Supplemental material

Volk et al., https://doi.org/10.1084/jem.20190679

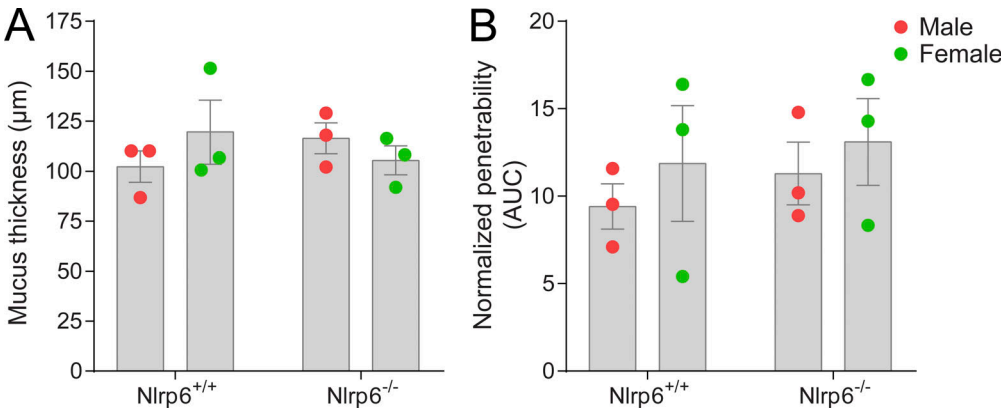

Figure S1. **Comparison of IML thickness and barrier function in *Nlrp6*$^{+/+}$ and *Nlrp6*$^{-/-}$ male and female mice. (A and B)** Data are pooled from two independent experiments (three animals per experiment). AUC, area under the curve. Error bars are SEM.

