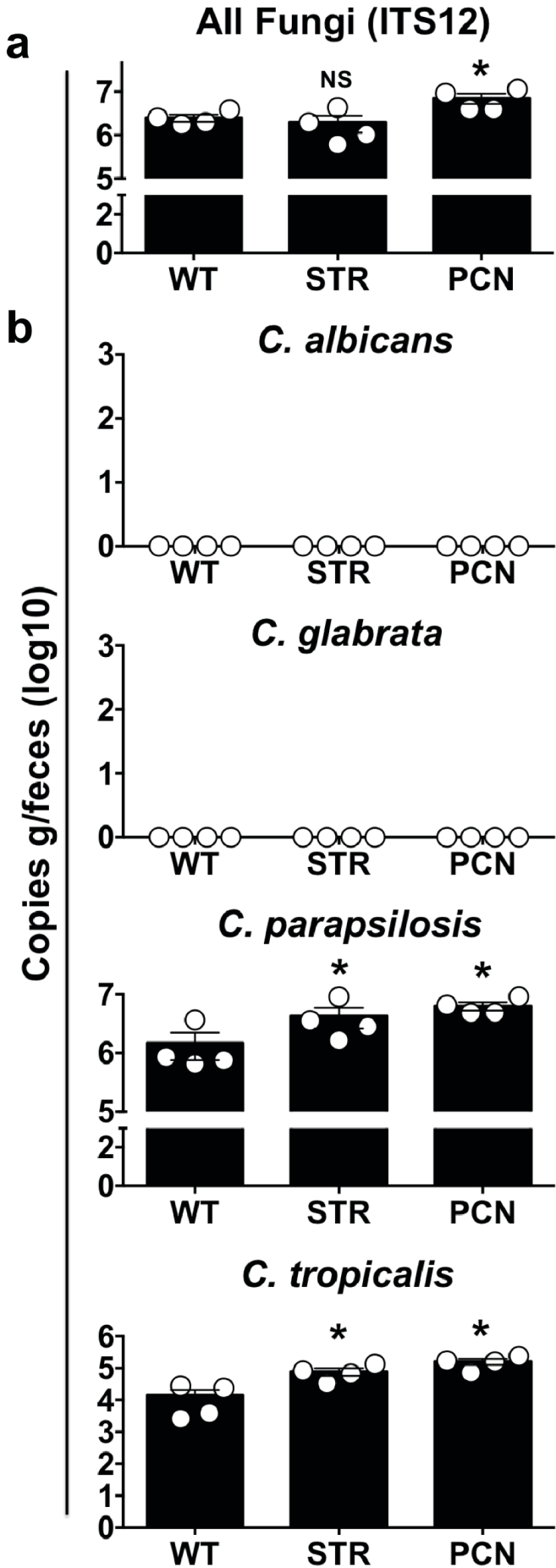
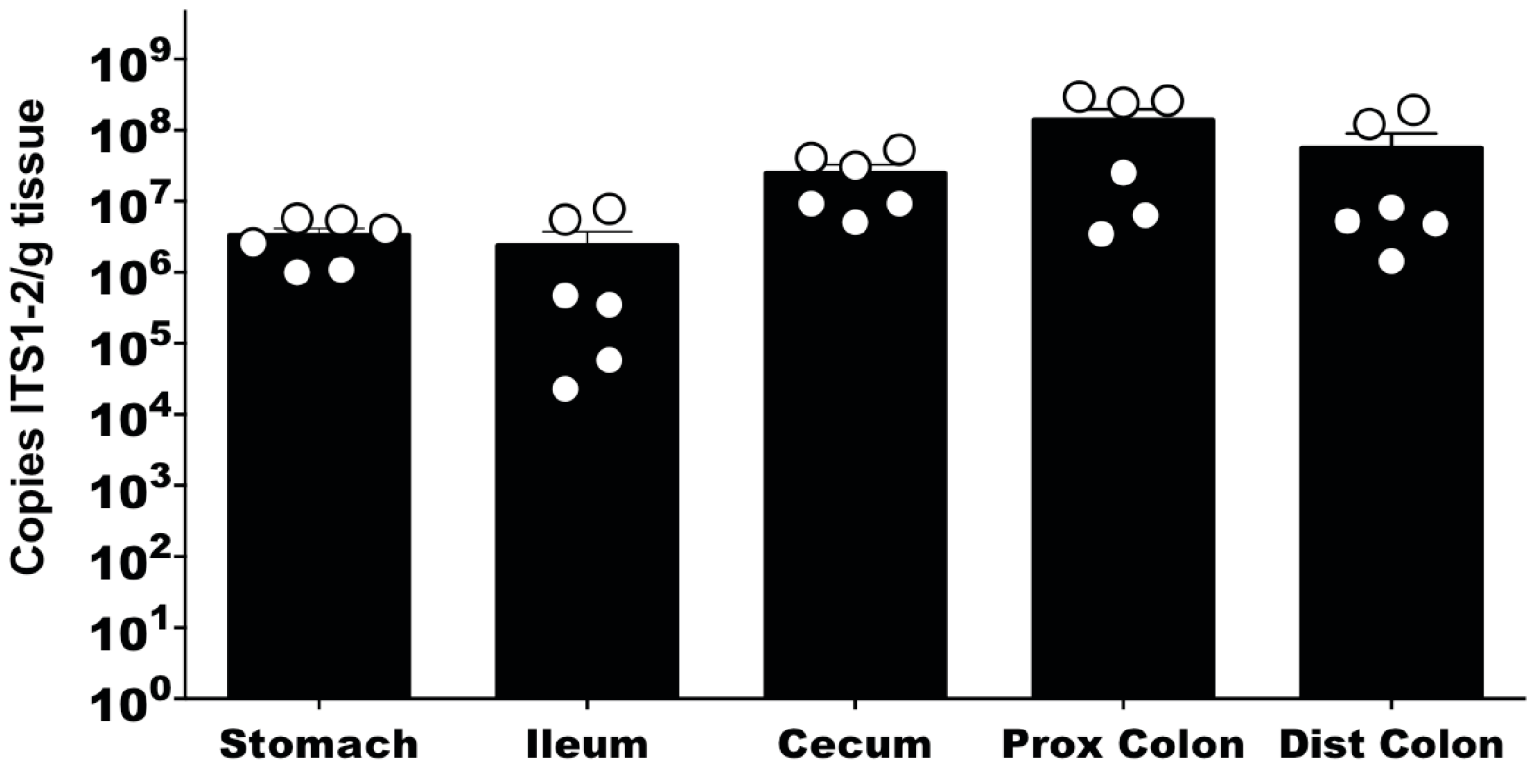


**Supplementary Figure 1. Murine-adapted *Candida albicans* GI colonization levels in adult mice.** Murine-adapted *C. albicans* strains (a) SC5314 and (b) CAF2-1 GI colonization levels in untreated (no antibiotics) C3H/HeN adult mice (Harlan, female, 6-8 weeks). n=4. Points represent results from individual animals, and horizontal lines with bars representing the median with interquartile range.

