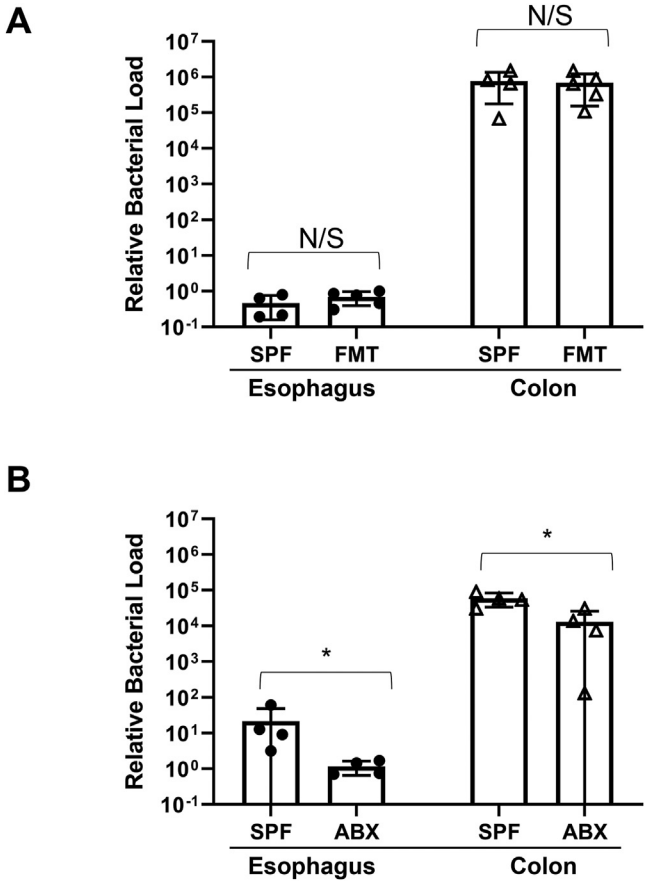
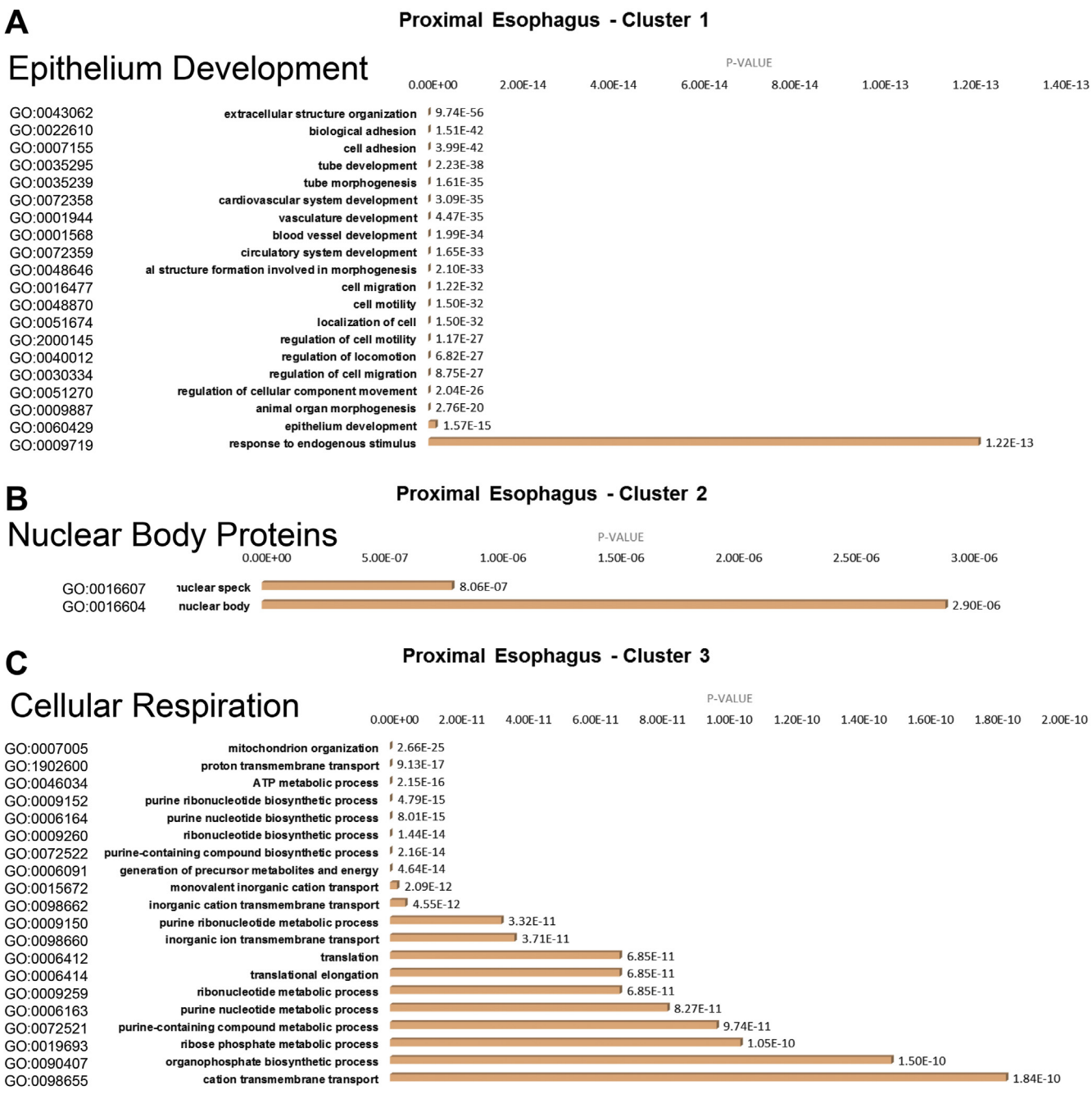
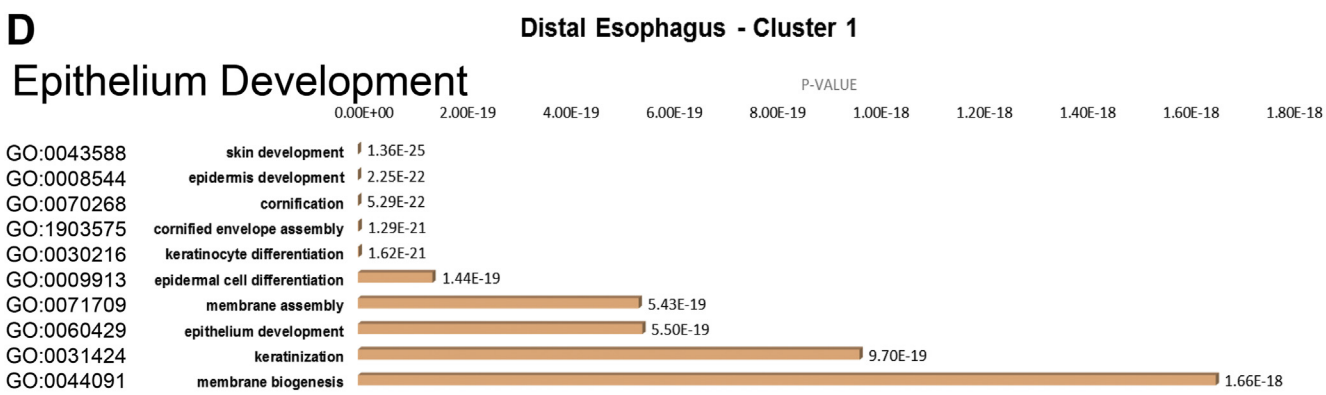
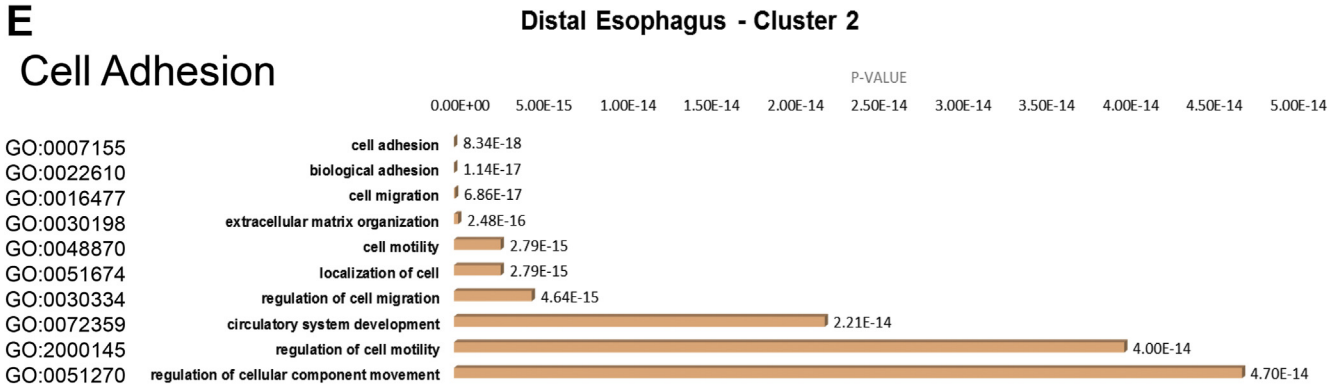


