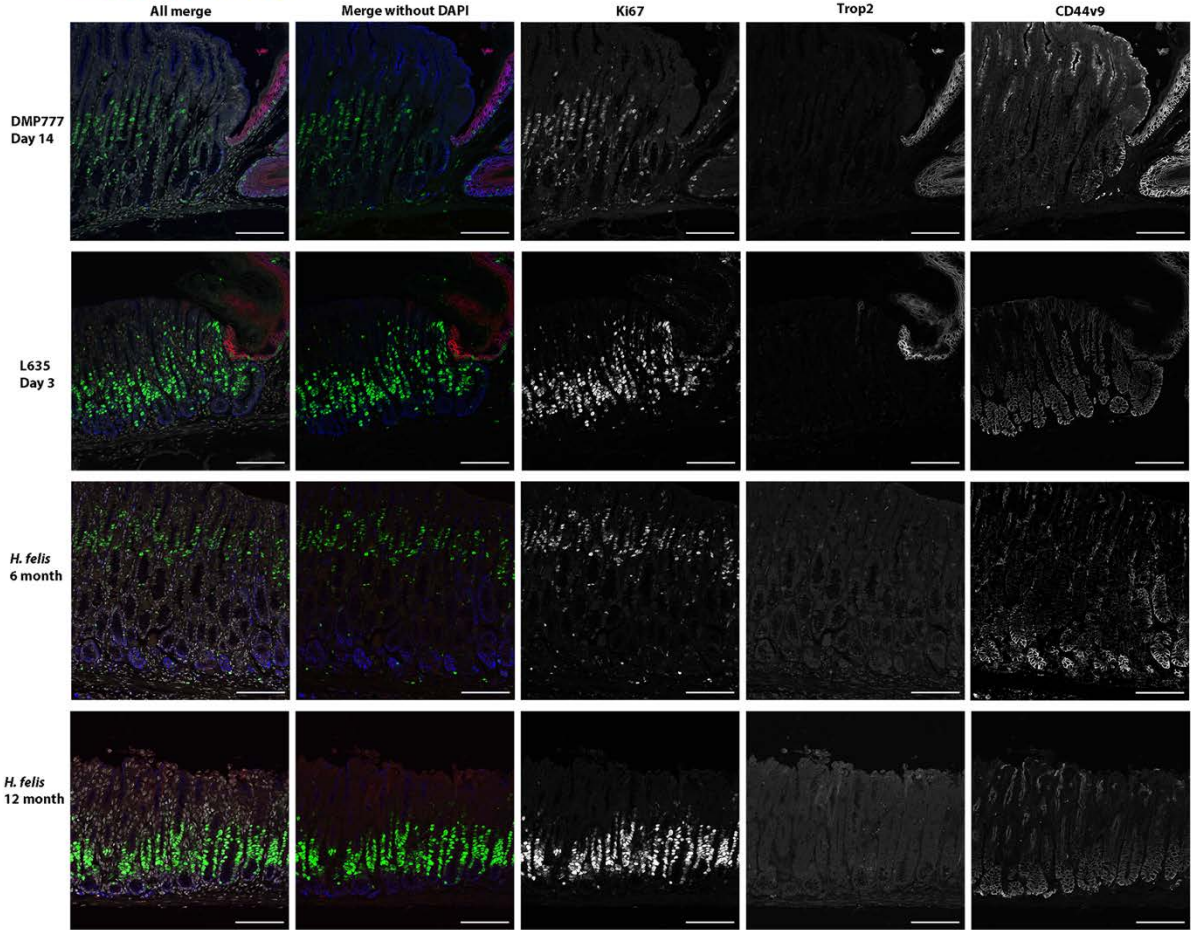
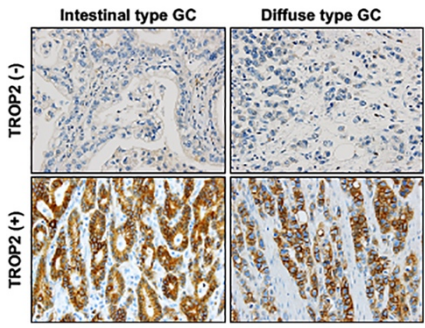