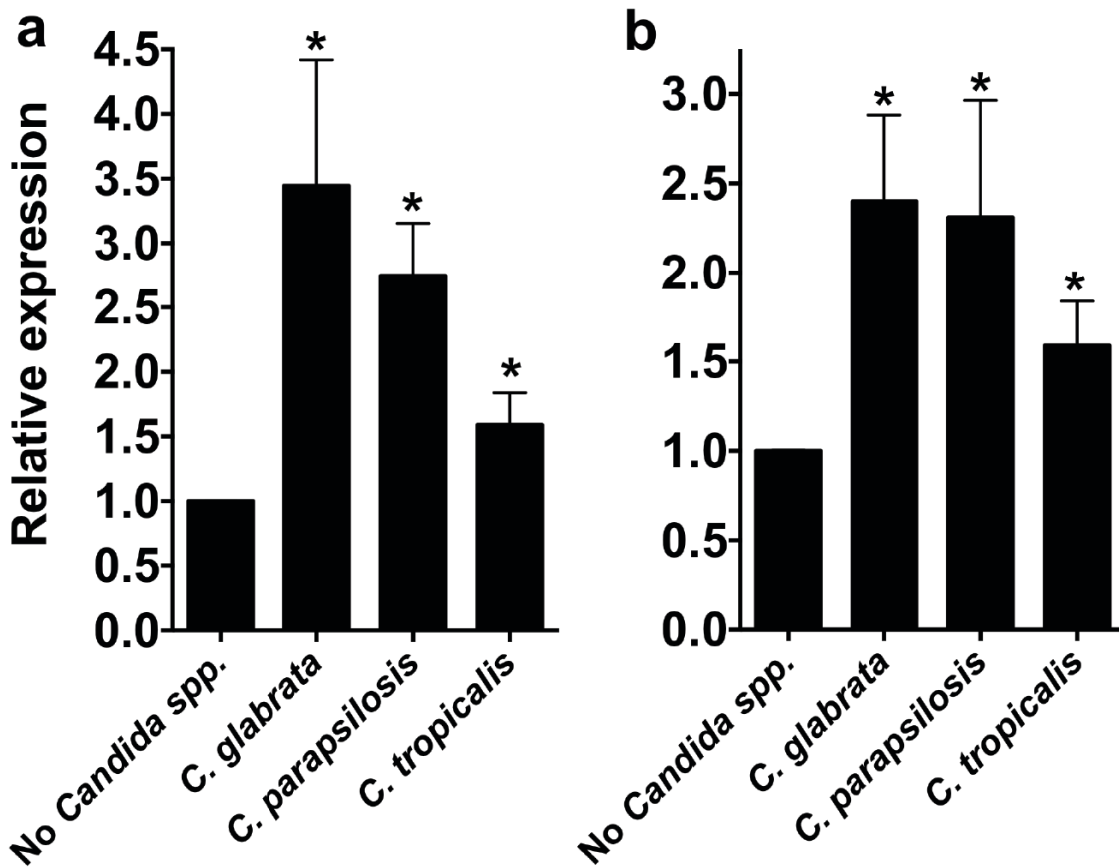


**Supplementary Figure 2. Quantification of endogenous fungal flora in the GI tracts of C3H/HeN Mice**

(a) ITS1-2 rDNA levels of gDNA recovered from fecal specimens of C3H/HeN mice (Harlan, female, 6-8 weeks old) treated with sterile water (WT), streptomycin (STR) or penicillin G (PCN) in the drinking water for 5 days. (b) *C. albicans*, *C. glabrata*, *C. parapsilosis*, and *C. tropicalis* levels as determined by qPCR on microbial gDNA recovered from fecal specimens of C3H/HeN adult mice pre-treated with or without antibiotics in the drinking water for 5 days. Points represent results from individual animals, and horizontal lines with bars representing the mean with SEM. n=4. Statistical analysis was performed by Mann-Whitney test. \* p< 0.05; ns, not significant.

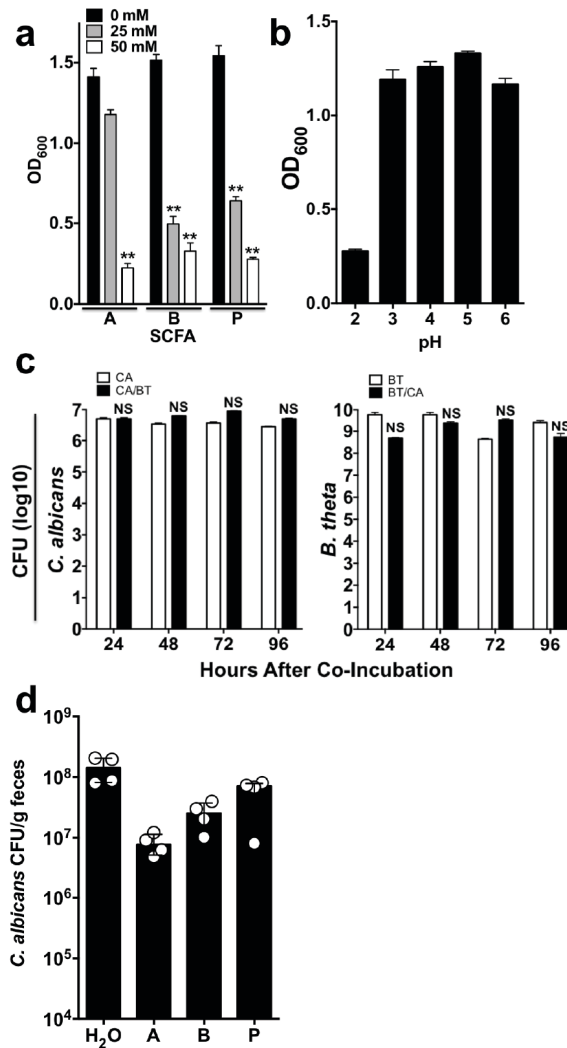


**Supplementary Figure 3. Quantification of fungi in mucosa isolated from stomach, ileum, cecum, proximal and distal colon of mice.** ITS1-2 rDNA level of intestinal segments of C3H/HeN mice (Harlan, female, 6-8 weeks old) treated with penicillin/streptomycin and colonized with *C. albicans* strain SC5314. Data was generated by qPCR and normalized to 18S rDNA. Points represent results from individual animals, and horizontal lines with bars representing the mean with SEM. n=6.

