SUPPLEMENTAL METHODS

Strain recovery from mouse stomachs for culture and *H. pylori*-specific PCR. *H. pylori* PMSS1 was routinely grown on Columbia blood agar (CBA) plates at 37°C in a microaerobic atmosphere prior to mouse infection. Following sacrifice, for each mouse (including controls), a longitudinal quarter of the stomach was collected, weighed and grinded in 250 µl PBS. Different dilutions of the suspension were plated on CBA (with added amphotericin B, vancomycin. and polymyxin B). CBA-plates were incubated for up to 17 days at 37°C under microaerobic atmosphere and *H. pylori* CFU (colony forming units) were determined. 100 µl of the grinded stomach suspension was used for chromosomal DNA isolation and *glmM* PCR was performed to verify *H. pylori* presence (Jenks et al., 1998; Lu et al., 1999). The *glmM* PCR also was applied for *H. pylori* detection in fecal samples; experiments involving spiking of fecal pellets with *H. pylori* revealed a threshold for detection of $5x10^5$ *H. pylori* per fecal pellet (or 10^4 *H. pylori*/mg of stool).

Measurement of *H. pylori*-specific antibodies and CagA antibodies in mice by Enyzme-linked immunosorbent assay. ELISA plates were coated with whole cell *H. pylori* PMSS1 protein, as described (Pohl et al., 2012). Plates were coated overnight at 4°C and then blocked for 2 h with 1x PBS containing 0.05% Tween-20, 0.1 mg/ml thimerosal, and 0.1% gelatin. Serum samples were diluted 1:600 and plates were incubated for 1 h at 37°C. All washing steps were performed with 1x PBS containing 0.05% Tween-20 and 0.1 mg/ml thimerosal. Goat anti-mouse IgG (Fc) or IgM conjugated to horseradish peroxidase (Life Technologies) was used as second antibody for detection of responses. An ELISA to detect anti-CagA IgG in plasma of the mice was performed using a purified recombinant CagA antigen, as described (Blaser et al., 1995). The assay was modified with the use of the goat anti-mouse IgG conjugate, and mouse plasma was diluted 1:100. For the whole cell and the CagA ELISAs, all samples were run in duplicate and optical density ratios (ODRs)

were determined by dividing the OD-value of the sample by the OD-value of a positive control for *H. pylori* or CagA, which were included on each ELISA plate as reference specimens; three to six mice were bled for each time point throughout the experiment.

Histopathology. For each mouse, stomach tissue was collected at each sacrifice time point, fixed in neutral-buffered formalin, routinely processed and stained with hemotoxylin and eosin (H&E). Histopathology of stomachs was scored according to the Sidney Classification (Mainguet et al., 1993) for chronic and active inflammation in corpus and antrum. For overall analysis, the sum of active and chronic inflammatory scores for corpus and antrum was compared and expressed as inflammation score.

Nanostring. RNA was isolated using the QIAshredder and the miRNeasy Mini Kit (Qiagen, Redwood City CA). Expression levels of 547 transcripts related to immunity were measured by the nCounter GX Mouse Immunology Panel (NanoString, Seattle WA) at 1, 3, and 6 month after challenge for Cohort 1 mice. Gene counts were normalized per manufacturers instructions, and expression levels were visualized on a heat map with hierarchical clustering of samples using the R statistical framework. Significant differences were detected by t-test with p-values adjusted by false-discovery rate; changes in canonical pathways and biological functions were predicted using Ingenuity Pathway Analysis (Qiagen).

Hormone measurements. Blood cells and serum were separated through centrifugation (3000 g for 10 min at RT) and the serum frozen at -80°C. Ghrelin, insulin, leptin, and peptide YY were measured using the Millipore Mouse Gut Hormone Panel (Millipore Corp., St. Charles MO) using a Luminex 200 (Millipore) analyzer.

DNA library preparation, sequencing and sequence analysis. After DNA isolation and 16s rRNA gene amplification, DNA concentrations of each amplicon were measured using Quant-iT PicoGreen dsDNA regent (Invitrogen), and pooled at equal

DNA quantities. After samples were pooled in 5 groups of 96 samples each, excess primers were removed with the Qiaquick PCR purification kit (Qiagen). DNA concentration in these sub-pools were quantified with the Qubit high sensitivity dsDNA Assay (Invitrogen), and combined at equal concentration for a pool with unique molecular barcodes. The amplicons were sequenced on the Illumina MiSeq I platform, with 50% PhiX spiked into the amplicon pool to improve the signal from a low diversity library. The sequencing was carried out in three separate reads, (i) 151 base pair forward read, (ii) 12 base pair barcode read, and (iii) 151 base pair reverse read. Only reads that passed the Illumina quality filter were used for downstream analysis. Paired end reads were joined with EA-utils; only reads that were a perfect match were kept. QIIME (Caporaso et al., 2010) was used to demultiplex and quality-filter the samples. Reads were truncated at a stretch of 4 or more low quality bases (phred q score < 20), and only reads ≥ 75% of the original length were retained; 1,972,991 sequences were retained after demultiplexing and quality filtering.

Calculation of alpha-diversity (richness, Shannon-index), beta-diversity (UniFrac distances), and generation of relative abundance and PCoA plots were performed using QIIME (Caporaso et al., 2010) and plots were generated by KiNG Kinemage Next Generation version 2.16. Alpha- and beta-diversity were analyzed with even sampling (500, 1,000 and for stomach 3,000) depth by accepting a loss of 4 samples or 25 samples, respectively. Differences of microbial compositions were measured by unweighted UniFrac distances and significance testing was performed using the ADONIS test, with 999 permutations. P-values ≤ 0.05 were considered significant. Linear discrimination analysis effect size (LEfSE) (Segata et al., 2011) was used via the Galaxy Browser (Blankenberg et al., 2010; Giardine et al., 2005; Goecks et al., 2010) to detect significant changes in relative abundance of microbial taxa.

age at infection

4-weeks

+ BB

+ Hp PMSS1

Control (C) (n=22)

Infected (I) (n=22)

Cohort 1

6-weeks

+ BB

+ Hp PMSS1

Control (C) (n=18)

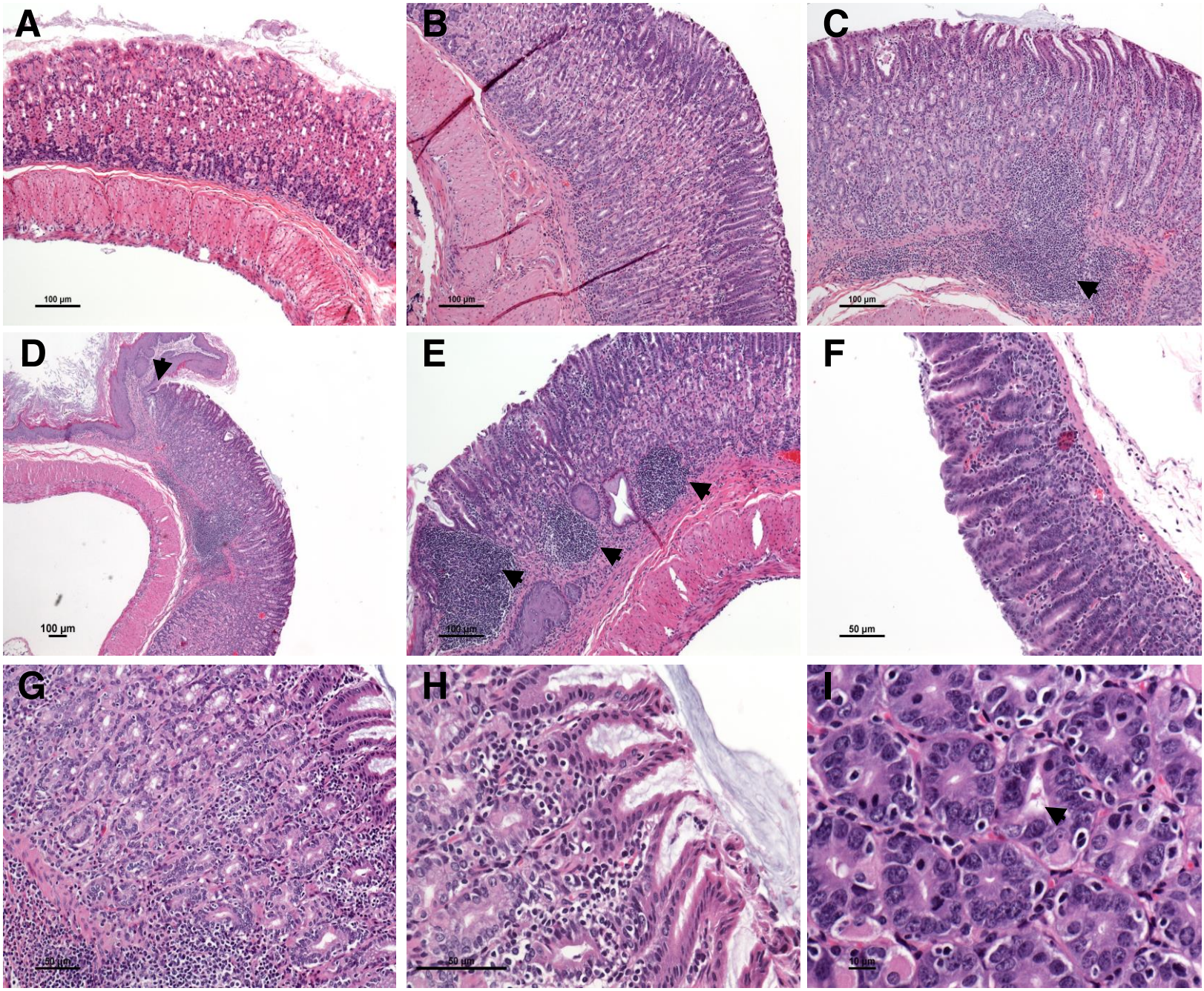
Infected (I) (n=24)