Supplementary Figure 1

Ki67/Trop2/CD44v9

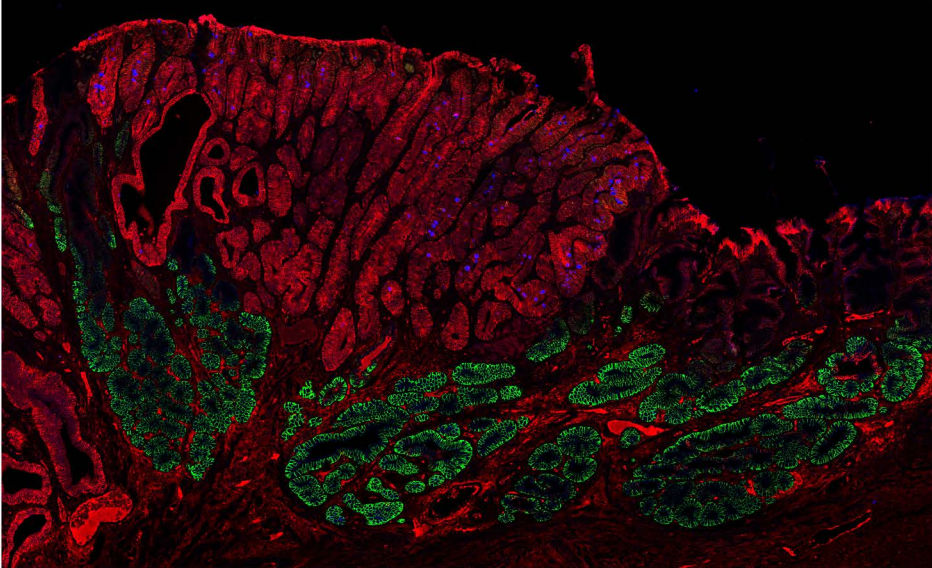
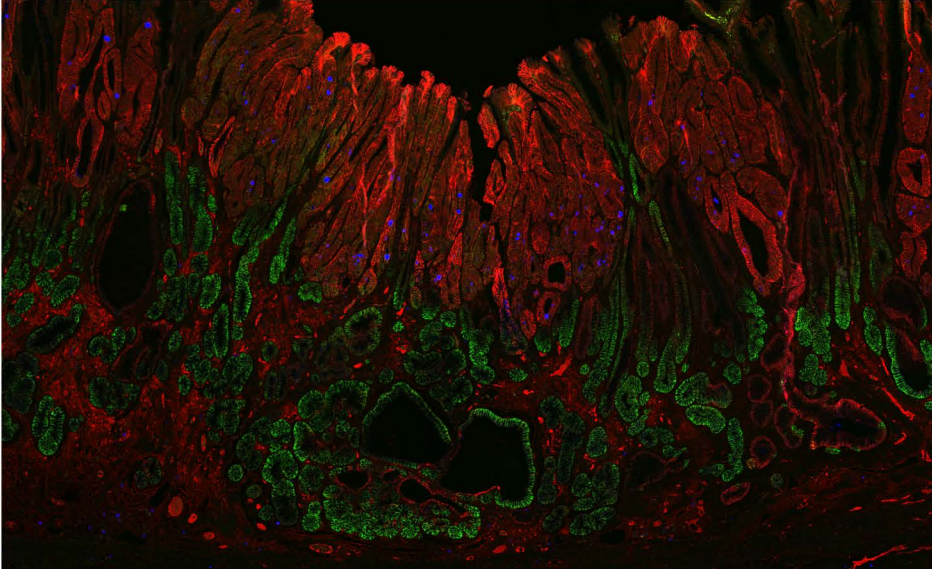


Supplementary Figure 2



Supplementary Figure 3

TROP2/CD44v9/TFF3



**Supplemental Figure 1: Trop2 is not observed in SPEM induced by acute oxyntic atrophy or *H. felis* infection.** Sections of mouse stomach from mice (n=3 for all groups) treated with 14 days of DMP-777 or 3 days of L635 to induce acute SPEM or mice infected with *H. felis* for 6 or 12 months were stained for CD44v9 (blue), Ki67 (green) and Trop2 (red) along with nuclear staining with DAPI (greyscale). Squamous forestomach stained positively for Trop2 and CD44v9 as an internal control in DMP-777 and L635 mice. SPEM did not stain for Trop2 in any of the models. Scale bar = 100  $\mu$ m.