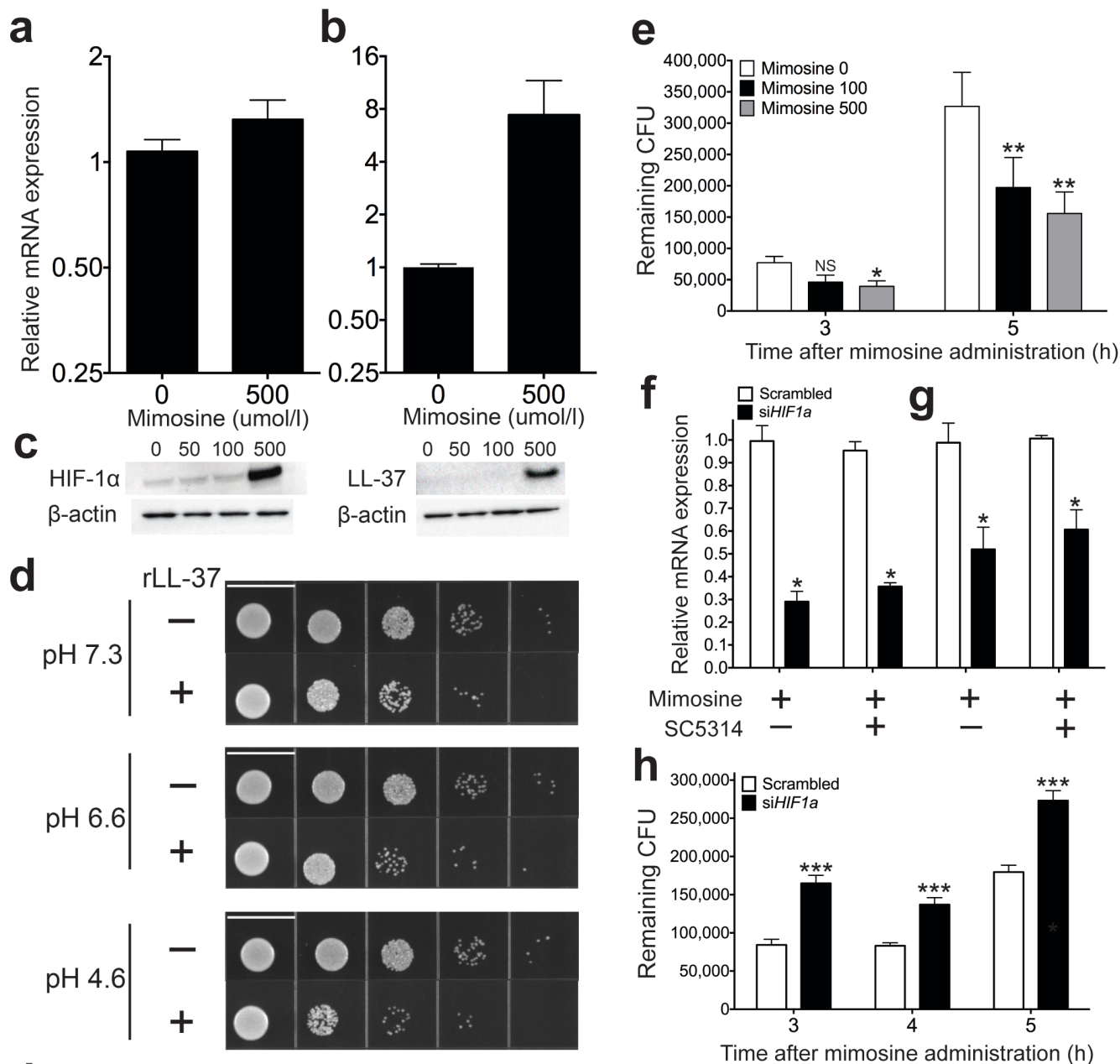


**Supplementary Figure 4. *C. glabrata*, *C. parapsilosis*, and *C. tropicalis* induce *Hif1a* and *Cramp* expression in colons of antibiotic-treated mice.**

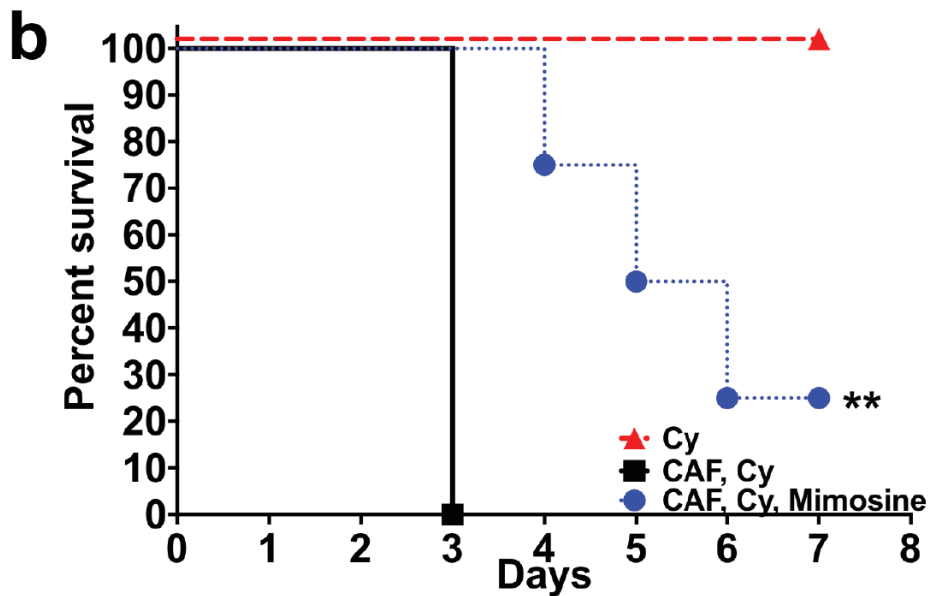
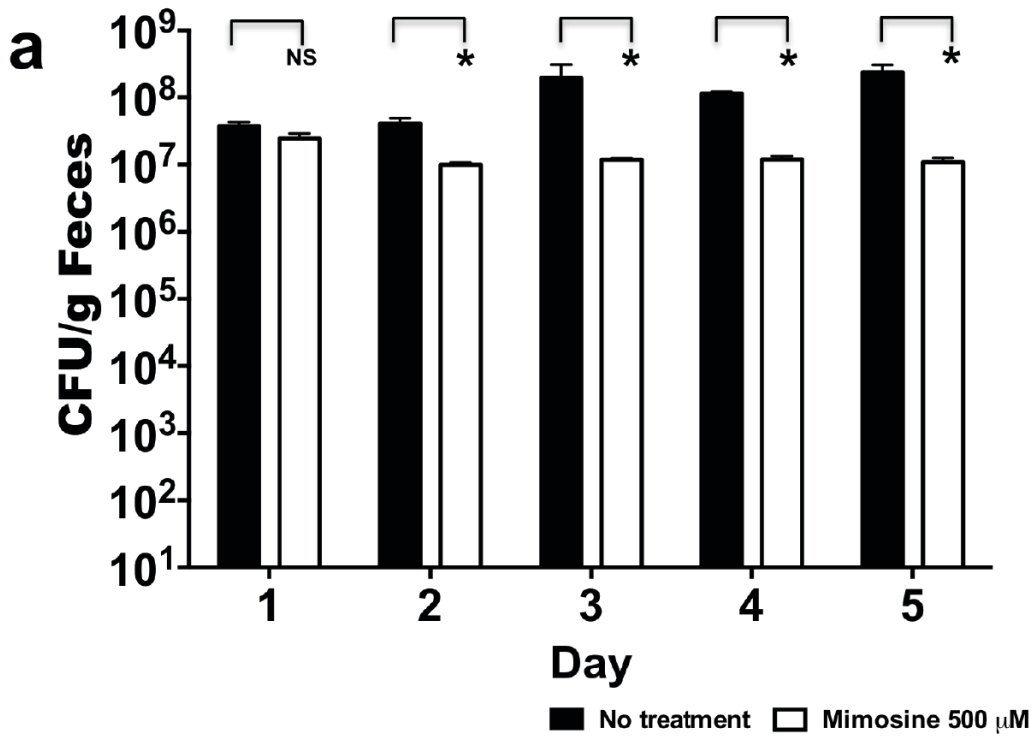
(a) *Hif1a* and (b) *Cramp* gene expression in colons of antibiotic (PS)-treated mice +/- oral gavage with *Candida* spp. ( $2 \times 10^8$  cfu). *Candida* spp.: *C. glabrata*, ATCC 15126; *C. parapsilosis*, clinical isolate; and *C. tropicalis*, ATCC 66029. Mice (C3H/HeN, Harlan, female, 6-8 weeks) were maintained on PS water, and colons were resected 7 days after *Candida* gavage. For all experiments,  $n=4$ . All data shown are means  $\pm$  SEM. Assays were performed in triplicate. Statistical analysis was performed by Mann-Whitney test. \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; ns, not significant.