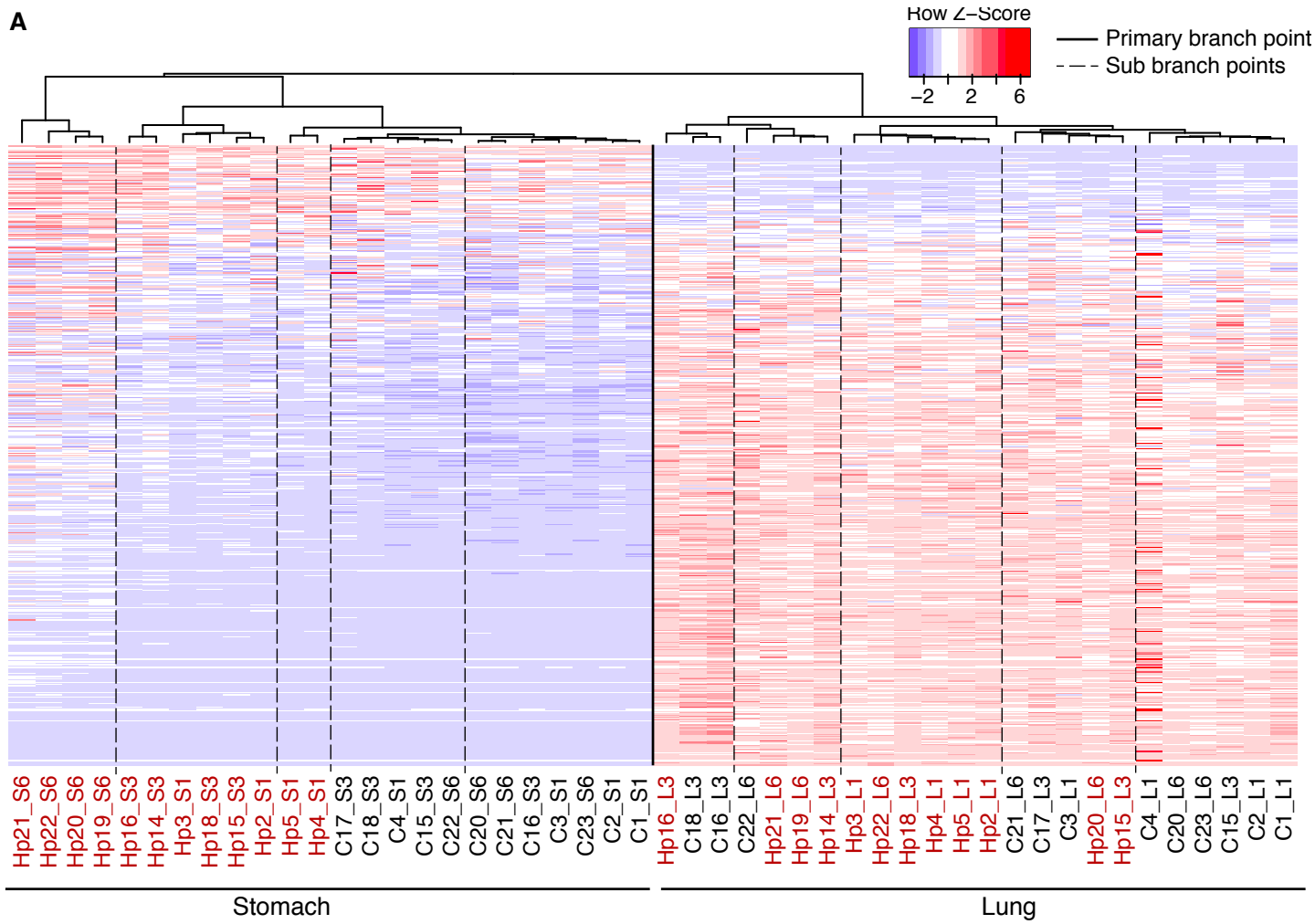
Cohort 2

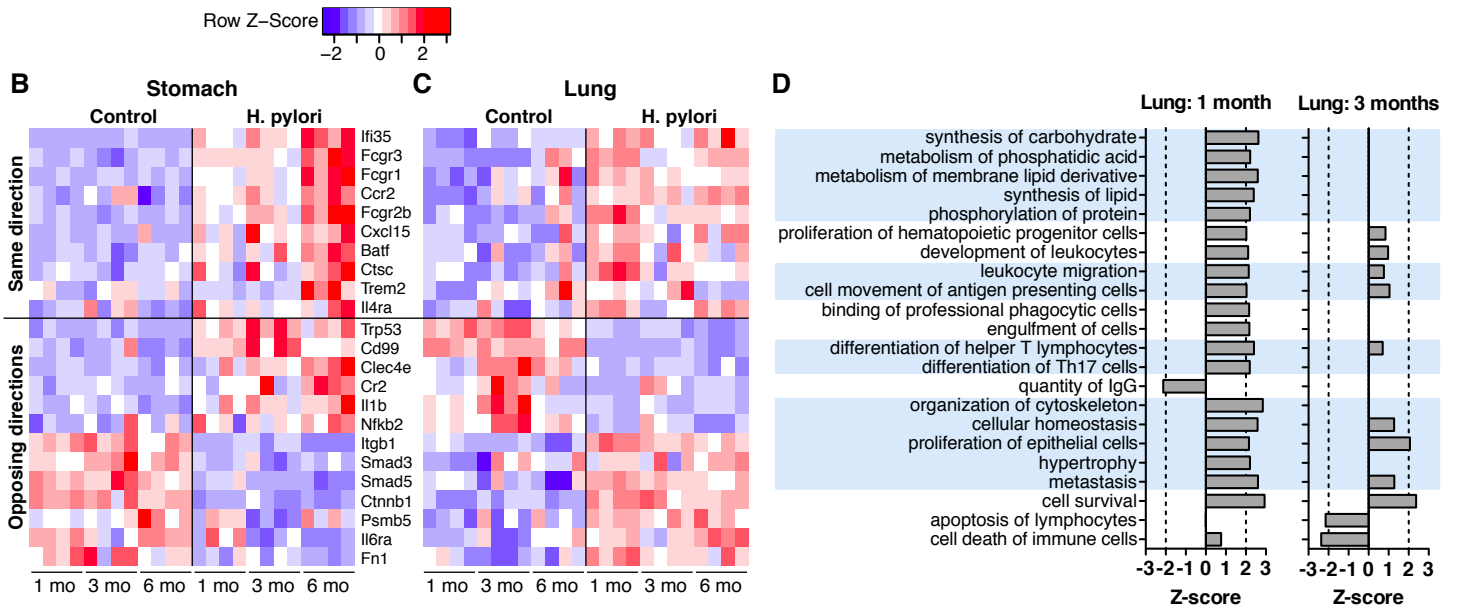
Infection	+					
Blood	+	+	+	+	+	+
Feces	+	+	+	+	+	+
Sacrifice		+	+	+		+
Month (post-infection)	0	1	2	3	4.5	6
Total Mouse # (I/C)		12/11	12/11	11/9	11/9	11/9

