Supporting Information Appendix

Secretory Antibodies in Breast Milk Promote Long-Term Intestinal Homeostasis by Regulating the Gut Microbiota and Host Gene Expression. Eric W. Rogier, Aubrey L. Frantz, Maria E.C. Bruno, Leia Wedlund, Donald A. Cohen, Arnold J. Stromberg, Charlotte S. Kaetzel.

Supplementary Methods:

Tissue histology and immunofluorescence microscopy (Figs. S1, S2, S3, S10). Mouse tissues were dissected at various time points as noted in the figures. Tissues were fixed in buffered formalin (Sigma-Aldrich, St. Louis, MO), embedded in paraffin and sectioned. Serial sections were stained with hematoxylin and eosin or by immunofluorescence for pIgR/SC and IgA as described (1).

Quantification of IgA in mouse milk and stomach contents (Fig. S1). Milk was collected from nursing dams as described (2) at the indicated times postpartum. For analysis of stomach contents, suckling mice were sacrificed at 10 days of age, stomachs were dissected, the entire contents were removed by gentle scraping, weighed and resuspended in 1mL sample buffer for enzyme-linked immunosorbent assay (ELISA) (50 mM Tris, pH 7.4, 0.14 M NaCl, 1% bovine serum albumin, 0.05% Tween 20). ELISA sample buffer. All samples were stored at -20ºC until analysis. Total IgA was quantified by ELISA as described (3). Total protein was quantified in milk samples by the Pierce BCA Protein Assay (ThermoFisher Scientific, Rockford, IL).

Imaging of colonic bacteria by fluorescence *in situ* hybridization (FISH) (Fig. S3). Colons were harvested from mice at the indicated ages and fixed in Carnoy's fixative (60% ethanol, 30% chloroform, 10% acetic acid), embedded in paraffin and sectioned. After rehydration, tissue sections were hybridized with a universal 16S rRNA probe (EUB338) (4) at a concentration of 10ng/μL as previously described (5). The EUB338 probe, which was labeled on the 5' end with the AlexaFluor647 fluorophore and purified by high performance liquid chromatography agarose gel electrophoresis, was obtained from Invitrogen (Carlsbad, CA). Tissue sections were counterstained with DAPI to visualize eukaryotic cell nuclei.

Identification of bacterial species in mesenteric lymph nodes (Fig. S4). MLNs were homogenized and cultured as described for **Fig. 2** of the main text. Representative colonies from two different 21 day-old offspring of *Pigr*$^{-/-}$ dams were cultured for four days under aerobic conditions at 37^{o}C in Schaedler broth. Bacteria were collected by centrifugation, and DNA was extracted by column purification with the QIAmp DNA Stool Mini Kit (Qiagen Inc., Valencia CA). The bacterial 16S rRNA gene was amplified by real-time PCR using universal EUB338/EUB518R primers (6) as previously described (3). The PCR product was isolated by agarose gel electrophoresis, excised, and purified using the QIAEX II gel Extraction Kit (Qiagen). Purified DNA was ligated into the pGEM-T vector (Promega, Madison, WI), then used to transform frozen competent *E. coli* DH5α (Promega) to ampicillin resistance by standard protocols. Two ampicillin-resistant colonies were harvested and cultured in Schaedler broth containing 100μg/mL ampicillin. Plasmid DNA was purified using the QIAprep Spin Miniprep Kit (Qiagen), and shipped on ice to ACGT, Inc. (Wheeling, IL) for sequence analysis. 16S rRNA sequences were compared with the sequences of known bacterial genomes by BLAST analysis through the National Center for Biotechnology Information database (http://blast.ncbi.nlm.nih.gov/Blast). The highest alignment score (99.8% identity) was observed by comparison to the16S rRNA gene from *Ochrobactrum anthropi*. The relative abundance of *O. anthropi* in fecal samples was based on hybridization values from the PhyloChip™ analysis as described in the main text, calculated as a trimmed average of fluorescence intensity with maximum and minimum values removed before averaging. Scores are expressed as log2 (hybridization value) x1000, meaning that a difference of 1000 units corresponds to a two-fold difference in abundance.

Quantitative real-time PCR analysis of fecal bacteria (Fig. S5). DNA was isolated from freshly collected stools using the QIAmp DNA Stool Mini Kit (Qiagen) and stored at -20oC until analysis. Bacterial 16S rRNA genes were amplified by real-time PCR using universal EUB338/EUB518R primers (6) as previously described (3). To quantify total numbers of bacteria (Fig. S5A), C_T values from individual samples were compared to regression lines of C_T values generated using defined quantities of bacterial DNA from representative species

from the four major phyla of colonic bacteria: Firmicutes, Lactobacillus acidophilus; Bacteroidetes, Bacteroides thetaiotaomicron; Proteobacteria, Escherichia coli; Actinobacteria, Bifidobacterium longum. For approximation of the relative proportion of each phylum in the fecal microbiota over time (Fig. S5D), phyla-specific primers were all divided by the total Eub C_T with primers for Firmicutes (Firm934F/Firm1060R) (6), Bacteroidetes (Bact934F/Bact1060R, 0.21μM) (6), Proteobacteria (Eub338F, 0.1 μM, Bet680, 5 μM) (7), and Actinobacteria (Actino235F, 5 μM, Eub518R, 0.1 μM) (7).

Analysis of gene expression in colonic epithelial cells (Figs. S7, S8, S9). ECs were isolated and purified from mouse colons as described in the main text. RNA was isolated using the MagNA Pure Compact RNA Isolation Kit and automated LightCycler System (Roche Applied Science, Indianapolis, IN). RNA concentration and purity were analyzed using the Agilent 2100 Expert Eukaryotic Total RNA Nanodrop System (Agilent Technologies, Santa Clara, CA). Only samples with an RNA Integrity Number of 8.5 or greater were used for microarray analysis. Two independent pooled RNA samples were made from each treatment group of 6 mice, by combining equal amounts of RNA from 3 individual mice, thereby generating RNA samples for 16 microarray chips (8 treatment groups, 2 independent chips per group). An aliquot of 250 ng of RNA from each pool was used to generate reverse-transcribed cDNA, of which 2 μg were hybridized to each microarray chip. Samples were analyzed at the University of Kentucky Microarray Core Facility using the GeneChip Whole Transcript Sense Target Labeling Assay protocol and GeneChip Mouse Gene 1.0 ST arrays (Affymetrix, Santa Clara, CA). Hybridization signals were annotated with gene symbol and functional information. Probe level data were produced using Affymetrix Expression Console with the RMA output option. Probe sets were retained for analysis if they had gene symbol level annotations. Statistical modeling and data analysis was performed using a 2 x 2 x 2 ANOVA model-based approach. This analysis produced a list of genes that were regulated to a highly significant degree ($P < 0.01$) in colonic ECs by passive SIgA, active SIgA, DSS, or a combination of these factors (Fig. S7 and Table S1). The abundance of mRNA transcripts for 16 selected genes was validated by analyzing RNA from individual mice, using aliquots of the same RNA samples that had previously been used for the microarray analysis. Transcript levels were quantified by Nanostring nCounter™ hybridization (8), and normalized to hybridization signals for 6 "housekeeping" genes using an algorithm developed by NanoString Technologies (Seattle, WA) (www.nanostring.com).

1. Frantz AL, Bruno ME, Rogier EW, Tuna H, Cohen DA, Bondada S, Chelvarajan RL, Brandon JA, Jennings CD, Kaetzel CS (2012) Multifactorial patterns of gene expression in colonic epithelial cells predict disease phenotypes in experimental colitis. *Inflamm Bowel Dis* 18:2138-2148.
2. Garvy BA, Harmsen AG (1996) Susceptibility to *Pneumocystis carinii* infection: host responses of neonatal mice from immune or naive mothers and of immune or naive adults. *Infect Immun* 64:3987-3992.
3. Frantz AL, Rogier EW, Weber CR, Shen L, Cohen DA, Fenton LA, Bruno ME, Kaetzel CS (2012) Targeted deletion of MyD88 in intestinal epithelial cells results in compromised antibacterial immunity associated with downregulation of polymeric immunoglobulin receptor, mucin-2, and antibacterial peptides. *Mucosal Immunol* 5:501-512.
4. Johansson ME, Phillipson M, Petersson J, Velcich A, Holm L, Hansson GC (2008) The inner of the two Muc2 mucin-dependent mucus layers in colon is devoid of bacteria. *Proc Natl Acad Sci U S A* 105:15064-15069.
5. Amann RI, Binder BJ, Olson RJ, Chisholm SW, Devereux R, Stahl DA (1990) Combination of 16S rRNA-targeted oligonucleotide probes with flow cytometry for analyzing mixed microbial populations. *Appl Environ Microbiol* 56:1919-1925.
6. Guo X, Xia X, Tang R, Zhou J, Zhao H, Wang K (2008) Development of a real-time PCR method for Firmicutes and Bacteroidetes in faeces and its application to quantify intestinal population of obese and lean pigs. *Lett Appl Microbiol* 47:367-373.
7. Fierer N, Jackson JA, Vilgalys R, Jackson RB (2005) Assessment of soil microbial community structure by use of taxon-specific quantitative PCR assays. *Appl Environ Microbiol* 71:4117-4120.
8. Geiss GK, Bumgarner RE, Birditt B, Dahl T, Dowidar N, Dunaway DL, Fell HP, Ferree S, George RD, Grogan T *et al.* (2008) Direct multiplexed measurement of gene expression with color-coded probe pairs. *Nat Biotechnol* 26:317-325.

Table S1. Identification of regulated genes in mouse colonic epithelial cells by microarray analysis.

A. List of genes up-regulated by the designated factor(s)

Passive SIgA only	Active SIgA only	DSS only	Passive and Active SIgA	Passive SIgA and DSS	Active SIgA and DSS	Passive and Active SIgA and DSS
Acp5	*Ctsm*	*Abce1*	*Ccl5*	*Aaas*	*Acoxl*	*Cenpi*
Ap2a2	*Cyp4a12b*	*Abhd13*	*Cyp11b1*	*Acss1*	*Atp2c2*	*Ctse*
Arf1	*Ear10*	*Acadl*	*Sirpb1*	*Ak3*	*Baat*	*E2f8*
Bace2	*Gabrg1*	*Ada*	*Sprr2d*	*Alg3*	*Bcl2*	*Farsb*
Cd151	*Gm906*	*Adam10*	*Tas2r139*	*Alg8*	*Bcl2a1d*	*Ide*
Cmah	*Igh*	*Adcy2*	*Zfand2a*	*Alg9*	*Calcb*	*Mrps18b*
Dsg1a	*Il7r*	*Adprh*		*Anxa4*	*Ccdc93*	*Ndufaf4*
Ggcx	*Olfr1052*	*Ak3l1*		*Ap1s1*	*Cyp3a41a*	*Nlk*
Gltpd1	*Olfr1090*	*Akr1c18*		*Ap3d1*	*Cyp4x1*	*Olfr105*
Mbnl3	*Olfr1141*	*Aldh1a3*		*Aqp4*	*Defb39*	*Olfr270*
Nov	*Olfr1197*	*Ankrd50*		*Arpc1b*	*Dirc2*	*Smarcb1*
Olfr101	*Olfr1280*	*Apaf1*		*Arpc4*	*Dnajc24*	*Vmn2r109*
Olfr866	*Olfr1301*	*Apobec3*		*Asf1b*	*Ear6*	*Wbscr22*
Pold2	*Olfr1308*	*Arf2*		*B3gnt3*	*F10*	*Xlr5b*
Pole2	*Olfr132*	*Arrdc3*		*Bpnt1*	*Ggta1*	
Rab7l1	*Olfr1335*	*Asprv1*		*Calm3*	*Gm1527*	
Rnf181	*Olfr1385*	*Atic*		*Car9*	*Meis3*	
Slc31a2	*Olfr154*	*Atp8a1*		*Ccdc109a*	*Mlph*	
Sumo2	*Olfr171*	*Atpif1*		*Ccnd1*	*Mlxipl*	
Taf6	*Olfr19*	*B3galt5*		*Cct6a*	*Mpeg1*	
Topbp1	*Olfr380*	*Basp1*		*Cd72*	*Olfr1104*	
Twsg1	*Olfr574*	*Bcl2a1a*		*Cd80*	*Olfr1138*	
	Olfr582	*Bcl2a1b*		*Cd97*	*Olfr1328*	
	Olfr668	*Bloc1s3*		*Cdk2ap1*	*Olfr138*	
	Olfr670	*Bpgm*		*Chek1*	*Olfr23*	
	Olfr688	*Bst1*		*Cks2*	*Olfr395*	
	Olfr706	*C1s*		*Cpne3*	*Olfr533*	
	Olfr835	*C3*		*Ctsc*	*Olfr643*	
	Olfr934	*C5ar1*		*Dcbld1*	*Olfr657*	
	Olfr988	*Calr*		*Ddah1*	*Olfr813*	
	Pigr	*Capg*		*Ddost*	*Olr1*	
	Rnase12	*Caprin1*		*Dock10*	*Ott*	
	Rpe65	*Car12*		*Elavl1*	*Parp3*	
	Taar8b	*Ccdc134*		*Eno1*	*Pilrb1*	
	Tmem160	*Ccdc80*		*Enpp5*	*Ptch1*	
	Tmprss11b	*Ccl3*		*Epsti1*	*S100pbp*	
	V1rc7	*Ccl9*		*Expi*	*Siglece*	
	V1rg2	*Ccrl2*		*Fads3*	*Slamf7*	
	Vmn2r18	*Cd14*		*Fam57a*	*Spam1*	
	Xlr5a	*Cd33*		*Fut2*	*St6gal1*	
	Zfy1	*Cd38*		*Gatad1*	*Tdo2*	
		Cd47		*Gna14*	*Tnni1*	

