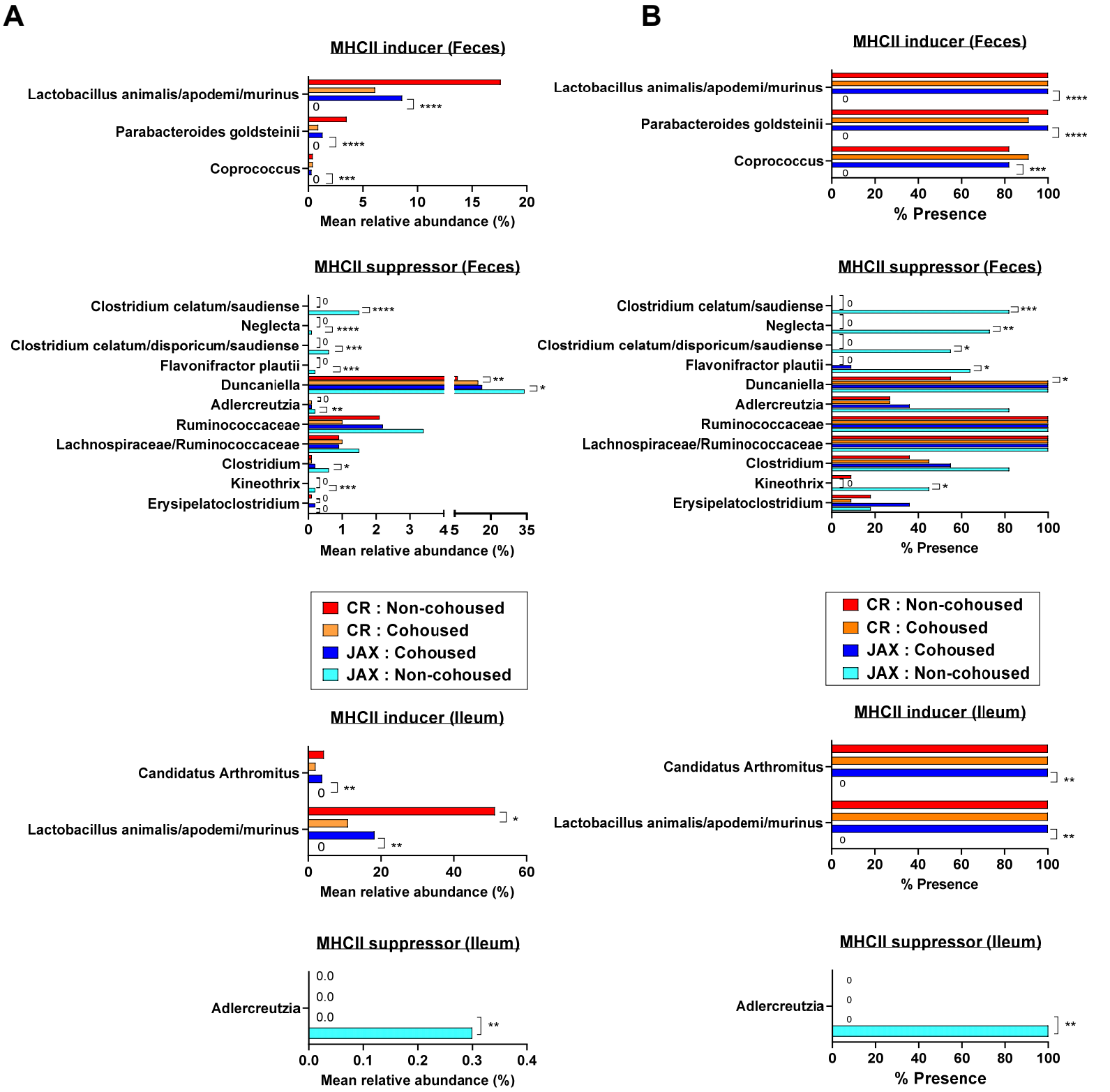

A
MHCII inducer (Feces)
Lactobacillus animalis/apodemi/murinus
Parabacteroides goldsteinii
Coprococcus
Mean relative abundance (%)
MHCII suppressor (Feces)
Clostridium celatum/saudiense
Neglecta
Clostridium celatum/disporicum/saudiense
Flavonifractor plautii
Duncaniella
Adlercreutzia
Ruminococcaceae
Lachnospiraceae/Ruminococcaceae
Clostridium
Kineothrix
Erysipelatoclostridium
Mean relative abundance (%)
CR : Non-cohoused
CR : Cohoused
JAX : Cohoused
JAX : Non-cohoused
MHCII inducer (Ileum)
Candidatus Arthromitus
Lactobacillus animalis/apodemi/murinus
Mean relative abundance (%)
MHCII suppressor (Ileum)
Adlercreutzia
Mean relative abundance (%)
B
MHCII inducer (Feces)
% Presence
MHCII suppressor (Feces)
% Presence
MHCII inducer (Ileum)
% Presence
MHCII suppressor (Ileum)
% Presence
C
Polyclonal CD4+ T cell-induced GVHD (MHC mismatched model)
GVHD survival (%)
Days after BMT
Non-cohoused JAX
Non-cohoused CR
Cohoused JAX
Cohoused CR
Non-cohoused JAX (TCD)
NS

Figure S1, related to Figure 4. MHC II-inducing microbiota are transfered after cohousing and promote GVHD lethality.

JAX B6N and CR B6N mice were housed separately (non-cohoused) or cohoused for 4 weeks as described in **Figure 4**. The relative abundance (**A**) and frequency of presence (**B**) of MHC-II inducers and MHC-II suppressors in CR non-cohoused, CR cohoused, JAX-cohoused and JAX non-cohoused mice in feces (top) and ileum (bottom). Wilcoxon rank-sum test with p-values adjusted using Holm's method. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$. (**C**) After 4 week cohousing or separate housing (non-cohoused), female JAX and CR B6N mice were lethally irradiated and transplanted with BM and 5 x 10^6 $CD4^+$ T cells from PC61-treated BALB/c mice. Survival by Kaplan-Meier analysis, combined from 2 replicate experiments (n = 20 per T cell-replete group, n = 10 in TCD group). ***$p < 0.001$, NS: not significant.