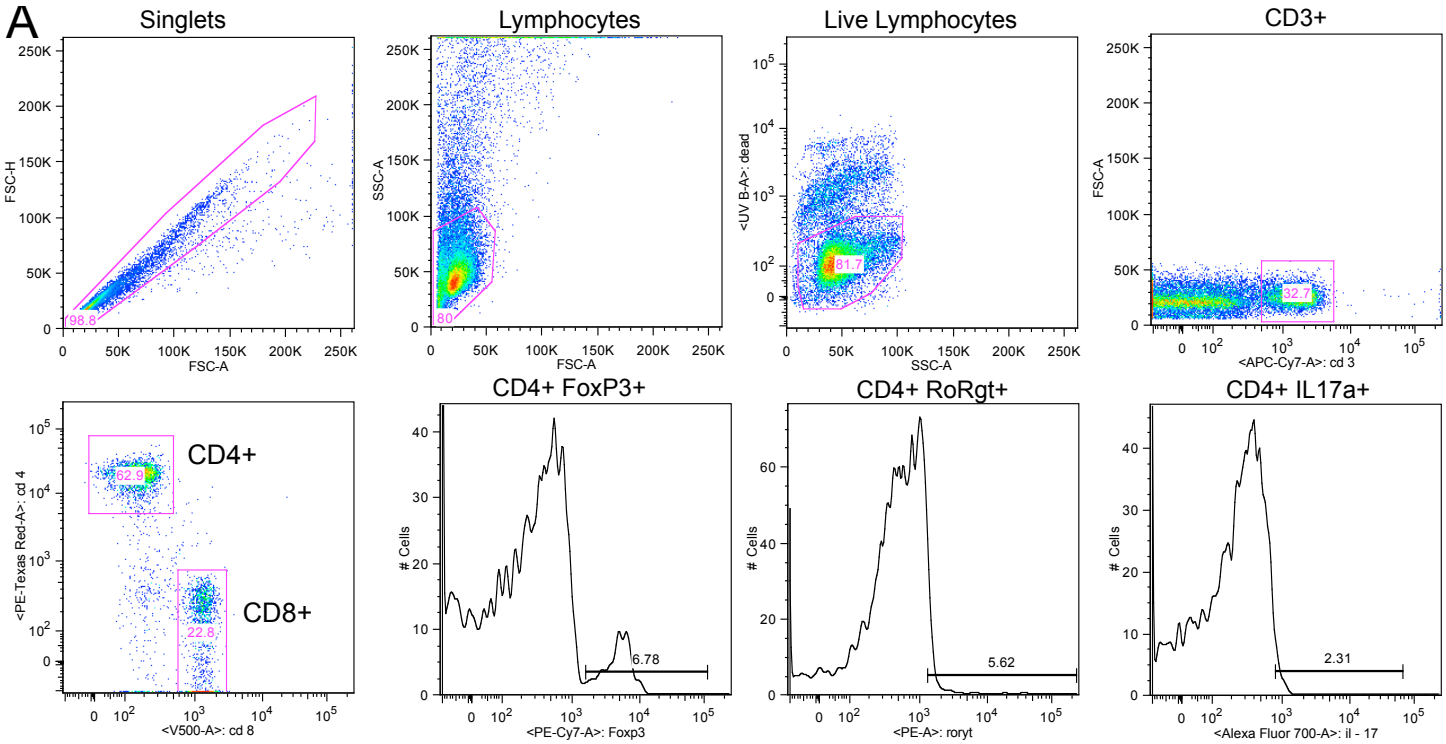
Colonization Status (I/C)

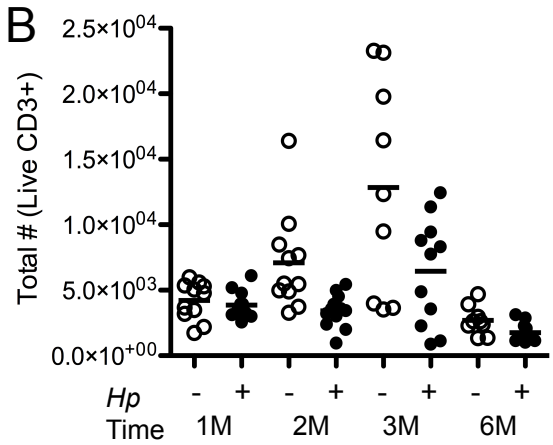
Cohort 1	Mouse #	6/6	6/6	5/5	5/5
	Culture +	5/0	5/0	5/0	4/0
	PCR +	3/0	1/0	3/0	5/0
	Overall +	6/0	5/0	5/0	5/0
Cohort 2	Mouse #	6/5	6/5	6/4	6/4
	Culture +	5/0	3/0	3/0	4/0
	PCR +	6/0	3/0	6/0	5/0
	Overall +	6/0	5/0	6/0	6/0

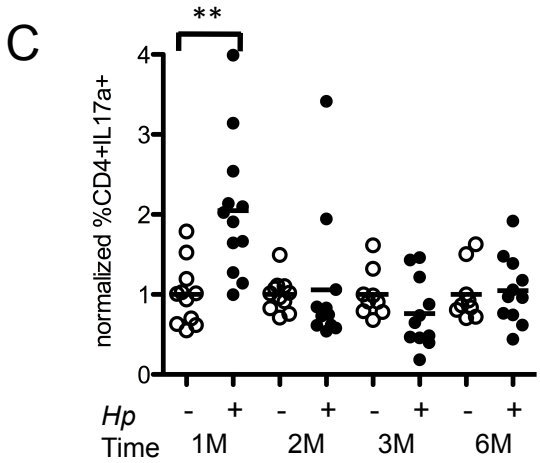

A
100 µm
B
100 µm
C
100 µm
D
100 µm
E
100 µm
F
50 µm
G
50 µm
H
50 µm
I
10 µm

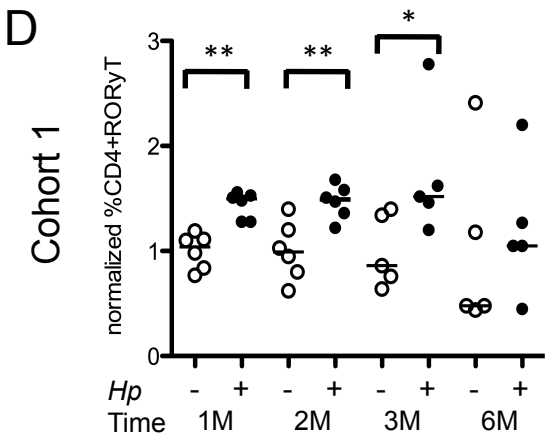

A
Row Z−Score
−2
2
6
Primary branch point
Sub branch points
Hp21_S6
Hp22_S6
Hp20_S6
Hp19_S6
Hp16_S3
Hp14_S3
Hp3_S1
Hp18_S3
Hp15_S3
Hp2_S1
Hp5_S1
Hp4_S1
C17_S3
C18_S3
C4_S1
C15_S3
C22_S6
C20_S6
C21_S6
C16_S3
C3_S1
C23_S6
C2_S1
C1_S1
Hp16_L3
C18_L3
C16_L3
C22_L6
Hp21_L6
Hp19_L6
Hp14_L3
Hp3_L1
Hp22_L6
Hp18_L3
Hp4_L1
Hp5_L1
Hp2_L1
C21_L6
C17_L3
C3_L1
Hp20_L6
Hp15_L3
C4_L1
C20_L6
C23_L6
C15_L3
C2_L1
C1_L1
Stomach
Lung

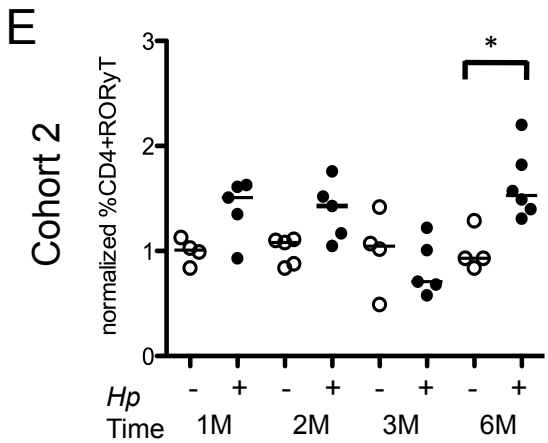

Row Z−Score
−2
0
2
B
Stomach
Control
H. pylori
C
Lung
Control
H. pylori
Same direction
Opposing directions
Ifi35
Fcgr3
Fcgr1
Ccr2
Fcgr2b
Cxcl15
Batf
Ctsc
Trem2
Il4ra
Trp53
Cd99
Clec4e
Cr2
Il1b
Nfkb2
Itgb1
Smad3
Smad5
Ctnnb1
Psmb5
Il6ra
Fn1
1 mo
3 mo
6 mo
1 mo
3 mo
6 mo
1 mo
3 mo
6 mo
1 mo
3 mo
6 mo
D
Lung: 1 month
Lung: 3 months
synthesis of carbohydrate
metabolism of phosphatidic acid
metabolism of membrane lipid derivative
synthesis of lipid
phosphorylation of protein
proliferation of hematopoietic progenitor cells
development of leukocytes
leukocyte migration
cell movement of antigen presenting cells
binding of professional phagocytic cells
engulfment of cells
differentiation of helper T lymphocytes
differentiation of Th17 cells
quantity of IgG
organization of cytoskeleton
cellular homeostasis
proliferation of epithelial cells
hypertrophy
metastasis
cell survival
apoptosis of lymphocytes
cell death of immune cells
-3 -2 -1 0 1 2 3
Z-score
-3 -2 -1 0 1 2 3
Z-score