Table S1, continued

DSS only	Passive SIgA and DSS	Active SIgA and DSS	DSS only	Passive SIgA and DSS
Cd53	*Gnpda1*	*Treml4*	*Fam118b*	*S100a11*
Cd74	*Golm1*	*Trim6*	*Fam124a*	*Scamp4*
Chi3l1	*Gorasp2*	*Zeb2*	*Fam3b*	*Scfd2*
Chmp4b	*Gstk1*		*Fam3c*	*Sec61a1*
Ckap4	*Guca2a*		*Fbln1*	*Sema7a*
Clca2	*H2afy*		*Fcer1g*	*Sh3bgrl2*
Clec4d	*H2-Eb1*		*Fcgr2b*	*Slc39a11*
Clec4e	*Hspd1*		*Fcgr3*	*Slc7a7*
Clec7a	*Kcnk6*		*Fkbp1a*	*Snap23*
Cnp	*Lin54*		*Fpr1*	*Spcs3*
Cox18	*Lrrc59*		*Fry*	*Srgn*
Cpne2	*M6pr*		*Fxyd5*	*Srm*
Csf1r	*Mif*		*Fzd1*	*Ssr3*
Csf2rb	*Mipep*		*Gars*	*Sub1*
Csf2rb2	*Mki67ip*		*Gbp2*	*Sulf1*
Ctps	*Mrps27*		*Gbp4*	*Tbccd1*
Cxcl2	*Mtap*		*Gbp5*	*Tcof1*
Cxcl9	*Mtpn*		*Gcnt2*	*Thg1l*
Cyba	*Nadk*		*Gda*	*Tpm3*
Cybb	*Ndrg3*		*Glo1*	*Tuba1b*
Daglb	*Nmt1*		*Gm379*	*Twf1*
Dapk2	*Npn2*		*Gp49a*	*Ube2l3*
Dcp2	*Nrbp2*		*Gpr110*	*Ubqln1*
Degs1	*Nudt4*		*Gpx2*	*Usp39*
Dgat2	*P2ry5*		*Gsdmc2*	*Vamp3*
Dhrs9	*Pdlim1*		*Gsdmd*	*Vkorc1l1*
Dhx29	*Pglyrp1*		*Gusb*	*Wrb*
Dis3	*Pigu*		*H13*	*Yars2*
Dnaja2	*Pklr*		*H2-Aa*	*Ywhah*
Dpp9	*Plrg1*		*H6pd*	*Zdhhc15*
Dsc2	*Pmepa1*		*Hars*	*Zdhhc3*
Duox2	*Pnp2*		*Hdc*	*Zfp27*
Duoxa2	*Ppih*		*Heatr1*	*Zfp652*
Dus1l	*Prpf4*		*Hk2*	
Dynll1	*Prps1*		*Hyou1*	
Efhd2	*Psmb2*		*Icam1*	
Egln3	*Psmd14*		*Ick*	
Eif3b	*Psme3*		*Idh1*	
Eif4a3	*Rad18*		*Ido1*	
Eif4e3	*Rbp4*		*Ier3*	
Entpd1	*Reep6*		*Ifi205*	
Epb4.1l2	*Rpn1*		*Ifitm1*	
Ermp1	*Rpn2*		*Ifitm3*	
Ero1l	*Rrm2*		*Ifnar2*	

Table S1, continued

DSS only						
Igsf6	*Lpcat4*	*Ncf1*	*Phf5a*	*Rassf4*	*Slc35b1*	*Tlr2*
Iigp1	*Lrg1*	*Ndufa12*	*Pilra*	*Rbm12b*	*Slc3a1*	*Tmc5*
Il1a	*Lrp8*	*Nek6*	*Pion*	*Reg3b*	*Slc5a9*	*Tmcc3*
Il1b	*Lsp1*	*Nfkbiz*	*Pla2g5*	*Reg3g*	*Slc7a11*	*Tmem54*
Il1f9	*Ltf*	*Ngly1*	*Pla2g7*	*Retnlg*	*Slfn2*	*Tmem55a*
Il1r2	*Ly6a*	*Niacr1*	*Plat*	*Ripk1*	*Smad4*	*Tmsb10*
Il23a	*Ly6c1*	*Nlrp3*	*Plcl2*	*Ripk2*	*Smpd3*	*Tnf*
Il34	*Ly6c2*	*Nop2*	*Plek*	*Ripk3*	*Snd1*	*Tnfaip2*
Il4ra	*Ly6i*	*Nos2*	*Plek2*	*Rnf114*	*Snx4*	*Tnfrsf1b*
Il5ra	*Lyn*	*Noxo1*	*Polg*	*Rnf121*	*Socs3*	*Tnik*
Il6	*Marcksl1*	*Nsun2*	*Ppp1r14b*	*Robo2*	*Srms*	*Trem1*
Il8rb	*Me1*	*Nupr1*	*Prdm1*	*Rps19bp1*	*Ssh1*	*Trim15*
Irf8	*Med21*	*Osmr*	*Prom1*	*Rps2*	*Stat1*	*Trim29*
Irg1	*Mfsd2*	*Ostf1*	*Psat1*	*Rrbp1*	*Stat3*	*Trim40*
Itga2	*Micall2*	*Otud7b*	*Psmb3*	*S100a8*	*Steap4*	*Trim65*
Jagn1	*Mid1*	*P4ha1*	*Psmb9*	*S100a9*	*Stip1*	*Trps1*
Jak3	*Mlkl*	*P4hb*	*Psmd2*	*Samsn1*	*Stt3b*	*Twf2*
Jmjd6	*Mmp28*	*Pdcd11*	*Psmd3*	*Sar1b*	*Stx7*	*Tyrobp*
Kctd5	*Mrpl3*	*Pde11a*	*Ptafr*	*Scmh1*	*Sulf2*	*Ube2s*
Lap3	*Ms4a8a*	*Pde9a*	*Ptges*	*Sdf2l1*	*Tac1*	*Upk1b*
Lbp	*Msn*	*Pdgfc*	*Ptgs2*	*Sec61a2*	*Taok3*	*Vim*
Lcn2	*Mst1r*	*Pdia4*	*Ptk2*	*Sema6d*	*Tfdp1*	*Xdh*
Lcp1	*Mtap7d1*	*Pdss1*	*Ptprd*	*Serpinb2*	*Tgtp*	*Xpo1*
Lcp2	*Mtrr*	*Pgam5*	*Purb*	*Serping1*	*Thsd4*	*Zbp1*
Lgmn	*Myl7*	*Pgap1*	*Rab32*	*Sh3kbp1*	*Tifa*	*Zc3h12a*
Lilrb4	*N4bp1*	*Pgk1*	*Rab8b*	*Slc15a3*	*Tinagl1*	*Zranb1*
Lipk	*Ncald*	*Pgs1*	*Ranbp17*	*Slc16a3*	*Tln2*	

Table S1, continued

B. List of genes down-regulated by the designated factor(s)

Passive SIgA only	Active SIgA only	DSS only	Passive and Active SIgA	Passive SIgA and DSS	Active SIgA and DSS	Passive and Active SIgA and DSS
Akap8l	*Aen*	*Abat*	*Cpt1b*	*Abcb1a*	*Agpat3*	*Csnk2b*
Apbb3	*Akt1*	*Abhd2*	*Dgcr2*	*Abi3*	*Aqp1*	*Efcab4b*
Apol8	*Alox5*	*Abp1*	*Dhx30*	*Akt3*	*Aqr*	*Fryl*
Blcap	*B3galtl*	*Abr*	*Epha1*	*Alpk1*	*Arhgef2*	*Ilkap*
Ccdc3	*Cep68*	*Abtb2*	*Fer1l6*	*Ank3*	*Axin2*	*Junb*
Clip2	*Ddx56*	*Acaa1a*	*Gripap1*	*Ano1*	*Cbfa2t3*	*Lrig1*
Cxadr	*Far2*	*Acer1*	*Huwe1*	*Apitd1*	*Cdc25a*	*Map3k9*
Cyp27a1	*Gzf1*	*Acsl1*	*Nacc1*	*Arrdc2*	*Chmp1a*	*Mier3*
D1Pas1	*Hp1bp3*	*Acss2*	*Naf1*	*Atg16l2*	*Clcn6*	*Rbbp6*
Ddit3	*Mcph1*	*Adam15*	*Nfx1*	*Atg7*	*Dach1*	*Snord49a*
Dppa3	*Mettl1*	*Adck5*	*Plk4*	*Atp12a*	*Def8*	*Spata13*
Dsg2	*Mre11a*	*Add3*	*Rasa4*	*Bach2*	*Dennd1a*	*Whsc1l1*
Dyrk2	*N4bp2*	*Adh1*	*Snora7a*	*Bfsp1*	*Dpyd*	*Yaf2*
Fam83e	*Phf12*	*Agap1*	*Syt7*	*Btg2*	*Ern2*	
Fbxo4	*Rhobtb1*	*Agfg2*	*Tdp1*	*Ccdc116*	*Exosc1*	
Gtf2ird1	*Setd1a*	*Ahcyl2*	*Zer1*	*Ccrn4l*	*Fam115c*	
Herc2	*Spats2*	*Ahnak2*	*Zfp407*	*Chd7*	*Farp1*	
Ip6k1	*Trdn*	*AI854703*	*Zfp687*	*Clcn2*	*Foxk2*	
Ipo7	*Ubtf*	*Akap2*		*Clic5*	*Gbe1*	
Irf1		*Alb*		*Coq7*	*Glt1d1*	
Map2k7		*Aldh6a1*		*Crim1*	*Gm1123*	
Myo18a		*Amotl1*		*Cyp4f13*	*Gpam*	
Myo1h		*Ankrd10*		*Dll1*	*Greb1*	
Nr1d2		*Ankrd9*		*Dot1l*	*Gsr*	
Numb		*Ap4b1*		*Eppk1*	*Gsta2*	
Pex12		*Appl2*		*Erbb3*	*Gtf2i*	
Prpsap2		*Aqp8*		*Etl4*	*Iars*	
Rapgef4		*Arhgap27*		*Fam161a*	*Idua*	
Rnu12		*Ascl2*		*Foxo3*	*Ikbkb*	
Rnu1b1		*Atad4*		*Gse1*	*Insig2*	
Rnu3a		*Atoh1*		*Hdac5*	*Kank1*	
Rny1		*Atp6v1e1*		*Hoxd11*	*Kat2a*	
Rpl27a		*Atxn2*		*Hps4*	*Kcne3*	
Rprl1		*Best2*		*Il17rc*	*Kpnb1*	
Rprl2		*Boc*		*Irs2*	*Ldb1*	
Rps12		*Cabc1*		*Kalrn*	*Lgr5*	
Setd1b		*Cachd1*		*Kdm4a*	*Mrps22*	
Slc36a1		*Car2*		*Klc1*	*Olfr1380*	
Smg1		*Caskin2*		*Klf3*	*Olfr148*	
Snora62		*Casp14*		*Klf4*	*Pabpc4*	
Snord52		*Ccbl1*		*Lmo4*	*Pacs1*	
Snord85		*Cd200*		*Meg3*	*Pcgf2*	

Table S1, continued

Passive SIgA only	Active SIgA only	DSS only	Passive and Active SIgA	Passive SIgA and DSS	Active SIgA and DSS	Passive and Active SIgA and DSS
Spg7		*Cd83*		*Mtmr4*	*Pla2g2a*	
Ston1		*Cdc42bpb*		*Myh14*	*Pm20d1*	
Supt5h		*Cdkl1*		*Myo7b*	*Ppt2*	
Vasp		*Cdo1*		*Neu1*	*Prl2b1*	
Zc3hav1l		*cela1*		*Nr1d1*	*Prl3a1*	
		Chdh		*Nr3c2*	*Qdpr*	
		Clps		*Pacrgl*	*Qtrt1*	
		Clybl		*Peli2*	*Rab27a*	
		Cnksr3		*Pik3c2b*	*Sdr16c5*	
		Cnnm4		*Plec1*	*Senp1*	
		Cobl		*Plekhg5*	*Slc24a3*	
		Col8a1		*Pmvk*	*Smg6*	
		Coq10a		*Ppp1r10*	*Smoc2*	
		Cotl1		*Rab11fip4*	*Tas2r120*	
		Cox7a1		*Rgs3*	*Tns3*	
		Cpa2		*Rnf152*	*Trappc9*	
		Cpm		*Sema4g*	*Trmt2b*	
		Cps1		*Sipa1l3*	*Tut1*	
		Crip1		*Slc20a1*	*Ugt1a9*	
		Csad		*Slc26a3*	*Xpo5*	
		Cth		*Slc9a2*	*Zbtb38*	
		Ctns		*Snora30*		
		Cttnbp2		*Snord118*		
		Cyp2c40		*Snord32a*		
		Cyp2d13		*Snord33*		
		Cyp2d22		*Snord34*		
		Cyp2f2		*Spnb3*		
		Cyp2s1		*Spry2*		
		Cyp4a32		*Syne2*		
		Cyp4f16		*Synj2*		
		Ddc		*Synpo*		
		Dennd2c		*Tat*		
		Dgkh		*Tgm3*		
		Dhrs11		*Tns4*		
		Dip2a		*Trak1*		
		Dixdc1		*Unc84b*		
		Dpep1		*Unkl*		
		Dusp5		*Usp54*		
		Edn2		*Vdr*		
		Eef2k		*Zfhx3*		
		Efna1		*Zfp710*		
		Efna3		*Zfyve1*		
		Ell3		*Zfyve27*		
		Entpd5		*Zmiz1*		

Table S1, continued

DSS only						
Ephb3	*Higd1c*	*Lmna*	*Olfr309*	*Ptpn13*	*Sfxn5*	*Syn2*
Fabp2	*Hk1*	*Lrat*	*Olfr497*	*Ptpn3*	*Shisa2*	*Sytl1*
Fam134b	*Hmcn1*	*Lsr*	*Olfr669*	*Ptpn9*	*Sik1*	*Tas2r131*
Fam3a	*Hnf4a*	*Luzp4*	*Olfr812*	*Pttg1*	*Slc15a1*	*Tbc1d19*
Fam55b	*Hpcal1*	*Ly6g6c*	*Pacsin2*	*Pyroxd2*	*Slc16a12*	*Tbc1d8*
Fam55d	*Hpgd*	*Maob*	*Papss1*	*Rab5b*	*Slc16a7*	*Tceal8*
Farp2	*Hsd17b2*	*Mbc2*	*Pccb*	*Ramp1*	*Slc22a23*	*Tcn2*
Fbxo32	*Hsd3b7*	*Mcoln1*	*Pck1*	*Rapgefl1*	*Slc24a6*	*Timp3*
Fgfr3	*Htr4*	*Mep1a*	*Pcx*	*Rasd1*	*Slc25a23*	*Tm6sf2*
Fhl1	*Hunk*	*Mettl7a1*	*Pdk2*	*Rasd2*	*Slc25a25*	*Tmem171*
Fkbp9	*Id2*	*Mgrn1*	*Pdxk*	*Rasgef1b*	*Slc27a1*	*Tmem35*
Fmo1	*Id3*	*Mkx*	*Pdzd7*	*Rbp2*	*Slc34a2*	*Tmx4*
Frmd8	*Iffo2*	*Mme*	*Perld1*	*Repin1*	*Slc46a1*	*Tpcn1*
Fut9	*Ifi27l1*	*Mrgpra2*	*Pfkfb4*	*Rftn2*	*Slc6a4*	*Tppp*
Fxyd4	*Ifna7*	*Msi2*	*Pfkm*	*Rfxank*	*Slc6a8*	*Tppp3*
Fzd7	*Igsf9*	*Mtmr3*	*Phlppl*	*Rgs17*	*Slc9a3r1*	*Trib1*
Garnl4	*Inpp5j*	*Mupcdh*	*Pisd-ps1*	*Rhoc*	*Slco1a6*	*Trpm6*
Gas6	*Insr*	*Naaladl1*	*Pkhd1l1*	*Rhot2*	*Slco2a1*	*Trpv3*
Gba2	*Insrr*	*Ndrg2*	*Pla2g3*	*Rhou*	*Smad6*	*Trpv6*
Gdf15	*Ipmk*	*Nek5*	*Plbd1*	*Rin3*	*Smad7*	*Tshz1*
Glul	*Irf6*	*Nelf*	*Plcb1*	*Ror1*	*Smpx*	*Tspan33*
Gm967	*Itih2*	*Nit1*	*Plekhg6*	*Rtn1*	*Sned1*	*Ttll6*
Gnb5	*Itm2b*	*Nnt*	*Plekhh1*	*Saps1*	*Sorbs2*	*Ttr*
Golph3l	*Itpr1*	*Npc1*	*Plk3*	*Scamp1*	*Spdya*	*Unc45a*
Gpr175	*Itpr2*	*Npc2*	*Pmp22*	*Scamp5*	*Sstr1*	*Unc5b*
Gpt	*Kcnh8*	*Nr4a1*	*Pnpo*	*Scin*	*St3gal6*	*Upk1a*
Gramd1a	*Kcnk5*	*Odf3b*	*Ppargc1a*	*Scnn1a*	*Steap3*	*V1re12*
Gramd4	*Kif1c*	*Oit1*	*Ppp1r3b*	*Selenbp1*	*Stim1*	*Wdr59*
Grb7	*Kit*	*Olfr107*	*Prelp*	*Selenbp2*	*Stk10*	*Wee1*
Grik5	*Klhl21*	*Olfr1247*	*Prkar2b*	*Sema5a*	*Stox2*	*Wfdc2*
Gstm1	*Klk1b26*	*Olfr130*	*Prkcd*	*Sema6a*	*Sult1a1*	*Xpnpep1*
Gstm7	*Ldlrad3*	*Olfr181*	*Prlr*	*Serinc5*	*Sult2b1*	*Ypel3*
Gstt1	*Lgals3*	*Olfr204*	*Prss23*	*Sfxn3*	*Sycn*	*Zfp36l2*
Hexb	*Lhfpl2*					