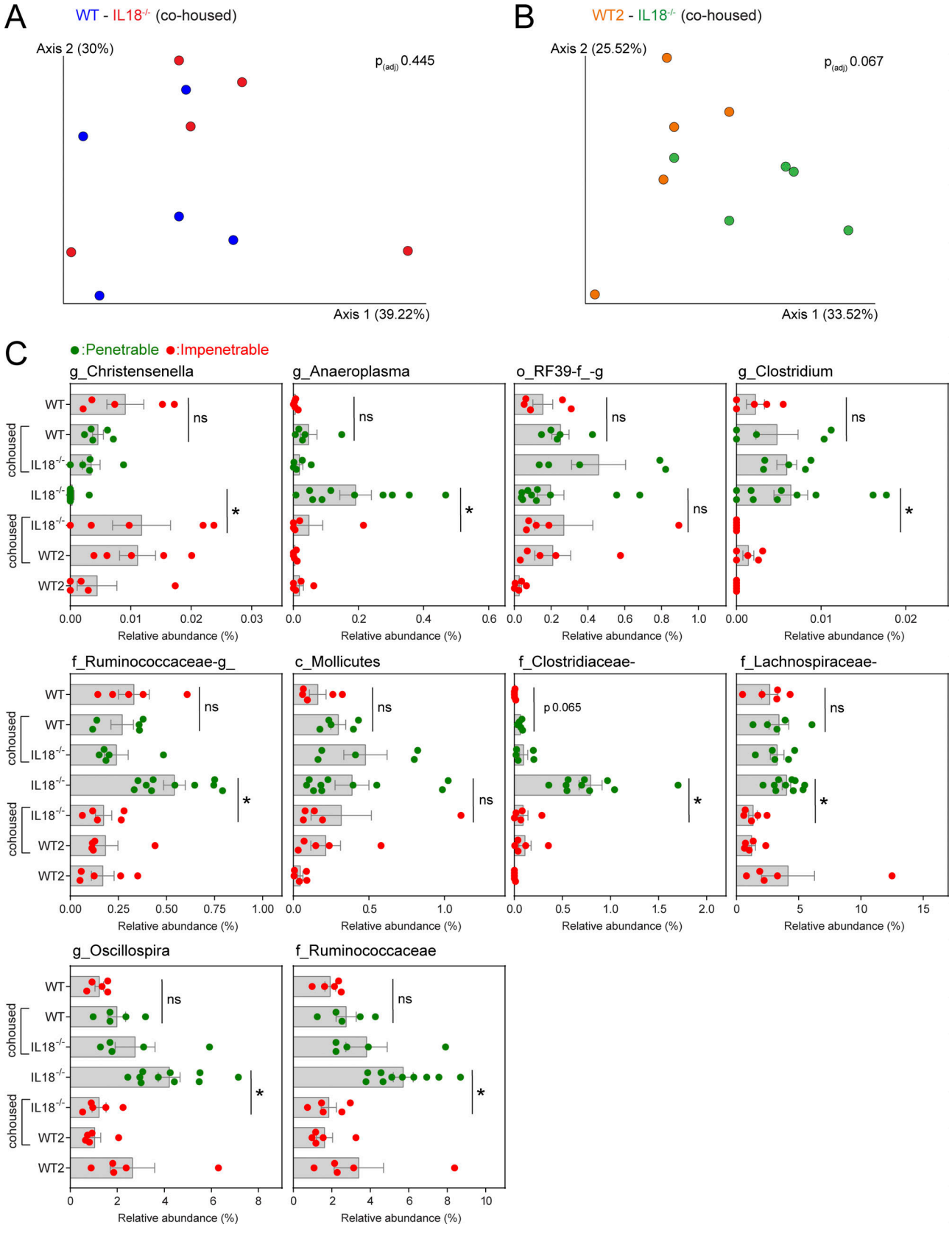

Figure S2. **Microbiota profiling in mice with divergent IML phenotypes continued.** Related to Fig. 6. **(A and B)** Principal component analysis of β-diversity (weighted UniFrac) from bacterial communities in experiments cohousing WT with *Il18*$^{-/-}$ (A) and WT2 with *Il18*$^{-/-}$ mice (B). **(C)** Relative abundance of specific taxa identified by LEfSe (Fig. 6 E) in different experimental groups; error bars represent SEM of n = 5–10 mice; *, P < 0.05, significance determined by Dunn's multiple comparison. All data are pooled from two independent experiments (five animals per experiment). ns, not significant.