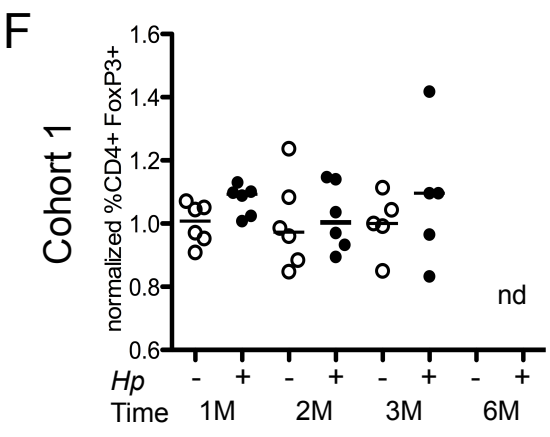

A
Singlets
Lymphocytes
Live Lymphocytes
CD3+
FSC-H
FSC-A
SSC-A
<UV B-A>: dead
<APC-Cy7-A>: cd 3
98.8
80
81.7
32.7
CD4+
CD8+
62.9
22.8
<PE-Texas Red-A>: cd 4
<V500-A>: cd 8
CD4+ FoxP3+
CD4+ RoRgt+
CD4+ IL17a+
Cells
6.78
5.62
2.31
<PE-Cy7-A>: Foxp3
<PE-A>: roryt
<Alexa Fluor 700-A>: il - 17