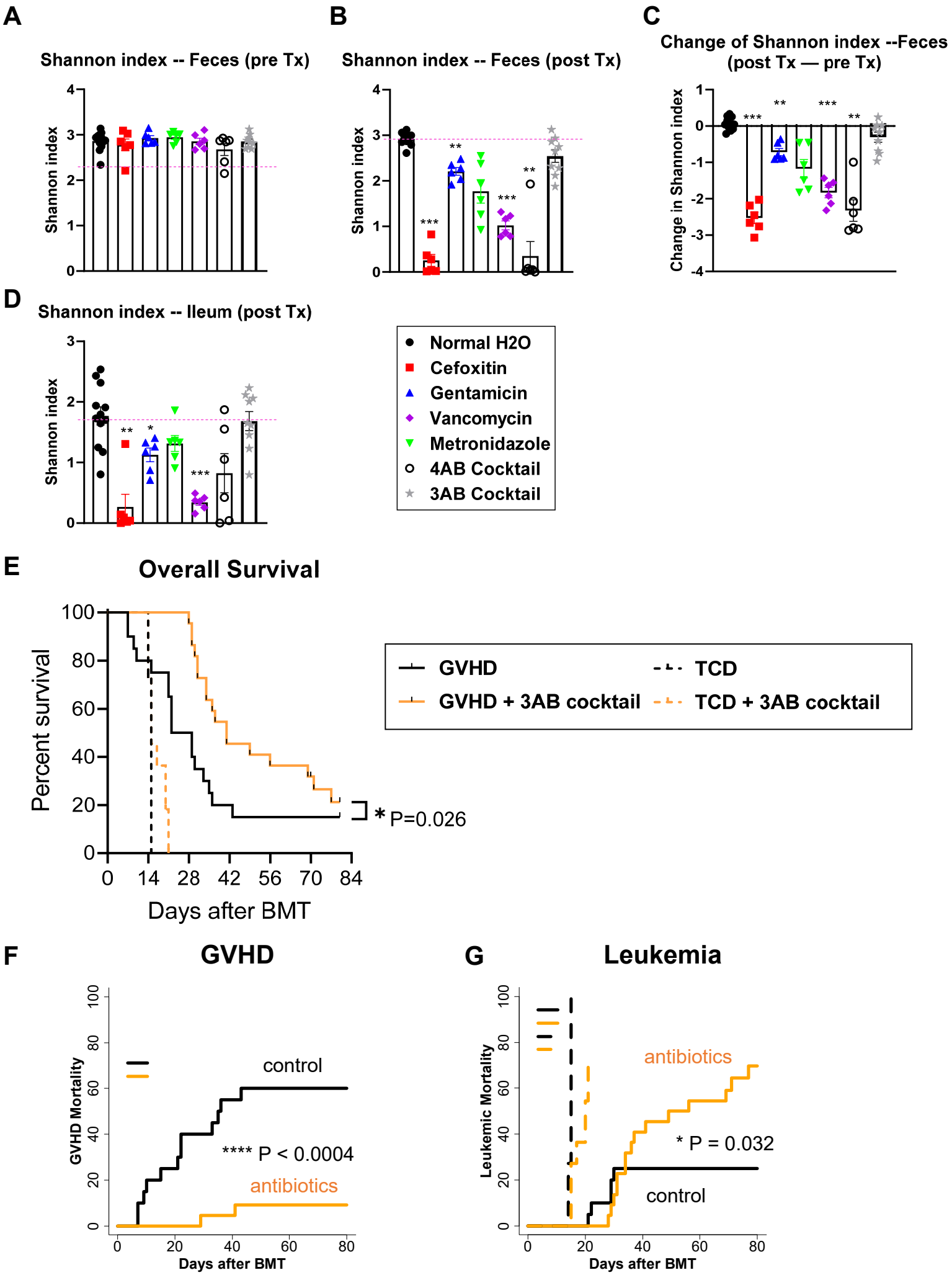

A
Shannon index -- Feces (pre Tx)
Shannon index
B
Shannon index -- Feces (post Tx)
Shannon index
C
Change of Shannon index --Feces (post Tx — pre Tx)
Change in Shannon index
D
Shannon index -- Ileum (post Tx)
Shannon index
Normal H2O
Cefoxitin
Gentamicin
Vancomycin
Metronidazole
4AB Cocktail
3AB Cocktail
E
Overall Survival
Percent survival
Days after BMT
GVHD
GVHD + 3AB cocktail
TCD
TCD + 3AB cocktail
* P=0.026
F
GVHD
GVHD Mortality
control
**** P < 0.0004
antibiotics
Days after BMT
G
Leukemia
Leukemic Mortality
antibiotics
* P = 0.032
control
Days after BMT

Figure S2, related to Figure 5. Microbial abundance and evenness of species following antibiotic treatment, and effects on leukemia relapse.

ADFH B6N mice were treated with the antibiotics shown for 2 weeks as described in **Figure 5A-E**. Fecal and ileal samples were collected before (feces only) and after treatment. Two sets of comparisons as 4AB cocktail, single antibiotics vs. normal H_2O (n = 6 per group combined from 2 replicate experiments) and 3AB cocktail vs. normal H_2O (n = 6, 9 per group combined from 2 replicate experiments).Shannon diversity index in pre-treatment (**A**), post-treatment fecal (**B, C**) and ileal (**D**) samples. Data presented as mean ± SEM and analyzed with Welch's t-test with p-value adjusted using Holm's method. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001. (**E – G**) Lethally irradiated B6N CR mice were transplanted with 10 x 10^6 BM and 0.5 x 10^6 $CD4^+$ T cells from BALB/c mice with C57Bl/6-background MHC-II-expressing primary B cell acute lymphoblastic leukemia (*Arf*$^{-/-}$ *MSCV-RCSD1-ABL2-ires-GFP* + *MSCV-IK6-ires-RFP*) on day 0. The recipients of T cell depleted grafts (TCD) served as negative controls. The recipients in antibiotics groups received 3AB antibiotic water (Cefoxitin, Gentamicin and Vancomycin) as described in Methods. The recipients in control groups received normal water throughout. (**E**) Overall survival, (**F**) GVHD and (**G**) Leukemia death are shown. (3 experiments combined, n = 20 – 22 per T cell deplete group, n = 11 per TCD group, Log-rank test)

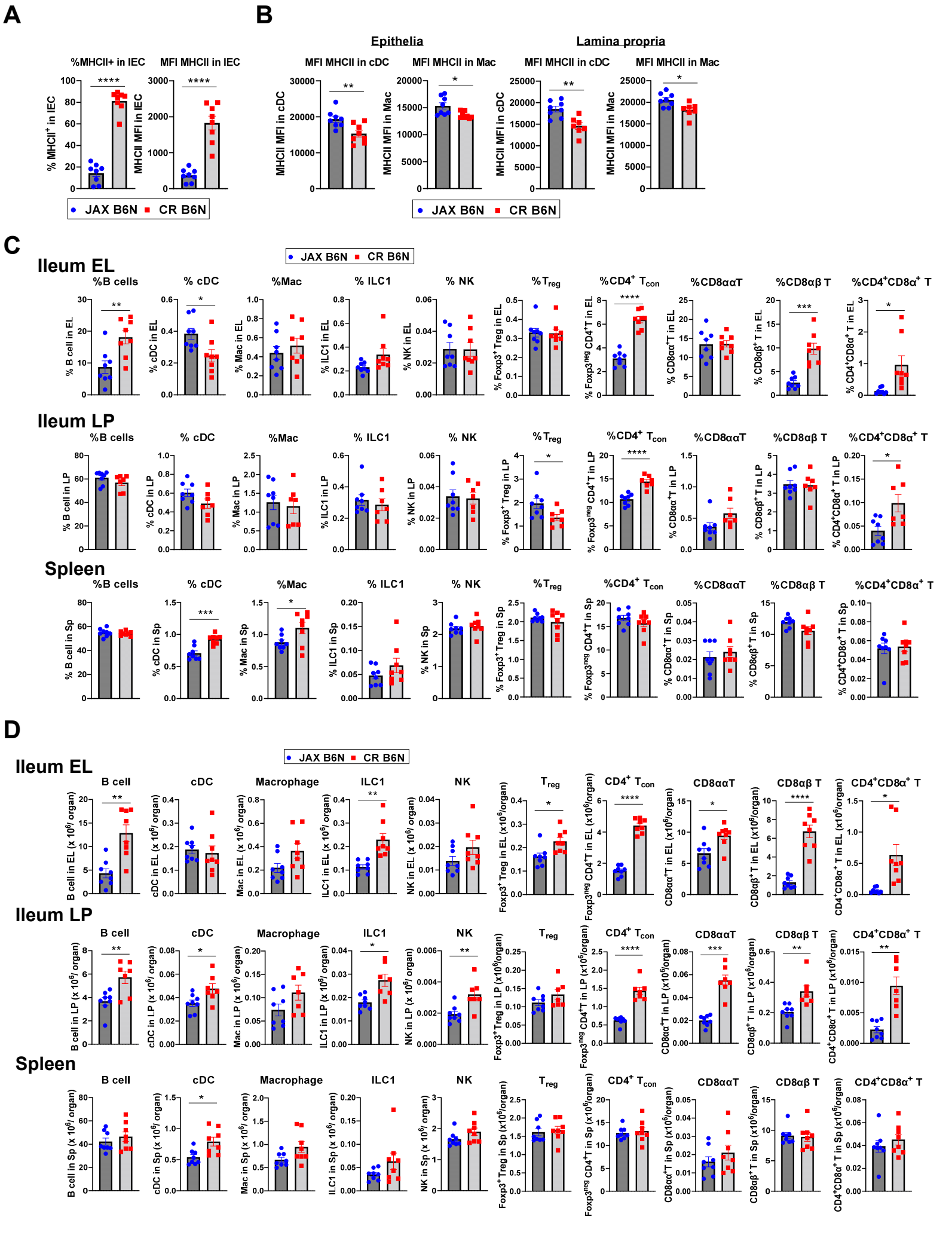

A
%MHCII+ in IEC
MFI MHCII in IEC
% MHCII+ in IEC
MHCII MFI in IEC
JAX B6N
CR B6N
B
Epithelia
Lamina propria
MFI MHCII in cDC
MFI MHCII in Mac
MHCII MFI in cDC
MHCII MFI in Mac
C
Ileum EL
Ileum LP
Spleen
%B cells
% cDC
%Mac
% ILC1
% NK
%Treg
%CD4+ Tcon
%CD8αα T
%CD8αβ T
%CD4+CD8α+ T
D
Ileum EL
Ileum LP
Spleen
B cell
cDC
Macrophage
ILC1
NK
Treg
CD4+ Tcon
CD8αα T
CD8αβ T
CD4+CD8α+ T

Figure S3, related to Figure 1–5. Mice with high MHC-II expression on IEC have expanded numbers of T cells in the ileum.

