KEY RESOURCES TABLE

| REAGENT or RESOURCE S | OURCE | IDENTIFIER |
|--|--------------------------|---------------------|
| Antibodies | | |
| PE anti-mouse CD45 antibody | Biolegend | Clone no. 30-F11 |
| APC anti-mouse CD3ε antibody | Biolegend | Clone no. 145-2C11 |
| FITC anti-mouse CD8a antibody | Biolegend | Clone no. 53-6.7 |
| PerCP/Cyanine5.5 anti-mouse CD223 (LAG- | Biolegend | Clone no. C9B7W |
| 3) antibody | | |
| PE/Cyanine7 anti-mouse CD279 antibody | Biolegend | Clone no. 29F.1A12 |
| Brilliant Violet 421 anti-mouse CD366 (Tim-3) | Biolegend | Clone no. B8.2C12 |
| antibody | | |
| Brilliant Violet 421 anti-mouse Ki-67 antibody | Biolegend | Clone no.16A8 |
| Brilliant Violet 421 anti-mouse IFN-γ antibody | Biolegend | Clone no. XMG1.2 |
| PE anti-mouse F4/80 antibody | Biolegend | Clone no. BM8 |
| Alexa Fluor® 700 anti-mouse/human CD11b | Biolegend | Clone no. M1/70 |
| antibody | | |
| APC anti-mouse CD206 antibody | Thermo Fisher Scientific | Clone no. MR6F3 |
| APC anti-mouse iNOS antibody | Thermo Fisher Scientific | Clone no. CXNFT |
| APC anti-mouse CD3 antibody | Thermo Fisher Scientific | Clone no. 145-2C11 |
| FITC anti-mouse CD45 antibody | Biolegend | Clone no. 30-F11 |
| PerCP/Cyanine5.5 anti-mouse NK1.1 | Biolegend | Clone no. PK136 |
| antibody | | |
| FITC anti-mouse CD4 antibody | Biolegend | Clone no. RM4-5 |
| Brilliant Violet 421 anti-mouse CD8 antibody | Biolegend | Clone no. 53-6.7 |
| Brilliant Violet 421 anti-mouse Ly6G antibody | Biolegend | Clone no. 1A8 |
| PE-Cyanine 7 anti-mouse Ly6C antibody | Biolegend | Clone no. HK1.4 |
| APC anti-mouse IL10 antibody | Biolegend | Clone no. JES5-16E3 |
| Brilliant Violet 421 anti-mouse CD45.1 | Biolegend | Clone no. A20 |
| antibody | | |
| APC-Cyanine 7 anti-mouse CD45.2 antibody | Biolegend | Clone no. 104 |
| PE/Cyanine7 anti-mouse CD19 antibody | Biolegend | Clone no. 6D5 |
| Brilliant Violet 510 anti-mouse CD11b | Biolegend | Clone no. M1/70 |
| antibody | | |
| Anti-mouse CD16/32 antibody | Biolegend | Clone no. 93 |
| Anti-mouse CD45 antibody | Biolegend | Clone no. 30-F11 |
| Anti-mouse CD3ε Antibody | Biolegend | Clone no. 145-2C11 |
| Anti-mouse CD103 antibody | Biolegend | Clone no. 2E7 |
| Anti-mouse CD95(Fas) antibody | Biolegend | Clone no. SA367H8 |
| Anti-mouse MHC II(I-A/I-E) antibody | Biolegend | Clone no. |
| | | M5/114.15.2 |
| Anti-mouse CD44 antibody | Biolegend | Clone no. IM7 |
| Anti-mouse Gr-1(Ly-6G/Ly-6C) antibody | Biolegend | Clone no. RB6-8C5 |
| Anti-mouse CD206(MMR) antibody | Biolegend | Clone no. C068C2 |

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---------------------------------------|----------------|---------------------|
| Anti-mouse Ly6C antibody | Biolegend | Clone no. HK1.4 |
| Anti-mouse Ly6G antibody | Biolegend | Clone no. 1A8 |
| Anti-mouse CX3CR1 antibody | Biolegend | Clone no. SA011F11 |
| Anti-mouse CD127(IL-7Rα) antibody | Biolegend | Clone no. A7R34 |
| Anti-mouse CD19 antibody | Biolegend | Clone no. 6D5 |
| Anti-mouse CD278(ICOS) antibody | Biolegend | Clone no.C398.4A |
| Anti-mouse SiglecF antibody | BD Biosciences | Clone no. E50-2440 |