**Supplemental Figure 2: Trop2 immunostaining in gastric cancers.** Examples of negative and positive TROP2 immunostaining in intestinal type and diffuse gastric cancers.

**Supplemental Figure 3. Trop2 staining in dysplastic lesions from Canadian patients.** Representative immunostaining of intramucosal dysplasia in two of four samples from non-Asian Canadian gastric cancer patients. Sections were stained for TROP2 (red), CD44v9 (green) and TFF3 (blue). Note the separation of CD44v9 staining lineages (SPEM) from Trop2-stained dysplastic cells. Bar = 100  $\mu$ m.

Supplemental Table 1: Association between the TROP2 expression and the clinicopathological characteristics

	Total (%)	TROP2		<i>p</i> -value <sup>#</sup>
		Low (%)	High (%)	
Patients	740 (100)	459 (62)	282 (38)	
Age				
<65	482 (65)	313 (65)	169 (35)	0.02
≥65	258 (34)	145 (56)	113 (44)	
Gender (n = 739)				
Female	233 (32)	158 (68)	75 (32)	0.028
Male	506 (68)	300 (59)	206 (41)	
Location (n = 732)				
Upper	101 (14)	57 (56)	44 (34)	0.028
Middle	284 (39)	195 (69)	89 (31)	
Lower	337 (46)	195 (58)	142 (42)	
Whole	10 (1)	6 (60)	4 (40)	
Lauren				
Intestinal	289 (39)	175 (61)	114 (39)	0.241
Diffuse	334 (45)	216 (65)	118 (35)	
Mixed	111 (15)	62 (56)	49 (44)	
Undetermined	6 (1)	5 (67)	1 (33)	
Histological				
Papillary	15 (2)	6 (40)	9 (60)	0.000
Tubular				
Well	134 (18)	61 (45)	73 (55)	
Moderate	296 (40)	185 (63)	111 (37)	
Poor	182 (25)	123 (68)	59 (32)	
Signet ring cell	91 (12)	70 (77)	21 (23)	
Mucinous	15 (2)	14 (93)	1 (7)	
Others	7 (1)	4 (57)	3 (43)	
Lymphatic invasion				
Negative	262 (35)	173 (66)	89 (34)	0.086
Positive	478 (65)	285 (60)	193 (40)	
Venous invasion				
Negative	612 (83)	382 (63)	230 (37)	0.519
Positive	128 (17)	76 (60)	52 (41)	
Perineural invasion				
Negative	323 (44)	201 (62)	122 (37)	0.868
Positive	417 (56)	257 (62)	160 (38)	
Tumor stage				
I	186 (25)	117 (63)	69 (37)	0.957
II	208 (28)	129 (62)	79 (38)	
III	270 (36)	167 (62)	103 (38)	
IV	76 (10)	45 (59)	31 (40)	
CDX2 (n = 679)				

Negative	546 (80)	338 (62)	208 (38)	0.831
Positive	133 (20)	81 (61)	52 (39)	
<hr/>				
#Pearson Chi-square				