The ileal epithelial layer (EL), ileal lamina propria (LP) and spleen of naïve age-matched female B6N mice from JAX and CR were analyzed. (**A**) Quantification of MFI and % MHC-II expression by IEC ($CD45^{neg}CD326^{+}$). (**B**) Quantification of MHC-II MFI on conventional dendritic cells (cDC) ($CD45^{+}CD326^{neg}CD3^{neg}CD19^{neg}NK1.1^{neg}Ly6G^{neg}SiglecH^{neg}CD11c^{high}CD64^{neg}$) and macrophages ($CD45^{+}CD326^{neg}CD3^{neg}CD19^{neg}NK1.1^{neg}Ly6G^{neg}SiglecH^{neg}CD64^{+}$) from ileal EL and LP. (**C-D**) Frequency and (**C**) absolute number (**D**) of each cell fraction: B cell ($CD3^{neg}CD19^{+}$), cDC, macrophage (Mac), innate lymphoid cell type 1 (ILC1) ($CD3^{neg}CD19^{neg}NK1^{+}CD49b^{neg}CD11b^{neg}CD200R^{+}$), NK cell ($CD3^{neg}CD19^{neg}NK1^{+}CD49b^{+}CD200R^{neg}$), regulatory T cell (Treg) ($CD3^{+}CD19^{neg}NK1^{neg}CD4^{+}CD8a^{neg}Foxp3^{+}$), conventional CD4 T cell ($CD4^{+}$ Tcon) ($CD3^{+}CD19^{neg}NK1^{neg}CD4^{+}CD8a^{neg}Foxp3^{neg}$), CD8αα T cell ($CD3^{+}CD19^{neg}NK1^{neg}CD4^{neg}CD8a^{+}CD8\beta^{neg}$), CD8αβ T cell ($CD3^{+}CD19^{neg}NK1^{neg}CD4^{neg}CD8a^{+}CD8\beta^{+}$), $CD4^{+}CD8\alpha^{+}$ T cell ($CD3^{+}CD19^{neg}NK1^{neg}CD4^{+}CD8a^{+}$). (**A-D**) Data shown with mean ± SEM (n = 8 per group combined from 2 replicate experiments). t-test with Welch's correction. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

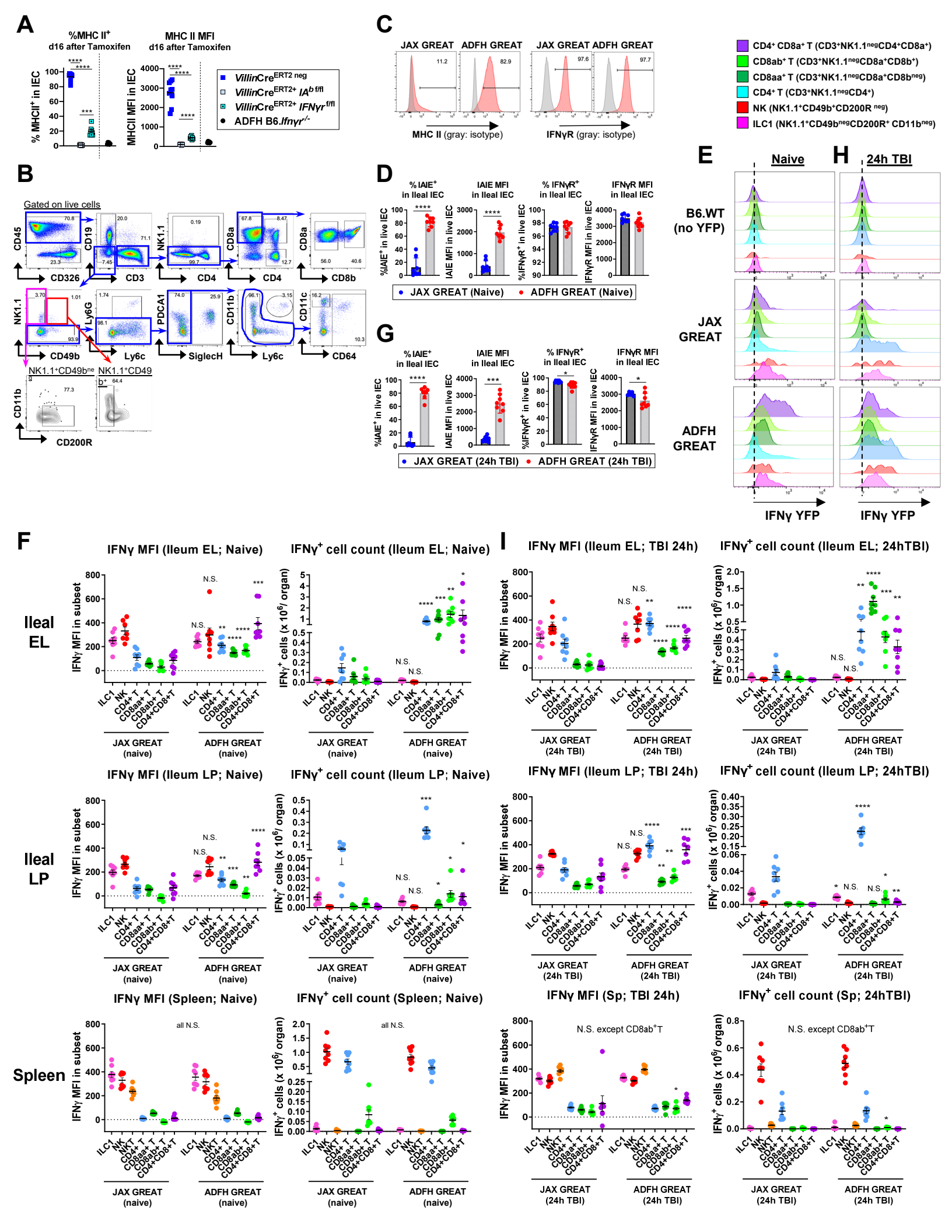
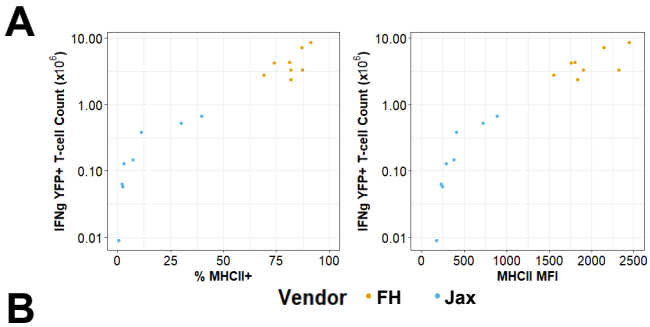
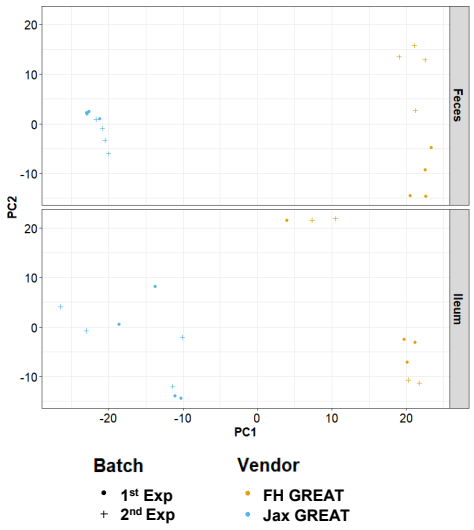
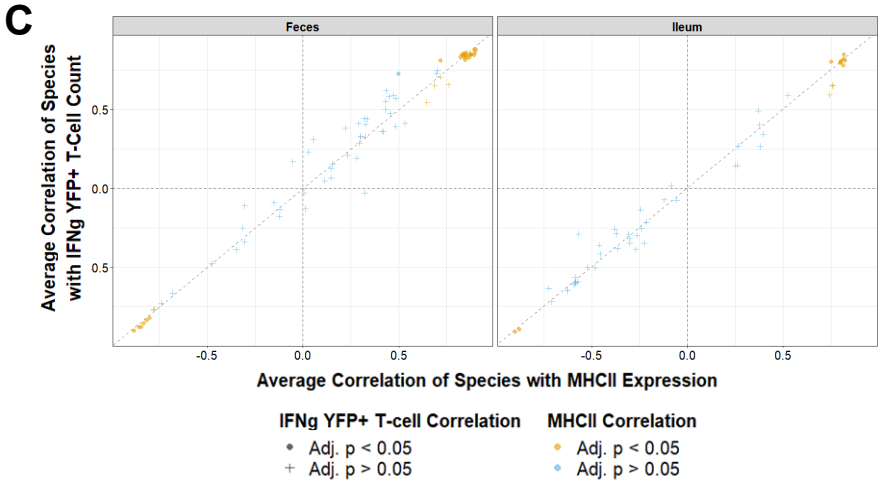