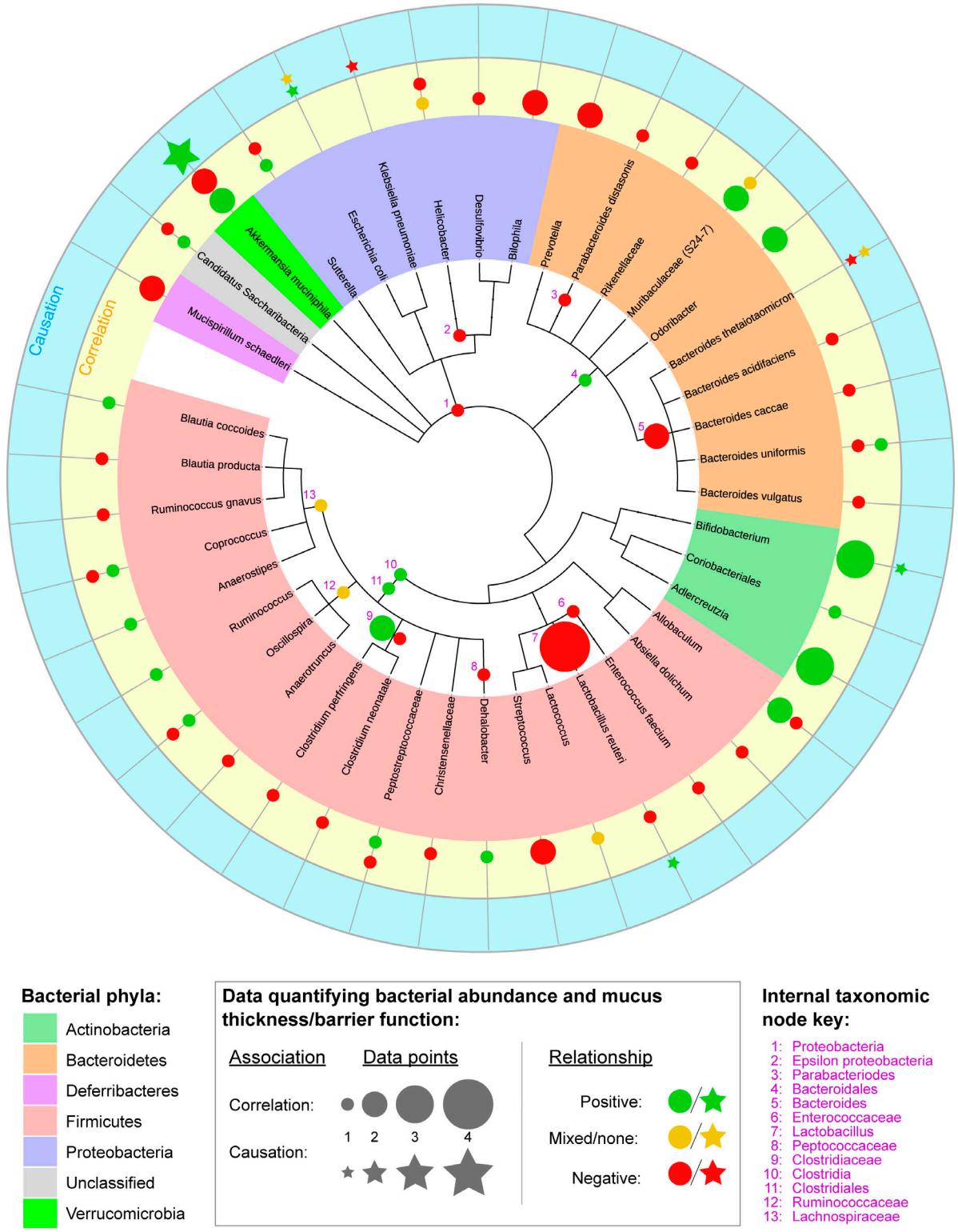

Figure S3. **Correlative and causative relationships between IML thickness and/or barrier function and the abundance of bacterial taxons in the colonic microbiota.** Related to Fig. 6. Phylogenetic tree displaying bacteria that covary with IML thickness and/or barrier function identified in public datasets. Each data point represents one independent observation. Branches terminate in the lowest ranked taxon (genus or species) identified. Positive (green), mixed/none (yellow), or negative (red) associations between taxon abundance and IML function are indicated in the inner (correlative association; circles) and outer (causative association; stars) rings. IML associations with higher ranked taxons are indicated on tree nodes and identified in the internal taxonomic node key.

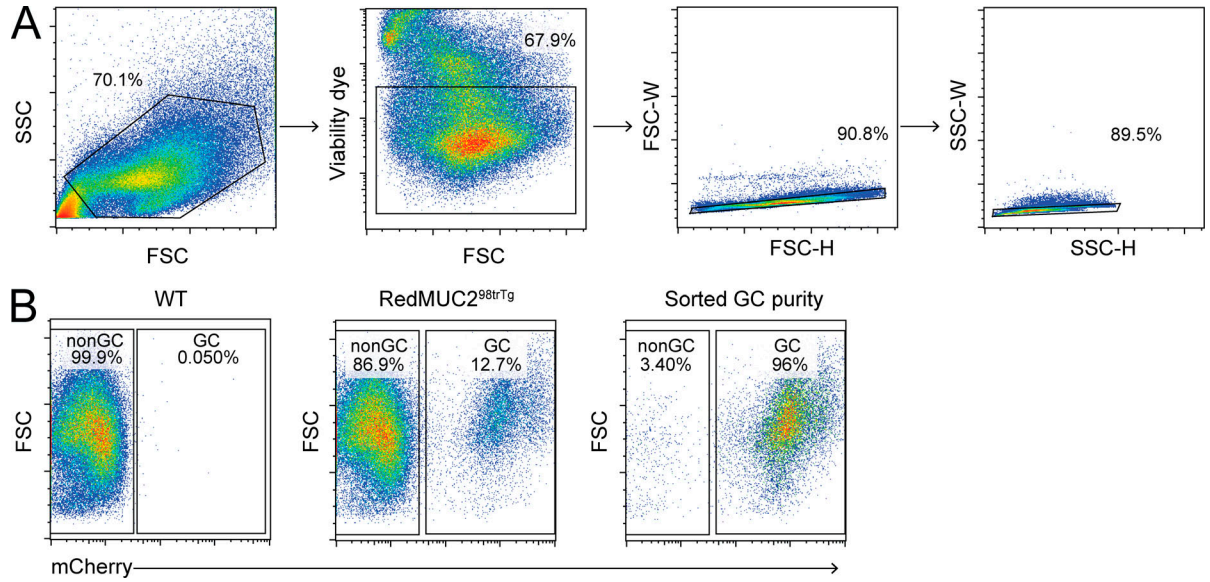

Figure S4. **Gating and sorting strategy for FACS isolation of mCherry^{+ve} and mCherry^{-ve} cells.** Related to Fig. 1, B and C; Fig. 4 A; and Fig. 5 A. **(A)** Gating strategy to isolate live single cells from debris, dead cells, and doublets. **(B)** Gating of live single cells based on mCherry signal to sort non-goblet cell (nonGC; mCherry^{-ve}) and goblet cell (GC; mCherry^{+ve}) fractions. Isolated goblet cells were resorted to check purity. Data are representative of four independent experiments.