Supplemental Table 2: List of all resource information

<b>Primary</b>	<b>Company, Location</b>	<b>Product Number</b>
Mouse Trop2 (1:200 for immunostaining, 1:2000 for western blot)	R&D Systems, Minneapolis, MN	AF1122
Human Trop2 (1:200)	R&D Systems, Minneapolis, MN	AF650
Mouse CD44v9 (1:25,000)	Cosmo Bio, Carlsbad, CA	CAC-LKG-M002
Human CD44v9 (1:10,000)	Cosmo Bio, Carlsbad, CA	CAC-LKG-M001
TFF3 (1:1000)	Atlas Antibodies, Bromma, Sweden	HPA035464
Muc2 (1:300)	Santa Cruz Biotechnology, Dallas, TX	sc-15334
Ki67 (1:100)	Abcam, Cambridge, MA	ab16667
PCNA (1:2000)	Cell Signaling Technology, Danvers, MA	2586S
$\beta$ -Actin (1:5000)	Sigma-Aldrich, St. Louis, MO	A5316
Villin (1:300)	Cell Signaling Technology	2369
<b>Secondary</b>		
Donkey anti-rabbit Cy2 (1:500)	Jackson Laboratories	
Donkey anti-goat Cy3 (1:500)	Jackson Laboratories	
Donkey anti-rat Cy5 (1:500)	Jackson Laboratories	
Donkey anti-mouse Alexa 750 (1:500)	Abcam, Cambridge, MA	ab175738
DAPI (1:3000, 1:5000)		
Hoechst 33342 Solution (1:1000, 1:5000)	Thermo Scientific, Waltham, MA	62249
IRDye 800CW donkey anti-goat (1:10000)	LI-COR Biosciences	926-32214
IRDye 680LT donkey anti-mouse (1:10000)	LI-COR Biosciences	926-68022
<b>Immunofluorescence Staining Resources</b>		
Histoclear	National Diagnostics, Atlanta, GA	
Dako Target Retrieval Solution 10x	Dako North America, Inc, Carpinteria, CA	S1699
Dako Protein Block Serum-Free solution	Dako North America, Inc, Carpinteria, CA	X0909

Dako Antibody Diluent with Background Reducing Components	Dako North America, Inc, Carpinteria, CA	S3022
Dako Antibody Diluent	Dako North America, Inc, Carpinteria, CA	S0809
Prolong Gold		
N-acetylcysteine		
<b>Culture media, harvest materials, other reagents or kit</b>		
Intesticult Organoid Growth Medium (mouse)	StemCell Technologies, Cambridge, MA	06005
ECM Gel	Sigma-Aldrich, St. Louis, MO	E1270
Penicillin/Streptomycin Solution	Corning, Corning, NY	30-002-CI
MycoZap Plus PR	Lonza, Basel, Switzerland	VZA-2021
4% Paraformaldehyde (PFA)	Affymetrix, Santa Clara, CA	19943
Y-27632 (ROCK inhibitor)	StemCell Technologies, Cambridge, MA	72304
DMEM/F12	Thermo Fisher, Waltham, MA	10-092-CV
Fetal Bovine Serum (FBS)		
HistoGel	Thermo Scientific, Waltham, MA	HG-4000-012
TrypLE	Thermo Fisher, Waltham, MA	12604013
Polybrene		
QIAprep Spin miniprep Kit	Qiagen, Hilden, Germany	27106
Lenti-X	Takara Bio Inc., Shiga, Japan	631232
<b>Experimental Models and Cell lines</b>		
Mist1-Kras mice		n/a
Meta4 organoids		n/a
Meta4 Trop2 knock down organoids		n/a



<b>Imaging Equipment</b>		
Nikon A1R		n/a
Versa		n/a
Cytell		n/a
EVOS	Thermo Fisher, Waltham, MA	n/a
JuLI™ Stage	Nanoentek	n/a

Supplemental Table 3: Resource information on TACSTD2 Mission shRNA bacterial glycerol stock (Sigma-Aldrich, St. Louis, MO, SHCLNG-NM\_020047, species: mouse)

Lab viral name	Product number	Region	Sequence
Virus 1	TRCN00001127 <u>00</u>	3UTR	CCGGGCTAGATAGCTTGGTTAAGAACTCGAGTT CTTAACCAAGCTATCTAGCTTTTTG
Virus 2	TRCN00001127 <u>01</u>	CDS	CCGGGCTCTTCCAAGAACGCTACAACCTCGAGTT GTAGCGTTCTTGAAGAGCTTTTTG
Virus 3	TRCN00001127 <u>04</u>	CDS	CCGGCCACCACATCCTCATTGAGTTCTCGAGAA CTCAATGAGGATGTGGTGGTTTTG