A
%MHC II+ d16 after Tamoxifen
MHC II MFI d16 after Tamoxifen
% MHCII+ in IEC
MHCII MFI in IEC
VillinCreERT2 neg
VillinCreERT2+ IAb f/fl
VillinCreERT2+ IFNγr f/fl
ADFH B6.Ifnγr-/-
B
Gated on live cells
CD45
CD19
CD326
CD3
NK1.1
CD4
CD8a
CD8b
Ly6G
Ly6c
CD49b
PDCA1
SiglecH
CD11b
CD11c
CD64
NK1.1+CD49bne
NK1.1+CD49b+
CD200R
C
JAX GREAT
ADFH GREAT
JAX GREAT ADFH GREAT
MHC II (gray: isotype)
IFNγR (gray: isotype)
CD4+ CD8a+ T (CD3+NK1.1negCD4+CD8a+)
CD8ab+ T (CD3+NK1.1negCD8a+CD8b+)
CD8aa+ T (CD3+NK1.1negCD8a+CD8bneg)
CD4+ T (CD3+NK1.1negCD4+)
NK (NK1.1+CD49b+CD200R neg)
ILC1 (NK1.1+CD49bnegCD200R+ CD11bneg)
D
% IAIE+ in Ileal IEC
IAIE MFI in Ileal IEC
% IFNγR+ in Ileal IEC
IFNγR MFI in Ileal IEC
%IAIE+ in live IEC
IAIE MFI in live IEC
%IFNγR+ in live IEC
IFNγR MFI in live IEC
JAX GREAT (Naive)
ADFH GREAT (Naive)
E
Naive
H
24h TBI
B6.WT (no YFP)
JAX GREAT
ADFH GREAT
IFNγ YFP
G
JAX GREAT (24h TBI)
ADFH GREAT (24h TBI)
F
IFNγ MFI (Ileum EL; Naive)
IFNγ+ cell count (Ileum EL; Naive)
Ileal EL
IFNγ MFI in subset
IFNγ+ cells (x 10^6/ organ)
ILC1
NK
CD4+ T
CD8aa+ T
CD8ab+ T
CD4+CD8+T
JAX GREAT (naive)
ADFH GREAT (naive)
N.S.
I
IFNγ MFI (Ileum EL; TBI 24h)
IFNγ+ cell count (Ileum EL; 24hTBI)
JAX GREAT (24h TBI)
ADFH GREAT (24h TBI)
IFNγ MFI (Ileum LP; Naive)
IFNγ+ cell count (Ileum LP; Naive)
Ileal LP
IFNγ MFI (Ileum LP; TBI 24h)
IFNγ+ cell count (Ileum LP; 24hTBI)
IFNγ MFI (Spleen; Naive)
IFNγ+ cell count (Spleen; Naive)
Spleen
all N.S.
IFNγ MFI (Sp; TBI 24h)
IFNγ+ cell count (Sp; 24hTBI)
N.S. except CD8ab+T

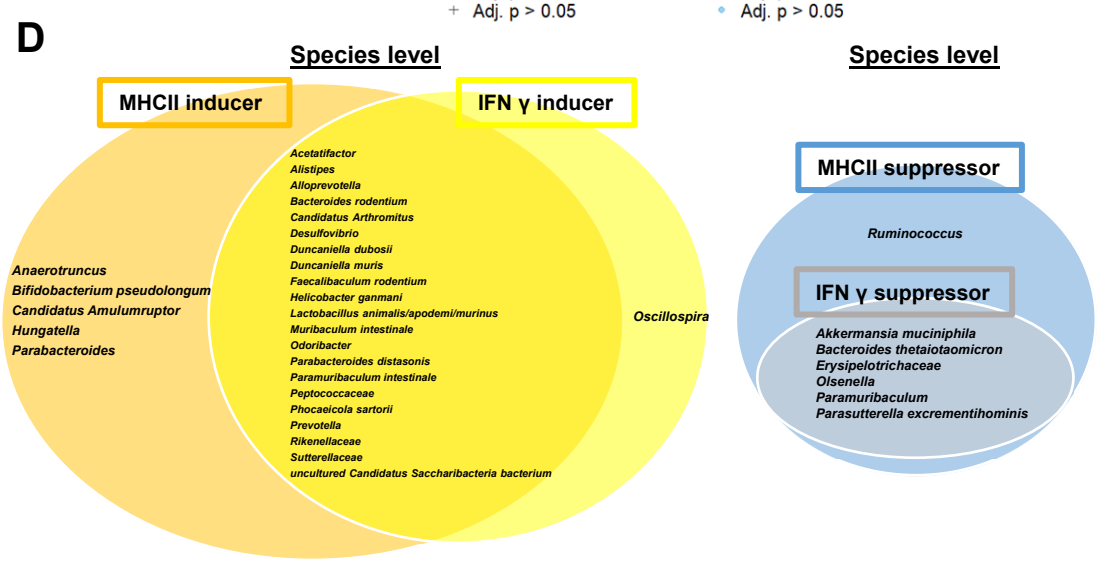
Figure S4, related to Figure 1–5. IFNγ secreting lymphocytes in the ileum control MHC II expression.

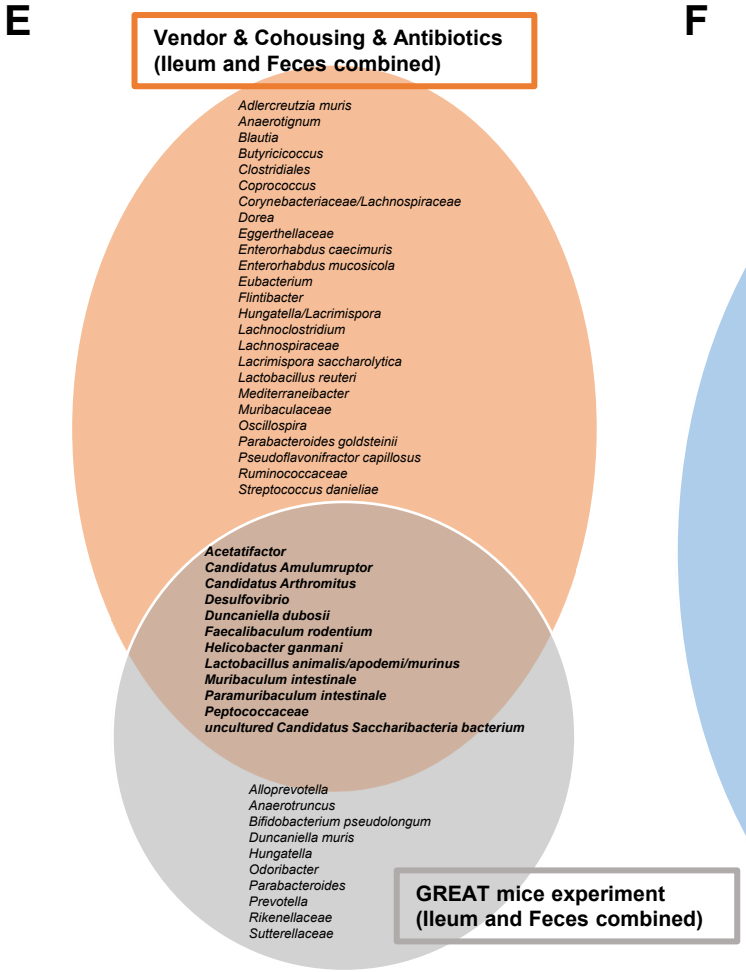
(**A**) Naïve *Villin*Cre-ER$^{T2\ neg}$, *Villin*Cre-ER^{T2+} *I-A*$^{b\ fl/fl}$, *Villin*Cre-ER^{T2+} *Ifnγr1*$^{fl/fl}$ were treated with tamoxifen for five days. 16 days after the initial tamoxifen administration, ileal IEC were assessed for MHC II expression. 2 experiments combined, n = 7-9 per group (mean ± SEM). Brown-Forsythe and Welch's ANOVA test and Dunnett's T3 multiple compatison test. ADFH B6.*Ifnγr*$^{-/-}$ data are shown as reference (n = 6). (**B - I**) Cellular compartments of naïve (**B – F**) or 24h post-TBI (1000 cGy) (**G – I**) age-matched female GREAT mice from JAX and ADFH. (**B**) Gating strategy for ileal EL, (**C**) MHC-II and IFNγR expression on IEC, (**D, G**) Quantification of MHC-II and IFNγR expression by IEC, (**E, H**) representative histograms of IFNγ-YFP MFI by each cell subset, and (**F, I**) IFNγ-YFP MFI and absolute number of IFNγ-expressing cells in the ileum and spleen. 2 experiments combined, n = 8 per group (mean ± SEM). t-test with Welch's correction. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001. N.S.: not significant. TBI: total body irradiation.