| Anti-mouse Ki67 antibody | eBioscience | Clone no. SoIA15 |
| Anti-mouse CD11c antibody | Biolegend | Clone no. N418 |
| Anti-mouse CD39 antibody | Biolegend | Clone no. 5F2 |
| Anti-mouse TIGIT(VSTM3) antibody | R&D Systems | Clone no. 2190A |
| Anti-mouse CD45R(B220) antibody | Biolegend | Clone no. RA3-6B2 |
| Anti-mouse F4/80 antibody | BioRAD | Clone no. C1:A3-1 |
| Anti-mouse TCRb antibody | Biolegend | Clone no. H57-597 |
| Anti-mouse iNOS antibody | eBioscience | Clone no. CXNFT |
| Anti-mouse PD-L1 antibody | Biolegend | Clone no.10F.9G2 |
| Anti-mouse CD25 antibody | Biolegend | Clone no. 3C7 |
| Anti-mouse CD192(CCR2) antibody | R&D Systems | Clone no. 475301 |
| Anti-mouse CD64(FcγRI) antibody | Biolegend | Clone no. X54-5/7.1 |
| Anti-mouse TCR γ/δ antibody | Biolegend | Clone no. GL3 |
| Anti-mouse CD49b antibody | Biolegend | Clone no. DX5 |
| Anti-mouse CD27 antibody | Biolegend | Clone no. LG.3A10 |
| Anti-mouse CD62L antibody | Biolegend | Clone no. MEL-14 |
| Anti-mouse T-bet antibody | Biolegend | Clone no. 4B10 |
| Anti-mouse CD69 antibody | Biolegend | Clone no. H1.2F3 |
| Anti-mouse PD-1(PD-1) antibody | Biolegend | Clone no. 29F.1A12 |
| Anti-mouse CD172a (SIRPα) antibody | Biolegend | Clone no. P84 |
| Anti-mouse Gata3 antibody | eBioscience | Clone no. TWAJ |
| Anti-mouse KLRG1 antibody | eBioscience | Clone no. 2F1 |
| Anti-mouse CD366(Tim-3) antibody | Biolegend | Clone no. RMT3-23 |
| Anti-mouse CD4 antibody | Biolegend | Clone no. RM4-5 |
| Anti-mouse CD8 antibody | Biolegend | Clone no. 53-6.7 |
| Anti-mouse CD11b antibody | Biolegend | Clone no. M1/70 |
| InVivoMab anti-mouse PD-1 | Bio X Cell | Cat no. BE0146 |
| InVivoMab rat IgG2a isotype control | Bio X Cell | Cat no. BE0089 |
| InVivoPlus anti-mouse CD8α | Bio X Cell | Cat no. BP0117 |
| InVivoPlus rat IgG2b I sotype control | Bio X Cell | Cat no. BP0090 |
| InVivoMAb anti-mouse CD28 | Bio X Cell | Cat no. BE0015 |
| InVivoMAb anti-mouse CD3 | Bio X Cell | Cat no. BE0002 |
| InVivoMAb anti-mouse CSF1R | Bio X Cel | Cat no. BE0213 |
| | | |

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|--|--------------------------|--------------------|
| Anti-human MS4A4A antibody | Abcam | Cat no. ab67134 |
| Anti-mouse MS4A4A mAb | This paper | Clone no. 3G7 |
| Anti-human MS4A4A antibody | Sigma-Aldrich | Cat no. HPA029323 |
| Anti-mouse MS4A4A antibody | ABclonal | Cat no. A18334 |
| Anti-human CD68 antibody | Abcam | Cat no. ab213363 |
| Anti-mouse AKT antibody | Proteintech | Cat no.10176-2-AP |
| Anti-mouse phospho-AKT (Ser473) antibody | Proteintech | Cat no. 66444-1 |
| Anti-mouse STAT6 antibody | Proteintech | Cat no. 51073-1-AP |
| Anti-mouse phospho-STAT6 (Y641) antibody | Abcam | Cat no. ab263947 |
| Anti-mouse STAT3 antibody | Proteintech | Cat no.10253-2-AP |
| Anti-mouse phospho-STAT3 (Y705) antibody | ABclonal | Cat no. AP0070 |
| Anti-mouse alpha Tubulin antibody | Proteintech | Cat no.11224-1-AP |
| Anti-mouse/human β-actin antibody | Proteintech | Cat no. 20536-1-AP |
| Anti-mouse F4/80 antibody | Cell Signaing Technology | Cat no. 70076S |
| Anti-mouse CD206 antibody | Cell Signaing Technology | Cat no. 24595S |