Table S1. **List of all mouse strains used in the current study**

Mouse strain	Designation	Source
WT	C57BL/6	Long-term colony established at University of Gothenburg
WT2	C57BL/6	Colony purchased from Taconic Biosciences
mCherry-MUC2 transgenic mouse	RedMUC2^{98trTg}	Birchenough et al., 2016
Nlrp3$^{-/-}$	B6.Nlrp3^{tm1}	Martinon et al., 2006
Nlrc4$^{-/-}$	B6.C2-Nlrc4^{tm1Vmd}	Mariathasan et al., 2004
Nlrp6$^{-/-}$	B6.129/Sv-Nlrp6$^{tm1.1Kuv/LAS}$	Chen et al., 2011
Casp1/11$^{-/-}$	B6.129S2-Casp1^{tm1Sesh}	Li et al., 1995
Casp11$^{-/-}$	B6.Casp11^{tm1}	Kayagaki et al., 2011
Il1ab$^{-/-}$	B6.D-IL1a^{tm1Yiw}/IL1b^{tm1Yiw}	Horai et al., 1998
Il18$^{-/-}$	B6.129P2-Il18^{tm1Aki}	Takeda et al., 1998

Table S2. **List of all qRT-PCR primers**

Gene	Primer (F/R)	Source/sequence (5′–3′)	Primer ID
Aim2	F	Sigma-Aldrich	FM1_Aim2
Aim2	R	Sigma-Aldrich	RM1_Aim2
Asc	F	Sigma-Aldrich	FM1_Pycard
Asc	R	Sigma-Aldrich	RM1_Pycard
Car1	F	Sigma-Aldrich	FM1_Car1
Car1	R	Sigma-Aldrich	RM1_Car1
Casp1	F/R	Bio-Rad	qMmuCID0026983
Casp11	F/R	Bio-Rad	qMmuCID0005809
Clca1	F	Sigma-Aldrich	FM1_Clca3
Clca1	R	Sigma-Aldrich	RM1_Clca3
Clca4a	F	Sigma-Aldrich	FM1_Clca6
Clca4a	R	Sigma-Aldrich	RM1_Clca6
Gapdh	F	GGAGAAACCTGCCAAGTATG	N/A
Gapdh	R	GGAGTTGCTGTTGAAGTCG	N/A
Ifi204	F	Sigma-Aldrich	FM1_Ifi204
Ifi204	R	Sigma-Aldrich	RM1_Ifi204
Il13ra1	F	Sigma-Aldrich	FM1_Il13ra1
Il13ra1	R	Sigma-Aldrich	RM1_Il13ra1
Il18	F	Sigma-Aldrich	FM1_Il18
Il18	R	Sigma-Aldrich	RM1_Il18
Il18r1	F	Sigma-Aldrich	FM1_Il18r1
Il18r1	R	Sigma-Aldrich	RM1_Il18r1
Il18rap	F	Sigma-Aldrich	FM1_Il18rap
Il18rap	R	Sigma-Aldrich	RM1_Il18rap
Il1b	F	Sigma-Aldrich	FM1_Il1b
Il1b	R	Sigma-Aldrich	RM1_Il1b
Il4ra	F	Sigma-Aldrich	FM1_Il4ra
Il4ra	R	Sigma-Aldrich	RM1_Il4ra
Nlrc4	F	Sigma-Aldrich	FM1_Nlrc4
Nlrc4	R	Sigma-Aldrich	RM1_Nlrc4
Nlrp12	F	Sigma-Aldrich	FM1_Nlrp12
Nlrp12	R	Sigma-Aldrich	RM1_Nlrp12
Nlrp1b	F	Sigma-Aldrich	FM1_Nlrp1b
Nlrp1b	R	Sigma-Aldrich	RM1_Nlrp1b
Nlrp2	F	Sigma-Aldrich	FM1_Nlrp2
Nlrp2	R	Sigma-Aldrich	RM1_Nlrp2
Nlrp3	F	Sigma-Aldrich	FM1_Nlrp3
Nlrp3	R	Sigma-Aldrich	RM1_Nlrp3
Nlrp6	F/R	Bio-Rad	qMmuCID0024291
Nlrp9b	F	Sigma-Aldrich	FM1_Nlrp9b
Nlrp9b	R	Sigma-Aldrich	RM1_Nlrp9b
Nos2	F	CTTGGTGAAAGTGGTGTTCTTTG	N/A
Nos2	R	TCAGACTTCCCTGTCTCAGTAG	N/A