A
IFNg YFP+ T-cell Count (x10^6)
% MHCII+
MHCII MFI
Vendor
FH
Jax


B
PC1
PC2
Feces
Ileum
Batch
1st Exp
2nd Exp
Vendor
FH GREAT
Jax GREAT


C
Feces
Ileum
Average Correlation of Species with IFNg YFP+ T-Cell Count
Average Correlation of Species with MHCII Expression
IFNg YFP+ T-cell Correlation
Adj. p < 0.05
Adj. p > 0.05
MHCII Correlation
Adj. p < 0.05
Adj. p > 0.05


D
Species level
MHCII inducer
IFN γ inducer
Anaerotruncus
Bifidobacterium pseudolongum
Candidatus Amulumruptor
Hungatella
Parabacteroides
Acetatifactor
Alistipes
Alloprevotella
Bacteroides rodentium
Candidatus Arthromitus
Desulfovibrio
Duncaniella dubosii
Duncaniella muris
Faecalibaculum rodentium
Helicobacter ganmani
Lactobacillus animalis/apodemi/murinus
Muribaculum intestinale
Odoribacter
Parabacteroides distasonis
Paramuribaculum intestinale
Peptococcaceae
Phocaeicola sartorii
Prevotella
Rikenellaceae
Sutterellaceae
uncultured Candidatus Saccharibacteria bacterium
Oscillospira
Species level
MHCII suppressor
Ruminococcus
IFN γ suppressor
Akkermansia muciniphila
Bacteroides thetaiotaomicron
Erysipelotrichaceae
Olsenella
Paramuribaculum
Parasutterella excrementihominis


E
MHCII inducers (Species level)
Vendor & Cohousing & Antibiotics (Ileum and Feces combined)
Adlercreutzia muris
Anaerotignum
Blautia
Butyricicoccus
Clostridiales
Coprococcus
Corynebacteriaceae/Lachnospiraceae
Dorea
Eggerthellaceae
Enterorhabdus caecimuris
Enterorhabdus mucosicola
Eubacterium
Flintibacter
Hungatella/Lacrimispora
Lachnoclostridium
Lachnospiraceae
Lacrimispora saccharolytica
Lactobacillus reuteri
Mediterraneibacter
Muribaculaceae
Oscillospira
Parabacteroides goldsteinii
Pseudoflavonifractor capillosus
Ruminococcaceae
Streptococcus danieliae
Acetatifactor
Candidatus Amulumruptor
Candidatus Arthromitus
Desulfovibrio
Duncaniella dubosii
Faecalibaculum rodentium
Helicobacter ganmani
Lactobacillus animalis/apodemi/murinus
Muribaculum intestinale
Paramuribaculum intestinale
Peptococcaceae
uncultured Candidatus Saccharibacteria bacterium
Alloprevotella
Anaerotruncus
Bifidobacterium pseudolongum
Duncaniella muris
Hungatella
Odoribacter
Parabacteroides
Prevotella
Rikenellaceae
Sutterellaceae
GREAT mice experiment (Ileum and Feces combined)

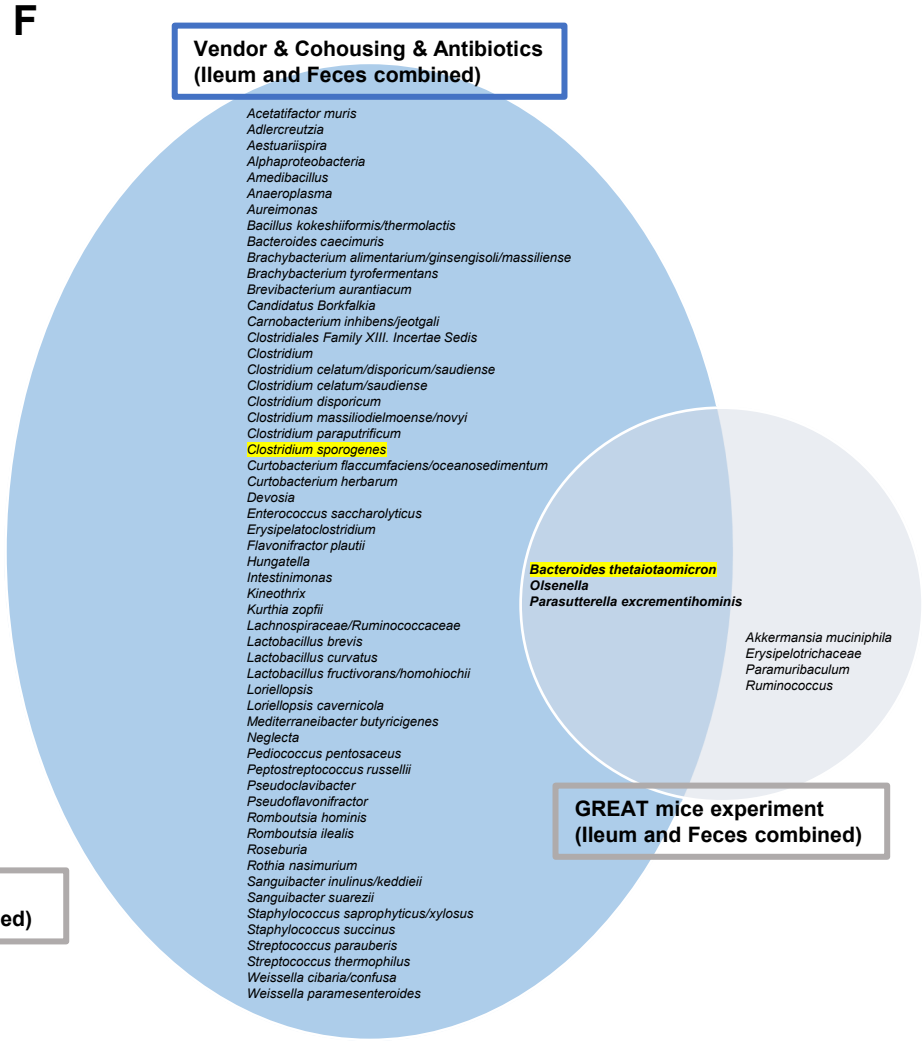
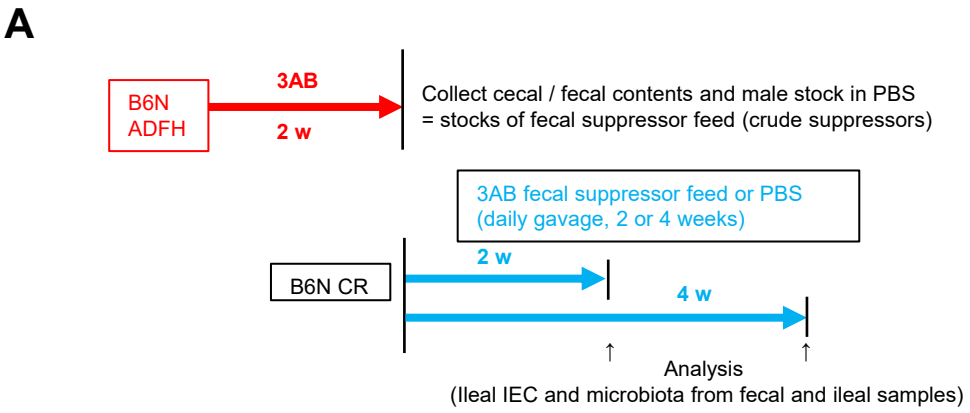
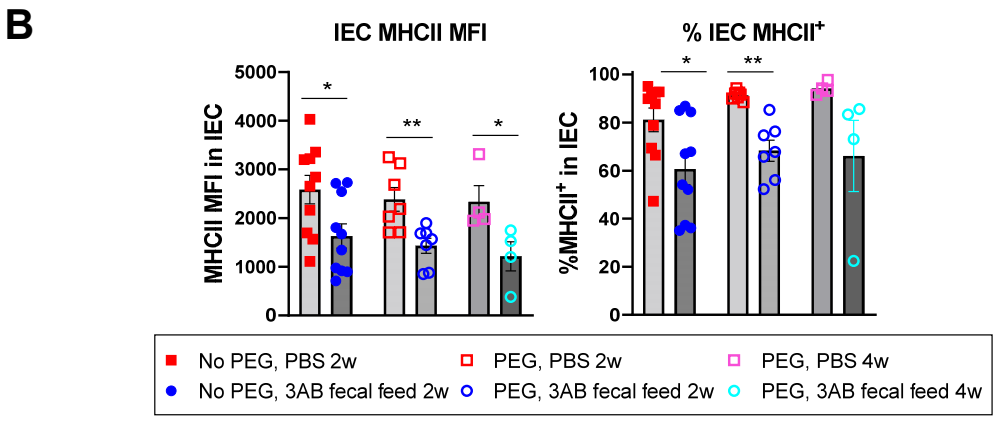
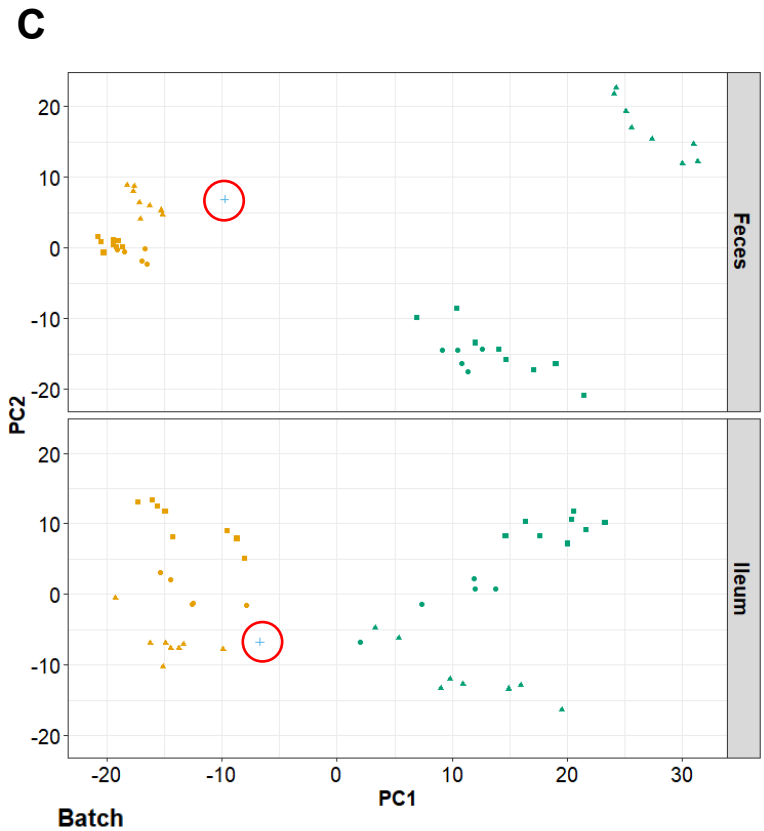