Adult *Pigr* $^{+/-}$ and *Pigr* $^{-/-}$ offspring from *Pigr* $^{+/-}$ and *Pigr* $^{-/-}$ dams were given 2% DSS in the drinking water or plain water for 8 days, and RNA was purified from isolated colonic epithelial cells. Gene expression was analyzed using an Affymetrix GeneChip Mouse Gene 1.0 ST array. Normalized data were analyzed by 3-way ANOVA for effects of passive SIgA (maternal *Pigr* genotype), active SIgA (offspring *Pigr* genotype) and DSS treatment (see Fig. S7). Genes included in this list were significantly regulated by the designated factor or combination of factors ($P < 0.01$).

Table S2. Regulated genes in mouse colonic epithelial cells that are orthologous to human disease-associated gene loci.

Human disease association:

- Crohn's disease (CD)
- Ulcerative colitis (UC)
- IBD (CD and UC)
- Adult and early onset IBD
- Celiac disease (CelD)
- CelD and adult IBD
- CelD and early onset IBD

A. Disease-associated genes up-regulated by the designated factor(s)

Passive SIgA only	Active SIgA only	DSS only	Passive and Active SIgA	Passive SIgA and DSS	Active SIgA and DSS	Passive and Active SIgA and DSS
	Il7r	*Nos2*		*Fut2*	*Slamf7*	
	Pigr	*Ripk2*		*Calm3*		
		Ada		*Ube2l3*		
		Il8rb				
		Prdm1				
		Psmd3				
		Smpd3				
		Xpo1				
		Cxcl2				
		Fcgr2b				
		Icam1				
		Il1r2				
		Irf8				
		Lilrb4				
		Lsp1				
		Mst1r				
		Nupr1				
		Stat1				
		Stat3				
		Ltf				
		Plek				

B. Disease-associated genes down-regulated by the designated factor(s)

Passive SIgA only	Active SIgA only	DSS only	Passive and Active SIgA	Passive SIgA and DSS	Active SIgA and DSS	Passive and Active SIgA and DSS
Irf1		*Fam55d*		*Nr1d1*	*Pla2g2a*	
		Grb7		*Slc26a3*		
		Hnf4a		*Ccdc116*		
		Perld1		*Vdr*		
		Prkcd		*Bach2*		
		Rftn2		*Zmiz1*		
		Tppp				
		Tspan33				
		Ipmk				
		Pfkfb4				
		Smad7				
		Trib1				
		Mtmr3				
		Sult1a1				
		Atxn2				

The list of regulated genes in mouse colonic epithelial cells (**Table S1**) was scanned for orthologous human gene loci that have been identified in genome-wide association studies for Crohn's disease, ulcerative colitis, early-onset IBD and celiac disease. See Materials and Methods for a detailed description of inclusion criteria.

Table S3. List of biological pathways predicted to be regulated by passive SIgA, active SIgA and DSS. Genes that were determined by microarray analysis to be significantly up- or down-regulated by one or more of these factors (see **Table S1**) were scanned for matches in biological pathways indexed in the Reactome pathway database (www.reactome.org). Based on the number of matching genes and the relationships among their biological activities, pathways were identified that are statistically predicted to be regulated by passive SIgA, active SIgA and/or DSS. Pathways highlighted in red are predicted to be up-regulated by the indicated factor, and pathways highlighted in green are predicted to be down-regulated by the indicated factor. For a detailed description of the criteria for pathway selection and statistical methods, see www.reactome.org. Additional information on individual genes and pathways can be obtained by opening the hyperlinks in the tables below.

Biological pathways predicted to be regulated by early exposure to passive SIgA in breast milk		
Statistical likelihood that the indicated pathway is regulated by passive SIgA (*P*-value)	Genes that map to this pathway	Name of this pathway
3.8e-04	Pold2, Pole2	Repair synthesis of patch ~27-30 bases long by DNA polymerase
3.8e-04	Pold2, Pole2	Repair synthesis for gap-filling by DNA polymerase in TC-NER
4.3e-04	Pold2, Pole2	Gap-filling DNA repair synthesis and ligation in GG-NER
4.3e-04	Pold2, Pole2	Gap-filling DNA repair synthesis and ligation in TC-NER
8.3e-04	Pold2, Pole2	Telomere C-strand (Lagging Strand) Synthesis
1.1e-03	Pold2, Pole2	Extension of Telomeres
1.9e-03	Pold2, Pole2	Global Genomic NER (GG-NER)
3.3e-03	Pold2, Pole2	Transcription-coupled NER (TC-NER)
3.6e-03	Arf1, Ap2a2	Nef Mediated CD4 Down-regulation
4.1e-03	Pold2, Pole2	Nucleotide Excision Repair
5.3e-03	Pold2, Pole2	Telomere Maintenance
5.7e-03	Arf1, Ap2a2	Nef-mediates down modulation of cell surface receptors by recruiting them to clathrin adapters
7.1e-03	Arf1, Ap2a2	The role of Nef in HIV-1 replication and disease pathogenesis
2.9e-03	Rps12, Rpl27a, Smg1	UPF1 Binds an mRNP with a Termination Codon Preceding an Exon Junction Complex
2.9e-03	Rps12, Rpl27a, Smg1	SMG1 Phosphorylates UPF1 (Enhanced by Exon Junction Complex)
3.4e-03	Rps12, Rpl27a, Smg1	Nonsense-Mediated Decay
3.4e-03	Rps12, Rpl27a, Smg1	Phosphorylated UPF1 Recruits SMG5, SMG7, SMG6, and PP2A
3.4e-03	Rps12, Rpl27a, Smg1	Nonsense Mediated Decay Enhanced by the Exon Junction Complex

Biological pathways predicted to be regulated by active SIgA derived from endogenous transport		
Statistical likelihood that the indicated pathway is regulated by active SIgA (*P*-value)	Genes that map to this pathway	Name of this pathway
9.5e-09	Olfr19, Olfr1385, Olfr582, Olfr706, Olfr171, Olfr1141, Olfr688, Olfr380, Olfr1090, Olfr1052, Olfr835	Olfactory Receptor - G Protein olfactory trimer complex formation
9.5e-09	Olfr19, Olfr1385, Olfr582, Olfr706, Olfr171, Olfr1141, Olfr688, Olfr380, Olfr1090, Olfr1052, Olfr835	Olfactory Signaling Pathway
3.0e-06	Olfr19, Olfr1385, Olfr582, Olfr706, Olfr171, Olfr1141, Olfr688, Olfr380, Olfr1090, Olfr1052, Olfr835	GPCR downstream signaling
5.1e-06	Olfr19, Olfr1385, Olfr582, Olfr706, Olfr171, Olfr1141, Olfr688, Olfr380, Olfr1090, Olfr1052, Olfr835	Signaling by GPCR
4.3e-04	Olfr19, Olfr1385, Olfr582, Olfr706, Olfr171, Olfr1141, Olfr688, Olfr380, Olfr1090, Olfr1052, Olfr835	Signal Transduction

Table S3, continued.

Biological pathways predicted to be regulated by oral administration of DSS		
Statistical likelihood that the indicated pathway is regulated by DSS (*P*-value)	Genes that map to this pathway	Name of this pathway
6.9e-07	Psmd3, Nlrp3, Csf2rb, Cyba, Gbp2, Tyrobp, Stat1, Lcp2, Cd14, Il5ra, Sec61a2, Ube2s, Il6, Fcgr3, Lyn, Ifnar2, Ifitm1, Il1a, Icam1, Gbp4, Ifitm3, Tlr2, Ripk3, Lbp, Psmb3, Ripk1, Psmd2, Il1b, Calr, Eif4a3, Psmb9, Sar1b, Fcgr2b, Socs3, Eif4e3, Stat3, Ptafr, Gbp5, Irf8, Jak3, Cybb, Lgmn, Lilrb4, Zbp1, Ripk2, C3, Ncf1, Il1r2, Sh3kbp1, C1s	Immune System
1.7e-06	Eif4a3, Csf2rb, Gbp2, Stat1, Il5ra, Socs3, Eif4e3, Stat3, Ptafr, Irf8, Gbp5, Jak3, Il6, Lyn, Ifitm1, Ifnar2, Ripk2, Il1a, Icam1, Gbp4, Ifitm3, Il1r2, Il1b	Cytokine Signaling in Immune system
6.8e-06	Lyn, Csf2rb, Ripk2, Il1a, Stat1, Il5ra, Socs3, Stat3, Il1r2, Jak3, Il1b, Il6	Signaling by Interleukins
1.2e-05	Il1a, Il1r2, Il1b	Interleukin-1 receptor type 2 binds Interleukin 1
1.2e-05	Zbp1, Ripk1, Ripk3	DAI recruits RIP1 and RIP3
7.7e-05	Socs3, Stat3, Stat1, Il6	Interleukin-6 signaling
1.0e-04	Psmd3, Dapk2, Psmb9, Ptk2, H13, Tnf, Dynll1, Vim, Psmb3, Ripk1, Psmd2, Apaf1	Apoptosis
1.1e-04	Ncf1, Cyba, Cybb	Alkalization of the phagosomal lumen by NOX2
5.2e-04	Cd14, Lbp	LPS transferred from LBP carrier to CD14
5.2e-04	Cd14, Lbp	GPI-bound CD14 binds LPS
5.2e-04	Cd14, Lbp	Secreted CD14 binds LPS
5.2e-04	Stat3, Stat1	Phosphorylated STAT1, STAT3 form dimers
5.2e-04	Stat3, Stat1	STAT1/3 dimers translocate to the nucleus
6.1e-04	Stat3, Stat1, Il6	STATs bind gp130 phosphotyrosines
6.1e-04	Stat3, Stat1, Il6	Tyrosine phosphorylation of STATs by IL6 receptor
6.1e-04	Stat3, Stat1, Il6	Phosphorylated STATs are released
6.1e-04	Stat3, Stat1, Il6	Serine phosphorylation of STATs
6.1e-04	Ncf1, Cyba, Cybb	Cross-presentation of particulate exogenous antigens (phagosomes)
1.5e-03	Psmd3, Calr, Cyba, Psmb9, Psmb3, Ncf1, Psmd2, Sec61a2, Cybb	Antigen processing-Cross presentation
1.5e-03	Il1a, Il1b	Interleukin-1 receptor type 1 binds Interleukin 1
1.5e-03	Il1a, Il1b	Interleukin-1 family are secreted
1.7e-03	Lyn, Socs3, Stat3, Stat1	Growth hormone receptor signaling
1.7e-03	Zbp1, Ripk1, Ripk3	RIP-mediated NFkB activation via DAI
1.9e-03	Ifnar2, Ifitm1, Eif4a3, Icam1, Gbp2, Ifitm3, Gbp4, Stat1, Socs3, Eif4e3, Ptafr, Irf8, Gbp5	Interferon Signaling
2.2e-03	Lyn, Stat3, Stat1	Recruitment of STATs
2.2e-03	Lyn, Stat3, Stat1	Phosphorylation of STATs
2.2e-03	Lyn, Stat3, Stat1	Dimerization of STATs
2.2e-03	Lyn, Stat3, Stat1	Disassociation and translocation of STATs to the nucleus
2.9e-03	Lyn, Itga2, Fcer1g	Platelet Adhesion to exposed collagen
2.9e-03	Zbp1, Ripk1, Ripk3	DAI mediated induction of type I IFNs
2.9e-03	Zbp1, Ripk1, Ripk3	Cytosolic sensors of pathogen-associated DNA
3.0e-03	Plat, Pdgfc	Extracellular processing of novel PDGFs
3.0e-03	Cd47, Ptk2	Phosphorylation of ITIM in SIRP alpha
3.0e-03	Tyrobp, Sema6d	Sema6D binds PlexinA1-Trem2-DAP12
3.0e-03	Lyn, Fcer1g	GPVI binds Fyn and Lyn
3.0e-03	Il1a, Il1b	Interleukin-1 receptor type 1: Interleukin 1 binds Interleukin-1 receptor accessory protein, membrane associated isoform
3.0e-03	Il1a, Il1b	Interleukin-1 family precursors are cleaved by caspase-1
3.0e-03	Il1a, Il1b	Interleukin-1 processing
3.0e-03	Il5ra, Csf2rb	Interleukin-5:Interleukin-5 receptor alpha binds IL3RB:JAK2
3.4e-03	Xpo1, Psmd3, Psmb3, Dcp2, Psmd2, Psmb9, Dis3	Regulation of mRNA Stability by Proteins that Bind AU-rich Elements
5.0e-03	Ripk1, Tnf	TRADD:TRAF2:RIP1 complex dissociates from the TNF-alpha:TNF-R1 complex.
5.0e-03	Ripk1, Tnf	TNF:TNF-R1 binds TRADD, TRAF2 and RIP Complex
5.0e-03	Ifitm1, C3	C3d-complexed antigen binds to complement receptor
5.0e-03	Il1a, Il1b	IL1R1:IL1:IL1RAP binds MYD88 homodimer

Table S3, continued.

