Supplementary Methods

Treatment

Cre recombinase was induced by oral administration of tamoxifen (Sigma; 3mg/0.2ml unless otherwise indicated). All experiments were repeated at least three times with three biological replicates. For all experiments gender-matched mice in C57BL/6 background at the age of 6-9 weeks were used. *Helicobacter* infection was performed by oral gavage of *Helicobacter felis* in 0.2mL trypticase broth three times per week, achieving a total dose of 100 million colony-forming units (CFU)/mouse. Diphtheria toxin (DT, EMD Millipore) was applied i.p. at a dose of 40µg/Kg at the indicated timepoints. CD90.2 depletion was performed by application of 200µg anti-CD90.2 (BioXCell) twice a week during the healing period.

Acetic ulcer induction

The acetic acid ulcer was applied to the serosal surface of the gastric corpus as previously described [1]. For this procedure a median laparotomy was performed under general inhalative anesthesia using Isofluoran, and the gastric corpus was identified. After luxation of the stomach outside the abdominal cavity. 100% acetic acid was applied to the outer surface of the gastric corpus using a capillary tube for 45 seconds. After removal of the capillary tube the acetic acid was wiped off using a sterile cotton tip. The gastric corpus was repositioned, and the peritoneum was closed using a 5-0 absorbable running suture. The skin was closed using single 5-0 nonabsorbable sutures. Suture material was removed after 7-10 days. For analysis the animals were euthanized, and the median laparotomy was re-opened. Intraabdominal adhesions were dissected and the stomach

was removed and immediately transferred into cold PBS. Adjacent organs were removed and the stomach was opened along the greater curvature using microdissection scissors. Macroscopic imaging was performed, and tissue was collected for the corresponding experiments.

Quantification of partially *traced glands and macroscopic ulcer imaging*

For quantification of partially traced glands complete slides were examined blindly and the number of partially traced glands per sections was assessed. Definition of partially traced glands vs. not partially traced glands is provided in Figure S2B. To measure macroscopic ulcer size the stomach was opened along the greater curvature and ulcer area was measured using ImageJ software.

Immunofluorescence

Tissue was fixed in 4% paraformaldehyde for 4h and 30% sucrose for 24h. After embedding, 7µm sections were washed with 0.1% Tween 20 in PBS and blocked with a 5% FBS/2% BSA solution in PBs for 1h. Sections were incubated with the indicated primary antibodies overnight at 4°. Fluorescence-conjugated antibodies were added as indicated and cells were mounted with DAPI containing mounting medium (Vector).

Immunhistochemistry

Tissue was fixed in 10% Formalin for 24h and embedded in paraffin with standard protocols. After embedding, 7µm sections were deparaffinized and heat-mediated antigen retrieval was performed. Endogenous peroxidase was blocked using hydrogen peroxide

and slides were blocked with 10% serum. Sections were incubated with the indicated primary antibody overnight at 4°. Secondary antibody was added at the indicated concentration and signal was detected using ABC vectastain and DAB. Slides were then rehydrated and mounted using permount mounting medium. Steiner-Silver staining was performing using Steiner Microorganism staining kit (Abcam) following the manufacturer's instruction.

Antibodies:

The following antibodies were used for this study. Ki-67 (abcam; 1:200), gastric intrinsic factor (kind gift from Dr. Alpers, 1:2000), DCLK-1 (abcam; 1:500), GS-II lectin (Invitrogen; 1:200), eGFP (abcam 1:500), RFP (Rockland, 1:500), HK-ATPase (Santa Cruz, 1:200), Frizzled5 (Sigma, 1:400), CD45 (Novus Biologicals, 1:100).

RNA Scope

RNA Scope experiments were performed by the Human Immune Monitoring Core (HIMC) at Columbia University using a commercially available Wnt5a probe (Advanced Cell Diagnostics, 316791)

RT-PCR

Tissue was homogenized and RNA was extracted by using either Nucleo spin. (Macherey-Nagel) or the RNA plus micro kit (Qiagen)cDNA was synthetized using a cDNA Superscript amplification system (Invitrogen). RT-PCR primers used are listed in supplementary; CT values were expressed relative to ß-actin or Gapdh as indicated. All samples were at least analyzed in duplicates. ΔΔ*CT* method was used to compare the individual values.

Flow cytometry

Tissue preparation was performed depending on the population of interest. For isolation of stromal cells, the gastric corpus was dissected from the antrum and chopped into small pieces and washed in HBSS (Gibco). Tissue was digested using Collagenase Type IV (Worthington) and Dispase (Gibco) followed by pipetting of the pellet. Digestion was stopped by adding 100% FBS. Cells were washed, centrifuged, filtered through a 40μm cell strainer (Fisher Science) and resuspended in PBS containing 2% FBS.

For isolation of epithelial cells, cells were dissected as described and washed in PBS followed by incubation with 10mM EDTA (Invitrogen). After this step, cells were pipetted up and down followed by filtration through a 100μm cell strainer (Fisher Science). Collected cells were washed, centrifuged, and incubated in TrypLE^{TM} Express Enzyme mix (Fisher Scientific). Digestion was stopped by adding 100% FBS and cells were washed and resuspended in PBS containing 2% FBS.