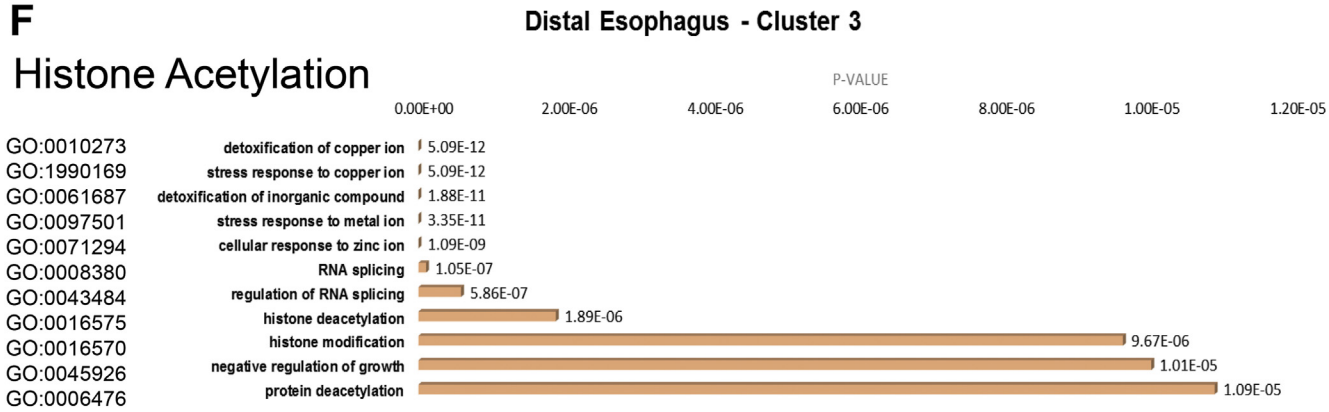
Supplementary Figure 1. Relative tissue bacterial load. (*A*) Bacterial load from PHF SPF FMT mice and (*B*) antibiotic-treated mice in esophagus and colon. Relative bacterial load was examined by quantitative reverse transcriptase polymerase chain reaction compared with host genomic DNA via the $2^{-\Delta\Delta Ct}$ method. Data are from corresponding esophageal microbiota analysis (Figures 1 and 5). ABX, antibiotics. Data are represented as mean ± standard deviation and are pooled from 3 independent experiments. Statistics by unpaired *t* test. *$P \leq .05$; N/S, nonsignificant.