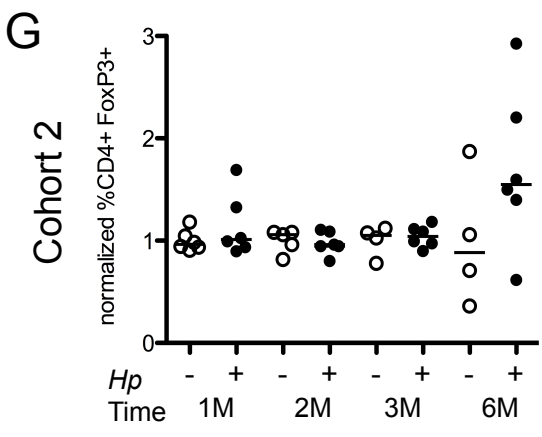

B
Total # (Live CD3+)
Hp
Time
1M
2M
3M
6M

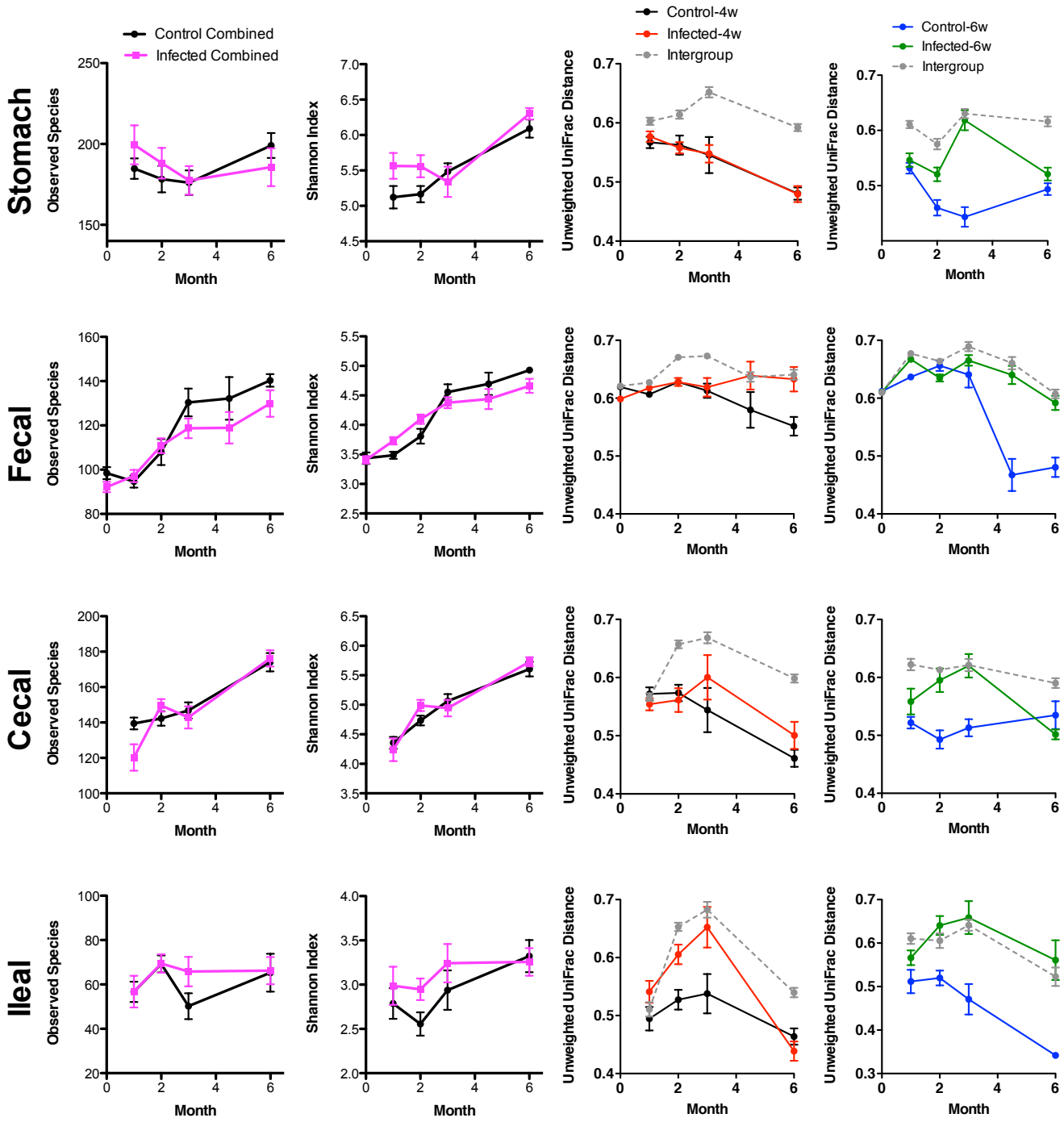

C
**
normalized %CD4+IL17a+
Hp
Time
1M
2M
3M
6M

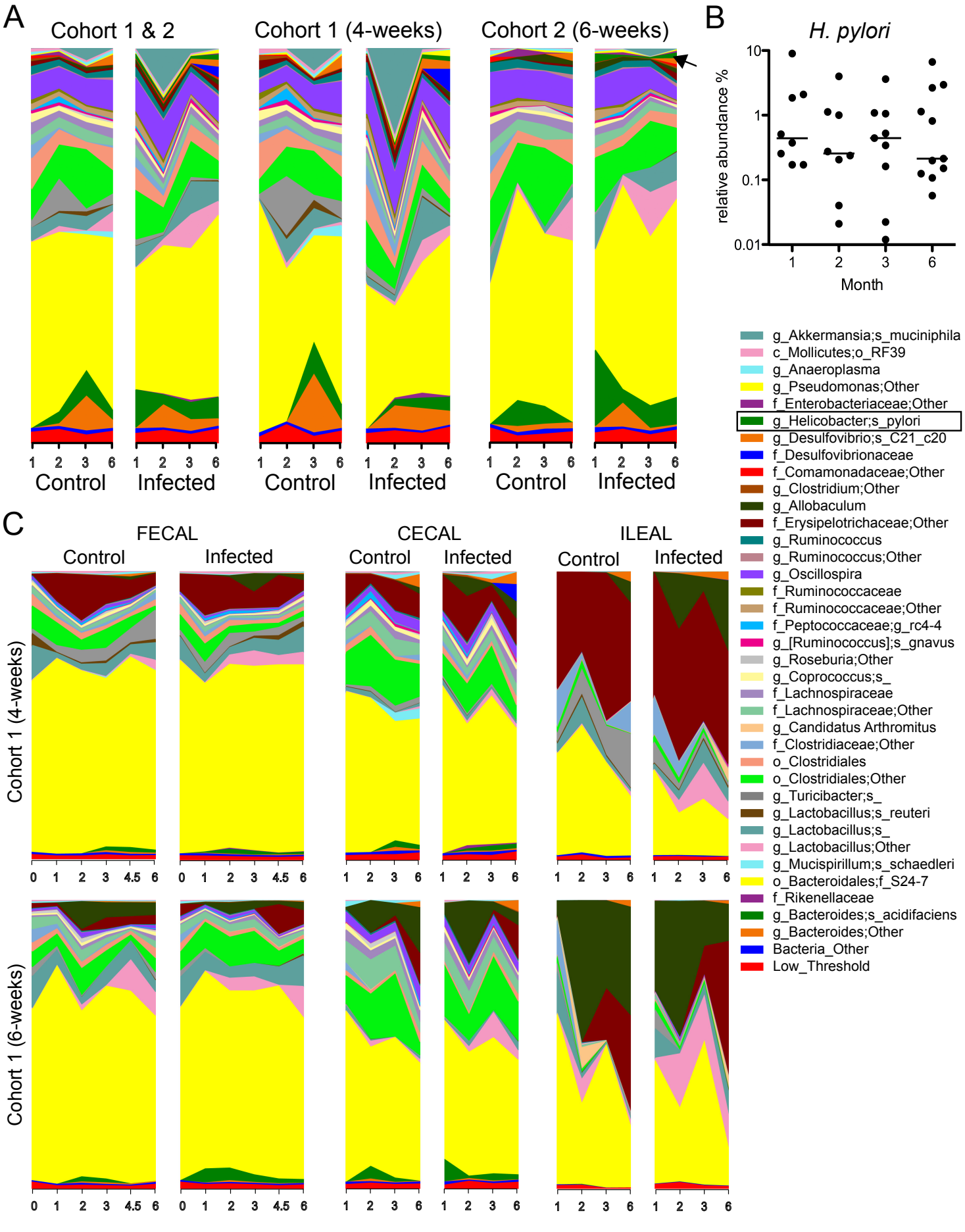

D
Cohort 1
**
**
*
normalized %CD4+RORγT
Hp
Time
1M
2M
3M
6M


E
Cohort 2
*
normalized %CD4+RORγT
Hp
Time
1M
2M
3M
6M


F
Cohort 1
normalized %CD4+ FoxP3+
nd
Hp
Time
1M
2M
3M
6M


G
Cohort 2
normalized %CD4+ FoxP3+
Hp
Time
1M
2M
3M
6M


Stomach
Fecal
Cecal
Ileal
Control Combined
Infected Combined
Control-4w
Infected-4w
Intergroup
Control-6w
Infected-6w
Intergroup
Observed Species
Shannon Index
Unweighted UniFrac Distance
Month


A
Cohort 1 & 2
Cohort 1 (4-weeks)
Cohort 2 (6-weeks)
Control
Infected
B
H. pylori
relative abundance %
Month
C
FECAL
CECAL
ILEAL
Cohort 1 (4-weeks)
Cohort 1 (6-weeks)
g_Akkermansia;s_muciniphila
c_Mollicutes;o_RF39
g_Anaeroplasma
g_Pseudomonas;Other
f_Enterobacteriaceae;Other
g_Helicobacter;s_pylori
g_Desulfovibrio;s_C21_c20
f_Desulfovibrionaceae
f_Comamonadaceae;Other
g_Clostridium;Other
g_Allobaculum
f_Erysipelotrichaceae;Other
g_Ruminococcus
g_Ruminococcus;Other
g_Oscillospira
f_Ruminococcaceae
f_Ruminococcaceae;Other
f_Peptococcaceae;g_rc4-4
g_[Ruminococcus];s_gnavus
g_Roseburia;Other
g_Coprococcus;s_
f_Lachnospiraceae
f_Lachnospiraceae;Other
g_Candidatus Arthromitus
f_Clostridiaceae;Other
o_Clostridiales
o_Clostridiales;Other
g_Turicibacter;s_
g_Lactobacillus;s_reuteri
g_Lactobacillus;s_
g_Lactobacillus;Other
g_Mucispirillum;s_schaedleri
o_Bacteroidales;f_S24-7
f_Rikenellaceae
g_Bacteroides;s_acidifaciens
g_Bacteroides;Other
Bacteria_Other
Low_Threshold

SUPPLEMENTAL FIGURE LEGENDS

Figure S1. Study overview, related to Figure 1. Mice were challenged with *H. pylori* strain PMSS1 at the age of 4-weeks (Cohort 1) or 6-weeks (Cohort 2 and Cohort 3). Mice of each cohort were either gavaged with Brucella Broth (BB) (Control) or 10^9 CFU *H. pylori* suspended in BB (Infected) at day 0. Before sacrifice, blood was collected from Cohorts 1 and 2 every other day and analyzed for early antibody responses and antibody and ghrelin responses at the time of sacrifice (indicated by +). Fecal samples from mice in all two Cohorts were collected and subjected to 16S rRNA sequencing (time points indicated by +). The time of sacrifice and organ collection (stomach, lung, ileum, and cecum) was 1, 2, 3 and 6 months (Cohorts 1 and 2) and 2 months (Cohort 3) after challenge (indicated by +). Numbers of control (C) and infected (I) mice is shown below the thick arrows. Colonization status of *H. pylori*-infected and non-infected control mice of each cohort at sacrifice as verified by culture and *H. pylori glmM* PCR.

Figure S2. Histopathology of C57/Bl6 mice three months post-infection, related to Figure 2. Compared to an uninfected control **(A),** infected mice showed moderate **(B)** to severe **(C)** chronic active inflammation in the gastric corpus. Inflammatory cells were arranged around gastric glands in the lamina propria and extended to the submucosa in severe cases (arrow head in **C**). Inflammation was pronounced in the gastric corpus adjacent to the esophageal-gastric junction (arrow head in **D**). In severe cases, lymphoid follicles were evident (arrow heads in **E**) and chronic inflammation also was evident in the gastric antrum **(F)**. Higher magnification indicates a mixed inflammatory infiltrate scattered around gastric glands mirroring human type B gastritis **(G, H)**. Infrequent rod-shaped bacteria typical for *H. pylori* were visible within gastric glands **(I)**. Scale bars represent 100 µm **(A-E)**, 50 µm **(F-H)** and 10 µm **(I);** Representative photomicrographs were obtained from mice sacrificed 3 or 6 months post-infection.

Figure S3. Tissue-specific immune gene expression profiles, related to Figure 3. (A) Expression of 547 genes related to mouse immunity were measured with the Nanostring n-counter Mouse Immunology Kit from mouse pulmonary and gastric tissues collected 1, 3, or 6 months following gavage with either *H. pylori* (Hp) or brucella broth alone (control, C). Heatmap showing relative gene expression values, with rows ordered by the ratio of average gastric expression divided by average pulmonary expression, and columns ordered by hierarchical clustering. Sample names are colored by colonization status (control, black; *H. pylori*, red). **(B-C)** Heat maps show expression levels of genes significantly different (FDR-adjusted p-value < 0.05, t-test) for ≥1 time point in both tissues. **(D)** Induced or repressed predicted biological functions in the lung in response to *H. pylori*-infection.