Live/dead staining was achieved by addition of DAPI (BD Pharmingen) right before data acquisition/sorting. Data was acquired on either a BD Fortessa Flow Cytometer or using a FACS Aria III. FACS Diva and FCS Software (https://www.denovosoftware.com) were used for analysis of the data.

Statistical analysis

The differences between the means were compared using either the Student's t-test or the Wilcoxon test. p values < 0.05 were considered to indicate statistical significance. Graphical measurements were acquired using ImageJ software (https://imagej.nih.gov/ij) Statistical analysis was performed by Graphpad Prism 8 software.

Primers used for RT-PCR (in alphabetical order)

Gene	Forward 5'-3'	Reverse 3'-5'
ß-actin	*TAGACTTCGAGCAGGAGATGG*	*CAGGATTCCATACCCAAGAAGG*
Dclk1	*GGACTTTCCATCTCCGTATTGG*	*CTGGGAGACCATCATCATTAACC*
Fzd5	*GCTTGTCGTTAAACTTTCCCA*	*GCACTCAGTTCCACACCA*
Gapdh	*CGTCCCGTAGACAAAATGGT*	*TCAATGAAGGGGTCGTTGAT*
GIF	*GAAAAGTGGATCTGTGCTACTTGCT*	*AGACAATAAGGCCCCAGGATG*
HKATPase	*CCCAGCTTCGGCTTCGA*	*TGGAGACTGAAGGTGCCATTG*
Lgr5	*CAGCCAGCTACCAAATAGGTGCTC*	*GACGCTGGGTTATTTCAAGTTCAA*
Mist1	*TTAATAAGGAGGGTGAGTGGT*	*ATTCTAAAGGTGGGTGTGGG*
Ror1	*TCAATGCATACAAGCCCAAG*	*TTCTTCCATGAAACGCACAG*
Ror2	*TCATCAGCCAGCACAAACA*	*GTGGCCTTTGTAGACCTTGC*
Sox9	*AGGAAGCTGGCAGACCAGTA*	*TCCACGAAGGGTCTCTTCTC*
Wnt1	*ATGAACCTTCACAACAACGAG*	*GGTTGCTGCCTCGGTTG*
Wnt2	*CTGGCTCTGGCTCCCTCTG*	*GGAACTGGTGTTGGCACTCTG*
Wnt2b	*CGTTCGTCTATGCTATCTCGTCAG*	*ACACCGTAATGGATGTTGTCACTAC*
Wnt3	*CAAGCACAACAATGAAGCAGGC*	*TCGGGACTCACGGTGTTTCTC*
Wnt3a	*CACCACCGTCAGCAACAGCC*	*AGGAGCGTGTCACTGCGAAAG*
Wnt4	*GAGAAGTGTGGCTGTGACCGG*	*ATGTTGTCCGAGCATCCTGACC*
Wnt5a	*CTCCTTCGCCCAGGTTGTTATAG*	*TGTCTTCGCACCTTCTCCAATG*
Wnt 5b	*ATGCCCGAGAGCGTGAGAAG*	*ACATTTGCAGGCGACATCAGC*
Wnt 6	*TGCCCGAGGCGCAAGACTG*	*ATTGCAAACACGAAAGCTGTCTCTC*
Wnt7a	*CTTCATGTTCTCCTCCAGGATCTTC*	*CGACTGTGGCTGCGACAAG*
Wnt7b	*TCTCTGCTTTGGCGTCCTCTAC*	*GCCAGGCCAGGAATCTTGTTG*
Wnt8a	*ACGCTGGAATTGTCCTGAGCATG*	*GATGGCAGCAGAGCGGATGG*
Wnt8b	*AGTCATCACAGCCACAGTTGTC*	*TTGGGACCGTTGGAATTGCC*
Wnt9a	*GCAGCAAGTTTGTCAAGGAGTTCC*	*GCAGGAGCCAGACACACCATG*
Wnt9b	*AAGTACAGCACCAAGTTCCTCAGC*	*GAACAGCACAGGAGCCTGACAC*
Wnt10a	*CCTGTTCTTCCTACTGCTGCTGG*	*CGATCTGGATGCCCTGGATAGC*
Wnt10b	*TTCTCTCGGGATTTCTTGGATTC*	*TGCACTTCCGCTTCAGGTTTTC*
Wnt 11	*CTGAATCAGACGCAACACTGTAAAC*	*CTCTCTCCAGGTCAAGCAGGTAG*
Wnt 16	*AGTAGCGGCACCAAGGAGAC*	*GAAACTTTCTGCTGAACCACATGC*

Supplementary References

1. Okabe, S. and K. Amagase, *An overview of acetic acid ulcer models--the history and state of the art of peptic ulcer research.* Biol Pharm Bull, 2005. **28**(8): p. 1321-41.