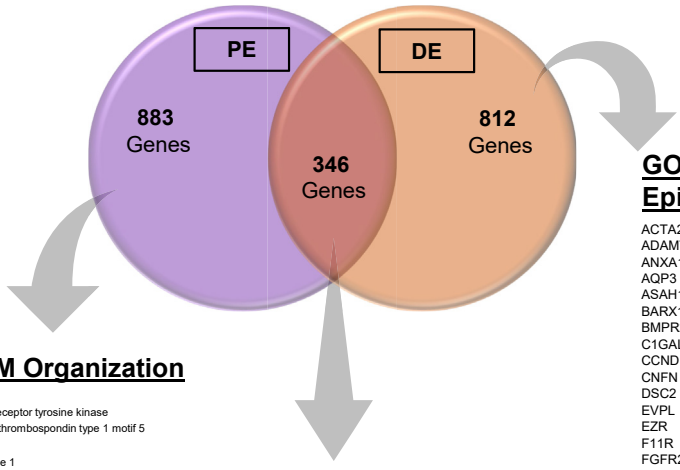
Supplementary Figure 2. Gene ontology (GO) functional enrichment analysis of gene clusters differentially expressed due to colonization. Differentially expressed genes in the PE (*A*–*C*) and DE (*D*–*F*) as measured by RNA-seq in Figure 2 were analyzed with TOPPFUN (false discovery rate [FDR]-adjusted $P < .05$ and gene limit $n \leq 2000$), and top significantly enriched GO terms with corresponding *P* values were plotted.







Supplementary Figure 2. continued



GO:0030198 - ECM Organization

ABL2	ABL proto-oncogene 2, non-receptor tyrosine kinase
ADAMTS5	ADAM metallopeptidase with thrombospondin type 1 motif 5
AEBP1	AE binding protein 1
ANTXR1	ANTXR cell adhesion molecule 1
APLP2	amyloid beta precursor like protein 2
BGN	biglycan
COL12A1	collagen type XII alpha 1 chain
COL15A1	collagen type XV alpha 1 chain
COL16A1	collagen type XVI alpha 1 chain
COL18A1	collagen type XVIII alpha 1 chain
COL1A1	collagen type I alpha 1 chain
COL1A2	collagen type I alpha 2 chain
COL3A1	collagen type III alpha 1 chain
COL4A1	collagen type IV alpha 1 chain
COL4A2	collagen type IV alpha 2 chain
COL4A6	collagen type IV alpha 6 chain
COL5A1	collagen type V alpha 1 chain
COL5A2	collagen type V alpha 2 chain
COL5A3	collagen type V alpha 3 chain
COL6A1	collagen type VI alpha 1 chain
COL6A2	collagen type VI alpha 2 chain
COL6A3	collagen type VI alpha 3 chain
COL8A1	collagen type VIII alpha 1 chain
CREB3L1	cAMP responsive element binding protein 3 like 1
CRISPLD2	cysteine rich secretory protein LCCL domain containing 2
CTSK	cathepsin K
DCN	decorin
EMILIN1	elastin microfibril interfacer 1
FBLN2	fibulin 2
FBLN5	fibulin 5
FBN1	fibrillin 1
FERMT1	fermitin family member 1
GSN	gelsolin
HSPG2	heparan sulfate proteoglycan 2
ITGA5	integrin subunit alpha 5
ITGAM	integrin subunit alpha M
JAM2	junctional adhesion molecule 2
KLK5	kallikrein related peptidase 5
KLK7	kallikrein related peptidase 7
LAMA3	laminin subunit alpha 3
LAMC1	laminin subunit gamma 1
LOXL2	lysyl oxidase like 2
LRP1	LDL receptor related protein 1
MFAP4	microfibril associated protein 4
MMP14	matrix metallopeptidase 14
MMP19	matrix metallopeptidase 19
MMP2	matrix metallopeptidase 2
MYO1E	myosin IE
NF1	neurofibromin 1
NPNT	nephronectin
OLFML2A	olfactomedin like 2A
PDGFB	platelet derived growth factor subunit B
PDGFRA	platelet derived growth factor receptor alpha
PXDN	peroxidasin
SCX	scleraxis bHLH transcription factor
SERPINH1	serpin family H member 1
SFRP2	secreted frizzled related protein 2
SH3PXD2B	SH3 and PX domains 2B
SMPD3	sphingomyelin phosphodiesterase 3
SPARC	secreted protein acidic and cysteine rich
SPOCK2	osteonectin, cwcv and kazal like domains proteoglycan 2
TGFB2	transforming growth factor beta 2
TGFBI	transforming growth factor beta induced
TIMP2	TIMP metallopeptidase inhibitor 2
TNC	tenascin C
TNXB	tenascin XB
VCAN	versican
VTN	vitronectin