F
MHCII suppressors (Species level)
Vendor & Cohousing & Antibiotics (Ileum and Feces combined)
Acetatifactor muris
Adlercreutzia
Aestuariispira
Alphaproteobacteria
Amedibacillus
Anaeroplasma
Aureimonas
Bacillus kokeshiiformis/thermolactis
Bacteroides caecimuris
Brachybacterium alimentarium/ginsengisoli/massiliense
Brachybacterium tyrofermentans
Brevibacterium aurantiacum
Candidatus Borkfalkia
Carnobacterium inhibens/jeotgali
Clostridiales Family XIII. Incertae Sedis
Clostridium
Clostridium celatum/disporicum/saudiense
Clostridium celatum/saudiense
Clostridium disporicum
Clostridium massiliodielmoense/novyi
Clostridium paraputrificum
Clostridium sporogenes
Curtobacterium flaccumfaciens/oceanosedimentum
Curtobacterium herbarum
Devosia
Enterococcus saccharolyticus
Erysipelatoclostridium
Flavonifractor plautii
Hungatella
Intestinimonas
Kineothrix
Kurthia zopfii
Lachnospiraceae/Ruminococcaceae
Lactobacillus brevis
Lactobacillus curvatus
Lactobacillus fructivorans/homohiochii
Loriellopsis
Loriellopsis cavernicola
Mediterraneibacter butyricigenes
Neglecta
Pediococcus pentosaceus
Peptostreptococcus russellii
Pseudoclavibacter
Pseudoflavonifractor
Romboutsia hominis
Romboutsia ilealis
Roseburia
Rothia nasimurium
Sanguibacter inulinus/keddieii
Sanguibacter suarezii
Staphylococcus saprophyticus/xylosus
Staphylococcus succinus
Streptococcus parauberis
Streptococcus thermophilus
Weissella cibaria/confusa
Weissella paramesenteroides
Bacteroides thetaiotaomicron
Olsenella
Parasutterella excrementihominis
Akkermansia muciniphila
Erysipelotrichaceae
Paramuribaculum
Ruminococcus
GREAT mice experiment (Ileum and Feces combined)

Figure S5, related to Figure 1–5. Bacterial species in the GI tract correlate with both IEC MHC-II expression and IFNγ-producing T cells.

Fecal and ileal microbiota from naïve JAX and ADFH GREAT mice shown in **Figure S4** were analyzed by 16S rRNA gene sequencing. 2 experiments combined, n = 8 per group. (**A**) Spearman's correlation. Frequency of MHC-II$^+$ IEC vs. IFNγ-YFP$^+$ T cell counts: 0.92, $p < 0.001$. MHC-II MFI on IEC vs. IFNγ-YFP$^+$ T cell counts: 0.93, $p < 0.001$. (**B**) Principal component analysis (PCA) plot of centered log-ratio (CLR)-transformed abundance to visualize the fecal (**top**) and ileal (**bottom**) microbiota of mice from 2 batchs (experiments) and 2 vendors. (**C**) Spearman's correlation. Average correlation of species with MHC-II expression by IEC vs Average correlation of species with IFNγ-YFP$^+$ T cell counts of fecal samples (**left**: coeffifient = 0.98, $p < 0.001$) and ileal sample (**right**: coeffifient = 0.98, $p < 0.001$). (**D**) Venn diagrams of species level MHC-II inducers and IFNγ inducers (**left**) and MHC-II suppressors and IFNγ suppressors (**right**), combined from fecal and ileal samples. (**E – F**) Venn diagrams of species level of (**E**) MHC-II inducers and (**F**) suppressors determined across three experimental systems (Vendor, Cohousing and Antibiotic treatment) and vendor comparison of GREAT mice (JAX vs ADFH) combined from fecal and ileal samples. *Paramuribaculum, Ruminococcaceae, Bacteroides acidifaciens, Duncaniella, Prevotella, Alistipes, Bacteroides rodentium, Parabacteroides distasonis* and *Phocaeicola sartorii* had conflicting inducer and suppressor categorizations in separate experiments and are excluded here.


A
B6N
ADFH
3AB
2 w
Collect cecal / fecal contents and male stock in PBS
= stocks of fecal suppressor feed (crude suppressors)
3AB fecal suppressor feed or PBS
(daily gavage, 2 or 4 weeks)
B6N CR
2 w
4 w
Analysis
(Ileal IEC and microbiota from fecal and ileal samples)


B
IEC MHCII MFI
% IEC MHCII+
MHCII MFI in IEC
%MHCII+ in IEC
No PEG, PBS 2w
No PEG, 3AB fecal feed 2w
PEG, PBS 2w
PEG, 3AB fecal feed 2w
PEG, PBS 4w
PEG, 3AB fecal feed 4w


C
Feces
Ileum
PC1
PC2
Batch
1st exp (No PEG, 2w)
2nd exp (No PEG or with PEG, 2w)
3rd exp (with PEG, 2w or 4w Tx)
3AB-fecal Feed
Gavage Group
3AB-fecal
3AB-fecal Feed
PBS