Figure S4. Increased proportions of Th17 cells in the lungs of *H. pylori*-infected mice, related to Figure 4 and Table 1. (A) Representative gating strategy (control mouse). Cells isolated from pulmonary specimens were first gated for singlets (FSC-H vs. FSC-A) and lymphocytes (SSC-A vs. FSC-A). The lymphocyte gate was further analyzed for their uptake of the Live/Dead Fixable blue dead stain to obtain only viable T-cells (UV-B vs SSC-A) expressing CD3+ (FSC-A vs Cy7-A). From this gated population, CD4 and CD8 surface expression was determined and subsequently CD4+ cells were analyzed for RORγT+, FoxP3+ and IL17a+ expression (gated similarly but from a stimulated subpopulation of isolated lymphocytes) (also see **Figure 4**). **(B)** Total count of live CD3+ cells isolated from the lung of control and *H. pylori*-infected mice. **(C)** Quantitation of frequency of CD4+ IL17a+ cells in control and *H. pylori*-infected mice. **(D-G)** Proportions of CD3+ CD4+ RORγT+ (Th17) cells and CD3+ CD4+ FoxP3+ (T-reg) cells in the lungs of *H. pylori*-infected mice. Quantitation of frequency of CD4+ RORγT+ cells (Th17) for Cohort 1 **(D)** and Cohort 2 **(E)**. Frequency of CD4+ FoxP3+ cells (T-reg) for Cohort 1 **(F)** and Cohort 2 **(G)**. **(C-G)** Results for each mouse normalized to the respective controls for each time point (average of controls for each month). Horizontal bars indicate group mean values. (-) Uninfected control; (+) *H.*

pylori-infected; (M) month; Statistical analysis was performed using Mann-Whitney U-Test, * P<0.05; ** P<0.01;

Figure S5. Microbial diversity and unweighted UniFrac Distances of control and *H. pylori*-challenged mice, related to Figure 5 and Figure 6. Observed species and Shannon index for stomach, fecal, cecal, and ileal samples over the 6-month study period of the combined Cohorts (left panels). Unweighted UniFrac Distances for Cohort 1 and Cohort 2 over time, including the Intergroup distances (right panels).

Figure S6. Effects of *H. pylori* colonization on gastrointestinal microbial composition over 6 months, related to Figure 5 and Figure 6. Mean relative abundance of bacteria present in intestinal samples from control and *H. pylori*-infected mice**. (A)** Relative abundance in stomach samples. All species identified with abundance >0.1% were used to generate relative abundance plots. Shown is the combination of Cohort 1 (4-weeks) and Cohort 2 (6-weeks), as well as each Cohort separately. Arrow indicates *H. pylori*. **(B)** Relative abundance of *H*. *pylori* in the stomach, as determined by 16S rRNA gene high throughput sequencing. **(C)** Relative abundance in fecal, cecal, and ileal samples. Taxa listed have relative abundance >1% in any sample at the lowest possible level of identification; c, class; o, order; f, family; g, genus; s, species. Analysis at depth 3000 showed similar results, but with fewer samples (data not shown).

SUPPLEMENTAL TABLES

Table S1. Number of enriched taxa in the stomach according to LEfSe for each cohort vs controls, and significant taxa shared between cohorts, related to Figure 5 and Figure S6.

		Total				Phylum				Class				Order				Family				Genus				Species			
	Month	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**	**1**	**2**	**3**	**6**
Cohort 1 (4-week)	Total	57	78	48	77	2	3	3	3	5	6	4	8	8	6	4	11	9	13	7	14	13	22	14	20	20	28	16	21
	↓ 108	18	32	19	39	1	1	1	2	2	2	1	3	3	3	1	5	3	6	2	7	4	9	7	11	5	11	7	11
	↑ 152	39	46	29	38	1	2	2	1	3	4	3	5	5	3	3	6	6	7	5	7	9	13	7	9	15	17	9	10
Cohort 2 (6-week)	Total	61	50	42	75	2	3	0	2	4	6	2	6	5	7	4	10	12	9	8	16	17	10	13	19	20	15	15	22
	↓ 115	32	15	25	43	1	1	0	1	1	1	1	1	2	1	3	5	6	2	4	10	10	4	8	12	11	6	9	14
	↑ 113	29	35	17	32	1	2	0	1	3	5	1	5	3	6	1	5	6	7	4	6	7	6	5	7	9	9	6	8
Shared	Total	10	17	6	29	0	2	0	1	2	3	0	4	2	2	0	6	2	3	1	7	2	2	2	5	2	5	3	6
	↓	5	6	1	8	0	1	0	0	1	2	0	2	1	1	0	2	1	1	0	2	1	0	0	1	1	1	1	1
	↑	2	2	2	15	0	0	0	1	0	0	0	1	0	0	0	3	0	0	0	3	1	1	1	3	1	1	1	4
	↑↓	3	9	3	6	0	1	0	0	1	1	0	1	1	1	0	1	1	2	1	2	0	1	1	1	0	3	1	1

↓ down in *H. pyori*-infected compared to control, ↑ up in *H. pylori*-infected compared to control, ↑↓ same taxa affected but different direction in the two cohorts; shaded block indicates taxonomic differences vs. controls that are shared across both cohorts

Table S2. Gastric taxa affected ≥ two time points in the same direction, related to Figure 5 and Figure S6.*

	Log LDA scores by month			
Taxa – Cohort 1 (4-weeks)	**1**	**2**	**3**	**6**
p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides.s_		**3.56**	**3.88**	
p_B.c_B.o_Bacteroidales.f_Rikenellaceae		**3.40**	**3.79**	**3.65**
p_B.c_B.o_Bacteroidales.f_Rikenellaceae.g_		**3.40**	**3.78**	**3.11**
p_B.c_B.o_Bacteroidales.f_Rikenellaceae.g_.s_		**3.40**	**3.78**	**3.11**
p_B.c_B.o_Bacteroidales.f_S24_7	-5.06	-4.94		
p_B.c_B.o_Bacteroidales.f_S24_7.g_	-5.06	-4.94		
p_B.c_B.o_Bacteroidales.f_S24_7.g_.s_	-5.06	-4.94		
p_Firmicutes.c_Bacilli.o_Lactobacillales	3.87			4.19
p_F.c_B.o_Lactobacillales.f_Lactobacillaceae.g_Lactobacillus.Other			4.46	3.87
p_F.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Roseburia	3.52		3.37	
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Roseburia.Other	3.52		3.37	
p_F.c_C.o_Clostridiales.f_Ruminococcaceae.g_Oscillospira.Other	3.62	3.99		
p_F.c_Erysipelotrichi.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Coprobacillus			-3.54	-3.01
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Coprobacillus.s_			-3.52	-3.01
p_Proteobacteria			4.35	4.57
p_P.c_Deltaproteobacteria		**3.44**	**4.12**	**4.36**
p_P.c_D.o_Desulfovibrionales		**3.44**	**4.12**	**4.36**
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae		**3.44**	**4.12**	**4.36**
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Bilophila		3.39	3.54	
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Bilophila.s_		3.39	3.54	
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Desulfovibrio		3.18	4.10	
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Desulfovibrio.s_C21_c20		3.18	4.10	
p_P.c_Epsilonproteobacteria	3.14	*a*	*a*	3.77
p_P.c_E.o_Campylobacterales	3.14			3.77
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae	3.14			3.77
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae.g_Helicobacter	3.14			3.77
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae.g_Helicobacter.s_pylori	3.14			3.77
p_Tenericutes.c_Mollicutes.o_RF39	-3.47			-3.21
p_T.c_M.o_RF39.f_	-3.47			-3.21
p_T.c_M.o_RF39.f_.g_	-3.47			-3.21
p_T.c_M.o_RF39.f_.g_.s_	-3.47			-3.21
Taxa Cohort 2 (6-weeks)	**1**	**2**	**3**	**6**
p_Actinobacteria		3.28		3.18
p_A.c_Actinobacteria		3.27		3.09
p_A.c_A.o_Bifidobacteriales		3.15		3.10
p_A.c_A.o_Bifidobacteriales.f_Bifidobacteriaceae		3.15		3.10
p_A.c_A.o_Bifidobacteriales.f_Bifidobacteriaceae.g_Bifidobacterium		3.15		3.10
p_A.c_A.o_Bifidobacteriales.f_Bifidobacteriaceae.g_Bifidobacterium.Other		3.15		3.10
p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Bacteroidaceae	4.99			4.45
p_B.c_B.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides	4.99			4.45
p_B.c_B.o_Bacteroidales.Other	3.18		2.83	
p_B.c_B.o_Bacteroidales.Other.Other	3.18		2.80	
p_B.c_B.o_Bacteroidales.Other.Other.Other	3.18		2.79	

p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiaceae	**-4.36**	**-2.82**	**-3.14**	
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_	**-4.13**		**-3.80**	**-4.07**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_.s_	**-4.13**		**-3.81**	**-4.08**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Coprococcus	**-3.56**		**-3.62**	**-3.54**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Coprococcus.s_	**-3.56**		**-3.60**	**-3.50**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Roseburia		-3.18	-3.86	
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Roseburia.Other		-3.18	-3.87	
p_F.c_C.Other			-2.85	-2.89
p_F.c_C.Other.Other			-2.85	-2.94
p_F.c_C.Other.Other.Other			-2.88	-2.92
p_F.c_C.Other.Other.Other.Other			-2.94	-2.92
p_F.c_Erysipelotrichi	**4.03**	**3.72**		**4.11**
p_F.c_E.o_Erysipelotrichales	**4.03**	**3.72**		**4.08**
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae	**4.03**	**3.72**		**4.12**
p_Proteobacteria.c_Alphaproteobacteria		**2.65**		**3.49**
p_P.c_Epsilonproteobacteria	**4.04**	**3.34**	**3.33**	**3.86**
p_P.c_E.o_Campylobacterales	**4.04**	**3.34**	**3.33**	**3.86**
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae	**4.04**	**3.34**	**3.33**	**3.86**
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae.g_Helicobacter	**4.04**	**3.34**	**3.33**	**3.86**
p_P.c_E.o_Campylobacterales.f_Helicobacteraceae.g_Helicobacter.s_pylori	**4.04**	**3.34**	**3.33**	**3.86**

*Criteria for inclusion of taxa in table: significantly affected (LEfSe) at ≥ two time points but never in opposite direction at any other time point; Numbers in grey shading represent those, up in infected; no shading represents those down in infected. **bold;** taxa affected at three time points; *a,* although culture or PCR positive, in only 3 of 5 infected mice were *H. pylori* 16S sequences detected.