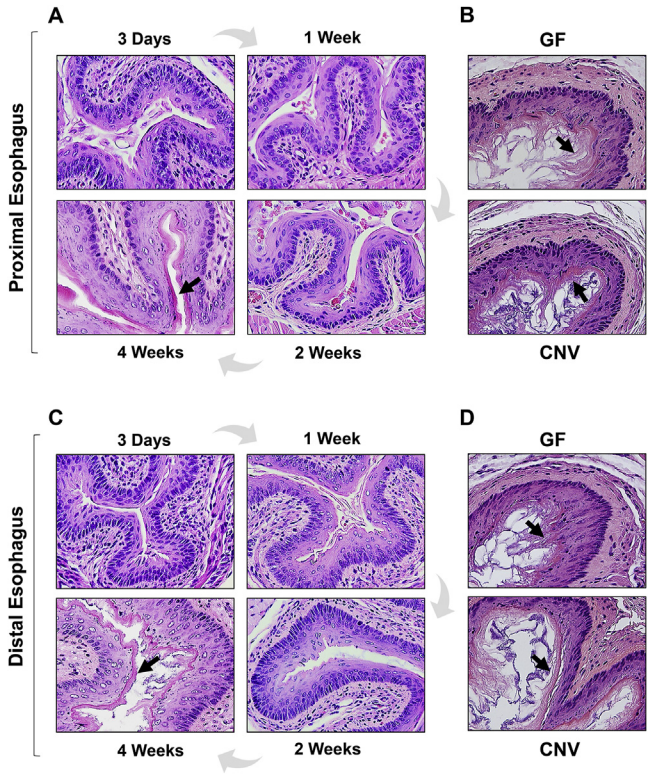
GO:0007155 - Cell Adhesion

ACTN1	actinin alpha 1
AOC3	amine oxidase copper containing 3
APOD	apolipoprotein D
APP	amyloid beta precursor protein
CAMSAP3	calmodulin regulated spectrin associated protein family member 3
CASP3	caspase 3
CAV1	caveolin 1
CCDC80	coiled-coil domain containing 80
CELSR1	cadherin EGF LAG seven-pass G-type receptor 1
CLSTN1	calsyntenin 1
COL14A1	collagen type XIV alpha 1 chain
COL7A1	collagen type VII alpha 1 chain
CTNND1	catenin delta 1
DLC1	DLC1 Rho GTPase activating protein
DOCK1	dedicator of cytokinesis 1
DSC3	desmocollin 3
DSG3	desmoglein 3
EMILIN2	elastin microfibril interfacer 2
ENG	endoglin
ENTPD1	ectonucleoside triphosphate diphosphohydrolase 1
FBLN1	fibulin 1
FLNA	filamin A
FN1	fibronectin 1
GPNMB	glycoprotein nmb
IGFBP7	insulin like growth factor binding protein 7
ITGA6	integrin subunit alpha 6
ITGAV	integrin subunit alpha V
KDR	kinase insert domain receptor
KITLG	KIT ligand
L1CAM	L1 cell adhesion molecule
LAMA2	laminin subunit alpha 2
LAMA4	laminin subunit alpha 4
LAMB1	laminin subunit beta 1
LGALS4	galectin 4
LPP	LIM domain containing preferred translocation partner in lipoma
MCAM	melanoma cell adhesion molecule
MEGF9	multiple EGF like domains 9
MPZ	myelin protein zero
MYH9	myosin heavy chain 9
NFKBIZ	NFKB inhibitor zeta
NID1	nidogen 1
NID2	nidogen 2
NRP2	neuropilin 2
NTN1	netrin 1
PDE5A	phosphodiesterase 5A
PECAM1	platelet and endothelial cell adhesion molecule 1
PODXL	podocalyxin like
POSTN	periostin
PRNP	prion protein
RND3	Rho family GTPase 3
SMOC2	SPARC related modular calcium binding 2
SPARCL1	SPARC like 1
THBS1	thrombospondin 1
THBS2	thrombospondin 2
VCL	vinculin
VEGFA	vascular endothelial growth factor A
ZBTB16	zinc finger and BTB domain containing 16