Table S2. **List of all qRT-PCR primers (*Continued*)**

Gene	Primer (F/R)	Source/sequence (5′–3′)	Primer ID
Pyrin	F	Sigma-Aldrich	FM1_Mefv
Pyrin	R	Sigma-Aldrich	RM1_Mefv
Rig1	F	Sigma-Aldrich	FM1_Ddx58
Rig1	R	Sigma-Aldrich	RM1_Ddx58
Rplpo	F	GCGACCTGGAAGTCCAACTA	N/A
Rplpo	R	TCTCCAGAGCTGGGTTGTTT	N/A
Tff3	F	Sigma-Aldrich	FM1_Tff3
Tff3	R	Sigma-Aldrich	RM1_Tff3
Tnfa	F	CAGGCGGTGCCTATGTCTC	N/A
Tnfa	R	CGATCACCCCGAAGTTCAGTAG	N/A

F, forward; N/A, not applicable; R, reverse.

Table S3. **Data references for identified microbiota–IML associations**

Bacterial taxon	Effect on colonic mucus layer	Reference
Adlercreutzia	Positively correlated with mucus barrier function	Chassaing et al., 2015
Adlercreutzia	Multiple positive correlations with mucus barrier function	Schroeder et al., 2018
Adlercreutzia	Multiple positive correlations with mucus barrier function	Current study
Akkermansia muciniphilia	Positively correlated mucus thickness	Zhu et al., 2018
A. muciniphilia	Increases mucus thickness	Everard et al., 2013
A. muciniphilia	Increases mucus thickness	Ganesh et al., 2013
A. muciniphilia	Increases mucus thickness	Dingemanse et al., 2015
A. muciniphilia	Negatively correlated with mucus thickness	Desai et al., 2016
A. muciniphilia	Negatively correlated with mucus barrier function	Chassaing et al., 2015
A. muciniphilia	Positively correlated with mucus barrier function	Schroeder et al., 2018
Allobaculum	Positively correlated with mucus barrier function	Jakobsson et al., 2015
Allobaculum	Positively correlated with mucus barrier function	Chassaing et al., 2015
Allobaculum	Multiple negative correlations with mucus barrier function	Schroeder et al., 2018
Anaerostipes	Positively correlated with mucus barrier function	Jakobsson et al., 2015
Anaerotruncus	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Bacteriodes	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
Bacteriodes	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Bacteriodes acidifaciens	Negatively correlated with mucus barrier function	Thaiss et al., 2016
Bacteriodes uniformis	Negatively correlated with mucus thickness	Desai et al., 2016
Bacteroidales	Positively correlated with mucus thickness	Wlodarska et al., 2011
Bacteroides caccae	Negatively correlated with mucus thickness	Desai et al., 2016
Bacteroides thetaiotomicron	No effect on mucus thickness	Li et al., 2015
B. thetaiotomicron	Decreases mucus thickness (monocolonization)	Earle et al., 2015
Bacteroides vulgatus	Negatively correlated with mucus thickness	Elderman et al., 2017
Bifidobacteria	Increased mucus growth	Schroeder et al., 2018
Bifidobacteria	Positively correlated with mucus thickness	Pélissier et al., 2010
Bifidobacteria	Positively correlated with mucus barrier function	Chassaing et al., 2015
Bifidobacteria	Positively correlated with mucus barrier function	Zou et al., 2018
Bilofila	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Bilofila	Multiple negative correlations with mucus barrier function	Schroeder et al., 2018
Blautia coccoides	Positively correlated with mucus thickness	Wlodarska et al., 2011
Blautia producta	Negative correlations with mucus barrier function	Chassaing et al., 2015
Christensenellaceae	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Clostridia	Positively correlated with mucus barrier function	Johansson et al., 2015
Clostridiaceae	Positively correlated with increased mucus thickness	Wlodarska et al., 2015
Clostridiaceae	Negative correlations with mucus barrier function	Chassaing et al., 2015
Clostridiaceae	Positively correlated with mucus barrier function	Schroeder et al., 2018
Clostridiales	Positively correlated with mucus thickness	Glymenaki et al., 2017
Clostridium neonatale	Negative correlations with mucus barrier function	Chassaing et al., 2015
Clostridium perfringens	Negative correlations with mucus barrier function	Chassaing et al., 2015
Coprococcus	Positively correlated with mucus barrier function	Chassaing et al., 2015
Coprococcus	Multiple negative correlations with mucus barrier function	Schroeder et al., 2018
Coriobacteriales	Positively correlated with mucus barrier function	Chassaing et al., 2015
Dehalobacteriaceae	Positively correlated with mucus barrier function	Chassaing et al., 2015