| Anti-mouse CD8 antibody | Abcam | Cat no. ab209775 |
| Anti-mouse CD206 antibody | Proteintech | Cat no.18704-1-AP |
| Anti-mouse/human GFP antibody | Cell Signaing Technology | Cat no. 2956S |
| Anti-human CD31 antibody | Proteintech | Cat no. 66065-2-lg |
| Anti-human MPO antibody | Proteintech | Cat no. 22225-1-AP |
| Anti-human SMA antibody | Proteintech | Cat no. 14395-1-AP |
| Anti-human EPCAM antibody | Proteintech | Cat no. 21050-1-AP |
| Anti-human CD11c antibody | Proteintech | Cat no. 60258-1-lg |
| Anti-mouse Arg1 antibody | Proteintech | Cat no. 16001-1-AP |
| Anti-mouse/human CD3 antibody | Proteintech | Cat no. 17617-1-AP |
| Chemicals | | |
| Collagenase IV | Sigma-Aldrich | Cat no. C4-22-1G |
| DNase I | Sigma-Aldrich | Cat no. D5025 |
| Puromycin dihydrochloride | Sigma-Aldrich | Cat no. P883 |
| Azoxymethane | Sigma-Aldrich | Cat no. A5486 |
| Dextran sodium sulfate | MP Biomedicals | Cat no. 0216011080 |
| Recombinant Murine IL-2 | PeproTech | Cat no. 212-12 |
| Phorbol 12-myristate 12-acetate (PMA) | InvivoGen | Cat no. tlrl-pma |
| Recombinant Human IL-4 | PeproTech | Cat no. 200-04 |
| Recombinant Murine IL-4 | PeproTech | Cat no. 214-14 |
| Recombinant Human IL-13 | PeproTech | Cat no. 200-13 |
| Recombinant Murine IL-13 | PeproTech | Cat no. 210-13 |
| Recombinant Human IFN-γ | PeproTech | Cat no. 300-02 |
| Recombinant Murine IFN-γ | PeproTech | Cat no. 315-05 |
| Dactolisib (BEZ235) | Selleck | Cat no. S1009 |

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| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
| AS1517499 | Selleck | Cat no. S8685 |
| PI3Kα inhibitors (HS-173) | Selleck | Cat no. S7356 |
| PI3Kδ inhibitors (IPI-3063) | Selleck | Cat no. S7335 |
| PI3Kβ inhibitors (IPI-3063) | Selleck | Cat no. S7335 |
| PI3Ky inhibitors (IPI-549) | Selleck | Cat no. S8330 |
| CFSE | eBioscience | Cat no. 65-0850-84 |
| ACK Lysis Buffer | Leagene | Cat no. CS0001 |
| Fixation Buffer | Biolegend | Cat no. 420801 |
| Cell Staining Buffer | Biolegend | Cat no. 420201 |
| RPMI-1640 | GIBCO | Cat no. C11875 |
| DMEM | GIBCO | Cat no. C11995500BT |
| Monocyte attachment medium | PromoCell | Cat no. C-28051 |
| Macrophage Detachment Solution DXF | PromoCell | Cat no. C-41330 |
| Macrophages Base Medium | PromoCell | Cat no. C-28057 |
| Histopaque®-1077 (1.077g/ml) | Sigma-Aldrich | Cat.no. S-10771 |
| PrimeScriptTM RT reagent Kit | Takara | Cat.no. S-10771 |
| SYBR Green 2xTaq mix | Takara | Cat no. RR820A |
| · · · · · · · · · · · · · · · · · · · | Ianaia | Cat 110. INNOZUA |
| Critical commercial assays | Dakowa | Cat no.1217102 |
| Mouse TGF-β1 Precoated ELISA Kit Mouse IL-10 Precoated ELISA Kit | Dakewe Dakewe | Cat no.1217102 |
| - | Absin | |
| 4-color multiple fluorescent immunohistochemical staining kit | ADSIII | Cat no. abs50012 |
| | TIANGEN | Cat no. DP103 |
| TIANprep Mini Plasmid Kit Advanced DNA BNA Transfection Respect | Zeta Life | Cat no. AD600075 |
| Advanced DNA RNA Transfection Reagent Cell Activation Cocktail (with Brefeldin A) | | Cat no. 423303 |
| - | Biologend | |
| Intracellular Staining Permeabilization Wash Buffer (10X) | Biolegend | Cat no. 421002 |