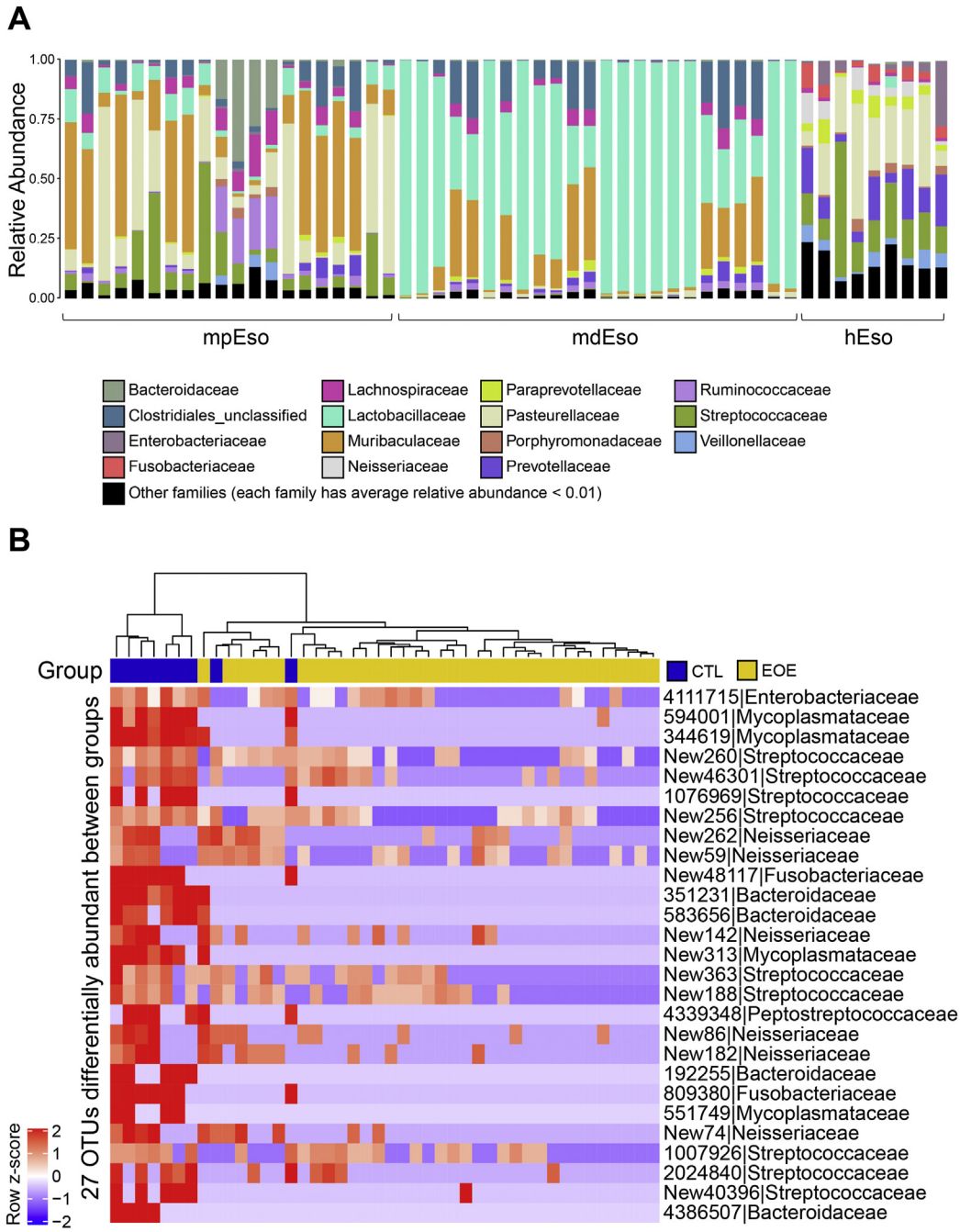
GO:0060429 – Epithelial Differentiation

ACTA2	actin alpha 2, smooth muscle
ADAMTSL4	ADAMTS like 4
ANXA1	annexin A1
AQP3	aquaporin 3 (Gill blood group)
ASAH1	N-acylsphingosine amidohydrolase 1
BARX1	BARX homeobox 1
BMPR2	bone morphogenetic protein receptor type 2
C1GALT1	C1 galactosyltransferase 1
CCND1	cyclin D1
CNFN	cornifelin
DSC2	desmocollin 2
EVPL	envoplakin
EZR	ezrin
F11R	F11 receptor
FGFR2	fibroblast growth factor receptor 2
FGFR3	fibroblast growth factor receptor 3
FOXF1	forkhead box F1
FRMD6	FERM domain containing 6
GJA1	gap junction protein alpha 1
GPSM2	G protein signaling modulator 2
GREM1	gremlin 1, DAN family BMP antagonist
GSTA1	glutathione S-transferase alpha 1
HEG1	heart development protein with EGF like domains 1
HIF1A	hypoxia inducible factor 1 subunit alpha
HNRNPH3	heterogeneous nuclear ribonucleoprotein H3
IL1B	interleukin 1 beta
IRF6	interferon regulatory factor 6
JUP	junction plakoglobin
KLF15	Kruppel like factor 15
KLF4	Kruppel like factor 4
KLK13	kallikrein related peptidase 13
KLK14	kallikrein related peptidase 14
KRT10	keratin 10
KRT13	keratin 13
KRT14	keratin 14
KRT15	keratin 15
KRT17	keratin 17
KRT18	keratin 18
KRT19	keratin 19
KRT32	keratin 32
KRT4	keratin 4
KRT5	keratin 5
KRT6A	keratin 6A
KRT8	keratin 8
KRT80	keratin 80
LATS2	large tumor suppressor kinase 2
LBH	LBH regulator of WNT signaling pathway
LCE3C	late cornified envelope 3C
MAFG	MAF bZIP transcription factor G
MET	MET proto-oncogene, receptor tyrosine kinase
NOTCH1	notch receptor 1
NPY	neuropeptide Y
NR2F2	nuclear receptor subfamily 2 group F member 2
PALLD	palladin, cytoskeletal associated protein
PBRM1	polybromo 1
PERP	p53 apoptosis effector related to PMP22