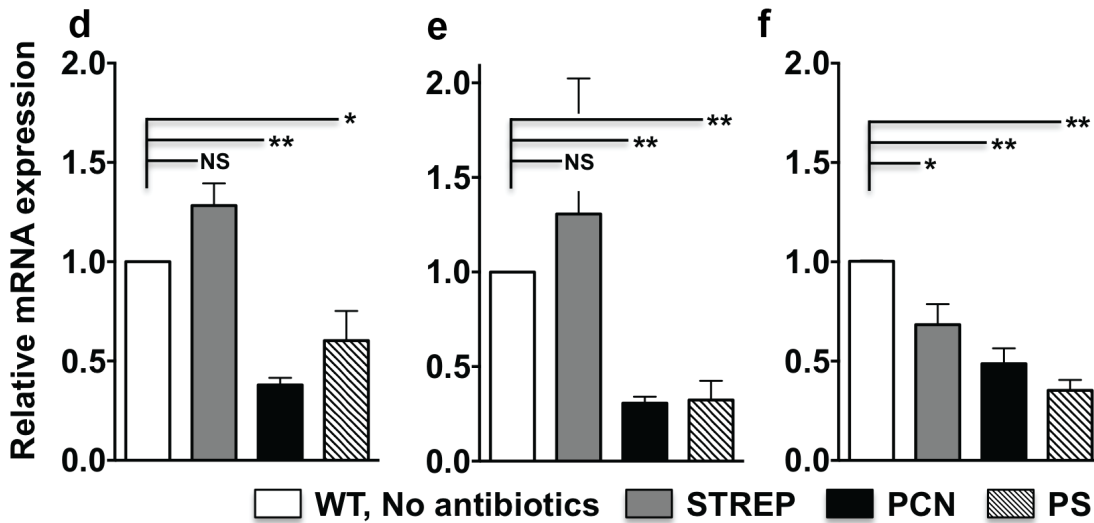
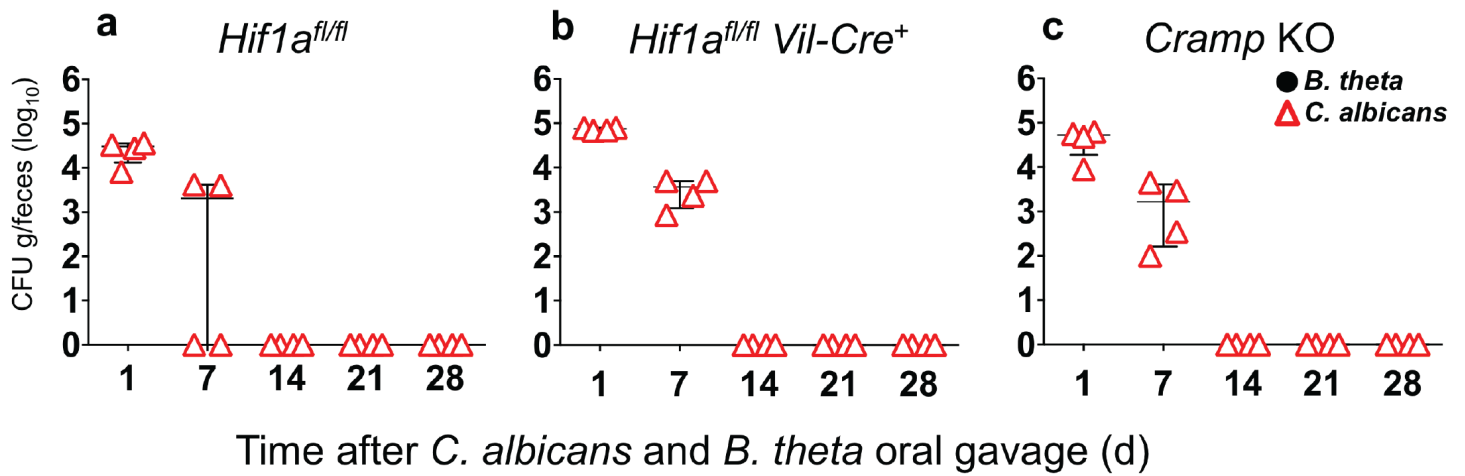
**Supplementary Figure 5. Small-chain fatty acids (SCFAs) inhibit *C. albicans* growth *in vitro* and decrease *C. albicans* colonization in mice.** OD<sub>600</sub> readings of *C. albicans* grown (a) aerobically ± SCFA in YPD media (pH 3-6) at 30°C for 12 hours and (b) aerobically in YPD media (pH 2-6, adjusted by HCl) at 30°C for 12 hours. A = acetic, B = butyric, P=propionic acid. Means ± SEM. Assays were performed in triplicate. Mann-Whitney test. \* p< 0.05; \*\* p<0.01 (c) Quantification of *C. albicans* strain SC5314 and *B. theta* grown in TYG media at 37°C under anaerobic conditions. CA and *B. theta* were first grown individually in TYG media at 37°C under anaerobic conditions. Cultures were then diluted to an OD<sub>600</sub> = 0.2 for the initial time point (0 hours). CA and *B. theta* co-cultures were created by combining equivalent volumes of CA and *B. theta* individual diluted cultures. Cultures were samples at selected time points and CA and *B. theta* (CFU) were enumerated by plating on YVG agar (aerobically) and BHI/Blood agar (anaerobically), respectively. Bars represent means ±SEM. Assays were performed in triplicate. Mann-Whitney test. ns, non-significant. (d) *C. albicans* GI colonization levels in mice pre-treated with antibiotics (PS water), colonized with *C. albicans*, and then treated with PS water ± 50 mM SCFAs. Colonization levels were checked after 14 days of SCFA water treatment. n=4. Points represent results from individual animals. Horizontal lines with bars represent the median with interquartile range. Mann-Whitney test. \* p<0.05. A= acetic, B= butyric, P=propionic acid, H20 = PS water adjusted for pH. (Supplementary Table 2).



**Supplementary Figure 6. Pharmacologic activation of HIF-1 $\alpha$  induces LL-37 expression and boosts *C. albicans* clearance by human colonocytes.** (a) HIF1a and (b) LL-37 mRNA and (c) protein expression in HT-29 human colonocytes treated with L-mimosine. (d) Spot assay to determine Candidacidal activity of recombinant LL-37 (30  $\mu$ g/ml) in the setting of varying pH. Scale bar, 13 mm. (e) Extracellular killing of *C. albicans* strain SC5314 (multiplicity of infection, 1 yeast per cell) by HT-29 cells incubated with 0-500  $\mu$ M L-mimosine. Three separate experiments with three replicates per experiment were conducted. (f) HIF1a and (g) LL-37 gene expression in human colonocytes treated with siRNAHIF1a while concurrently being exposed to L-mimosine  $\pm$  *C. albicans*. Assays were performed in triplicate. (h) Extracellular killing of *C. albicans* strain SC5314 by HT-29 cells incubated with 0-500  $\mu$ M L-mimosine and then transfected  $\pm$  siRNAHIF1a. Three separate experiments with three replicates per experiment were conducted. For all experiments, statistical analysis by Mann-Whitney test, \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ . (i) Quantification of *Candida albicans* strain SC5314 grown in RPMI-1640 with 10% FCS  $\pm$  L-mimosine at 37°C for 8 hours. Bars represent means  $\pm$  SEM. Assays were performed in triplicate. Statistical analysis was performed by unpaired Student's t-test. \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; ns, not significant.

