Supplementary Methods

Antibodies and other reagents

The Abs for immunofluorescence: mouse anti-human IL-22R1, and rat anti-mouse IL-22R1 from R&D Systems; rat anti-mouse CD11b, rat anti-mouse Ly6C from Biolegend; goat anti-mouse-TRITC, goat anti-rat-TRITC, goat anti-rat-FITC from Zhongshan Biotechnology. The Abs for flow cytometry: for human, anti-CD3-APC-H7 from BD Pharmingen; anti-CD4-PE, anti-IL-22-Alexa Fluor 647, anti-IFN-γ-APC, anti-CD14-PerCP-Cy5.5, and anti-CXCR2-PerCP-eFluor 710 from eBioscience; anti-CD45-PE-Cy7, anti-HLA-DR-Alexa Fluor 647, anti-HLA-DR-FITC, and anti-CD14-PE from Biolegend; anti-IL-22R1-APC from R&D Systems; for mouse, anti-CD3-FITC, anti-CD4-APC, anti-IL-22-PE, anti-IFN-γ-PE from eBioscience, anti-CD45-PE-Cy7, anti-CD11b-PerCP-Cy5.5, anti-Gr1-FITC, anti-CXCR2-Alexa Fluor 647, anti-Ly6G-APC-Cy7, anti-Ly6C-PE, anti-lineage panel-biotin, streptavidin-APC-Cy7, anti-NKp46-PE, and anti-IL-7Rα-FITC from Biolegend. The Abs for neutralizing and blocking were as follows: anti-human/mouse IL-22, anti-mouse IL-17A, anti-mouse IL-17F, and anti-mouse IFN-γ from eBioscience; anti-mouse CXCR2 and anti-mouse CXCL2 from R&D Systems. The Abs for Western blot: anti-human IL-22R1 and anti-mouse IL-22R1 from R&D Systems; anti-human STAT3 from Santa Cruz; anti-human p-STAT3 (Y705) from Cell signaling technology; anti-human S100A8 and anti-human S100A9 from Abcom. Purified anti-CD3 and anti-CD28 Abs were from Biolegend. ELISA kits for human IL-22, mouse IL-22, and mouse CXCL2 were from R&D Systems; ELISA kits for human S100A8, mouse S100A8, human S100A9, mouse S100A9, and human CXCL2 were from Uscn Life Science; ELISA kit for human IFN-γ was from eBioscience. Collagenase IV, DNase I, DMSO, PMA, ionomycin, and gentamycin were from Sigma-Aldrich. The potent and selective nonpeptide CXCR2 antagonist SB225002 (*N*-(2-hydroxy-4-nitrophenyl)-*N*′-(2-bromophenyl)urea) was from R&D Systems. The potent STAT3 inhibitor FLLL32 was from MedKoo Biosciences. CFSE was from eBioscience. Protein Extraction Reagent was from Pierce. All recombinant cytokines and chemokines were from PeproTech except recombinant murine IL-22 that was from eBioscience.

Generation of BM chimera mice

The following BM chimeric mice were prepared: male WT BM→female IL-23 KO mice, male IL-23 KO BM→female IL-23 KO mice, male WT BM→female WT mice, and male IL-23 KO BM→female WT mice; or male WT BM→female IL-22 KO mice, male IL-22 KO BM→female IL-22 KO mice, male WT BM→female WT mice, and male IL-22 KO BM→female WT mice. BM cells were collected from the femurs and tibia of donor mice by aspiration and flushing, and were suspended in PBS at the concentration of 5×10^7/ml. The BM in recipient mice was ablated with lethal irradiation (8 Gy). Then, the animals received intravenously 5×10^6 BM cells from donor mice in a volume of 300 μl sterile PBS under the anaesthesia. Thereafter, the transplanted BM was allowed to regenerate for 4-6 weeks before subsequent experimental procedures were performed. To verify successful engraftment and reconstitution of the BM in the transplanted mice, genomic DNA was isolated from tail tissues of each chimera mouse 4 weeks after BM transplantation. Quantitative PCR was performed to detect the *Sry* gene present in the Y chromosome (primers seen in Supplementary Table 3) and mouse β2-microglobulin (β2-M) gene as an internal control. The chimeric rates were calculated on the assumption that the ratio of the Sry to β2-M gene was 100% in male mice. We confirmed that the chimeric rates were consistently higher than 80%. After BM reconstitution was confirmed, mice were infected with bacteria as described above.