Table S3. **Data references for identified microbiota–IML associations (*Continued*)**

Bacterial taxon	Effect on colonic mucus layer	Reference
Desulfovibrio	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
Enterococcaceae	Negatively correlated with mucus barrier function	Zou et al., 2018
Enterococcus faecium	Negatively correlated with mucus thickness	Hendrickx et al., 2015
Epsilon proteobacteria	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
E. coli	Increases mucus thickness (monocolonization)	Tomas et al., 2015
E. coli	No effect on mucus thickness	Li et al., 2015
Eubacterium dolichum	Negative correlations with mucus barrier function	Chassaing et al., 2015
Helicobacter	Negative and positive correlations with mucus barrier function	Chassaing et al., 2015
Helicobacter	Multiple negative correlations with mucus barrier function	Schroeder et al., 2018
Klebsiella pneumoniae	Decreases mucus barrier function	Caballero et al., 2015
Lachnospiraceae	Negative and positive correlations with mucus barrier function	Chassaing et al., 2015
Lactobacillaceae	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Lactobacillus	Negatively correlated with mucus thickness	Wlodarska et al., 2011
Lactobacillus	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Lactobacillus	Negatively correlated with mucus barrier function	Johansson et al., 2015
Lactobacillus	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Lactobacillus reuteri	Negatively correlated with mucus barrier function	Thaiss et al., 2016
L. reuteri	Increases mucus thickness	Ahl et al., 2016
Lactococcus	Multiple negative correlations with mucus barrier function	Schroeder et al., 2018
Mucispirillum schaedleri	Negatively correlated with mucus barrier function	Thaiss et al., 2016
M. schaedleri	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Odoribacter	Positively correlated with mucus barrier function	Chassaing et al., 2015
Odoribacter	Multiple positive correlations with mucus barrier function	Schroeder et al., 2018
Oscillospira	Positively correlated with mucus barrier function	Chassaing et al., 2015
Oscillospira	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Parabacteroides	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
Parabacteroides distasonis	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Peptococcaceae	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Peptostreptococcaceae	Positively correlated with increased mucus thickness	Wlodarska et al., 2015
Peptostreptococcaceae	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Prevotella	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
Prevotella	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Proteobacteria	Negatively correlated with mucus barrier function	Zou et al., 2018
Rikenellaceae	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Ruminococcaceae	Negative and positive correlations with mucus barrier function	Chassaing et al., 2015
Ruminococcus	Multiple positive correlations with mucus barrier function	Schroeder et al., 2018
Ruminococcus gnavus	Negatively correlated with mucus barrier function	Thaiss et al., 2016
S24-7	Negative and positive correlations with mucus barrier function	Chassaing et al., 2015
S24-7	Multiple positive correlations with mucus barrier function	Schroeder et al., 2018
S24-7	Multiple positive correlations with mucus barrier function	Current study
Streptococcus	Negatively correlated with mucus barrier function	Zou et al., 2018
Streptococcus	Negatively correlated with mucus barrier function	Schroeder et al., 2018
Sutterella	Negatively correlated with mucus barrier function	Chassaing et al., 2015
Sutterella	Multiple positive correlations with mucus barrier function	Schroeder et al., 2018

Table S3. **Data references for identified microbiota–IML associations (*Continued*)**

Bacterial taxon	Effect on colonic mucus layer	Reference
TM7	Negatively correlated with mucus barrier function	Jakobsson et al., 2015
TM7	Positively correlated with mucus barrier function	Chassaing et al., 2015

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