Biological pathways predicted to be regulated by DSS, continued		
Statistical likelihood that the indicated pathway is regulated by DSS (*P*-value)	Genes that map to this pathway	Name of this pathway
5.3e-03	Cd47, Tyrobp, Ptk2	Signal regulatory protein (SIRP) family interactions
5.8e-03	Atic, Ada, Xdh, Gda	Purine metabolism
6.4e-03	Il5ra, Csf2rb, Jak3	Phosphorylated SHC1 recruits GRB2:GAB2
6.4e-03	Il5ra, Csf2rb, Jak3	Phosphorylated SHC recruits GRB2:SOS1
6.4e-03	Il5ra, Csf2rb, Jak3	SHC1 mediates cytokine-induced phosphorylation of GAB2
6.4e-03	Il5ra, Csf2rb, Jak3	Phosphorylated SHC1 recruits SHIP
6.4e-03	Il5ra, Csf2rb, Jak3	The SHC1:SHIP1 complex is stabilized by GRB2
7.4e-03	Lyn, Fcer1g	Binding of GPVI:Fc Epsilon R1 gamma receptor complex with collagen
7.4e-03	Lyn, Fcer1g	Fyn/Lyn-mediated phosphorylation of FcR1 gamma
7.4e-03	Il1a, Il1b	IL1R1:IL1:IL1RAP:MYD88 homodimer binds IRAK4
7.4e-03	Stat3, Stat1	JAK2 phosphorylates STAT1/STAT3
7.4e-03	Stat3, Stat1	JAK2 binds STAT1/3
7.4e-03	Socs3, Ptafr, Irf8, Icam1, Gbp5, Gbp2, Gbp4, Stat1	Interferon gamma signaling
7.5e-03	Il5ra, Csf2rb, Jak3	SOS1 activates H-Ras
9.2e-03	Ifnar2, Ifitm1, Socs3, Irf8, Gbp2, Ifitm3, Stat1	Interferon alpha/beta signaling
1.9e-07	Acss2, Rbp2, Prkar2b, Ddc, Acer1, Slc27a1, Pccb, Pfkm, Itpr2, Pdk2, Pdxk, Adh1, Alb, Fmo1, Cyp2s1, Gpt, Acsl1, Aldh6a1, Papss1, Hexb, Lrat, Maob, Gnb5, Glul, Clps, Sult2b1, Slc46a1, Cth, Hk1, Slc6a8, Pnpo, Nnt, Csad, Gba2, Gstm1, Hsd3b7, Itpr1, Cps1, Sult1a1, Cdo1, Plcb1, Ccbl1, Pfkfb4, Pck1	Metabolism
2.7e-05	Stim1, Itpr2, Itpr1	Oligomerization of STIM1
2.3e-04	Rbp2, Lrat, Clps	Vitamin A uptake in enterocytes
3.6e-04	Cth, Csad, Cdo1	Degradation of cysteine and homocysteine
3.6e-04	Pdxk, Pnpo	Vitamins B6 activation to pyridoxal phosphate
3.6e-04	Rbp2, Lrat	Esterification of retinol
5.3e-04	Stim1, Itpr2, Itpr1	Elevation of cytosolic Ca2+ levels
1.1e-03	Itpr2, Itpr1	Transport of Ca++ from platelet dense tubular system to cytoplasm
1.1e-03	Itpr2, Itpr1	Binding of IP3 to IP3 receptor
1.1e-03	Itpr2, Itpr1	IP3 binds to the IP3 receptor, opening the endoplasmic reticulum Ca2+ channel
1.1e-03	Itpr2, Itpr1	Release of calcium from intracellular stores by IP3 receptor activation
1.1e-03	Itpr2, Itpr1	Opening of ER calcium channels by activated PKA
1.2e-03	Itpr2, Itpr1, Prkcd, Dgkh	Effects of PIP2 hydrolysis
1.2e-03	Fmo1, Acss2, Gstm1, Cyp2s1, Sult1a1, Sult2b1, Papss1, Adh1, Maob	Biological oxidations
1.3e-03	Itpr2, Prkar2b, Plcb1, Itpr1, Prkcd	PLC beta mediated events
1.4e-03	Itpr2, Prkar2b, Plcb1, Itpr1, Prkcd	G-protein mediated events
1.7e-03	Sult2b1, Papss1, Sult1a1	Cytosolic sulfonation of small molecules
2.7e-03	Itpr2, Prkar2b, Itpr1, Prkcd	DAG and IP3 signaling
3.2e-03	Glul, Ccbl1, Gpt	Amino acid synthesis and interconversion (transamination)
3.4e-03	Itpr2, Prkar2b, Itpr1, Prkcd	PLC-gamma1 signalling
3.4e-03	Itpr2, Prkar2b, Itpr1, Prkcd	EGFR interacts with phospholipase C-gamma
3.4e-03	Ddc, Glul, Cps1, Gpt, Cdo1, Aldh6a1, Cth, Slc6a8, Ccbl1, Csad	Metabolism of amino acids and derivatives
3.5e-03	Smad7, Smad6	I-SMAD competes with SMAD2/3 for type I receptor (TGFBR1)
3.5e-03	Smad7, Smad6	I-Smad competes with Co-Smad for R-Smad1/5/8
3.5e-03	Itpr2, Prkar2b, Itpr1, Prkcd, Fgfr3	Phospholipase C-mediated cascade
3.8e-03	Itpr2, Prkar2b, Itpr1, Prkcd	PLCG1 events in ERBB2 signaling
4.1e-03	Itpr2, Prkar2b, Plcb1, Itpr1, Prkcd, Gnb5	Opioid Signalling
5.2e-03	Kit, Grb7	Interaction of other adapter proteins with p-KIT
5.3e-03	Rhou, Rhot2, Rhoc	Rho GTPase:GTP activates downstream effectors
5.3e-03	Stim1, Itpr2, Itpr1	Platelet calcium homeostasis
6.2e-03	Slc46a1, Steap3, Atp6v1e1, Mcoln1	Iron uptake and transport
8.5e-03	Nr4a1, Itpr2, Prkar2b, Itpr1, Prkcd, Grb7	Downstream signal transduction
8.8e-03	Itpr2, Prkar2b, Itpr1, Gnb5	Regulation of Insulin Secretion by Glucagon-like Peptide-1
9.4e-03	Fmo1, Acss2, Cyp2s1, Adh1, Maob	Phase 1 - Functionalization of compounds
9.4e-03	Smad7, Smad6	I-Smad competes with R-Smad1/5/8 for type I receptor

Table S3, continued.

Biological pathways predicted to be coordinately regulated by passive SIgA and DSS		
Statistical likelihood that the indicated pathway is regulated by passive SIgA and DSS (*P*-value)	Genes that map to this pathway	Name of this pathway
1.3e-05	Rpn1, Ddost, Rpn2	Transfer of N-glycan to the protein
1.6e-05	Rpn1, B3gnt3, Alg9, Cct6a, Ddost, Alg8, Ssr3, Pigu, Spcs3, Sec61a1, Tuba1b, Hspd1, Rpn2, Alg3	Metabolism of proteins
9.0e-05	Rpn1, Alg9, Ddost, Alg8, Rpn2, Alg3	Asparagine N-linked glycosylation
1.7e-04	Rpn1, B3gnt3, Alg9, Ddost, Alg8, Pigu, Rpn2, Alg3	Post-translational protein modification
2.8e-04	Spcs3, Sec61a1, Rpn1, Ddost, Ssr3, Rpn2	Signal peptide cleavage from ribosome-associated nascent protein
4.5e-04	Spcs3, Sec61a1, Rpn1, Ddost, Ssr3, Rpn2	SRP-dependent cotranslational protein targeting to membrane
8.5e-04	Psme3, Ccnd1, Psmb2, Psmd14	Proteasome mediated degradation of Cyclin D1
9.2e-04	Psme3, Ccnd1, Psmb2, Psmd14	Ubiquitin-dependent degradation of Cyclin D1
9.2e-04	Psme3, Ccnd1, Psmb2, Psmd14	Ubiquitin-dependent degradation of Cyclin D
1.0e-03	Psme3, Ccnd1, Psmb2, Rrm2, Psmd14, Lin54	Mitotic G1-G1/S phases
1.1e-03	Psme3, Psmb2, Chek1, Psmd14	Ubiquitin Mediated Degradation of Phosphorylated Cdc25A
1.1e-03	Psme3, Psmb2, Chek1, Psmd14	p53-Independent DNA Damage Response
1.1e-03	Psme3, Psmb2, Chek1, Psmd14	p53-Independent G1/S DNA damage checkpoint
1.8e-03	Psme3, Psmb2, Chek1, Psmd14	G1/S DNA Damage Checkpoints
2.0e-03	Spcs3, Sec61a1, Rpn1, Ddost, Ssr3, Rpn2	Translation
2.2e-03	Alg9, Alg8, Alg3	Biosynthesis of the N-glycan precursor (dolichol lipid-linked oligosaccharide, LLO) and transfer to a nascent protein
2.6e-03	Sec61a1, Rpn1, Ddost, Ssr3, Rpn2	Translocation of signal-containing nascent peptide to Endoplasmic Reticulum
4.8e-03	Aaas, Eno1, Calm3, Prps1, Pklr	Metabolism of carbohydrates
6.6e-03	Psme3, Psmb2, Psmd14	Proteasomal clevage of exogenous antigen
6.7e-03	Psme3, Psmb2, Elavl1, Psmd14	Regulation of mRNA Stability by Proteins that Bind AU-rich Elements
7.1e-03	Psme3, Psmb2, Psmd14	Destruction of AUF1 and mRNA
7.4e-03	Srm, Mtap	Metabolism of polyamines
8.5e-03	Psme3, Psmb2, Psmd14	26S proteosome degrades ODC holoenzyme complex
8.5e-03	Psme3, Psmb2, Psmd14	Proteasomal cleavage of substrate
8.5e-03	Psme3, Psmb2, Psmd14	Proteasomal cleavage of substrate
9.0e-03	Psme3, Psmb2, Psmd14	Ubiquitinated geminin is degraded by the proteasome
9.0e-03	Psme3, Psmb2, Psmd14	Ubiquitinated Orc1 is degraded by the proteasome
9.0e-03	Psme3, Psmb2, Psmd14	Ubiquitinated Cdc6 is degraded by the proteasome
9.0e-03	Psme3, Psmb2, Psmd14	Proteolytic degradation of ubiquitinated-Cdc25A
9.0e-03	Psme3, Psmb2, Psmd14	Proteasome mediated degradation of PAK-2p34
9.0e-03	Psme3, Psmb2, Psmd14	Regulation of activated PAK-2p34 by proteasome mediated degradation
9.0e-03	Psme3, Psmb2, Psmd14	Proteasome mediated degradation of PAK-2p34
9.0e-03	Psme3, Psmb2, Psmd14	Proteasome mediated degradation of COP1
9.0e-03	Psme3, Psmb2, Psmd14	Cross-presentation of soluble exogenous antigens (endosomes)
9.5e-03	Psme3, Psmb2, Psmd14	CDK-mediated phosphorylation and removal of Cdc6
9.5e-03	Psme3, Psmb2, Psmd14	Regulation of ornithine decarboxylase (ODC)
9.5e-03	Psme3, Psmb2, Psmd14	Degradation of Ubiquitinated IkB (B cell)
3.8e-04	Foxo3, Akt3	AKT can phosphorylate forkhead box transcription factors
8.6e-04	Irs2, Foxo3, Akt3	PI3K/AKT activation
9.1e-04	Foxo3, Akt3	AKT phosphorylates targets in the nucleus
1.4e-03	Foxo3, Akt3, Erbb3	PI3K events in ERBB2 signaling
1.9e-03	Akt3, Erbb3	Downregulation of ERRB2:ERBB3 signaling
2.2e-03	Nr1d1, Nr3c2, Vdr	Formation of NR-MED1 Coactivator Complex
2.2e-03	Nr1d1, Nr3c2, Vdr	Nuclear Receptor transcription pathway
2.3e-03	Nr1d1, Ccrn4l	BMAL1:CLOCK/NPAS2 Activates Circadian Expression
5.1e-03	Irs2, Foxo3, Akt3, Plekhg5, Kalrn	Signalling by NGF
9.0e-03	Foxo3, Akt3	PIP3 activates AKT signaling

Biological pathways predicted to be coordinately regulated by active SIgA and DSS		
Statistical likelihood that the indicated pathway is regulated by passive SIgA and DSS (*P*-value)	Genes that map to this pathway	Name of this pathway
7.5e-03	Agpat3, Gpam	Triglyceride Biosynthesis
9.1e-03	Agpat3, Gpam, Ugt1a9	Fatty acid, triacylglycerol, and ketone body metabolism

Table S4. Principal component analysis of microarray gene expression.

	PC1	PC2
Contribution to overall variance	55%	17%
Eigenvalue	642.98	195.69

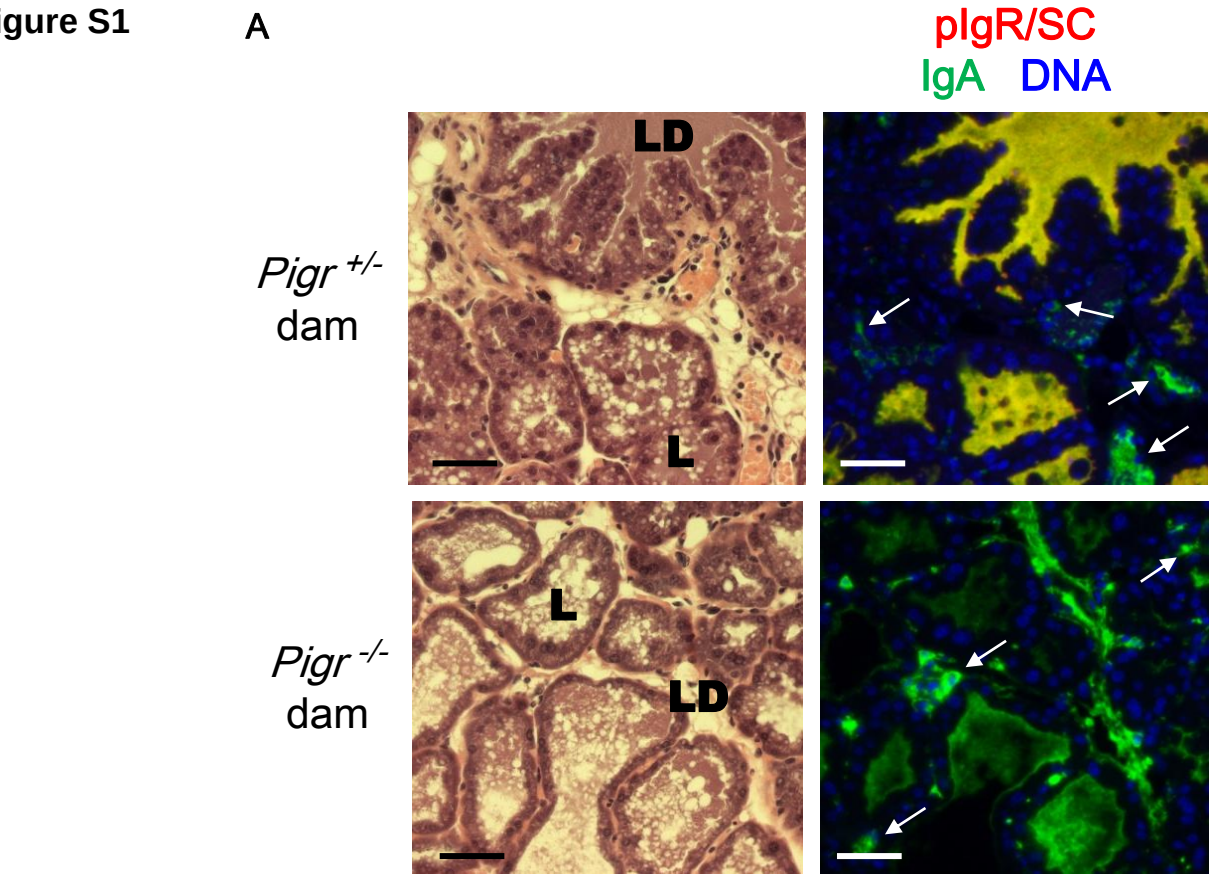
Scores for Principal Components (PCs):

