**Supplementary Data**

The prostate weights of the model mice showed stepwise increases following tumor progression, and adenocarcinoma existed in the prostatic tissues of the *Pten*-deficient model mice at more than 10 weeks of age (Supplementary Fig. S1a, b). MDSCs of the model mice were significantly higher than those of the normal mice (p < 0.001) (Supplementary Fig. S1c, d). There were no significant differences in the fractions of B cells, T cells, and CD8/CD4 ratio between the normal and model mice, whereas the numbers of macrophages of the model mice were significantly higher than those of the normal mice (p = 0.001) (Supplementary Fig. S1e). Mast cell counts of the model mice were significantly higher than those of the normal mice (p < 0.001) (Supplementary Fig. S1f, g).

There were no differences in the prostate weights and the glandular structures between the CD-fed and HFD-fed normal mice (Supplementary Fig. S2b-2d). MDSCs of the HFD-fed normal mice tended to be higher than those of the CD-fed normal mice (p = 0.006) (Supplementary Fig. S2e). The M2/M1 macrophage ratio of the HFD-fed normal mice tended to be lower than that of the CD-fed normal mice (p = 0.052) (Supplementary Fig. S2f, g). Mast cell counts of the HFD-fed normal mice were significantly higher than those of the CD-fed normal mice (p = 0.009), whereas there was no significant difference in those between the CD-fed and HFD-fed model mice (Supplementary Fig. S2i, j).

**Supplementary Methods**

**Mouse genotyping.** Genotyping was performed by PCR using tail genomic DNA, with the following primer sequences: *Pten* wild-type allele, forward 5′-GTCACCAGGATGCTTCTGAC-3′, reverse 5′-GTAAATTCAACTGCACTGACCCTG-3′; *Pten* flox allele, forward 5′-GTCACCAGGATGCTTCTGAC-3′, reverse 5′-GAAACGGCCTTAACGACGTAG-3′; and ARR2PB-Cre allele , forward 5′-CTGAAGAATGGGACAGGCATTG-3′, reverse 5′-CATCACTCGTTGCATCGACC-3′. Littermate mice that lacked the Cre transgene served as “normal” controls.

**Histopathology and immunohistochemistry.** Histopathology was examined by hematoxylin-eosin staining and assessed by a pathologist, and immunohistochemical staining was performed on 4-μm-thick sections of formalin-fixed, paraffin-embedded tissue. The slides were deparaffinized by heating to 68°C for 20 min. Antigen retrieval was performed by steamer in citrate buffer (pH 6.0) for 20 min before staining, and endogenous peroxidase activity was quenched with H2O2. A DAKO EnVision™ Kit was used according to the manufacturer’s instructions. SignalStain™ Boost Detection Reagent and the protocols of Cell Signaling were used for phosphorylated signal transducer and activator of transcription 3 (pSTAT3) staining only of the human prostatectomy specimens.

**Primary antibodies for immunohistochemistry.** The following primary antibodies were used: rabbit anti-mouse Ki67 (clone: D3B5, Cell Signaling), rabbit anti-mouse IL6 (ab7737, Abcam), rat anti-mouse F4/80 (clone: MCA497, AbD Serotec), rat anti-mouse CD68 (clone: FA-11, Abcam), rabbit anti-mouse and anti-human pSTAT3 (Tyr705) (clone: D3A7, Cell Signaling), rabbit anti-mouse COX2 (clone: EPR12012, Abcam), rabbit anti-human CD11b (clone: EP1345Y, Abcam), and mouse anti-human CD206 (clone: 685645, R&D). The antibodies were qualified using spleen or bladder cancer (Supplementary Fig. S4). Positive controls for the anti-mouse antibodies were prepared with the allograft tumor of RenCa (mouse renal cancer cell line), the prostate tumor of a *Pten*/*Tp53*-deficient model mouse (<Pb-Cre+;*Pten*(fl/fl);*Tp53*(fl/fl)>) or spleen (Supplementary Fig. S4a-d). Positive controls for the anti-human antibodies were prepared with spleen or bladder cancer specimens (Supplementary Fig. S4e-g).

**Tissue dissociation and single-cell suspension.** Single-cell suspensions were prepared from prostatic tissues. All tissues were minced in sterile tissue culture dishes and subjected to collagenase type I (1.0 mg/mL; Wako) in RPMI digestion for 1 hour at 37°C. Undigested tissues were passed through a 70-μm cell strainer to facilitate dissociation, followed by washes in phosphate-buffered saline (PBS) and subjected to a red blood cell lysis step using ammonium-chloride-potassium lysing buffer (Life Technologies). All cells were re-suspended in PBS plus 10% fetal bovine serum.