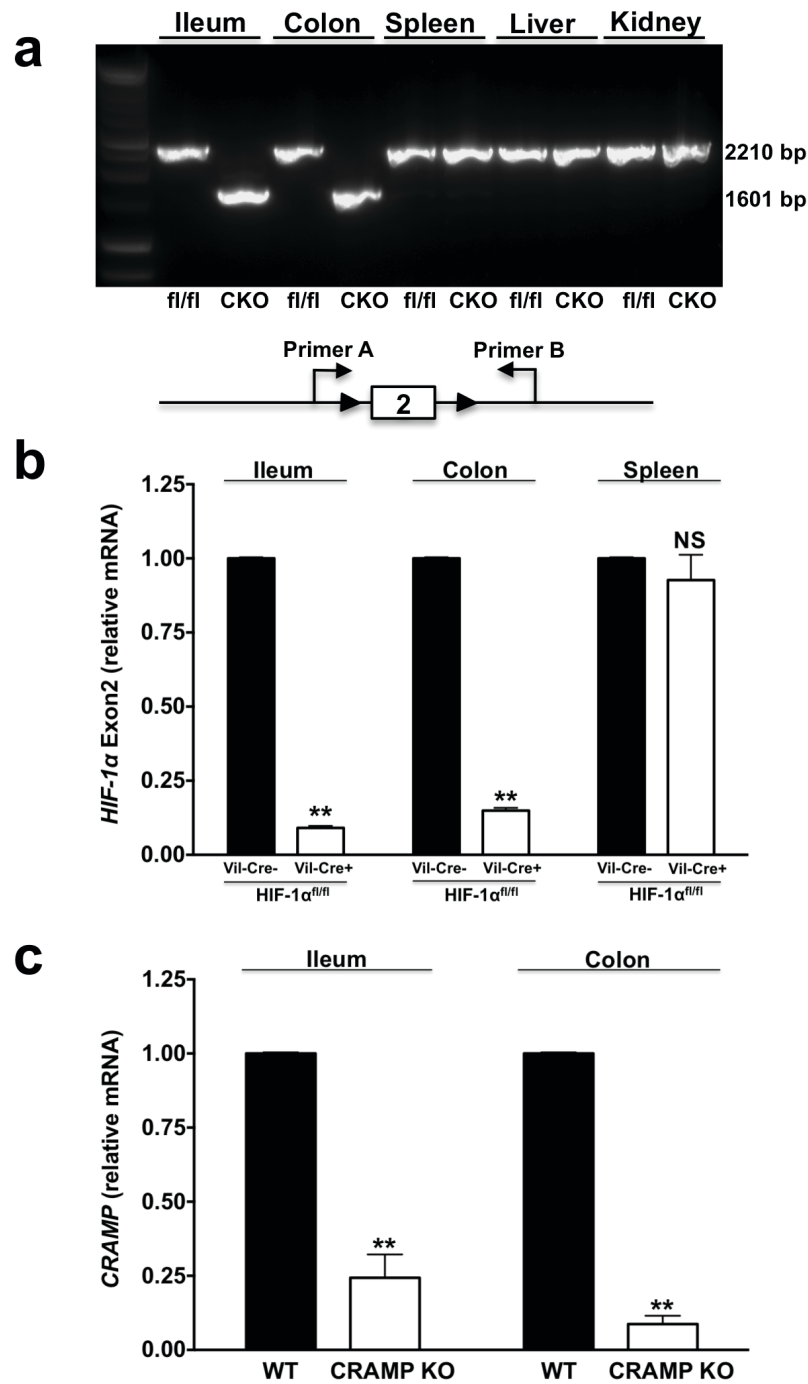


**Supplementary Figure 7. L-mimosine treatment decreases *Candida albicans* CAF2-1 GI colonization and decreases dissemination.** (a) *C. albicans* strain CAF2-1 GI colonization levels in *Hlf1a<sup>fl/fl</sup>* mice treated  $\pm$  L-mimosine. n=8. Bars represent the mean with SEM. Statistical analysis was performed by Mann-Whitney test. \* p<0.05; \*\* p<0.001; ns, not significant. (b) Survival curves of *Hlf1a<sup>fl/fl</sup>* mice treated  $\pm$  L-mimosine after the administration of cyclophosphamide. n=8. Statistical analysis was performed by log-rank test. \* p< 0.05; \*\* p<0.01; ns, not significant.

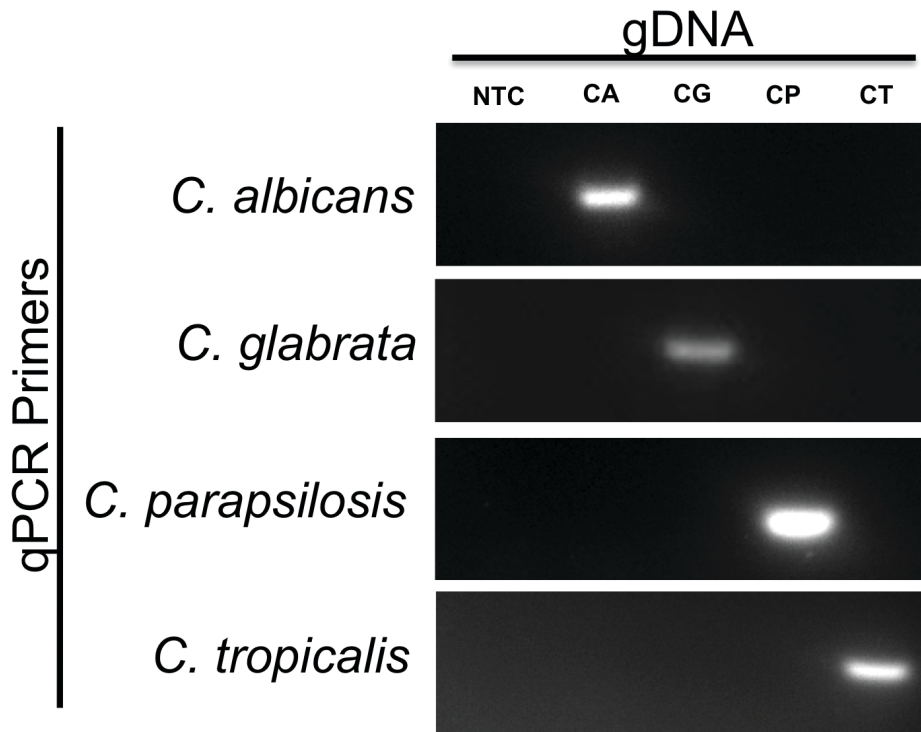


**Supplementary Figure 8** *Hif1a* and *Cramp* are not necessary for *C. albicans* GI colonization resistance in wild-type mice. *Candida albicans* (red triangle) GI colonization levels of (a) *Hif1a<sup>fl/fl</sup>*, (b) *Hif1a<sup>fl/fl</sup> Vil-Cre<sup>+</sup>*, and (c) *Cramp* KO mice not pre-treated with antibiotics and orally gavaged with *C. albicans* strain SC5314. n=4. Points represent results from individual animals. Horizontal lines with bars represent the median with interquartile range. (d) mouse  $\beta$ -defensin 1 (*mBD-1*), (e) mouse  $\beta$ -defensin 2 (*mBD-2*), and (f) *Ili7a* gene expression in murine colons. Colonic expression of *mBD-1*, *mBD-2*, and *Ili7a* in C3H/HeN mice treated with sterile water (WT), streptomycin (STREP), penicillin G (PCN), or penicillin/streptomycin (PS). Mice deficient in *Mmp7* (thus deficient in beta-defensins) or *Ili7a* still maintain resistance to CA colonization in the absence of antibiotics (data not shown). n=4. All data shown are means  $\pm$  SEM. Statistical analysis was performed by Mann-Whitney. \* p< 0.05; \*\* p<0.01; ns, not significant.





**Supplementary Figure 9. Molecular characterization of *Hif1a*<sup>fl/fl</sup>, *Hif1a*<sup>fl/fl</sup> *Vil-Cre*<sup>+</sup>, and *Cramp* KO mice.** (a) Deletion of *Hif1a* Exon 2 is confirmed in the small and large intestines, but is absent in the spleen, liver, and kidney of *Hif1a*<sup>fl/fl</sup> *Vil-Cre*<sup>+</sup> (CKO) mice. Primer pair A/B amplifies a 1601 bp product when exon 2 is deleted (ileum, colon) and a 2210 bp product when exon 2 is intact (spleen, liver, and kidney). (b) *Hif1a* Exon 2 mRNA levels in ileums, colons, and spleens of *Hif1a*<sup>fl/fl</sup> and *Hif1a*<sup>fl/fl</sup> *Vil-Cre*<sup>+</sup> mice as determined by qPCR. n=4. *Hif1a* Exon 2 expression levels were normalized to both *Hif1a* Exon 9 (which is not deleted) and 18s rRNA. (c) *Cramp* mRNA levels in ileums and colons of *Cramp* KO and WT (C57/BL6J) mice. n=4. Bars represent means  $\pm$ SEM. Assays were performed in triplicate. Statistical analysis was performed by unpaired Student's t-test. \* p<0.05; \*\* p<0.01; ns, not significant.



**Supplementary Figure 10. Specificity of *Candida spp.* qPCR.** *Candida spp.* specific qPCR (e.g. *C. albicans* qPCR) generates PCR products of the appropriate size when genomic DNA of corresponding *Candida spp.* (*C. albicans* gDNA) is used but not with gDNA of other *Candida spp.* (i.e. *C. glabrata*, *C. parapsilosis*, *C. tropicalis*). NTC, no template control; CA, *C. albicans*; CG, *C. glabrata*; CP, *C. parapsilosis*; CT, *C. tropicalis*.