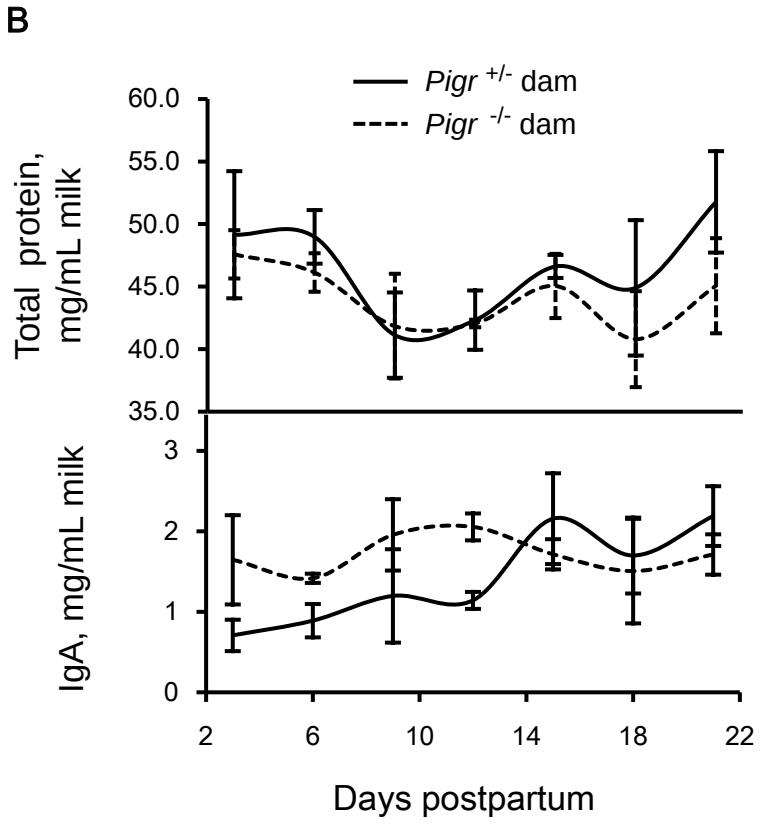
Samples	Groups	PC1	PC2
1	P-yes A-yes D-no	-22.95	-28.04
2		-23.37	-33.70
3	P-yes A-yes D-yes	25.82	-8.71
4		32.41	-5.00
5	P-yes A-no D-no	-19.65	1.53
6		-19.09	0.96
7	P-yes A-no D-yes	29.89	-3.05
8		28.03	3.56
9	P-no A-yes D-no	-26.96	5.07
10		-24.74	11.23
11	P-no A-yes D-yes	22.56	3.61
12		18.81	5.46
13	P-no A-no D-no	-28.86	19.18
14		-27.58	15.82
15	P-no A-no D-yes	17.82	4.53
16		17.88	7.55

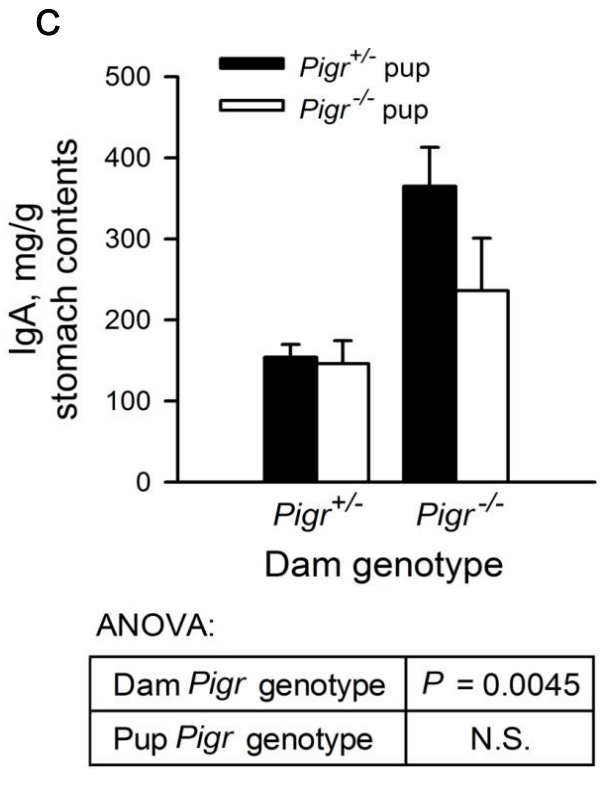
P = Passive SIgA
A = Active SIgA
D = DSS

Multifactorial principal component analysis (PCA) was conducted using expression levels of 1,130 genes identified by microarray analysis to be significantly regulated by passive SIgA, active SIgA and/or DSS ($P < 0.01$) (see **Fig. S7** for experimental design and **Table S1** for a list of regulated genes). Each sample represents pooled RNA from 3 mice, for a total of 6 mice/treatment group. **A**, Data for mRNA transcript levels from individual samples were reduced to two principal components (PC1 and PC2) that accounted for 72% of the overall variance in gene expression. PC1 and PC2 scores were calculated as the sum of normalized expression levels for each gene multiplied by weighted coefficients for that gene for PC1 and PC2.

Figure S1







ANOVA:

Dam *Pigr* genotype	$P = 0.0045$
Pup *Pigr* genotype	N.S.

Figure S1. Localization of IgA in the mammary glands of lactating *Pigr*$^{+/-}$ and *Pigr* $^{-/-}$ mice, and transit of IgA from milk to the stomach of suckling pups. **A.** Serial sections of mammary tissue stained with hematoxylin and eosin or labeled by immunofluorescence for pIgR/SC (red), IgA (green) and nuclei (blue). L, lobule; LD, lactiferous duct. White arrows in immunofluorescence images indicate clusters of IgA-secreting plasma cells. Scale bar = 50 μm. **B.** Total protein and IgA content of milk from *Pigr*$^{+/-}$ and *Pigr* $^{-/-}$ dams (mean ± SEM, n = 4). Effects of maternal *Pigr* genotype were not significant ($P > 0.05$). **C**. IgA levels of stomach contents of 10 day-old *Pigr*$^{+/-}$ and *Pigr* $^{-/-}$ neonates of different *Pigr* genotypes from *Pigr*$^{+/-}$ and *Pigr* $^{-/-}$ dams (mean ± SEM, n = 6). Significant effects of dam and pup *Pigr* genotype were determined by 2-way ANOVA. N.S., not significant ($P > 0.05$).

Figure S2

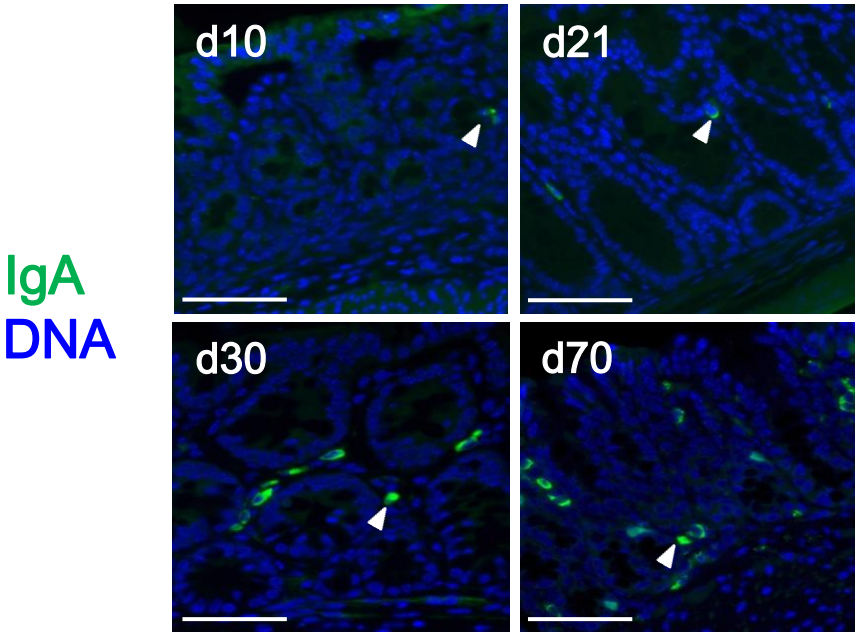


Figure S2. Numbers of IgA-secreting plasma cells in the colon increase as mice age. Sections of colon tissue from mice at the indicated ages were labeled by immunofluorescence for IgA (green) and nuclei (blue). Scale bar = 50 μm. Arrowheads indicate individual IgA^+ plasma cells. Images shown are from representative mice.

Figure S3

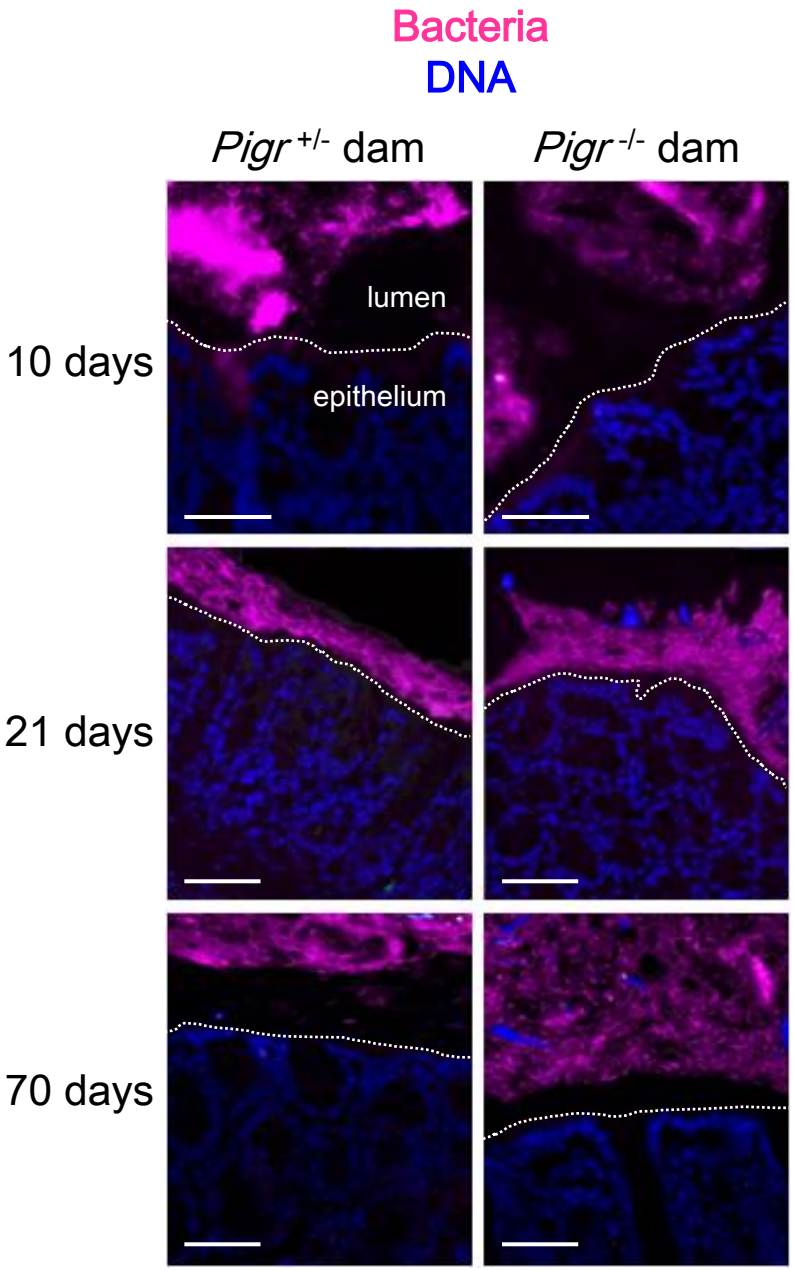


Figure S3. Localization of intestinal bacteria with respect to the epithelial surface changes with age. Segments of colon tissue from neonatal (10 days), weanling (21 days) and adult (70 days) offspring of *Pigr* $^{+/-}$ and *Pigr* $^{-/-}$ mice were treated with Carnoy's fixative to preserve the mucus layer. Sections of fixed tissue were labeled with fluorescent probes for bacterial 16S rRNA (magenta) and DNA (blue). White dotted lines denote the boundary between the epithelial surface and the colonic lumen. Scale bar = 50 μm.

Figure S4

A

Ochrobactrum anthropi ATCC 49188 chromosome 2, complete sequence

Sequence ID: gb|CP000759.1 Length: 1895911 Number of Matches: 1

Score	Expect	Identities	Gaps	Strand
329 bits(364)	4e-87	187/189 (99.8%)	1/189 (0.5%)	Plus/Plus

```
MLN clone 16S rRNA       1  GGCGTAAGGTTCAGGGCGCGCGCTGCTTCCCATTGTCCGCGCGGAATGGCCTCTATACCT
                            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
       O. anthropi  822431  GGCGTAAGGTTCAGGGCGCGCGCTGCTTCCCATTGTCCGCGCGGAATGGCCTCTATACCT

MLN clone 16S rRNA      61  CCGCGGTAAACCTCCGACGTATAGGCCGAATATTGAAGGCCAAGCGCCAGAGCGCCGGTC
                            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
       O. anthropi  822491  CCGCGGTAAACCTCCGACGTATAGGCCGAATATTGAAGGCCAAGCGCCAGAGCGCCGGTC

MLN clone 16S rRNA     121  AGGAATGCGGGCAGAACAATGCCATAGACAGGCAGCACGTAATACAGGAAAAACAACTGT
                            |||||||||||||||||||||||||| |||||||||||||||||||||||||||||||||
       O. anthropi  822551  AGGAATGCGGGCAGAACAATGCCATAGGCAGGCAGCACGTAATACAGGAAAAACAACTGT

MLN clone 16S rRNA     181  A-CAGCAGC
                            | |||||||
       O. anthropi  822611  ACCAGCAGC
```

B

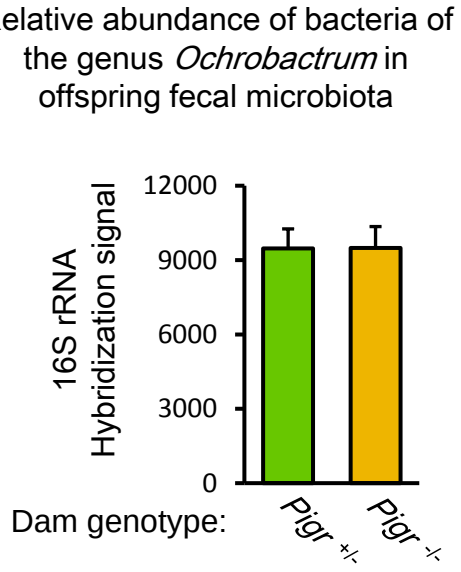


Figure S4. Identification of *Ochrobactrum anthropi* in the mesenteric lymph nodes (MLNs) of weanling offspring of *Pigr* $^{-/-}$ dams. **A.** The 16S rRNA gene was amplified, using universal primers, from a representative bacterial colony of the predominant type isolated from MLNs of 21 day-old *Pigr* $^{+/-}$ offspring of *Pigr* $^{-/-}$ dams (see **Fig. 2B** in the main text). The BLAST alignment compares the 16S rRNA sequence from the MLN clone to the genomic sequence of *Ochrobactrum anthropi* from the NCBI bacterial database. Red letters indicate mismatches or gaps in the alignment. **B.** Relative abundance of bacteria of the genus *Ochrobactrum* in fecal samples from 21 day-old *Pigr* $^{+/-}$ offspring of *Pigr* $^{+/-}$ and *Pigr* $^{-/-}$ dams. Bacterial abundance was determined by PhyloChip™ hybridization of the16S rRNA gene from fecal DNA samples. Data represent mean ± SEM (n = 5). No significant differences were observed between groups in the abundance of fecal *O. anthropi*.