| FOXP3 Fix/Perm Buffer Set | Biolegend | Cat no. 42140 |
| Clophosome® -Neutral Liposomal | FormuMax | Cat no. F70101C-N |
| Clodronate for Macrophage Depletion | TOTTIUWAX | Cat 110. 1 70 10 10-11 |
| Experimental models: Cell lines | | |
| SW480 | Fang Yuan et al., 2019 | N/A |
| HT29 | Fang Yuan et al., 2019 | N/A |
| LoVo | Fang Yuan et al., 2019 | N/A |
| RKO | Fang Yuan et al., 2019 | N/A |
| - | the Department of Pathology, | N/A |
| THP-1 | Southern Medical University | 1 W/ /** |
| HEK-293T | the Department of Pathology, | N/A |
| | Southern Medical University | 1 W/ /\text{\tint{\text{\text{\text{\text{\text{\tinit}}\\ \text{\ti}\\\ \text{\ti}\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\ti}\\\ \text{\text{\text{\text{\text{\text{\text{\text{\text{\tex{\tinit}\\ \text{\text{\text{\text{\text{\text{\text{\tinit}\\ \tinit{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\tinit}\\ \tinit{\text{\text{\text{\tinit}\\ \tinit{\text{\text{\text{\text{\text{\ti}\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\ti}\}\tittt{\text{\text{\text{\text{\text{\text{\text{\text{\text{\tinit}\tint{\text{\text{\text{\text{\texi}\tint{\text{\ti}\titt{\text{\ti}\tint{\text{\text{\tinit\tint{\tiint{\text{\tii}\tiint{\text{\tii}\tint{\text{\tiin}\tiint{\tii}\tiint{\tii}\t |
| | 22 anom modified Oniversity | |

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|--|------------------------------|-------------------------|
| Experimental models: Cell lines | SOURCE | IDENTIFIER |
| L929 | the Department of Pathology, | N/A |
| | Southern Medical University | |
| J774A.1 | the Department of Pathology, | N/A |
| | Southern Medical University | |
| RAW264.7 | the Department of Pathology, | N/A |
| | Southern Medical University | |
| MC38 | Mingdao Lin et al., 2021 | N/A |
| CT26 | Mingdao Lin et al., 2021 | N/A |
| B16F10 | the Department of Pathology, | N/A |
| | Southern Medical University | |
| Experimental models: | | |
| Organisms/strains | | |
| Mouse: C57BL/6J | Laboratory Animal Center, | N/A |
| | Southern Medical University. | |
| Mouse: BALB/c | Laboratory Animal Center, | N/A |
| | Southern Medical University. | |
| Oligonucleotides | | |
| siRNA targeting sequence: Ms4a4a #1: 5'- | GENECHEM Biotech | N/A |
| CCUUGGGAUUGUGCAGAUUTT -3' | | |
| siRNA targeting sequence: Ms4a4a #2: 5'- | GENECHEM Biotech | N/A |
| GCAGCCUAGGCUUGAACAUTT -3' | | |
| In vivo siRNA targeting sequence: Ms4a4a #1: | RiboBio | N/A |
| 5'- CCUUGGGAUUGUGCAGAUUTT -3' | | |
| In vivo siRNA targeting sequence: Ms4a4a #2: | RiboBio | N/A |
| 5'- GCAGCCUAGGCUUGAACAUTT -3' | | |
| Primers for qRT-PCR, see Table S2 | This paper | N/A |
| Recombinant DNA | | |
| pLent-EF1a-FH-CMV-Puro-Ms4a4a | Vigene Biosciences | N/A |
| pLent-EF1a-FH-CMV-Puro-MS4A4A | Vigene Biosciences | N/A |
| Software and Algorithms | | |
| GraphPad Prism 8 | GraphPad Software | https://www.graphpad |
| | | .com/scientific- |
| | | software/prism/ |
| ImageJ | NIH | https://imagej.nih.gov/ |
| | | ij/ |
| FlowJo | BD Biosciences | https://www.flowjo.co |
| | | m/solutions/flowjo/do |
| | | wnloads |