PKP1	plakophilin 1
POF1B	POF1B actin binding protein
PPL	periplakin
PRKCH	protein kinase C eta
PTN	pleiotrophin
RAP1A	RAP1A, member of RAS oncogene family
RAP1B	RAP1B, member of RAS oncogene family
RAP2B	RAP2B, member of RAS oncogene family
RARG	retinoic acid receptor gamma
REST	RE1 silencing transcription factor
S1PR3	sphingosine-1-phosphate receptor 3
SDC1	syndecan 1
SFN	stratifin
SMO	smoothened, frizzled class receptor
SPRR1A	small proline rich protein 1A
SPRR1B	small proline rich protein 1B
SPRR3	small proline rich protein 3
SRSF6	serine and arginine rich splicing factor 6
STAT1	signal transducer and activator of transcription 1
SULT2B1	sulfotransferase family 2B member 1
TAGLN	transgelin
TGFB1I1	transforming growth factor beta 1 induced transcript 1
TGM1	transglutaminase 1
TGM3	transglutaminase 3
TMEM38B	transmembrane protein 38B
TMEM79	transmembrane protein 79
TNFRSF1A	TNF receptor superfamily member 1A
TXNIP	thioredoxin interacting protein
UPK1B	uroplakin 1B
VSIG1	V-set and immunoglobulin domain containing 1
WNT7B	Wnt family member 7B
ZFP36	ZFP36 ring finger protein

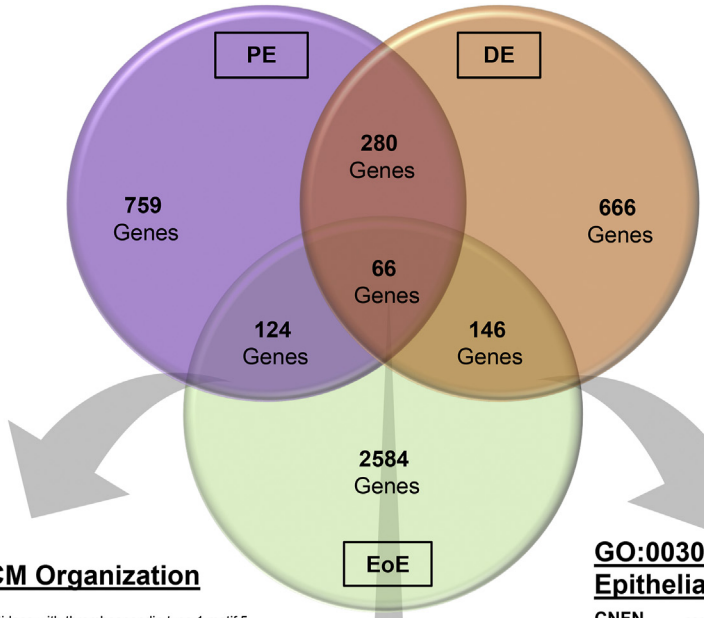
Supplementary Figure 3. Gene ontology (GO) functional enrichment analysis of genes differentially expressed due to colonization. Differentially expressed genes by RNA-seq from the PE and DE (Figure 2*B*; Supplementary Tables 1–2) were integrated, and common and unique gene groups were analyzed with TOPPFUN (FDR-adjusted $P < .05$ and gene limit $n \leq 2000$). The top representative, significantly enriched GO term with corresponding genes from input was summarized for each group. The complete GO functional analysis of gene groups is in Supplementary Table 3. ECM, extracellular matrix.