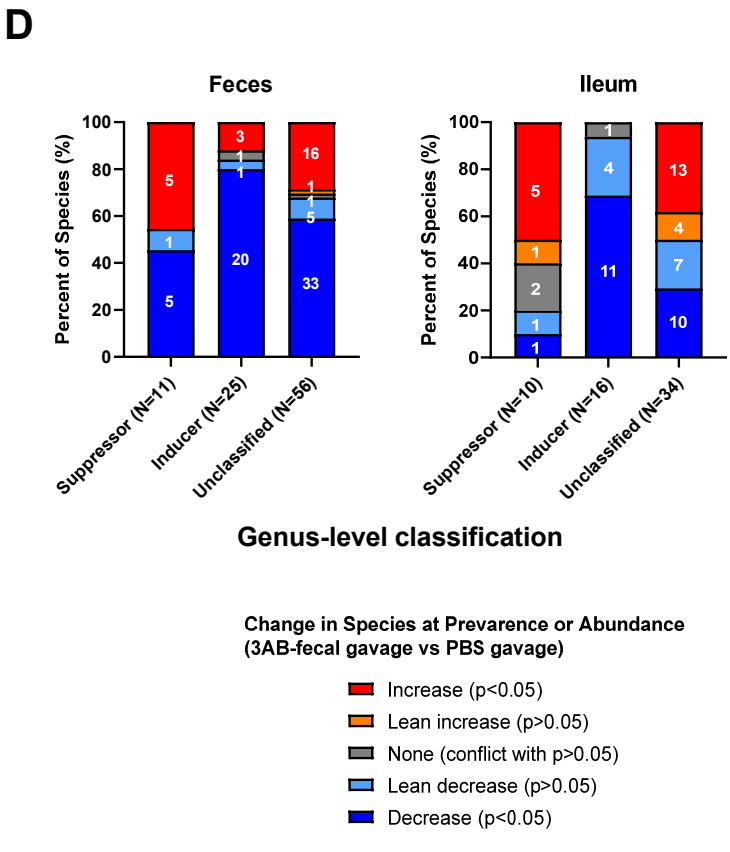
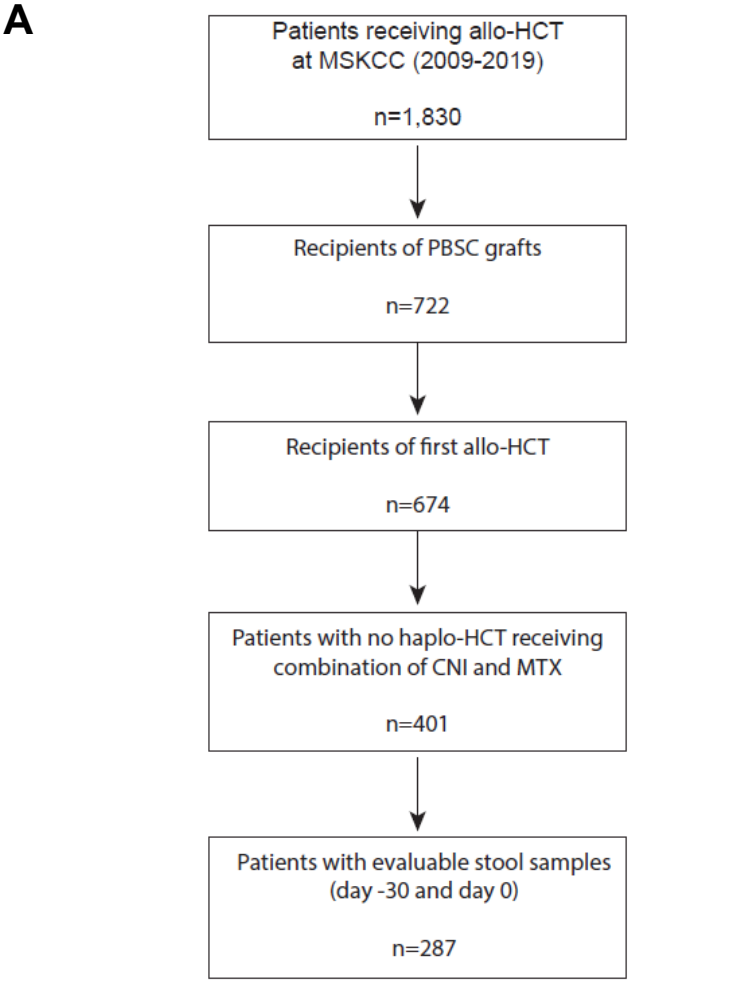
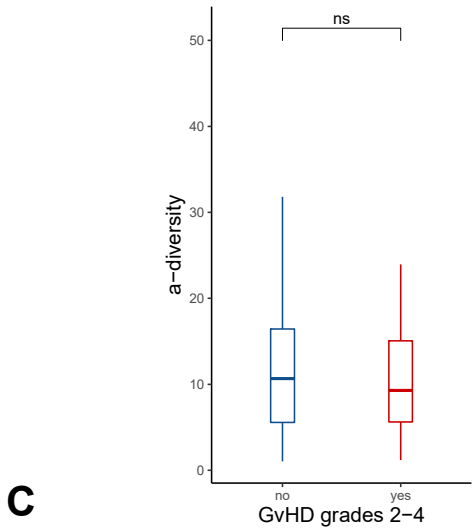

D
Feces
Ileum
Percent of Species (%)
Suppressor (N=11)
Inducer (N=25)
Unclassified (N=56)
Suppressor (N=10)
Inducer (N=16)
Unclassified (N=34)
Genus-level classification
Change in Species at Prevarence or Abundance
(3AB-fecal gavage vs PBS gavage)
Increase (p<0.05)
Lean increase (p>0.05)
None (conflict with p>0.05)
Lean decrease (p>0.05)
Decrease (p<0.05)

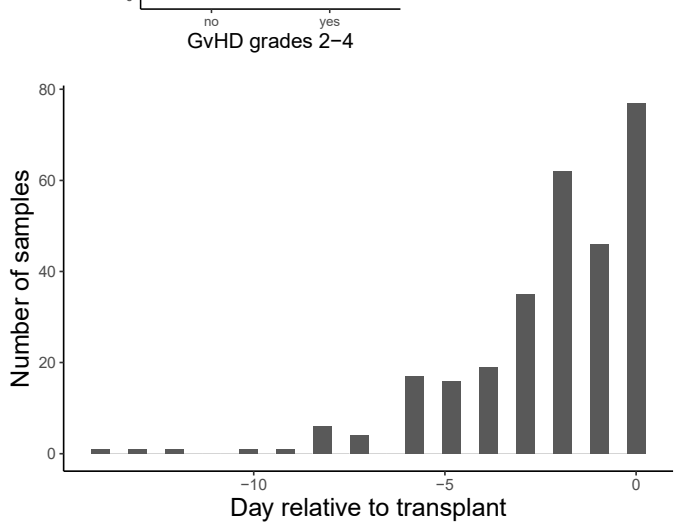
Figure S6, related to Figure 6. Transfer of MHC-II suppressors reduce MHC-II expression by IEC in the ileum.

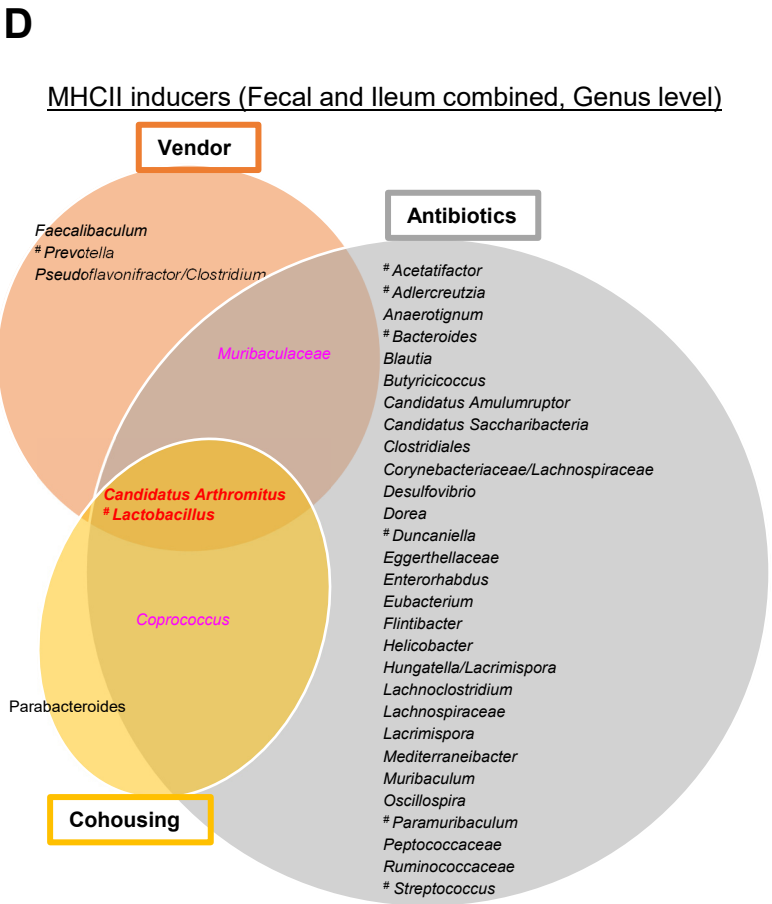
(**A**) Experimental schema. Naïve CR B6N mice were administered 3AB suppressor enriched fecal feed or PBS (200 µl/dose) by oral gavage daily for 2 or 4 weeks, then assessed for ileal IEC and fecal and ileal 16S rRNA gene sequencing analysis with or without PEG conditioning as described in Methods (**B**) Quantification of MFI and % MHC-II expression on IEC ($CD45^{neg}CD326^{+}$). No PEG, 2 week gavage treatment: n = 10 per group, 2 experiments combined. PEG conditioned, 2 week gavage treatment: n = 7 per group, 2 experiments combined. PEG conditioned, 4 week gavage treatment: n = 4 per group, 1 experiment. t-test with Welch's correction. *$p < 0.05$, **$p < 0.01$. (**C-D**) 16S rRNA gene sequencing of fecal and ileal samples. (**C**) PCA plot of CLR-transformed abundance of fecal (**top**) and ileal (**bottom**) microbiota of mice from 3 experiments. The contents of 3AB suppressor enriched feed was included in the sequencing. (**D**) Detected species were assigned as MHC-II inducers, suppressors or unclassified bacteria based on the classification at the genus-level from prior experimental systems (Vendor, Cohousing and Antibiotic treatment). The number of species that changed in terms of prevalence or abundance after 3AB suppressor enriched feed treatment versus PBS treatment is shown in each MHC-II group. Change was classified by the direction of change in prevalence or abundance (increased or decreased) if the corresponding unadjusted p-value was <0.05. If the p-value > 0.05, change was classified as "lean increased" or "lean decreased" unless the change in prevalence and abundance disagreed, in which case the change was classified as "none."



Allo-HCT: allogeneic hematopoietic cell transplant; MSKCC: Memorial Sloan Kettering Cancer Center; PBSC: peripheral blood stem cell graft; CNI: calcineurin inhibitor; MTX: methotrexate.