**Antibodies for flow cytometry.** The following antibodies were used: CD45-FITC (clone: 30-F11, BD Pharmingen), CD3e-Pacific blue (clone: 500A2, BD Pharmingen), CD4 APC (clone: RM4-5, BD Pharmingen), CD8a PE (clone:53-6.7, BD Pharmingen), CD19 V450 (clone: 1D3, BD Horizon), CD11b APC (clone: M1/70, BD Pharmingen), Ly-6G and Ly-6C PE (clone: RB6-8C5, BD Pharmingen), F4/80 PE (clone: T45-2342, BD Pharmingen), major histocompatibility complex (MHC) class II; BV421 (clone: AF6-120.1, BD Horizon), and CD206 APC (clone: 857615, R&D). The antibodies were qualified by positive controls (mouse spleen) and isotype controls (Fig. 1h, Supplementary Figs. S1c, S2f and S3e).

**RNA preparation.** Total RNA was isolated from prostatic tissues using an RNeasy™ Plus Mini Kit (Qiagen) according to the manufacturer’s instructions. The RNAs were reverse transcribed using a Prime Script™ RT Reagent Kit (Clontech).

**Mast cell count.** Paraffin-embedded sections were deparaffinized with xylene and stained with 0.1% toluidine blue in 1% sodium chloride solution. Staining with toluidine blue permits the identification of mast cells because mast cell granules stain metachromatically, resulting in deep purplish-blue granular cytoplasmic staining. The number of mast cells was counted at a magnification of 100× under light microscopy.

**Primary and secondary antibodies for immunofluorescence staining.** The following antibodies were used: Primary antibody: rabbit anti-mouse IL6 (ab7737, Abcam), rat anti-mouse F4/80 (clone: MCA497, AbD Serotec), and rat anti-mouse CD68 (clone: FA-11, Abcam). Secondary antibodies: Goat anti-rat Alexa Fluor 488-conjugated secondary antibody (Invitrogen) and goat anti-rabbit Alexa Fluor 568-conjugated secondary antibody (Invitrogen)

**Supplementary Table 1 The primers used in quantitative RT-PCR**

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| --- | --- | --- |
| ***Il1b*** | forward | 5′-TCAACCAACAAGTGATATTCTCCA-3′ |
| reverse | 5′-ACCGTTTTTCCATCTTCTTTGG-3′ |
| ***Il6*** | forward | 5′-TCCTCTCTGCAAGAGACTTCC-3′ |
| reverse | 5′-TTGTGAAGTAGGGAAGGCCG-3′ |
| ***Tnf*** | forward | 5′-TAGCCCACGTCGTAGCAAAC-3′ |
| reverse | 5′-GCAGCCTTGTCCCTTGAAGA-3′ |
| ***Il4*** | forward | 5′-CAGCAACGAAGAACACCACAG-3′ |
| reverse | 5′-AAGCCCGAAAGAGTCTCTGC-3′ |
| ***Il13*** | forward | 5′-TGGTATGGAGTGTGGACCTG-3′ |
| reverse | 5′-TTCGATTTTGGTATCGGGGAGG-3′ |
| ***Il10*** | forward | 5′-GGCGCTGTCATCGATTTCTC-3′ |
| reverse | 5′-ATGGCCTTGTAGACACCTTGG-3′ |
| ***Il17a*** | forward | 5′-CCTGGACTCTCCACCGCAA-3′ |
| reverse | 5′-TTCCCTCCGCATTGACACAG-3′ |
| ***Cxcl15*** | forward | 5′-AGGAAGTGATAGCAGTCCCAA-3′ |
| reverse | 5′-CAGAAGCTTCATTGCCGGTG-3′ |
| ***Ptgs2*** | forward | 5′-TTTGCATTCTTTGCCCAGCA-3′ |
| reverse | 5′-GGGATACACCTCTCCACCAA-3′ |
| ***Gapdh*** | forward | 5′-TGTGTCCGTCGTGGATCTGA-3′ |
| reverse | 5′-TTGCTGTTGAAGTCGCAGGAG-3′ |