Supplementary Figure 4. Esophageal tissue morphology as a function of microbiota colonization. H&E staining of proximal (*A, B*) and distal (*C, D*) esophagus (×20 magnification). Tissues obtained from SPF (*A, C*) and GF and CNV (*B, D*) mice. *Images* are representative from 3 independent experiments; n are for each proximal and distal site: 3 days, n = 10; 1 week, n = 6; 2 weeks, n = 10; 4 weeks, n = 9; GF, n = 9; CNV, n = 9.



Supplementary Figure 5. Mouse and human esophageal microbiota at homeostasis and in patients with EoE. (*A*) 16S rRNA analysis from murine proximal (mpEso) and distal (mdEso) esophagi of SPF littermates from Figure 4 and Supplementary Table 4 compared with non-EoE human samples (Supplementary Table 5). Taxonomic composition is represented at the family level, where each *vertical bar* represents 1 individual mouse or human. (*B*) 16S rRNA analysis from patients with EoE and human non-EoE controls (Supplementary Table 5). *Heatmap* of differentially abundant OTUs between sites (DS-FDR 0.10; Supplementary Table 5) labeled at the individual OTU level (*right*). Mouse data are pooled from 3 independent experiments (*A*); n = 24 for each site (48 total samples): 24 for mdEso and 24 for mpEso. Human data obtained from n = 9 control and n = 35 patients with EoE. CTL, control; DS-FDR, discrete false discovery rate; EoE, Eosinophilic esophagitis; hEso, human esophagus.



GO:0030198 - ECM Organization

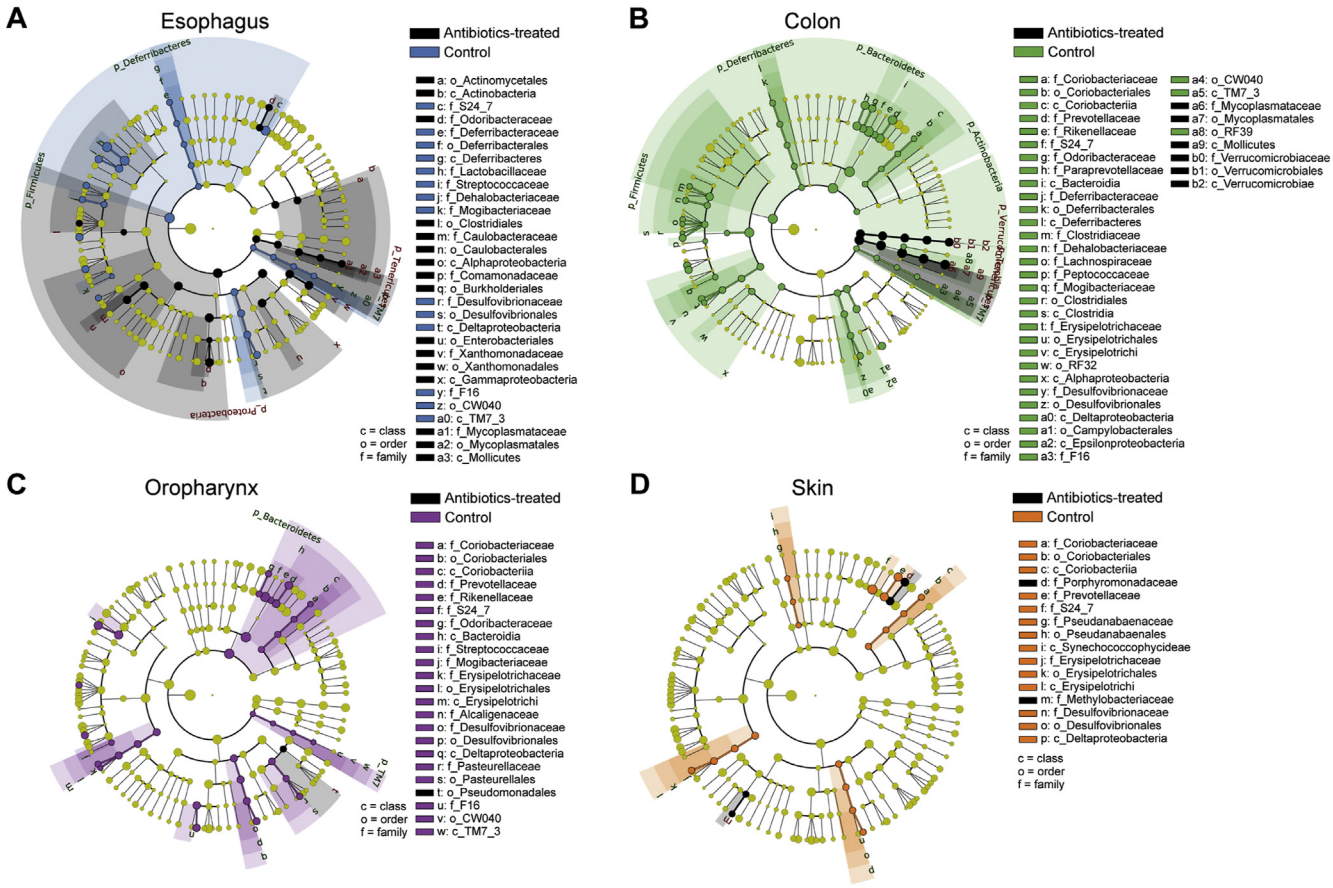
ADAMTS5	ADAM metallopeptidase with thrombospondin type 1 motif 5
COL12A1	collagen type XII alpha 1 chain
COL18A1	collagen type XVIII alpha 1 chain
COL1A1	collagen type I alpha 1 chain
COL1A2	collagen type I alpha 2 chain
COL3A1	collagen type III alpha 1 chain
COL4A6	collagen type IV alpha 6 chain
COL6A1	collagen type VI alpha 1 chain
COL6A2	collagen type VI alpha 2 chain
COL6A3	collagen type VI alpha 3 chain
CREB3L1	cAMP responsive element binding protein 3 like 1
CTSK	cathepsin K
EMILIN1	elastin microfibril interfacer 1
FBN1	fibrillin 1
ITGAM	integrin subunit alpha M
KLK5	kallikrein related peptidase 5
MMP14	matrix metallopeptidase 14
MMP19	matrix metallopeptidase 19
PDGFB	platelet derived growth factor subunit B
PDGFRA	platelet derived growth factor receptor alpha
PXDN	peroxidasin
SH3PXD2B	SH3 and PX domains 2B
TIMP2	TIMP metallopeptidase inhibitor 2