Table S3. Gastric species affected by *H. pylori* presence, over time and by cohort, related to Figure 5 and Figure S6.

		Log LDA scores by month and Cohort							
	Month	1		2		3		6	
A	Cohort	1	2	1	2	1	2	1	2
	p_Bacteroidetes	-5.06							
	c_Bacteroidia	-5.06							
	o_Bacteroidales	-5.06							
	f_Bacteroidaceae		4.99	4.56		-4.88			4.45
	g_Bacteroides		4.99	4.56		-4.88			4.45
2	**s_Bacteroides**			**3.56**	**2.68**	**3.88**			
	f_Rikenellaceae			3.40		3.79		3.65	-3.02
	g_Rikenellaceae			3.40		3.78		3.11	
1	**s_Rikenellaceae**			**3.40**		**3.78**		**3.11**	
	p_Firmicutes	5.05							
	c_Bacilli	4.18		-4.97					
	o_Lactobacillales	3.87						4.19	
	f_Lactobacillaceae							4.18	
	g_Lactobacillus							4.18	
2	**s_Other**					**4.46**	**4.82**	**3.87**	
	c_Clostridia	5.03							
	o_Clostridiales	5.03							
	f_Lachnospiraceae								-4.23
	g_Coprococcus	-3.69	-3.56				-3.62		-3.54
1,2	**s_Coprococcus**	**-3.69**	**-3.56**				**-3.60**		**-3.50**
	c_Erysipelotrichi	-4.02	4.03	3.95	3.72			3.74	4.11
	o_Erysipelotrichales	-4.02	4.03	3.95	3.72			3.74	4.08
	f_Erysipelotrichaceae	-4.02	4.03	3.95	3.72			3.74	4.12
	g_Allobaculum		3.97	3.66				3.71	
3	**s_Allobaculum**		**3.97**	**3.66**				**3.71**	
	c_Epsilonproteobacteria	3.14	4.04		3.34		3.33	3.77	3.86
	o_Campylobacterales	**3.14**	**4.04**		**3.34**		**3.33**	**3.77**	**3.86**
	f_Helicobacteraceae	3.14	4.04		3.34		3.33	3.77	3.86
	g_Helicobacter	3.14	4.04		3.34		3.33	3.77	3.86
1,2	**s_pylori**	**3.14**	**4.04**		**3.34**		**3.33**	**3.77**	**3.86**
	p_Tenericutes		-3.63	3.48	3.02			-3.65	-3.63
	c_Mollicutes		-3.63	3.48	3.02			-3.65	-3.66
	o_RF39	**-3.47**						**-3.21**	**-3.01**
	f_RF39	-3.47						-3.21	-3.02
	g_RF39	-3.47						-3.21	-3.04
2	**s_RF39**	**-3.47**						**-3.21**	**-3.00**

[A]Criteria for inclusion of species in Table: (1) significantly (LEfSe) up or down at three time points in one Cohort and not in the opposite direction in the other cohort; (2) shared between cohorts, same direction at specific time point, not affected in opposite direction; and affected in one cohort in the same direction ≥ one other time point**;** (3) family affected significantly in both cohorts, but no apparently shared taxa affected, when cohorts combined, only *Allobaculum* at the two time points was up in infected; numbers in grey shading represent those taxa up in infected; no shading represents those down in infected. **bold**; species level

Table S4. Affected species of Cohort 3, that are shared with Cohort 1 or 2, related to Figure 5 and Figure 6.

		Log LDA scores by month and Cohort								
	Month	1		2			3		6	
A	Cohort	1	2	1	2	3	1	2	1	2
ST	Turicibacter.s_	3.87		-4.48		-4.6			-4.26	-3.16
ST	Erysipelotrichaceae.other			3.94		3.00				3.87
ST	Desulfovibrio.s_C21_c20			3.18		4.00	4.12			
ST	Helicobacter.s_pylori	3.14	4.04		3.34	3.70		3.33	3.77	3.86
F	Turicibacter.s_	3.84	3.52		-3.39	-4.30	-4.14	-3.32	-4.62	-4.07
I	Erysipelotrichaceae.other			5.00		3.40				
I	Desulfovibrio.s_C21_c20			3.71		5.00				
C	Lachnospiraceae.other			-4.08		-3.60				
C	Oscilospira.s_	-3.75		3.78		4.30				-3.99
C	Desulfovibrio.s_C21_c20			3.44		4.40				

*Criteria for inclusion of species in Table: significantly affected (LEfSe) species from Cohort 3 that were also affected in the same direction in Cohort 1 or 2 and remained different over time or were later not affected at all. [A]sampling site; ST, stomach; F, feces; I, ileum; C, cecum;

Table S5. The effect of *H. pylori* infection on microbial community structure, related to Figure 5 and Figure 6.

ADONIS P-values, Control vs. Inoculated, in unweighted UniFrac analysis				
Location	**Month**	**Both Cohorts**	**4-week inoculation**	**6-week inoculation**
Ileum	**1**	0.131	0.577	**0.009**
	2	0.141	**0.001**	0.134
	3	**0.025**	**0.029**	**0.018**
	6	**0.011**	**0.005**	0.060
Cecum	**1**	0.192	0.631	**0.006**
	2	**0.043**	**0.003**	**0.007**
	3	0.080	**0.028**	**0.019**
	6	**0.001**	**0.011**	**0.006**
Fecal	**0**	0.168	**0.040**	0.940
	1	**0.019**	**0.035**	**0.002**
	2	**0.028**	**0.001**	0.127
	3	**0.050**	**0.003**	0.083
	4.5	**0.001**	**0.039**	**0.004**
	6	**0.031**	**0.006**	**0.006**

Compositional differences were measured by unweighted UniFrac distances and significance testing was performed using the ADONIS test, with 999 permutations. The table displays p-values, with values <0.05 in **bold** text.

Table S6. Fecal taxa affected at ≥ two time points in the same direction, related to Figure 6 and Figure S6.*

