NR_109-1	Sense: CUGUCAUCUACACAUGAAUTT Antisense: AUUCAUGUGUAGAUGACAGTT
NR_109-2	Sense: CUUGUCACCAUAACAUAUUTT Antisense: AUA AUGUUAUGGUGACAAGTT
FUBP1-1	Sense: GGUGCUGACAAACCUCUUATT Antisense: UAAGAGGUUUGUCAGCACCTT
FUBP1-2	Sense: GGUGUUCGCAUUCAGUUUATT Antisense: UAAACUGAAUGCGAACACCTT
c-Myc-1	Sense: CGUCCAAGCAGAGGAGCAATT Antisense: UUGCUCUCUGCUUGGACGTT
c-Myc-2	Sense: GCUUGUACCUGCAGGAUCUTT Antisense: AGAUCCUGCAGGUACAAGCTT