Isolation of single cells from tissues and dendritic cell (DCs) preparation

Fresh tissues were washed three times with Hank's solution containing 1% fetal calf serum (FCS) (Gibco) before being cut into small pieces. The specimen were then collected in RPMI 1640 containing 1mg/ml collagenase IV and 10 mg/ml DNase I, and mechanically dissociated by using the gentle MACS Dissociator (Miltenyi Biotec). Dissociated cell suspensions were further incubated 0.5-1 h at 37°C under continuous rotation. The cell suspensions were then filtered through a 70-μm cell strainer (BD Labware). Peripheral blood mononuclear cells (PBMCs) from healthy donors and gastric cancer patients were isolated by density gradient centrifugation using Ficoll-Paque Plus (GE Healthcare). Fresh human peripheral blood monocytes were selected using anti-CD14 magnetic beads (StemCell Technologies). To generate human DCs, monocytes were cultured (2×10^5 cells/well in 24-well culture plates) for 7 days in RPMI 1640 medium supplemented with

10% FCS (R-10) supplemented with recombinant human IL-4 (500 U/ml) and GM-CFS (100 ng/ml). The medium was changed every second day by removing half the medium and adding freshly made medium supplemented with full concentrations of cytokines. Morphologic analysis and high expression of CD1a and CD11c were parameters for quality and purity of DC preparations. To generate mouse bone marrow-derived DCs (BMDCs), BM cells were cultured in R-10 supplemented with 20 ng/ml recombinant murine GM-CSF (20 ng/ml) and IL-4 (10 ng/ml) for 7 days. DCs were purified using anti-CD11c magnetic beads (Miltenyi Biotec).

Immunofluorescence

Paraformaldehyde-fixed cryostat sections of tissues were washed in PBS and blocked for 30 min with 20% goat serum in PBS and stained for IL-22R1, and CD11b and/or Ly6C. Slides were examined with a confocal fluorescence microscope (LSM 510 META, Zeiss).

Real-time PCR

DNA of the biopsy specimens were extracted with QIAamp DNA Mini Kit (QIAGEN) and RNA of biopsy specimens and cultured cells were extracted with TRIzol reagent (Invitrogen). The RNA samples were reversed transcribed to cDNA with PrimeScript™ RT reagent Kit (TaKaRa). Real-time PCR was performed on the IQ5 (Bio-Rad) with the Real-time PCR Master Mix (Toyobo) according to the manufacturer's specifications. Expression of 16S rDNA, *cagA*, IL-23p19, IL-22, IL-22R1, CXCL2, S100A8, and S100A9 was measured using the TaqMan and/or SYBR green method with primers (Supplementary Table 3). For mice, mouse β2-microglobulin served as the normalizer, and uninfected stomach served as the calibrator. For human, human β-actin served as the normalizer, and unstimulated cells served as the calibrator. The relative gene expression was expressed as fold change calculated by the ΔΔCt method.

Flow cytometry

Cells were stained for Abs of surface markers or control isotype Abs. For intracellular molecules measurements, the cells were stimulated for 5 h with PMA (50 ng/ml) plus ionomycin (1 μg/ml) in the presence of Golgistop (BD Pharmingen). Intracellular cytokine staining was performed after

fixation and permeabilization, using Perm/Wash solution (BD Pharmingen). Then, the cells were analyzed by multicolour flow cytometry with FACSCanto II (BD Biosciences). Data were analyzed with Flowjo software (TreeStar) or FACSDiva software (BD Biosciences).

ELISA

Human and mouse gastric tissues from specimens were collected, homogenized in 1 ml sterile Protein Extraction Reagent, and centrifuged. Tissue supernatants were collected for ELISA. Concentrations of IL-22 in the tissue supernatants; concentrations of IL-23 in the DC culture supernatants; concentrations of CXCL2 in the gastric epithelial cell culture supernatants or tissue supernatants; concentrations of S100A8 and S100A9 in the MDSC culture supernatants or tissue supernatants; and concentrations of IFN-γ in the T cell culture system supernatants were determined using ELISA kits according to the manufacturer's instructions.

Western blot analysis

Western blot assays were performed on 10%-15% SDS-PAGE gels using equivalent amounts of cell or tissue lysate proteins of samples. Five percent skimmed milk or three percent BSA was used for blocking the PDF membranes. Mouse IL-22R1 was detected with rat anti-IL22R1 Abs; human IL-22R1, S100A8, S100A9, STAT3, and p-STAT3 were detected with mouse anti-IL-22R1 Abs, rabbit anti-S100A8 Abs, rabbit anti-S100A9 Abs, mouse anti-STAT3 Abs, and rabbit anti-p-STAT3 Abs, respectively. This was followed by incubation with HRP-conjugated secondary Abs (Zhongshan Biotechnology). Bound proteins were visualized by using SuperSignal® West Dura Extended Duration Substrate kit (Thermo).

Microarray experiments

Gene expression profiles of MDSCs were analyzed with the human Exon 1.0 ST GeneChip (Affymetrix), strictly following the manufacturer's protocol. Microarray experiments were performed at the Genminix Informatics (China) with the microarray service certified by Affymetrix.