Supplementary Table 1. Mouse strains used in this study

Strain	Source	Sex and Age	Experiments (n= number of mice used)
C57/BL6	Harlan	Female, 7 d to 8 weeks old	Fig. 1a (n=48)
Swiss Webster	Harlan	Female, 6-8 weeks old	Data not shown (n=4)
Balb/c	Harlan	Female, 6-8 weeks old	Data not shown (n=4)
C57/BL6	Taconic	Female, 6-8 weeks old	Data not shown (n=4)
C57/BL6J	Jackson	Female, 6-8 weeks old	Fig. 1b (n=4, germ-free) Fig. 2g (n=4, germ-free) Fig. 2h (n=4, germ-free) Fig. 3i-j (n=12, germ-free)
C3H/HeN	Harlan	Female, 6-8 weeks old	Fig. 1d (n=36), 1e (n=36) Supplementary Fig. 1 (n=8) Fig. 2a, 2c (n=32) Fig. 2b (n=3) Fig. 2d-3 (n=5) Fig. 2f (n=64) Supplementary Fig. 2 (n=12) Fig. 3a-b; Supplementary Fig. 8d-f (n=16) Fig. 3c-d (n=8) Fig. 3e-h (n=24) Supplementary Fig. 3 (n=6) Supplementary Fig. 4 (n=16) Supplementary Fig. 5d (n=16) Supplementary Fig. 6 (n=24)
<i>Hif1a<sup>fl/fl</sup></i>	Jackson	Sex-matched, 6-8 weeks old	Fig. 4a (n=16) Fig. 4c (n=24; 16 from Fig. 4a and 8 additional for <i>Hif1a<sup>fl/fl</sup></i> , Cy control) Fig. 4e-f (n=8) Fig 4g (n=6) Supplementary Fig. 8a (n=4) Supplementary Fig. 9 (n=4)
<i>Hif1a<sup>fl/fl</sup> Vil-Cre<sup>+</sup></i>	Jackson	Sex-matched, 6-8 weeks old	Fig. 4a (n=8) Fig. 4c (n=8; 8 from Fig 4a) Fig. 4e-f (n=4) Fig. 4g (n=5) Supplementary Fig. 8b (n=4) Supplementary Fig. 9 (n=4)

<i>Cramp</i> KO	Jackson	Sex-matched, 6-8 weeks old	Fig. 4b (n=16) Fig. 4d (n=24; 8 from Fig 4b and 8 additional for <i>Cramp</i> KO, Cy control) Fig. 4e-f (n=4) Fig. 4g (n=6) Supplementary Fig. 8b (n=4) Supplementary Fig 9 (n=4)
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Supplementary Table 2. *Candida albicans* and Bacterial GI Colonization Levels

<b>Antibiotic Experiments (Fig. 1a)</b>	<b>Median (cfu/g feces)</b>	<b>First Quartile (cfu/g feces)</b>	<b>Third Quartile (cfu/g feces)</b>
No antibiotics (WT)	0	0	0
Streptomycin (STR)	0	0	0
Penicillin (PCN)	$1.70 \times 10^7$	$1.34 \times 10^7$	$2.52 \times 10^7$
Penicillin/Streptomycin (PS)	$2.52 \times 10^7$	$1.04 \times 10^7$	$4.07 \times 10^7$
Clindamycin ( C )	$7.27 \times 10^4$	$4.97 \times 10^4$	$8.55 \times 10^4$
Metronidazole (M)	$1.38 \times 10^4$	$5.23 \times 10^3$	$8.37 \times 10^4$
<b>Germ Free (Fig. 1b)</b>			
Germ-Free Mice	$1.7 \times 10^7$	$1.02 \times 10^7$	$2.24 \times 10^7$
<b>Infant/Adolescent Mice (Fig. 1c)</b>			
14 day old	$2.56 \times 10^5$	$4.00 \times 10^4$	$7.38 \times 10^5$
28 day old	$3.06 \times 10^4$	$5.95 \times 10^3$	$8.30 \times 10^4$
42 day old	0	0	0
<b>Other CA (Fig. 1d)</b>			
WO-1, WT	0	0	0
WO-1, STR	0	0	0
WO-1, PCN	$2.59 \times 10^6$	$1.31 \times 10^6$	$1.49 \times 10^7$
Can098, WT	0	0	0
Can098, STR	0	0	0
Can098, PCN	$1.73 \times 10^5$	$7.76 \times 10^4$	$7.55 \times 10^5$
3153A, WT	0	0	0
3153A, STR	0	0	0
3153A, PCN	$9.62 \times 10^6$	$7.84 \times 10^6$	$1.42 \times 10^7$
<b>Other <i>Candida</i> spp. (Fig. 1e)</b>			
<i>C. glabrata</i> ATCC 15126, WT	0	0	0
<i>C. glabrata</i> ATCC 15126, STR	$5.35 \times 10^7$	$3.82 \times 10^7$	$7.36 \times 10^7$
<i>C. glabrata</i> ATCC 15126, PCN	$5.76 \times 10^7$	$4.74 \times 10^7$	$7.39 \times 10^7$

<i>C. parapsilosis</i> , clinical, WT	0	0	0
<i>C. parapsilosis</i> , clinical, STR	$9.62 \times 10^6$	$9.62 \times 10^6$	$9.62 \times 10^6$
<i>C. parapsilosis</i> , clinical, PCN	$9.62 \times 10^6$	$9.62 \times 10^6$	$9.62 \times 10^6$
<i>C. tropicalis</i> ATCC 66029, WT	0	0	0
<i>C. tropicalis</i> ATCC 66029, STR	0	0	0
<i>C. tropicalis</i> ATCC 66029, PCN	$2.49 \times 10^7$	$2.05 \times 10^7$	$4.13 \times 10^7$
<b>Bacterial Add Back (Fig. 2f)</b>			
No Bacteria			
<i>C. albicans</i>	$9.27 \times 10^3$	$1.81 \times 10^3$	$4.75 \times 10^5$
<i>E. coli</i>			
<i>E. coli</i>	$1.47 \times 10^8$	$7.64 \times 10^7$	$7.55 \times 10^8$
<i>C. albicans</i>	$7.33 \times 10^4$	$6.76 \times 10^2$	$2.00 \times 10^5$
<i>P. aeruginosa</i>			
<i>P. aeruginosa</i>	$2.52 \times 10^7$	$1.53 \times 10^7$	$1.03 \times 10^8$
<i>C. albicans</i>	$1.02 \times 10^5$	$5.10 \times 10^3$	$1.47 \times 10^5$
<i>B. fragilis</i>			
<i>B. fragilis</i>	$7.22 \times 10^8$	$2.03 \times 10^8$	$1.88 \times 10^{10}$
<i>C. albicans</i>	$1.83 \times 10^4$	$5.14 \times 10^3$	$2.77 \times 10^4$
<i>B. thetaiotamicron</i>			
<i>B. thetaiotamicron</i>	$5.27 \times 10^9$	$1.68 \times 10^9$	$6.15 \times 10^9$
<i>C. albicans</i>	0	0	0
<i>B. producta</i>			
<i>B. producta</i>	$9.98 \times 10^7$	$6.40 \times 10^6$	$3.69 \times 10^8$
<i>C. albicans</i>	0	0	0
<i>L. acidophilus</i>			
<i>L. acidophilus</i>	$4.40 \times 10^9$	$3.07 \times 10^8$	$2.94 \times 10^{10}$
<i>C. albicans</i>	$1.52 \times 10^4$	$3.21 \times 10^3$	$1.59 \times 10^5$
<i>L. reuteri</i>			
<i>L. reuteri</i>	$2.37 \times 10^8$	$3.70 \times 10^7$	$5.28 \times 10^8$