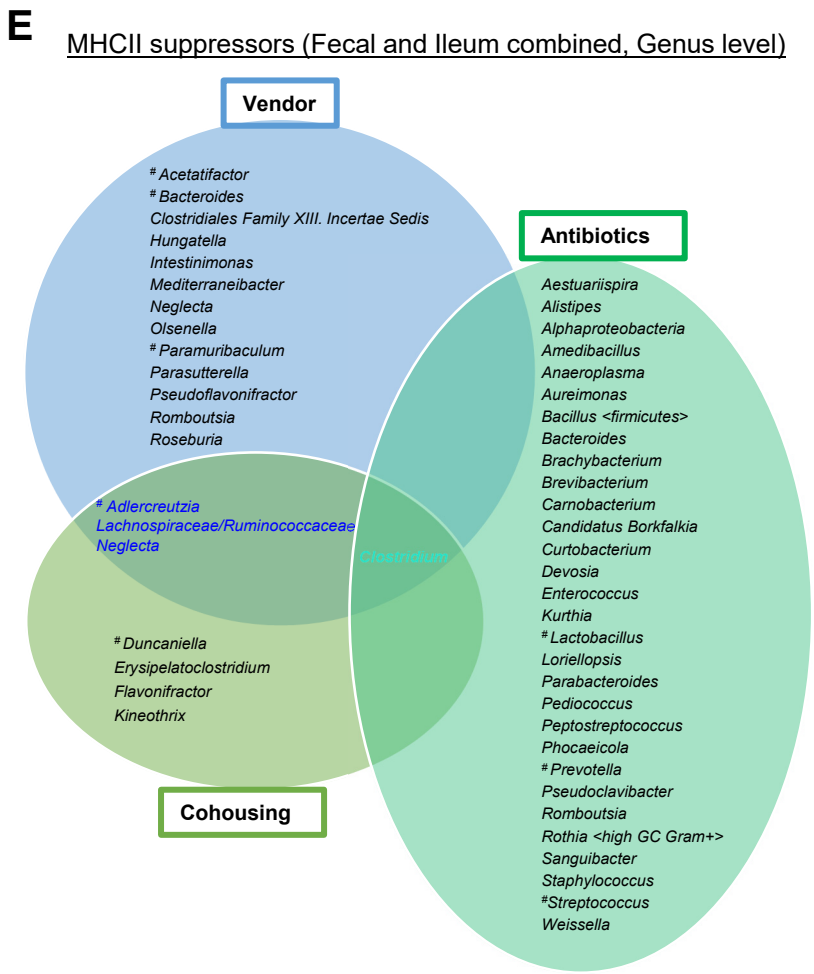


Figure S7, related to Figure 7. Consort flow diagram of clinical sample selection and genus-rank MHC-II inducers and suppressors.

(**A**) Patients receiving alloSCT at Memorial Sloan Kettering Cancer Center (MSKCC) were screened to include a total of 287 patients that received their first alloHCT with peripheral blood stem cells (PBSC) and GVHD prophylaxis with a calcineurin inhibitor (CNI) and methotrexate (MTX). (**B**) α-diversity using the Simpson reciprocal index in GVHD grades 2-4 vs grade 0-1. P = 0.36, one-way ANOVA. (**C**) Histogram demonstrating the distribution of samples included in this analysis. (**D – E**) Venn diagrams of genus rank of (**D**) MHC-II inducers and (**E**) suppressors determined across prior experimental systems (Vendor, Cohousing and Antibiotic treatment) combined from fecal and ileal samples. [#]These genera include species categorized as inducers or suppressors.

Table S1 , related to Figure 7. Patient characteristics.

	All patients n=287 (%)
Sex = M (%)	187 (65.2)
Age (mean (SD))	57.1 (12.3)
Disease	
Leukemia	131 (45.6)
Lymphoma	115 (40.0)
MDS/MPN	37 (12.9)
Multiple Myeloma	4 (1.4)
Conditioning Intensity (%)	
Ablative	77 (26.8)
Non-ablative	69 (24.0)
Reduced Intensity	141 (49.1)
Regimen	
Fludarabine/Melfalan	107 (37.3)
Cyclophosphamide/Fludarabine/TBI	70 (24.4)
Fludarabine/Busulfan	52 (18.1)
Cyclophsophamide/fludarabine/thiotepa/TBI	27 (9.4)
Busulfan/Melfalan	11 (3.8)
Cyclophosphamide/thiotepa/TBI	8 (2.8)
Clofarabine/melphalan/thiotepa	6 (2.1)
Busulfan/cyclophosphamide	2 (0.7)
Cyclophosphamide/TBI	2 (0.7)
Etoposide/TBI	1 (0.3)
Carmustine/Cytarabine/Etoposide/Melphalan	1 (0.3)
Donor match (%)	
Related Identical	94 (32.8)
Unrelated Identical	176 (61.3)
Unrelated Non-identical	17 (5.9)
Graft (%)	
PBSC	287 (100)
Commorbidity/age index (m=259)	
0	4 (1.5)
1-2	89 (34.4)
≥3	166 (64.1)
GVHD (first 100 days) = Y (%)	142 (49.5)
Grade 1	25 (17.6)
Grade 2	83 (58.5)
Grade 3	26 (18.3)
Grade 4	8 (5.6)
TRM	45 (15.7)

MDS/MPN: myelodysplastic syndrome/myeloproliferative neoplasm;
GvHD: graft versus host disease; TRM: transplant related mortality within 2 years.

Table S2, related to Figure 7. Antibiotic exposure prior to stool sample collection

	GVHD gr 0-1 (n=170)	GVHD gr 2-4 (n=117)	Total (n=287)
Cephalosporin IV	16	12	28
Cephalosporin PO	1	0	1
Trimethoprim/Sulfamethoxazole PO	20	9	29
Trimethoprim/Sulfamethoxazole IV	3	2	5
Vancomycin IV	14	11	25
Vancomycin PO	1	0	1
Quinolone IV	5	1	6
Quinolone PO	2	9	11
Piperacillin/Tazobactam IV	5	2	7
Metronidazole PO	1	1	2
Metronidazole IV	1	0	1
Clindamycin IV	1	0	1
Azithromycin PO	1	0	1
Nitrofurantoin PO	1	0	1
Penicillin V	1	0	1

Table S3, related to Figure 7. Immunofluorescence staining panel.

Position	Antibody	Manufacturer	catalog #	Host	Clone	Dilution	Concentration	Secondary	Fluorophore
1	EpCAM	Biolegend	32402	Mouse	9C4	1:400	1.25ug/ml	Leica Powervision mouse HRP	Akoya Opal 570 reagent
2	CD45 LCA	DAKO	M0701	Mouse	2B11 + PD7/26	1:500	0.75 ug/ml	Akoya Opal polymer ms+rbt HRP	Akoya Opal 520 reagent
3	HLA-DR+DP+DQ	Abcam	ab7856	Mouse	CR3/43	1:500	0.4ug/ml	Akoya Opal polymer ms+rbt HRP	Akoya Opal 690 reagent

Position	Antibody	Manufacturer	catalog #	Host	Clone	Dilution	Concentration	Secondary	Fluorophore
1	EpCAM	Biolegend	32402	Mouse	9C4	1:400	1.25ug/ml	Leica Powervision mouse HRP	Akoya Opal 570 reagent
2	CD45 LCA	DAKO	M0901	Mouse	2B11 + PD7/26	1:500	0.75 ug/ml	Akoya Opal polymer ms+rbt HRP	Akoya Opal 520 reagent
3	Mouse IgG1	R&D systems	MAB002	Mouse	11711	1:500	0.4ug/ml	Akoya Opal polymer ms+rbt HRP	Akoya Opal 690 reagent

Table S5, related to Figure 6. Culture media

Component	Amount (mg if there is no note)	Supplier	Catalog#
NaHCO3	28.75	Sigma	S4019
MgSO4.7H2O	14.38	Sigma	M63-500
NaCl	57.50	Sigma	S3014
CaCl2	0.58	Sigma	C7902
FeSO4	0.29	Sigma	F8048
BBL Tryptone peptone	10029.14	BD	211921
Bacto Yeast extract	5014.57	BD	212750
Glucose	2005.83	Sigma	G8270
Cysteine (free base)	501.46	Sigma	C1276
KH2PO4	4111.95	Sigma	P0662
K2HPO4	12235.56	Sigma	P3786
meat extract	5	Sigma	70164
Vitamin K	1	Sigma	M5625
Hematin	1 ml	Sigma	H3281
ATCC Viotamin mix	1 ml	ATCC	ATCC MD-VS
ATCC Mineral mix	1 ml	ATCC	ATCC MD-TMS
Tween 80	200 ul	Sigma	P1754
cellobiose	1	Sigma	C7252
maltose	1	Sigma	M5885
fructose	1	Sigma	F0127
sodium acetate	1	Fisher (Fluka)	BP333-500
sodium sulfate	2	Sigma	S9627
malic acid	1	Sigma	M7937
dH2O	1 L		