Figure S5

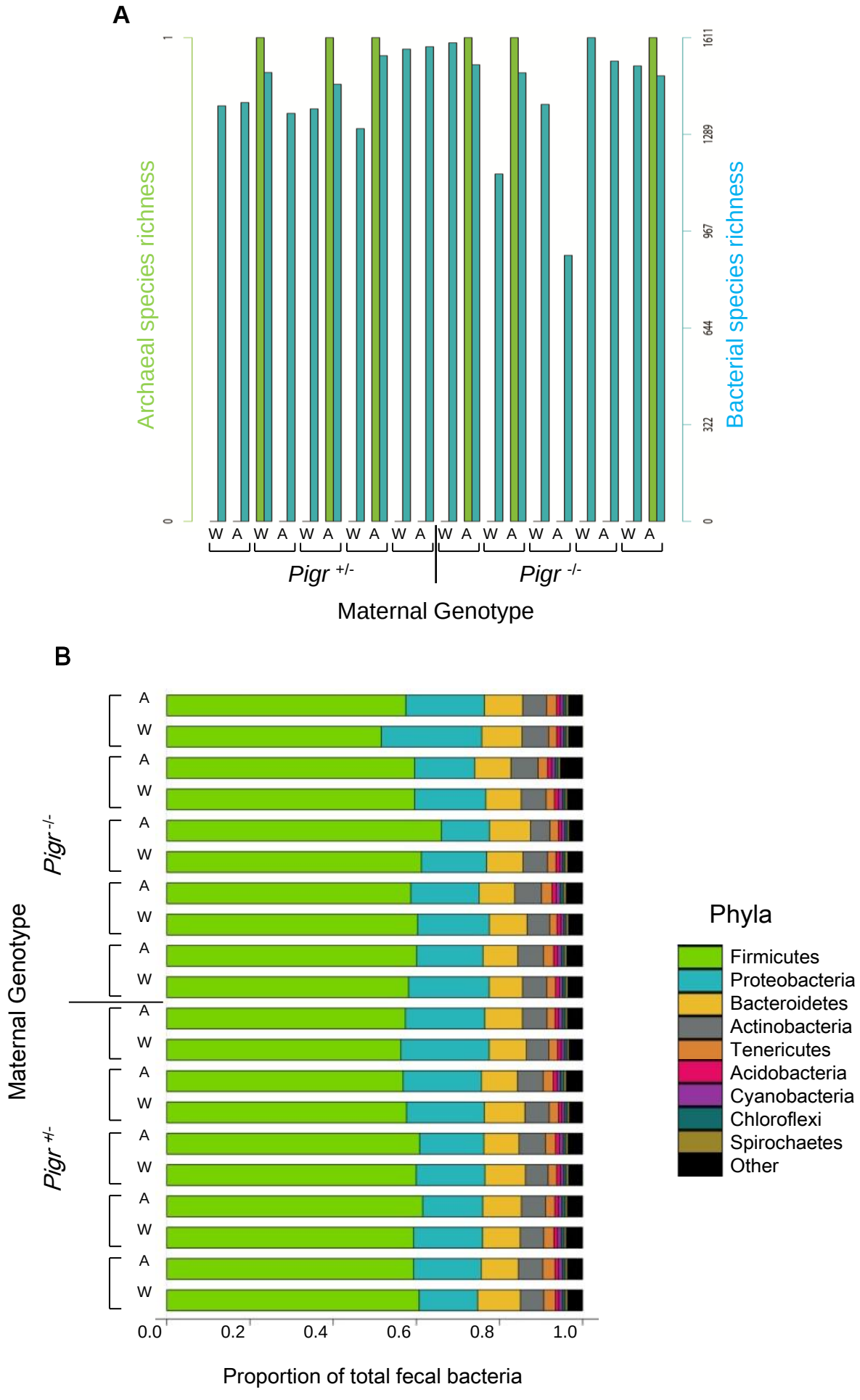

A
Archaeal species richness
Bacterial species richness
1
0
1611
1289
967
644
322
0
W A W A W A W A W A W A W A W A W A W A
Pigr +/-
Pigr -/-
Maternal Genotype
B
Maternal Genotype
Pigr -/-
Pigr +/-
A
W
0.0
0.2
0.4
0.6
0.8
1.0
Proportion of total fecal bacteria
Phyla
Firmicutes
Proteobacteria
Bacteroidetes
Actinobacteria
Tenericutes
Acidobacteria
Cyanobacteria
Chloroflexi
Spirochaetes
Other

Figure S5, continued

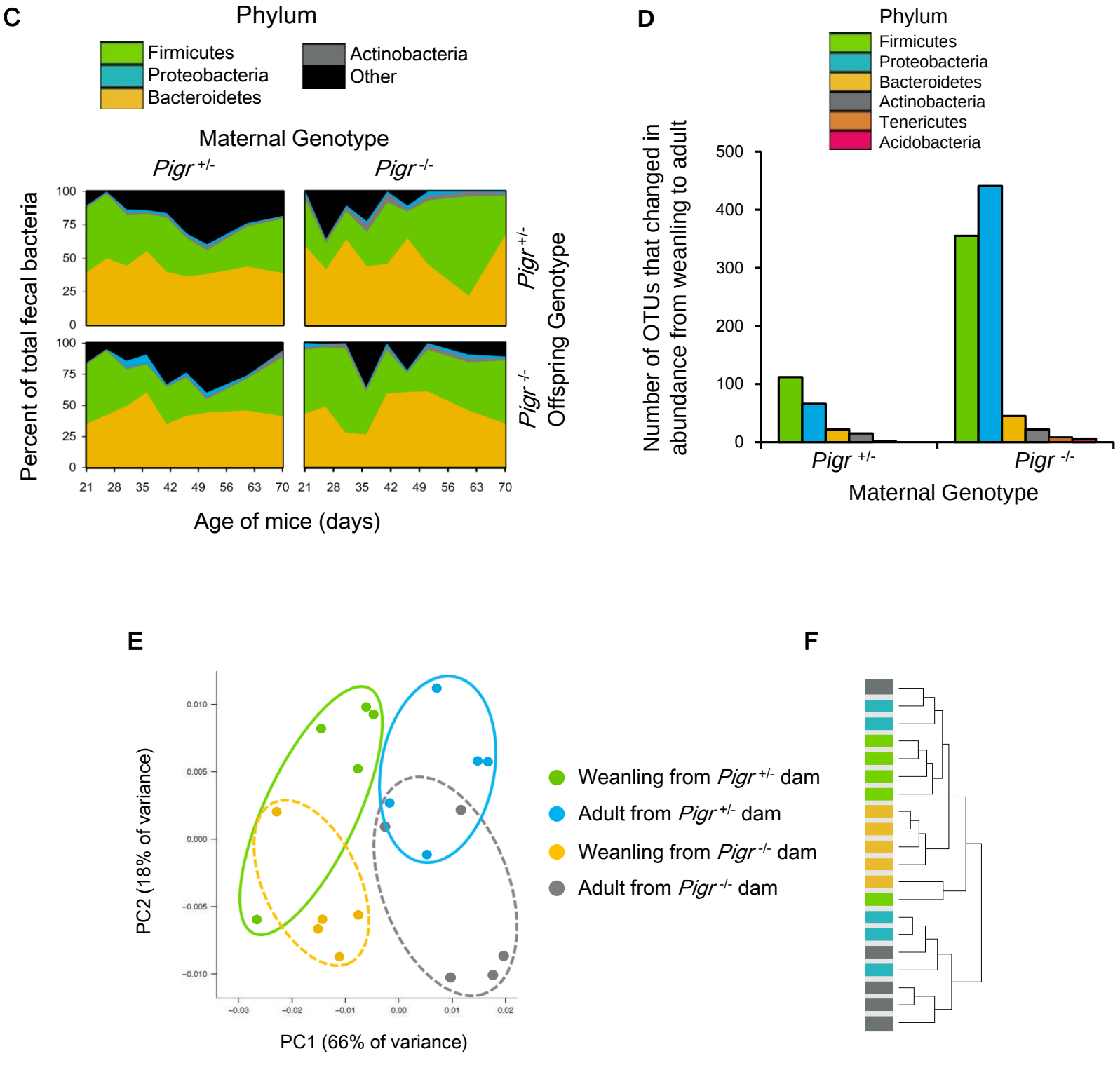


Figure S5. Changes in offspring bacterial abundance and diversity with age. **A.** Archaeal and bacterial taxon richness at the species level. Paired stool samples were collected from the same mice at 21 days (weaning, W) and 70 days (adult, A) of age, and numbers of unique operational taxonomic units (OTUs) were detected by PhyloChip™ analysis of microbial 16S rDNA. **B.** Change in the relative abundance of different phyla of fecal bacteria with age in individual mice. The abundance of unique taxa was detected in paired stool samples as described for panel B, and grouped by phylum. **C.** Change in the relative abundance of the dominant phyla of fecal bacteria with age, measured by real-time PCR using phylum-specific primers (mean, n = 6). **D.** Change in abundance of bacterial taxa from weaning (21 days) to adulthood (70 days). The abundance of unique taxa was detected in paired stool samples as described for panel B. Bars indicate the number of OTUs within the designated phyla which exhibited highly significant changes in abundance with age ($P < 0.01$). **E.** Principal coordinate analysis (PCoA) was used to generate two-dimensional ordination plots based on relative abundance (weighted Unifrac distances) of operational taxonomic units (OTUs) detected by PhyloChip™ analysis of microbial 16S rDNA in paired fecal samples from weanling and adult mice. **F.** Hierarchical clustering (average linkage) of the fecal microbiota, based on weighted Unifrac distance between samples in the abundance of 1684 taxa with significant differences across at least one of the categories (age or maternal *Pigr* genotype). It should be noted that the data in panels **E** and **F** are based on abundance of individual OTUs in individual samples (weighted Unifrac distance), whereas the data in **Fig. 3B** and **Fig. 3C** of the main article are based on the presence or absence of individual taxa (unweighted Unifrac distance).