<i>C. albicans</i>	0	0	1.78 x 10 <sup>3</sup>
<b>Bacterial Add Back Germ-free Mice (Fig. 2g-h) Day 20</b>			
<i>B. producta</i>			
<i>B. producta</i>	6.03 x 10 <sup>10</sup>	4.93 x 10 <sup>10</sup>	6.73 x 10 <sup>10</sup>
<i>C. albicans</i>	0	0	0
<i>B. thetaiotamicron</i>			
<i>B. thetaiotamicron</i>	2.08 x 10 <sup>10</sup>	1.06 x 10 <sup>10</sup>	2.78 x 10 <sup>10</sup>
<i>C. albicans</i>	3.72 x 10 <sup>2</sup>	2.22 x 10 <sup>2</sup>	4.56 x 10 <sup>2</sup>
<b>Mimosine Mouse Experiments <i>C. albicans</i> GI Colonization Levels (Fig. 4a)</b>			
Day 1			
<i>Hif1a</i> <sup>fl/fl</sup>	1.50 x 10 <sup>7</sup>	1.18 x 10 <sup>7</sup>	2.02 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> , Mimosine	2.07 x 10 <sup>7</sup>	1.21 x 10 <sup>7</sup>	2.34 x 10 <sup>7</sup>
HIF-1α <sup>H1H1</sup> Vil-Cre+, Mimosine	1.70 x 10 <sup>7</sup>	8.15 x 10 <sup>6</sup>	2.17 x 10 <sup>7</sup>
Day 2			
<i>Hif1a</i> <sup>fl/fl</sup>	1.54 x 10 <sup>7</sup>	1.06 x 10 <sup>7</sup>	2.70 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> , Mimosine	7.61 x 10 <sup>6</sup>	5.75 x 10 <sup>6</sup>	8.64 x 10 <sup>6</sup>
HIF-1α <sup>H1H1</sup> Vil-Cre+, Mimosine	1.35 x 10 <sup>7</sup>	7.69 x 10 <sup>6</sup>	2.00 x 10 <sup>7</sup>
Day 3			
<i>Hif1a</i> <sup>fl/fl</sup>	1.59 x 10 <sup>7</sup>	1.40 x 10 <sup>7</sup>	2.02 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> , Mimosine	9.25 x 10 <sup>6</sup>	8.09 x 10 <sup>6</sup>	1.05 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> Vil-Cre+, Mimosine	1.53 x 10 <sup>7</sup>	8.81 x 10 <sup>6</sup>	2.07 x 10 <sup>7</sup>
Day 4			
<i>Hif1a</i> <sup>fl/fl</sup>	1.60 x 10 <sup>7</sup>	1.25 x 10 <sup>7</sup>	1.98 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> , Mimosine	1.01 x 10 <sup>7</sup>	7.10 x 10 <sup>6</sup>	1.10 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> Vil-Cre+, Mimosine	1.29 x 10 <sup>7</sup>	1.10 x 10 <sup>7</sup>	2.05 x 10 <sup>7</sup>
Day 5			
<i>Hif1a</i> <sup>fl/fl</sup>	4.04 x 10 <sup>7</sup>	3.57 x 10 <sup>7</sup>	5.74 x 10 <sup>7</sup>
<i>Hif1a</i> <sup>fl/fl</sup> , Mimosine	4.66 x 10 <sup>5</sup>	1.69 x 10 <sup>5</sup>	6.80 x 10 <sup>5</sup>
<i>Hif1a</i> <sup>fl/fl</sup> Vil-Cre+, Mimosine	2.21 x 10 <sup>7</sup>	1.72 x 10 <sup>7</sup>	3.04 x 10 <sup>7</sup>

Mimosine			
<b><i>C. albicans</i> GI Colonization Levels in HIF and CRAMP KO mice (ANTIBIOTICS) (Fig. 4f)</b>			
<i>Hif1a<sup>fl/fl</sup></i>			
Day 1, CA	4.43 x 10 <sup>6</sup>	2.62 x 10 <sup>6</sup>	9.92 x 10 <sup>6</sup>
Day 1, <i>B. theta</i>	4.39 x 10 <sup>10</sup>	1.36 x 10 <sup>10</sup>	6.49 x 10 <sup>10</sup>
Day 7, CA	2.00 x 10 <sup>4</sup>	8.23 x 10 <sup>5</sup>	4.21 x 10 <sup>4</sup>
Day 7, <i>B. theta</i>	2.21 x 10 <sup>10</sup>	1.78 x 10 <sup>10</sup>	2.89 x 10 <sup>10</sup>
Day 14, CA	0	0	0
Day 14, <i>B. theta</i>	1.06 x 10 <sup>10</sup>	8.50 x 10 <sup>19</sup>	1.53 x 10 <sup>10</sup>
Day 21, CA	0	0	0
Day 21, <i>B. theta</i>	4.25 x 10 <sup>9</sup>	2.5 x 10 <sup>9</sup>	9.59 x 10 <sup>9</sup>
Day 28, CA	0	0	0
Day 28, <i>B. theta</i>	8.54 x 10 <sup>9</sup>	4.11 x 10 <sup>9</sup>	1.61 x 10 <sup>10</sup>
<i>Hif1a<sup>fl/fl</sup> Vil-Cre+</i>			
Day 1, CA	1.55 x 10 <sup>7</sup>	9.93 x 10 <sup>6</sup>	2.51 x 10 <sup>7</sup>
Day 1, <i>B. theta</i>	4.32 x 10 <sup>10</sup>	2.01 x 10 <sup>10</sup>	5.24 x 10 <sup>10</sup>
Day 7, CA	1.05 x 10 <sup>7</sup>	8.85 x 10 <sup>6</sup>	1.27 x 10 <sup>7</sup>
Day 7, <i>B. theta</i>	1.69 x 10 <sup>10</sup>	1.32 x 10 <sup>10</sup>	2.96 x 10 <sup>10</sup>
Day 14, CA	3.55 x 10 <sup>6</sup>	1.71 x 10 <sup>6</sup>	1.68 x 10 <sup>7</sup>
Day 14, <i>B. theta</i>	6.61 x 10 <sup>9</sup>	2.65 x 10 <sup>9</sup>	9.19 x 10 <sup>9</sup>
Day 21, CA	4.73 x 10 <sup>6</sup>	1.67 x 10 <sup>6</sup>	1.42 x 10 <sup>7</sup>
Day 21, <i>B. theta</i>	4.42 x 10 <sup>10</sup>	2.62 x 10 <sup>10</sup>	9.91 x 10 <sup>10</sup>
Day 28, CA	1.24 x 10 <sup>6</sup>	8.80 x 10 <sup>5</sup>	1.18 x 10 <sup>7</sup>
Day 28, <i>B. theta</i>	2.11 x 10 <sup>10</sup>	1.25 x 10 <sup>10</sup>	2.35 x 10 <sup>10</sup>
<b><i>Cramp</i> KO</b>			
Day 1, CA	2.01 x 10 <sup>7</sup>	1.10 x 10 <sup>7</sup>	5.29 x 10 <sup>7</sup>
Day 1, <i>B. theta</i>	4.39 x 10 <sup>10</sup>	1.36 x 10 <sup>10</sup>	6.49 x 10 <sup>10</sup>
Day 7, CA	2.40 x 10 <sup>7</sup>	2.31 x 10 <sup>7</sup>	2.82 x 10 <sup>7</sup>
Day 7, <i>B. theta</i>	2.21 x 10 <sup>10</sup>	1.78 x 10 <sup>10</sup>	2.89 x 10 <sup>10</sup>
Day 14, CA	1.01 x 10 <sup>7</sup>	6.39 x 10 <sup>6</sup>	1.98 x 10 <sup>7</sup>
Day 14, <i>B. theta</i>	4.34 x 10 <sup>9</sup>	2.25 x 10 <sup>9</sup>	8.18 x 10 <sup>9</sup>
Day 21, CA	5.17 x 10 <sup>6</sup>	3.34 x 10 <sup>6</sup>	1.67 x 10 <sup>7</sup>
Day 21, <i>B. theta</i>	7.10 x 10 <sup>9</sup>	4.63 x 10 <sup>9</sup>	3.68 x 10 <sup>10</sup>
Day 28, CA	1.25 x 10 <sup>7</sup>	8.24 x 10 <sup>6</sup>	2.14 x 10 <sup>7</sup>
Day 28, <i>B. theta</i>	1.85 x 10 <sup>10</sup>	1.67 x 10 <sup>10</sup>	3.02 x 10 <sup>10</sup>
<b><i>C. albicans</i>/ <i>B. theta</i> GI Colonization Levels in HIF and</b>			