GO:0030855 – Epithelial Differentiation

CNFN	cornifelin
DSC2	desmocollin 2
GJA1	gap junction protein alpha 1
HEG1	heart development protein with EGF like domains 1
HIF1A	hypoxia inducible factor 1 subunit alpha
KLF15	Kruppel like factor 15
KRT13	keratin 13
KRT32	keratin 32
KRT4	keratin 4
LBH	LBH regulator of WNT signaling pathway
MET	MET proto-oncogene, receptor tyrosine kinase
PALLD	palladin, cytoskeletal associated protein
PPL	periplakin
PTN	pleiotrophin
RAP2B	RAP2B, member of RAS oncogene family
SPRR1A	small proline rich protein 1A
SPRR1B	small proline rich protein 1B
SPRR3	small proline rich protein 3
SULT2B1	sulfotransferase family 2B member 1
TGM1	transglutaminase 1
TGM3	transglutaminase 3
TMEM79	transmembrane protein 79
UPK1B	uroplakin 1B
ZFP36	ZFP36 ring finger protein

GO:0016477 - Cell Migration

ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif 1
APCDD1	APC down-regulated 1
CAMSAP3	calmodulin regulated spectrin associated protein family member 3
EDNRB	endothelin receptor type B
F2R	coagulation factor II thrombin receptor
FN1	fibronectin 1
GPLD1	glycosylphosphatidylinositol specific phospholipase D1
ITGAV	integrin subunit alpha V
LIMA1	LIM domain and actin binding 1
MEGF9	multiple EGF like domains 9
NR4A1	nuclear receptor subfamily 4 group A member 1
NRP2	neuropilin 2
NTN1	netrin 1
PLAT	plasminogen activator, tissue type
POSTN	periostin
RND3	Rho family GTPase 3
SH3RF1	SH3 domain containing ring finger 1
THBS1	thrombospondin 1
WNT11	Wnt family member 11



Supplementary Figure 7. Taxonomic composition of bacteria in antibiotics-treated mice. (*A–D*) LEfSe analysis of taxa that are significantly enriched in microbiota samples at the indicated sites (esophagus, colon, oropharynx, or skin) from 8-week-old PHF SPF littermates treated with antibiotics or untreated controls. Kruskal-Wallis test was used in (*A–D*). LEfSe, linear discriminant analysis effect size.

Supplementary Figure 6. Gene ontology (GO) functional enrichment analysis of genes differentially expressed due to colonization and EoE. Differentially expressed genes from esophageal biopsies of EoE compared with control individuals (eg, the human EoE transcriptome; Supplementary Table 6) were integrated with the genes that changed after colonization of GF mice with FMT. The murine PE and DE genes were intersected (Figure 4*B*; Supplementary Tables 2–3), and common and unique genes were analyzed with TOPPFUN (false discovery rate–adjusted $P < .05$ and gene limit $n \leq 2000$). The top representative, significantly enriched GO term with corresponding genes from input was summarized for each group. The complete GO functional analysis of gene groups is in Supplementary Table 7.