Figure S6

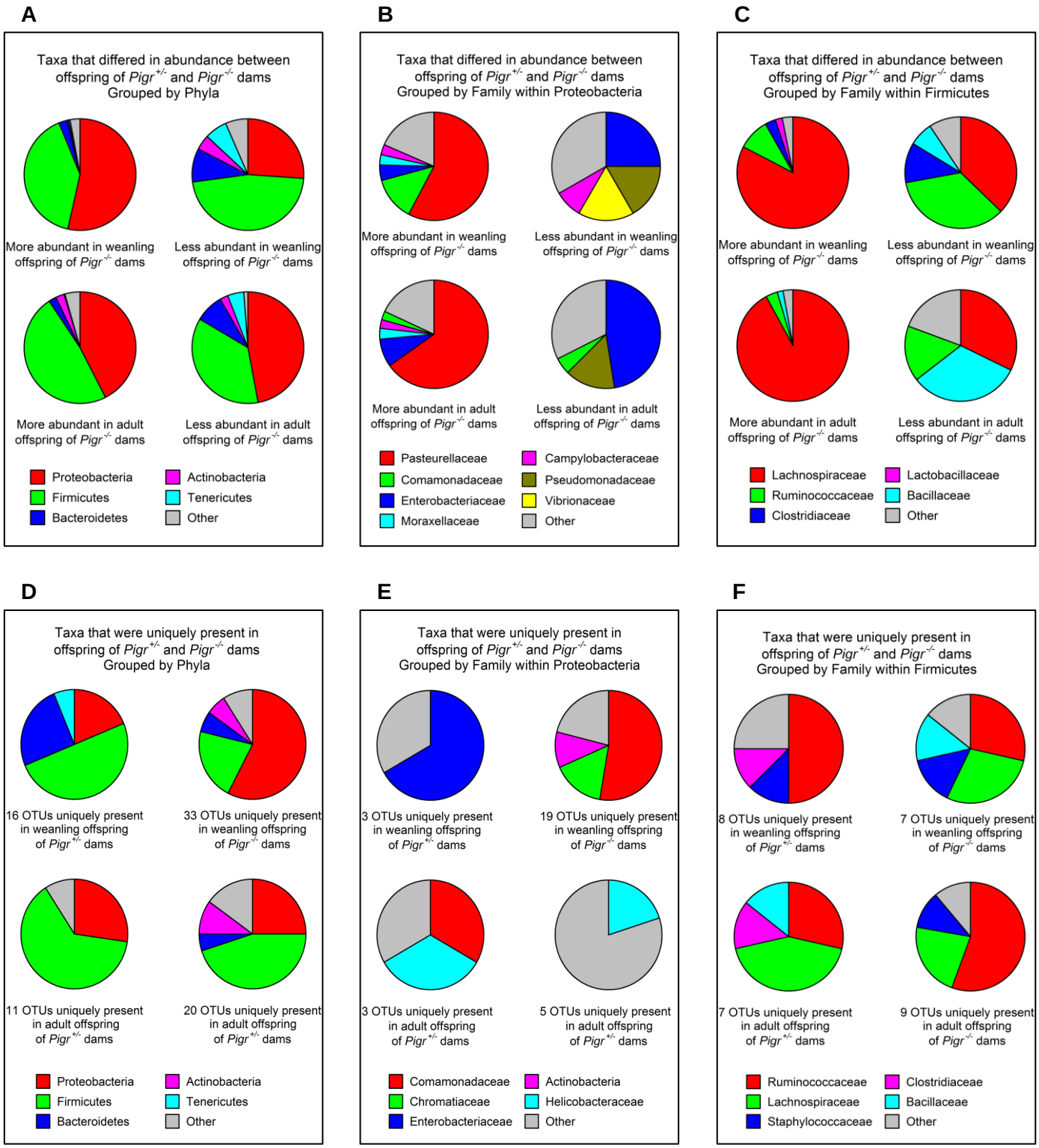

A
Taxa that differed in abundance between offspring of Pigr+/- and Pigr-/- dams Grouped by Phyla
More abundant in weanling offspring of Pigr-/- dams
Less abundant in weanling offspring of Pigr-/- dams
More abundant in adult offspring of Pigr-/- dams
Less abundant in adult offspring of Pigr-/- dams
Proteobacteria
Firmicutes
Bacteroidetes
Actinobacteria
Tenericutes
Other
B
Taxa that differed in abundance between offspring of Pigr+/- and Pigr-/- dams Grouped by Family within Proteobacteria
More abundant in weanling offspring of Pigr-/- dams
Less abundant in weanling offspring of Pigr-/- dams
More abundant in adult offspring of Pigr-/- dams
Less abundant in adult offspring of Pigr-/- dams
Pasteurellaceae
Comamonadaceae
Enterobacteriaceae
Moraxellaceae
Campylobacteraceae
Pseudomonadaceae
Vibrionaceae
Other
C
Taxa that differed in abundance between offspring of Pigr+/- and Pigr-/- dams Grouped by Family within Firmicutes
More abundant in weanling offspring of Pigr-/- dams
Less abundant in weanling offspring of Pigr-/- dams
More abundant in adult offspring of Pigr-/- dams
Less abundant in adult offspring of Pigr-/- dams
Lachnospiraceae
Ruminococcaceae
Clostridiaceae
Lactobacillaceae
Bacillaceae
Other
D
Taxa that were uniquely present in offspring of Pigr+/- and Pigr-/- dams Grouped by Phyla
16 OTUs uniquely present in weanling offspring of Pigr+/- dams
33 OTUs uniquely present in weanling offspring of Pigr-/- dams
11 OTUs uniquely present in adult offspring of Pigr+/- dams
20 OTUs uniquely present in adult offspring of Pigr-/- dams
Proteobacteria
Firmicutes
Bacteroidetes
Actinobacteria
Tenericutes
Other
E
Taxa that were uniquely present in offspring of Pigr+/- and Pigr-/- dams Grouped by Family within Proteobacteria
3 OTUs uniquely present in weanling offspring of Pigr+/- dams
19 OTUs uniquely present in weanling offspring of Pigr-/- dams
3 OTUs uniquely present in adult offspring of Pigr+/- dams
5 OTUs uniquely present in adult offspring of Pigr-/- dams
Comamonadaceae
Chromatiaceae
Enterobacteriaceae
Actinobacteria
Helicobacteraceae
Other
F
Taxa that were uniquely present in offspring of Pigr+/- and Pigr-/- dams Grouped by Family within Firmicutes
8 OTUs uniquely present in weanling offspring of Pigr+/- dams
7 OTUs uniquely present in weanling offspring of Pigr-/- dams
7 OTUs uniquely present in adult offspring of Pigr+/- dams
9 OTUs uniquely present in adult offspring of Pigr-/- dams
Ruminococcaceae
Lachnospiraceae
Staphylococcaceae
Clostridiaceae
Bacillaceae
Other

Figure S6, continued

Figure S6. Phylogenetic distribution of bacterial taxa that were altered in presence or abundance by early exposure to passive SIgA in breast milk. Paired stool samples were collected from *Pigr*$^{+/-}$ mice at 21 days of age (weanling) and from the same mice at 70 days of age (adult). Offspring of *Pigr*$^{+/-}$ dams received passive SIgA in breast milk, whereas offspring of *Pigr-/-* dams did not receive passive SIgA in breast milk (5 mice/group). Bacterial taxa were identified by PhyloChip™ analysis of microbial 16S rDNA. Operational taxonomic units (OTUs) are defined as bacterial taxa that share > 99% sequence identity of the 16S rRNA gene. **A-C,** Relative abundance of bacterial taxa was determined by weighted Unifrac distances. 1684 OTUs were identified with significant abundance differences across at least one of the categories (maternal *Pigr* genotype and/or age) ($p < 0.05$). OTUs were classified based on whether their abundance was up- or down-regulated in offspring of *Pigr*$^{-/-}$ dams relative to offspring of *Pigr*$^{+/-}$ dams. Charts in panel **A** illustrate the distribution of these taxa by bacterial phyla for each category, charts in panel **B** illustrate the distribution of taxa by family within the phylum Proteobacteria, and charts in panel **C** illustrate the distribution of taxa by family within the phylum Firmicutes. **D-F,** The presence or absence of bacterial taxa was determined by unweighted Unifrac distances. 80 OTUs were identified that were present in the majority of mice in one of the categories (maternal *Pigr* genotype and/or age) and absent in all other categories. Charts in panel **D** illustrate the distribution of these unique taxa by bacterial phyla for each category, charts in panel **E** illustrate the distribution of unique taxa by family within the phylum Proteobacteria, and charts in panel **F** illustrate the distribution of unique taxa by family within the phylum Firmicutes.

Figure S7

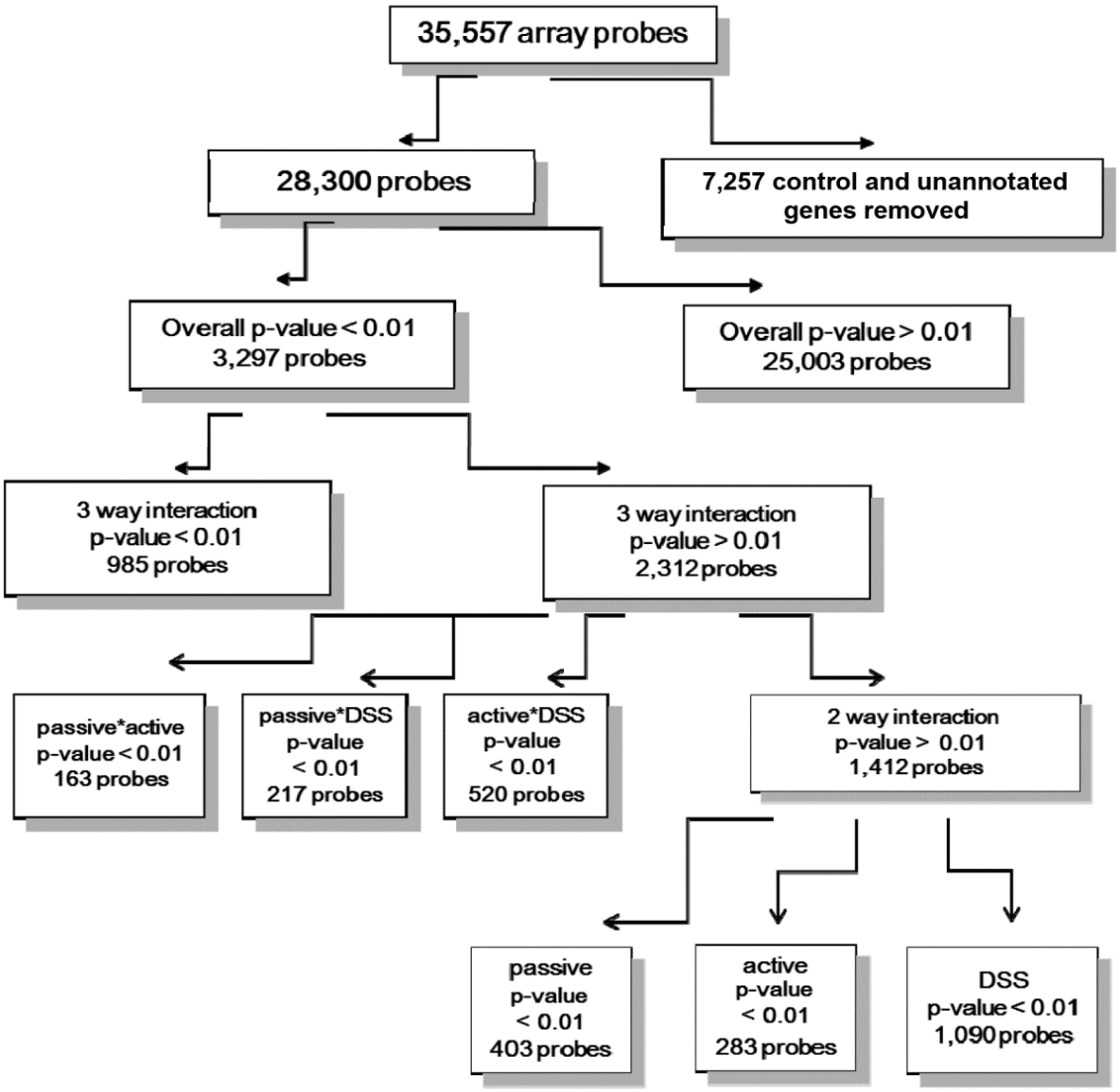


Figure S7. Three-way ANOVA of microarray gene expression data from colonic epithelial cells. Adult *Pigr*$^{+/-}$ and *Pigr*$^{-/-}$ offspring from *Pigr*$^{+/-}$ and *Pigr*$^{-/-}$ dams were given plain drinking water or 2% DSS in water for 8 days (6 mice/group). RNA was purified from isolated colonic epithelial cells and pooled into two samples for each treatment group (3 mice/sample). Gene expression was analyzed using the Affymetrix GeneChip Mouse Gene 1.0 ST array. Normalized data were analyzed by 3-way ANOVA for main effects of passive SIgA (maternal *Pigr*$^{+/-}$ or *Pigr*$^{-/-}$ genotype), active SIgA (offspring *Pigr*$^{+/-}$ or *Pigr*$^{-/-}$ genotype) and DSS treatment. Probes were discarded from the analysis when significant statistical interactions were observed between main effects, because of potential interference with the analysis of main effects. Following identification of probes that were significantly regulated by one or more of the main factors, the list was edited to remove probes for which a corresponding mouse gene has not been annotated, and to combine multiple probes that recognize different regions of the same gene. The edited list of regulated genes is shown in **Table S1.** Expression of some genes was significantly affected by more than one factor (passive SIgA, active SIgA and/or DSS).

Figure S8

A. Biological pathway predicted to be down-regulated by early exposure to passive SIgA in breast milk

Pathway Hierarchy:

Nonsense-Mediated Decay Enhanced by the Exon Junction Complex

⟶ Phosphorylated UPF1 recruits SMG5, SMG7, SMG6, and PP2A

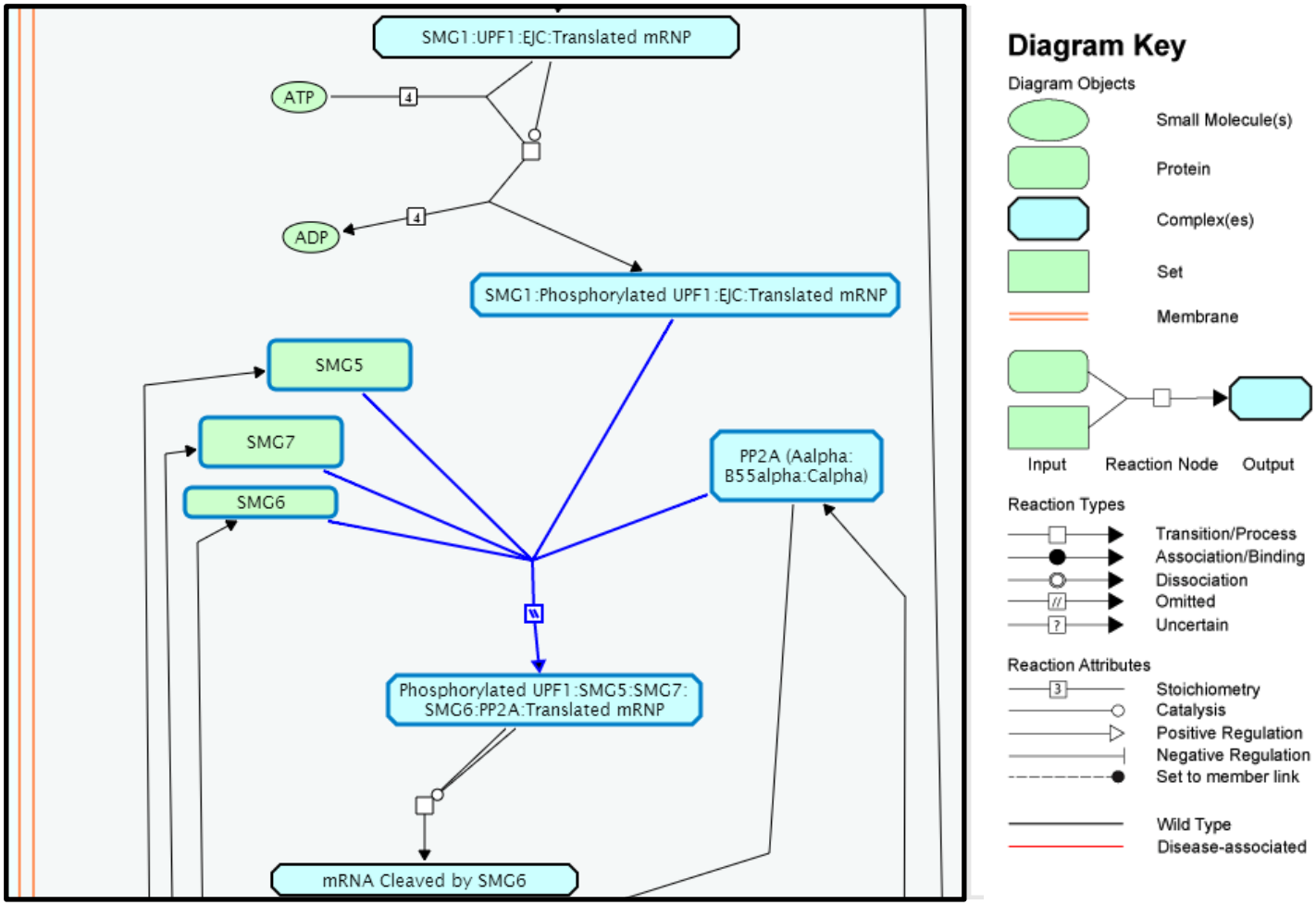


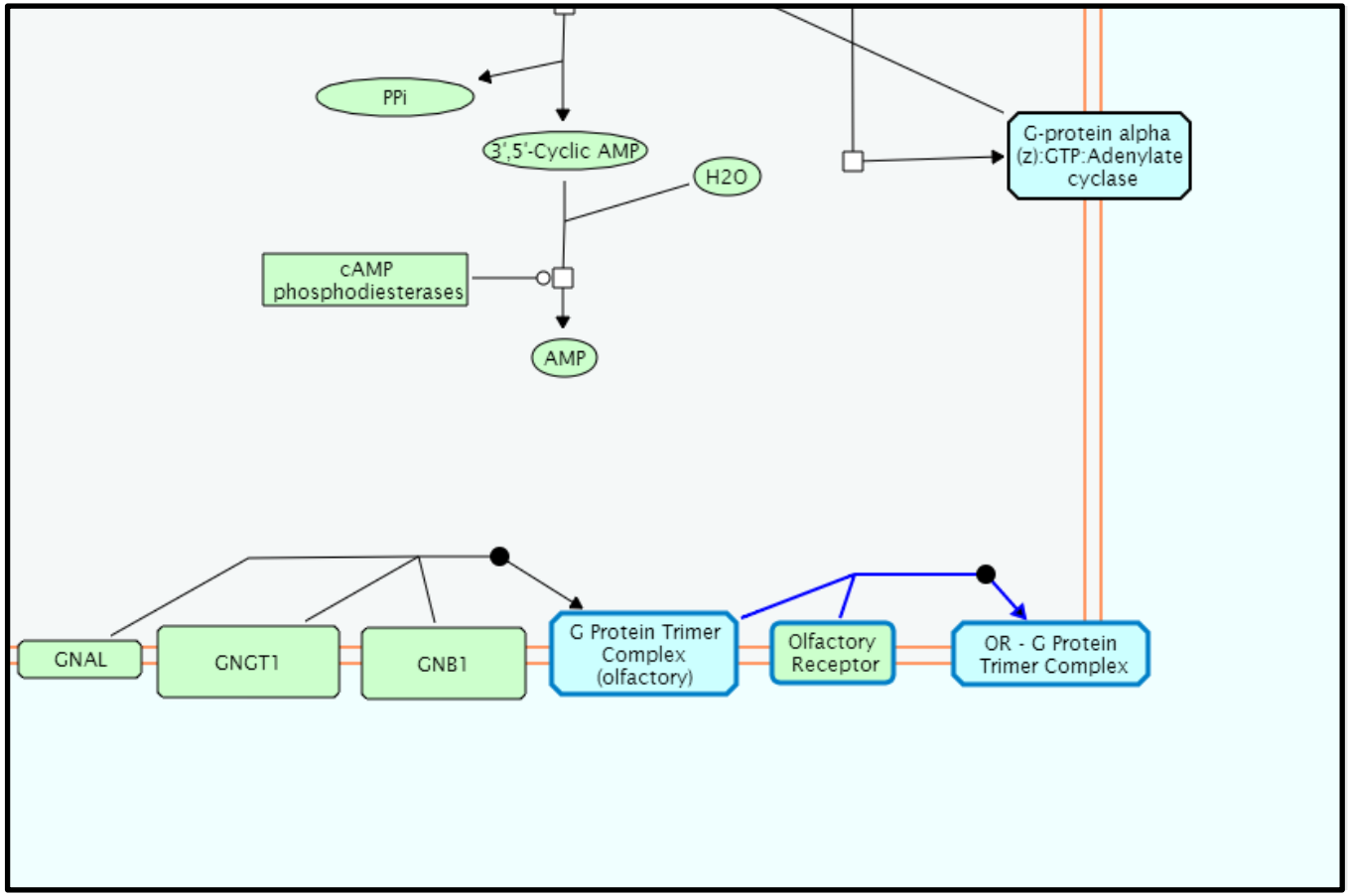
Figure S8, continued

B. Biological pathway predicted to be up-regulated by active SIgA derived from endogenous transport

Pathway Hierarchy:

Olfactory Signaling Pathway

⟶ Olfactory Receptor – G protein olfactory trimer complex formation



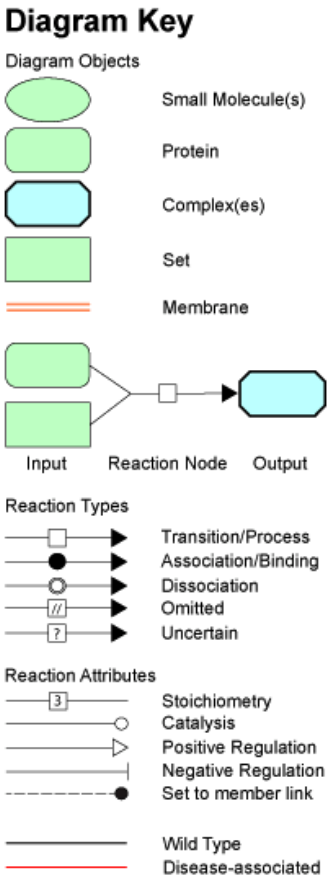


Figure S8. Representative biological pathways predicted by gene expression patterns to be regulated by passive or active SIgA in colonic epithelial cells from adult mice. Biological pathways associated with representative genes from **Table S3** were accessed by selecting the designated hyperlink for that pathway**.** These hyperlinks direct the user to the website http://www.reactome.org/PathwayBrowser, in which interactive graphs of biological pathways are displayed. In the pathways illustrated in panels **A** and **B**, specific segments influenced by passive or active SIgA are highlighted in blue. Two representative pathways are shown here, but any of the pathways listed in **Table S3** can be seen in graphical form by selecting the indicated hyperlink. **A,** The nonsense-mediated decay pathway for RNA degradation is predicted to be regulated by early exposure to passive SIgA.

Figure S9

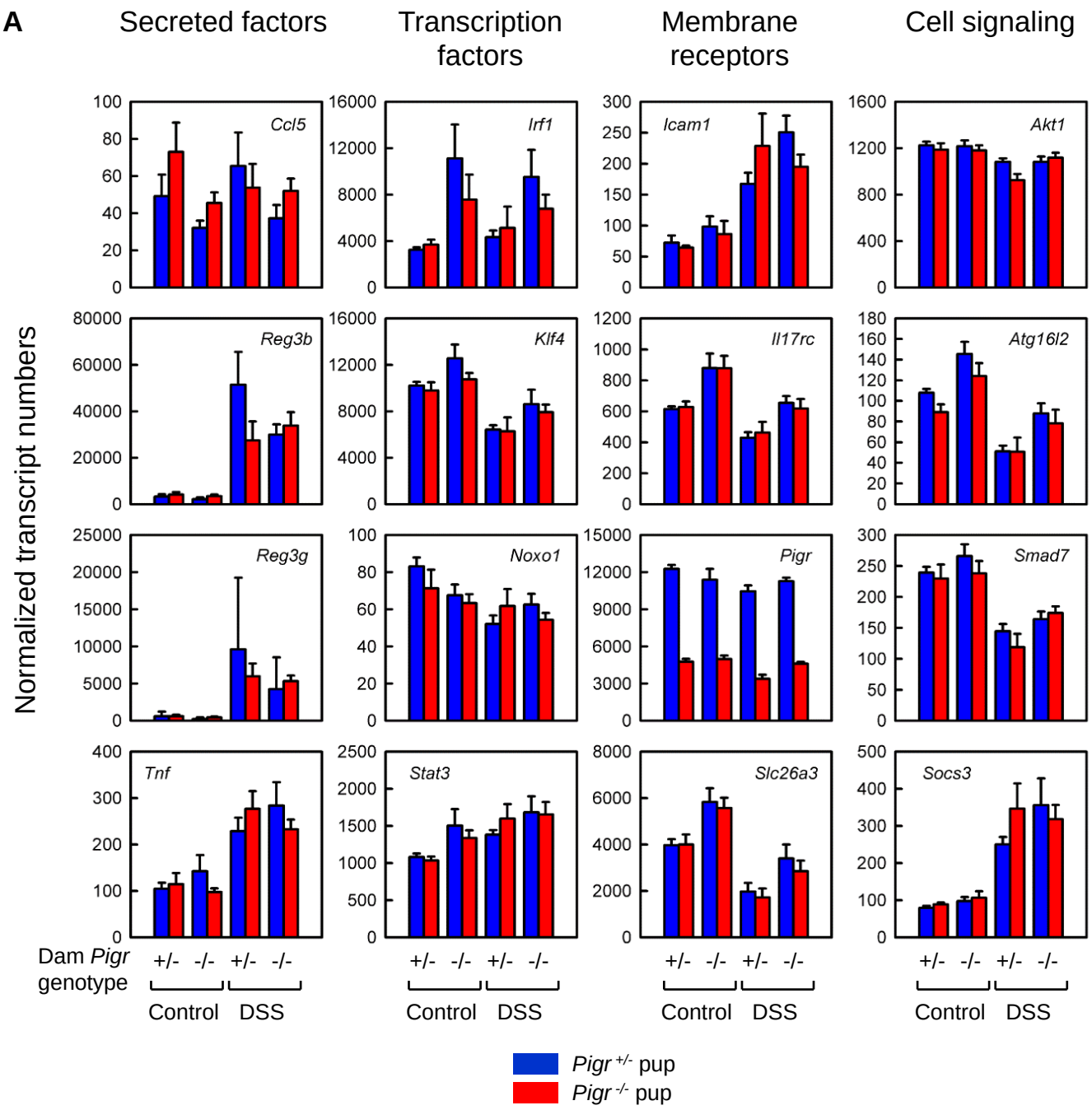

A
Secreted factors
Transcription factors
Membrane receptors
Cell signaling
Normalized transcript numbers
Ccl5
Irf1
Icam1
Akt1
Reg3b
Klf4
Il17rc
Atg16l2
Reg3g
Noxo1
Pigr
Smad7
Tnf
Stat3
Slc26a3
Socs3
Dam Pigr genotype
+/- -/- +/- -/-
Control DSS
Pigr +/- pup
Pigr -/- pup

Figure S9, continued

B

Factor	*P*-Value			
	Ccl5	***Irf1***	***Icam1***	***Akt1***
Dam *Pigr* genotype (passive SIgA)	0.0242	0.0005	0.2697	0.1720
Pup *Pigr* genotype (active SIgA)	0.2117	0.3111	0.8739	0.1324
DSS	0.7902	0.9775	< 0.0001	< 0.0001
	Reg3b	***Klf4***	***Il17rc***	***Atg16l2***
Dam *Pigr* genotype (passive SIgA)	0.3532	0.0055	< 0.0001	< 0.0001
Pup *Pigr* genotype (active SIgA)	0.3278	0.2122	0.9660	0.0944
DSS	< 0.0001	< 0.0001	< 0.0001	< 0.0001
	Reg3g	***Noxo1***	***Pigr***	***Smad7***
Dam *Pigr* genotype (passive SIgA)	0.0619	0.2625	0.2698	0.0264
Pup *Pigr* genotype (active SIgA)	0.4963	0.4298	< 0.0001	0.2665
DSS	< 0.0001	0.0043	0.0038	< 0.0001
	Tnf	***Stat3***	***Slc26a3***	***Socs3***
Dam *Pigr* genotype (passive SIgA)	0.7156	0.0163	< 0.0001	0.3128
Pup *Pigr* genotype (active SIgA)	0.6565	0.9462	0.4244	0.4866
DSS	< 0.0001	0.0029	< 0.0001	< 0.0001

Figure S9. Validation of selected genes by Nanostring nCounter™ gene expression analysis. The relative expression of each gene was determined as described in Supplemental Methods, using RNA from individual mice from the experiment described in **Figure S7**. **A**, Graphical representation of gene expression. Data are expressed as mean **±** SEM (n = 6). **B**, Three-way ANOVA of gene expression data from individual mice.

Figure S10

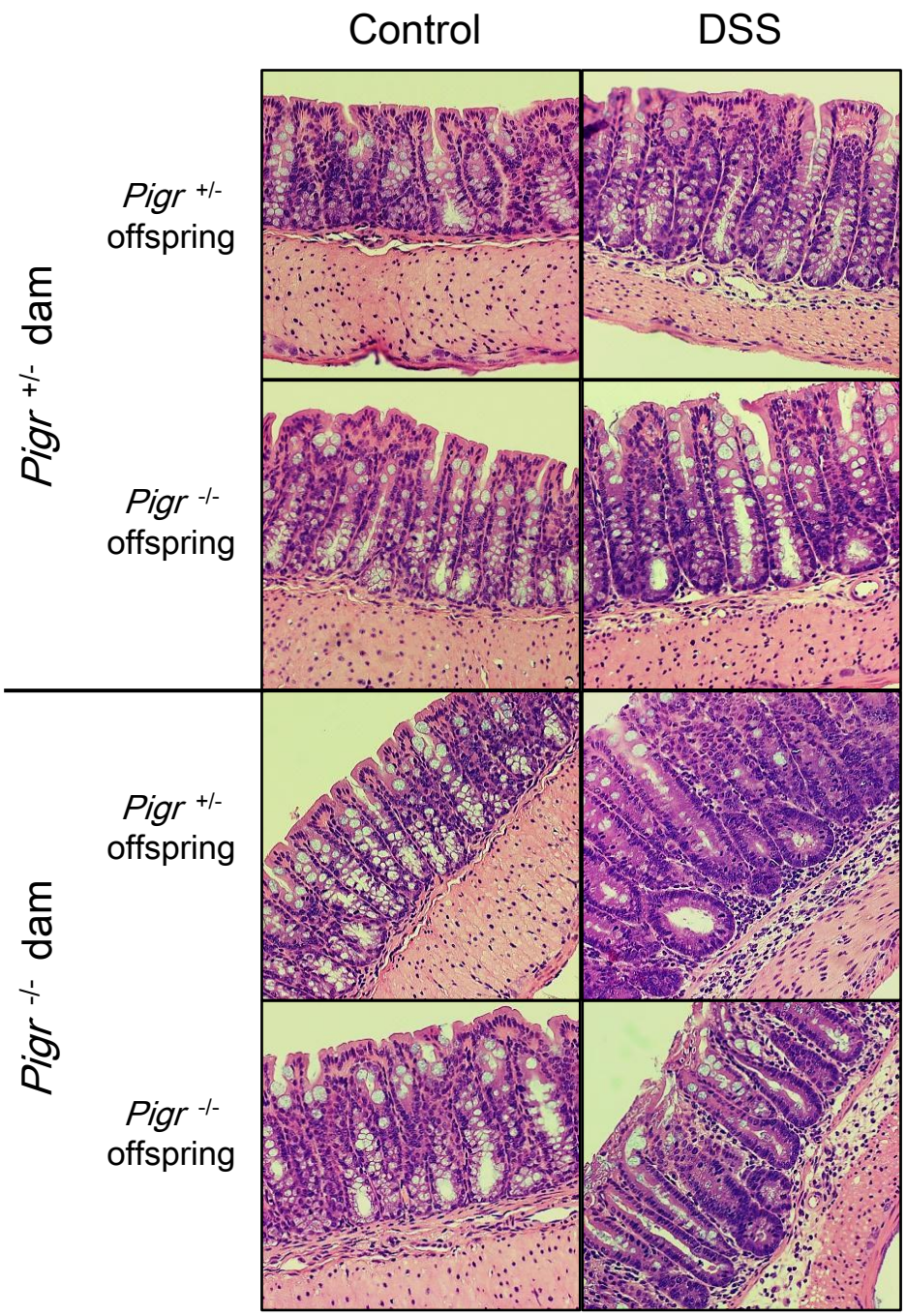


Figure S10. Effect of oral DSS administration on colon histology. Adult *Pigr*$^{+/-}$ and *Pigr*$^{-/-}$ offspring from *Pigr*$^{+/-}$ and *Pigr*$^{-/-}$ dams were given plain drinking water or 2% DSS in water for 8 days. Colons were removed, fixed in formalin, sectioned, and stained with hematoxylin and eosin. Images from representative mice from each treatment group are shown.