<b>CRAMP KO mice (NO ANTIBIOTICS) (Supplementary Figure 8a)</b>			
<i>Hif1a<sup>fl/fl</sup></i>			
Day 1, CA	3.07 x 10 <sup>4</sup>	1.31 x 10 <sup>4</sup>	3.56 x 10 <sup>4</sup>
Day 7, CA	2.03 x 10 <sup>3</sup>	0	4.19 x 10 <sup>3</sup>
Day 14, CA	0	0	0
Day 21, CA	0	0	0
Day 28, CA	0	0	0
<i>Hif1a<sup>fl/fl</sup> Vil-Cre+</i>			
Day 1, CA	7.45 x 10 <sup>4</sup>	6.93 x 10 <sup>4</sup>	7.96 x 10 <sup>4</sup>
Day 7, CA	3.67 x 10 <sup>3</sup>	1.22 x 10 <sup>3</sup>	4.99 x 10 <sup>3</sup>
Day 14, CA	0	0	0
Day 21, CA	0	0	0
Day 28, CA	0	0	0
<i>Cramp KO</i>			
Day 1, CA	5.29 x 10 <sup>4</sup>	1.89 x 10 <sup>4</sup>	6.11 x 10 <sup>4</sup>
Day 7, CA	1.66 x 10 <sup>3</sup>	1.63 x 10 <sup>2</sup>	4.12 x 10 <sup>3</sup>
Day 14, CA	0	0	0
Day 21, CA	0	0	0
Day 28, CA	0	0	0
<b><i>C. albicans</i> GI Colonization Levels after SCFA treatment (Supplementary Figure 5d)</b>			
Water	1.43 x 10 <sup>8</sup>	8.20 x 10 <sup>7</sup>	2.05 x 10 <sup>8</sup>
Acetic Acid	7.7 x 10 <sup>6</sup>	5.20 x 10 <sup>6</sup>	1.14 x 10 <sup>7</sup>
Butyric Acid	2.53 x 10 <sup>7</sup>	1.28 x 10 <sup>7</sup>	3.75 x 10 <sup>7</sup>
Propionic Acid	7.10 x 10 <sup>7</sup>	2.32 x 10 <sup>7</sup>	7.89 x 10 <sup>7</sup>

Supplementary Table 3. Bacterial and Fungal strains used in this study

Strain	Reference
<i>Candida albicans</i> SC5314	1
<i>C. albicans</i> CAF2-1	1
<i>C. albicans</i> BWP17	2
<i>C. albicans</i> SN152	3
<i>C. albicans</i> WO-1	4
<i>C. albicans</i> Can098 (Clinical isolate, blood)	This study
<i>C. albicans</i> 3153A (Clinical isolate, biofilm)	5
<i>Candida glabrata</i> , ATCC 15126	6
<i>Candida parapsilosis</i> , clinical isolate	This study
<i>Candida tropicalis</i> , ATCC 66029	7
<i>Bacteroidetes fragilis</i> ATCC 25285	8
<i>Bacteroidetes thetaiotamicron</i> VPI-5482	9
<i>Blautia producta</i> ATCC 27340	8
<i>Clostridium leptum</i> ATCC 29065	10
<i>Escherichia coli</i> ATCC 10798	8
<i>Lactobacillus acidophilus</i> ATCC 5357	8
<i>Lactobacillus reuteri</i> , clinical strain	This study
<i>Pseudomonas aeruginosa</i> , PAO1	11

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Supplementary Table 4: Primers used in this study

<b>Gene</b>	<b>Forward Primer</b>	<b>Reverse Primer</b>
<b><i>Genotyping Primers</i></b>		
HIF-1 $\alpha$ <sup>fl/fl</sup>	TGCTCATCAGTTGCCACTT	GTTGGGGCAGTACTGGAAAG
Vil-Cre	GTGTGGGACAGAGAACAAACC	ACATCTTCAGGTTCTGCGGG
Primer A, B (Figure S4A)	GAAGTGTGAGTGAATAAATCCCG	GAGAGAGAGACAAAGAGATACAGGTA
<b><i>qPCR Primers</i></b>		
Human HIF-1 $\alpha$	GCCGCTGGAGACACACAATCAT	CTGGTCATCAGTTTCTGTGTCG
Mouse HIF-1 $\alpha$ (exon 2)	ATCTCGGCGAAGCAAAGAGTC	TGGGGAAGTGGCAACTGAT
Mouse HIF-1 $\alpha$ (exon 9)	GTGGTATTATTCAGCAGACTTG	GGAGCCAGCAGAGTGAGAG
LL-37	GCAGTCACCAGAGGATTGTGAC	CACCGCTTCACCAGCCC
CRAMP	TCTCTACCGTCTCCTGGACCTG	CCACATACAGTCTCCTTCACTCG
IL-17A	GGACTCTCCACCGCAATGA	GGCACTGAGCTTCCCAGATC
Mouse $\beta$ -Defensin1	TCCTGGTGATGATATGTTTTCTTTCT	TGTTCTTCGTCCAAGACTTGTGA
Mouse $\beta$ -Defensin2	GGCATTCTCACAAAGTCTTGGACGAAG	AGCTCTTACAACAGTTGGGCTTATCTGG
Human $\beta$ -Defensin1	GTCGCCATGAGAACTTCCTACC	CATTGCCCTCCACTGCTGAC
Human $\beta$ -Defensin2	GGTGTTTTTGGTGGTATAGGCG	AGGGCAAAGACTGGATGAC
18S rRNA	CATTCGAACGTCTGCCCTAT	CCTGCTGCCTTCCTTGGA
<b><i>Bacterial 16S rRNA gene primers</i></b>		
Eubacteria (all bacteria)	ACTCCTACGGGAGGCAGCAGT	ATTACCGCGGCTGCTGGC
Bacteroides	GGTTCTGAGAGGAGGTCCC	GCTGCCTCCCGTAGGAGT
Mouse Intestinal Bacteroides (MIB)	CCAGCAGCCGCGGTAATA	CGCATTCCGCATACTTCTC
Lactobacillus/Enterococcus Group (LACT)	AGCAGTAGGGAATCTTCCA	CACCGCTACACATGGAG
Eubacterium rectale/Clostridium coccoides group (EREC)	ACTCCTACGGGAGGCAGC	GCTTCTTAGTCAGGTACCGTCAT
Clostridium leptum group (CLEPT)	GCACAAGCAGTGGAGT	CTTCCTCCGTTTTGTCAA
Enterobacteriaceae (ENTERO)	GTGCCAGCMGCCGCGGTAA	GCCTCAAGGGCACAACCTCCAAG
Segmented filamentous bacteria (SFB)	GACGCTGAGGCATGAGAGCAT	GACGGCACGGATTGTTATTCA
<b><i>Fungal ITS Primers</i></b>		
ITS1-2	CTTGGTCATTTAGAGGAAGTAA	GCTGCGTTCTTCATCGATGC

	Forward Primer	Reverse Primer	Probe
<i>Candida albicans</i>	GCCTTACCACTACCGTCT TTC	ATTGCGCCCTCT GGTATTC	FAM- AGGGAGAAACGACGCTCA AACAG
<i>Candida glabrata</i>	CACTCACTTATCCCTCCC TAGA	CGAGCGCAAGCTTCT CTATTA	FAM- CGCGCAAACGAGCAGCAG AT
<i>Candida parapsilosis</i>	TATCGCTCAACA CCAAACCC	TCGAATCTTTGA ACGCACATTG	FAM- AGGGTTTGAGGGAGAAAT GACGCT
<i>Candida tropicalis</i>	CGATGGAAGTTTGAGGC AATAAC	CTCTCGGCCAAGGTTT ATACT	FAM- TGTGATGCCCTTAGACGTT CTGGG