	Log LDA scores by month				
Taxa – Cohort 1 (4-weeks)	**1**	**2**	**3**	**4.5**	**6**
p_Actinobacteria.c_Coriobacteria		-3.26			-3.43
p_A.c_C.o_Coriobacteriales		-3.06			-3.43
p_A.c_C.o_Coriobacteriales.f_Coriobacteriaceae		-3.06			-3.43
p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Bacteroidaceae	3.74	4.00			
p_B.c_B.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides	3.72	4.00			
p_B.c_B.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides.Other	3.44	3.16			
p_B.c_B.o_Bacteroidales.Other		2.97			3.38
p_B.c_B.o_Bacteroidales.Other.Other		2.97			3.38
p_B.c_B.o_Bacteroidales.Other.Other.Other		2.97			3.38
p_Firmicutes.c_Bacilli.o_Lactobacillales.f_Lactobacillaceae.g_Lactobacillus.Other	3.40	4.2			
p_F.c_B.o_Lactobacillales.Other		2.63	3.13		
p_F.c_B.o_Lactobacillales.Other.Other		2.63	3.05		
p_F.c_B.o_Lactobacillales.Other.Other.Other		2.64	2.90		
p_F.c_Erysipelotrichi.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Clostridium	**-3.84**	**-3.04**	**-3.19**		
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Clostridium.Other	**-3.83**	**-3.05**	**-3.19**		
Taxa – Cohort 1 (6-weeks)	**1**	**2**	**3**	**4.5**	**6**
p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Bacteroidaceae	**4.39**	**4.12**		**3.82**	
p_B.c_B.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides	**4.4**	**4.12**		**3.82**	
p_B.c_B.o_Bacteroidales.f_Bacteroidaceae.g_Bacteroides.s_ovatus			**-3.43**	**-3.33**	**-3.83**
p_F.c_Clostridia.o_Clostridiales.f_	-3.57				-4.00
p_F.c_C.o_Clostridiales.f_.g_	-3.57				-4.05
p_F.c_C.o_Clostridiales.f_.g_.s_	-3.57				-4.03
p_F.c_C.o_Clostridiales.f_Clostridiaceae.g_CandidatusArthromitus		2.85	3.30		
p_F.c_C.o_Clostridiales.f_Clostridiaceae.g_CandidatusArthromitus.s_		2.85	3.39		
p_F.c_C.o_Clostridiales.f_Clostridiaceae.g_SMB53	**-2.64**	**-3.01**	**-3.52**	**-3.70**	
p_F.c_C.o_Clostridiales.f_Clostridiaceae.g_SMB53.s_	**-2.68**	**-2.95**	**-3.52**	**-3.76**	
p_F.c_C.o_Clostridiales.f_Clostridiaceae.Other	-3.87	-2.89			
p_F.c_C.o_Clostridiales.f_Clostridiaceae.Other.Other	-3.87	-2.96			
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Coprococcus		**-3.58**		**-3.53**	**-3.65**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Coprococcus.s_		**-3.58**		**-3.56**	**-3.66**
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Roseburia	**-3.64**	**-3.87**	**-3.50**		
p_F.c_C.o_Clostridiales.f_Lachnospiraceae.g_Roseburia.Other	**-3.64**	**-3.87**	**-3.50**		
p_F.c_C.o_Clostridiales.f_Peptococcaceae				-3.24	-3.35
p_F.c_C.o_Clostridiales.f_Peptococcaceae.g_rc4_4				-3.25	-3.33
p_F.c_C.o_Clostridiales.f_Peptococcaceae.g_rc4_4.s_				-3.22	-3.35
p_F.c_C.o_Clostridiales.Other	4.38			4.2	
p_F.c_C.o_Clostridiales.Other.Other	4.38			4.23	
p_F.c_C.o_Clostridiales.Other.Other.Other	4.38			4.22	
p_F.c_Erysipelotrichi.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Allobaculum			-4.17	-4.24	
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Allobaculum.s_			-4.17	-4.27	
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Clostridium	2.98		3.31		
p_F.c_E.o_Erysipelotrichales.f_Erysipelotrichaceae.g_Clostridium.Other	2.99		3.42		

p_Proteobacteria			-3.4	-3.28
p_P.c_Deltaproteobacteria			-3.39	-3.29
p_P.c_D.o_Desulfovibrionales			-3.39	-3.3
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae			-3.39	-3.31
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Desulfovibrio			-3.39	-3.28
p_P.c_D.o_Desulfovibrionales.f_Desulfovibrionaceae.g_Desulfovibrio.s_C21_c20			-3.39	-3.28
p_Tenericutes			-3.19	-3.52
p_T.c_Mollicutes			-3.19	-3.50
p_T.c_M.o_RF39	-3.04		-3.61	
p_T.c_M.o_RF39.f_	-3.04		-3.61	
p_T.c_M.o_RF39.f_.g_	-3.04		-3.61	
p_T.c_M.o_RF39.f_.g_.s_	-3.04		-3.61	

*Criteria for inclusion of taxa in Table: significantly affected (LEfSe) at ≥ two time points but never in opposite direction at any other time point; Numbers in grey shading represent those taxa up in infected; no shading represents those down in infected. **bold**; taxa affected at three time points;

Table S7. Fecal taxa affected by *H. pylori* presence, to species level, related to Figure 6 and Figure S6.[a]

		Log LDA scores by month and Cohort									
	Month	**1**		**2**		**3**		**4.5**		**6**	
A	**Cohort**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
	p_Bacteroidetes	-4.70									
	c_Bacteroidia	-4.70									
	o_Bacteroidales	-4.70									
	f_Bacteroidaceae	3.74	4.39	4.00	4.12				3.82		
	g_Bacteroides	3.72	4.40	4.00	4.12				3.82		
1	**s_ovatus**						-3.43		-3.33		-3.83
	p_Firmicutes	4.68									
	c_Bacilli	4.20		-4.23					-4.71		
	o_Turicibacteriales	3.84	3.44		-3.35	-4.14	-3-23			-4.62	-4.08
	f_Turicibacteraceae	3.84	3.24		-3.37	-4.14	-3-23			-4.62	-4.08
	g_Turicibacter	3.84	3.43		-3.39	-4.14	-3-23			-4.62	-4.06
2	**s_Turicibacter**	**3.84**	**3.42**		**-3.39**	**-4.14**	**-3-23**			**-4.62**	-4.07
	c_Clostridia								4.45		-4.54
	o_Clostridiales								4.44		-4.56
	f_Clostridiales	3.53	-3.57				-3.52				-4.00
	g_SMB53		-2.64		-3.01		-3.52		-3.70		
1	**s_SMB53**		**-2.68**		**-2.95**				**-3.76**		

[A]Criteria for inclusion of species in Table: (1) significantly (LEfSe) up or down at three time points in one Cohort and not in the opposite direction in the other cohort; (2) shared between cohorts, same direction at specific time point, not affected in opposite direction; and affected in one cohort in the same direction in ≥ one other time point; numbers in grey shading represent those taxa up in infected; no shading represents those down in infected. **bold**; species level

Supplemental File 1 (Table). Regulation of 547 immunological genes present in the nCounter GX Mouse Immunology Panel (NanoString, Seattle,WA), related to Figure 3 and Table 1.

SUPPLEMENTAL REFERENCES

Blankenberg, D., Von Kuster, G., Coraor, N., Ananda, G., Lazarus, R., Mangan, M., Nekrutenko, A., and Taylor, J. (2010). Galaxy: a web-based genome analysis tool for experimentalists. Curr Protoc Mol Biol *Chapter 19*, Unit 19 10 11-21.

Blaser, M.J., Perez-Perez, G.I., Kleanthous, H., Cover, T.L., Peek, R.M., Chyou, P.H., Stemmermann, G.N., and Nomura, A. (1995). Infection with *Helicobacter pylori* strains possessing CagA is associated with an increased risk of developing adenocarcinoma of the stomach. Cancer Res *55*, 2111-2115.

Caporaso, J.G., Kuczynski, J., Stombaugh, J., Bittinger, K., Bushman, F.D., Costello, E.K., Fierer, N., Pena, A.G., Goodrich, J.K., Gordon, J.I.*, et al.* (2010). QIIME allows analysis of high-throughput community sequencing data. Nat Methods *7*, 335-336.

Giardine, B., Riemer, C., Hardison, R.C., Burhans, R., Elnitski, L., Shah, P., Zhang, Y., Blankenberg, D., Albert, I., Taylor, J.*, et al.* (2005). Galaxy: a platform for interactive large-scale genome analysis. Genome Res *15*, 1451-1455.

Goecks, J., Nekrutenko, A., and Taylor, J. (2010). Galaxy: a comprehensive approach for supporting accessible, reproducible, and transparent computational research in the life sciences. Genome Biol *11*, R86.

Jenks, P.J., Megraud, F., and Labigne, A. (1998). Clinical outcome after infection with *Helicobacter pylori* does not appear to be reliably predicted by the presence of any of the genes of the *cag* pathogenicity island. Gut *43*, 752-758.

Lu, J.J., Perng, C.L., Shyu, R.Y., Chen, C.H., Lou, Q., Chong, S.K., and Lee, C.H. (1999). Comparison of five PCR methods for detection of *Helicobacter pylori* DNA in gastric tissues. J Clin Microbiol *37*, 772-774.

Mainguet, P., Jouret, A., and Haot, J. (1993). [The "Sidney System", a new classification of gastritis]. Gastroenterol Clin Biol *17*, T13-17.

Pohl, M.A., Kienesberger, S., and Blaser, M.J. (2012). Novel functions for glycosyltransferases Jhp0562 and GalT in Lewis antigen synthesis and variation in *Helicobacter pylori*. Infect Immun *80*, 1593-1605.

Segata, N., Izard, J., Waldron, L., Gevers, D., Miropolsky, L., Garrett, W.S., and Huttenhower, C. (2011). Metagenomic biomarker discovery and explanation. Genome Biol *12*, R60.