**Supplementary Figure legends**

**Fig. S1** (**a**) Prostate weights of normal and *Pten*-deficient model mice at every 8 weeks of age. (**b**) Representative images of H&E staining of the prostatic tissues of the model mice at 10, 22, and 38 weeks of age (black bars indicate 100 μm). (**c**) Representative images of MDSCs in the prostatic tissues of normal and model mice at 22 weeks of age after gating of CD45+ cells using flow cytometry (left: isotype). (**d**) The ratio of MDSCs to total viable cells of normal and model mice at 22 weeks of age (n = 12, 8, respectively). (**e**) The ratios of B cells (n = 9, 8, respectively), T cells (n = 10, 7, respectively), and macrophages (n = 10, 8, respectively) to total viable cells and the CD8/CD4 T-cell ratio (n = 10, 7, respectively) of normal and model mice at 22 weeks of age. (**f**) Representative images of toluidine blue staining of the prostatic tissues of normal and model mice at 22 weeks of age (black bars indicate 100 μm, and arrowheads indicate “mast cells”). (**g**) The counts of mast cells in the prostatic tissues of normal and model mice at 22 weeks of age (n = 10, 9, respectively). MDSCs, myeloid-derived suppressor cells; HPF, high-power field, \*\*p<0.01, \*\*\*p<0.001

**Fig. S2** (**a**) Body weights of the model mice at 22 weeks of age (n = 11, 11, 9, respectively). (**b**) Representative gross findings of the prostatic tissues of normal mice at 22 weeks of age (black bars indicate 5 mm). (**c**) Prostate weights of normal mice at 22 weeks of age (n = 15, 13, respectively). (**d**) Representative images of H&E staining of the prostatic tissues of normal mice at 22 weeks of age (black bars indicate 100 μm). (**e**) The ratio of MDSCs to total viable cells of normal mice at 22 weeks of age (n = 12, 13, respectively). (**f**) Representative images of M1 and M2 macrophages in the prostatic tissues of normal mice at 22 weeks of age after gating of macrophages (CD45+, F4/80+ cells) using flow cytometry. (**g**) M2/M1 ratio of normal mice at 22 weeks of age (n = 10, 12, respectively). (**h**) The ratios of B cells (n = 8, 8, 9, respectively), T cells (n = 7, 7, 5, respectively), and macrophages (n = 8, 11, 9, respectively) to total viable cells and the CD8/CD4 T-cell ratio (n = 7, 7, 5, respectively) of the model mice at 22 weeks of age. (**i**) The counts of mast cells in the prostatic tissues of normal mice at 22 weeks of age (n = 10, 4, respectively). (**j**) The counts of mast cells in the prostatic tissues of the model mice at 22 weeks of aged (n = 9, 9, respectively). CD, control diet; HFD, high-fat diet; MDSCs, myeloid-derived suppressor cells; HPF, high-power field, #p<0.1, \*p<0.05, \*\*p<0.01

**Fig. S3** (**a**) Relative mRNA expressions of *Tnf* and *Cxcl15* using RT-PCR in the prostatic tissues of the model mice at 22 weeks of age (n = 9, 8, 9, respectively). (**b**) Relative mRNA expression of *Ptgs2* using RT-PCR in the prostatic tissues of the model mice at 22 weeks of age (n = 9, 8, 9, respectively). (**c**) Representative images of COX2 staining of the prostatic tissues of the model mice at 22 weeks of aged (black bars indicate 100 μm). (**d**) Representative images of MDSCs in the prostatic tissues of the model mice at 22 weeks of age after gating of CD45+ cells using flow cytometry. (**e**) Representative images of M1 and M2 macrophages in the prostatic tissues of the model mice at 22 weeks of age after gating of macrophages (CD45+, F4/80+ cells) using flow cytometry. CD, control diet; HFD, high-fat diet; MDSCs, myeloid-derived suppressor cells; MHC, major histocompatibility complex.

**Fig. S4 (a)** RenCa tumor stained with anti-Ki67 antibody. **(b)** RenCa tumor stained with anti-IL6 antibody. **(c)** Prostate tumor of *Pten*/*Tp53*-deficient model mouse stained with anti-pSTAT3 antibody. **(d)** Mouse spleen stained withanti-COX2 antibody. **(e)** Human spleen stained with anti-CD11b antibody. **(f)** Human spleen stained with anti-CD206 antibody. **(g)** Human bladder cancer stained with anti-pSTAT3 antibody. Black bars indicate 100 μm. RenCa, mouse renal cancer cell line; pSTAT3, phosphorylated signal transducer and activator of transcription 3.