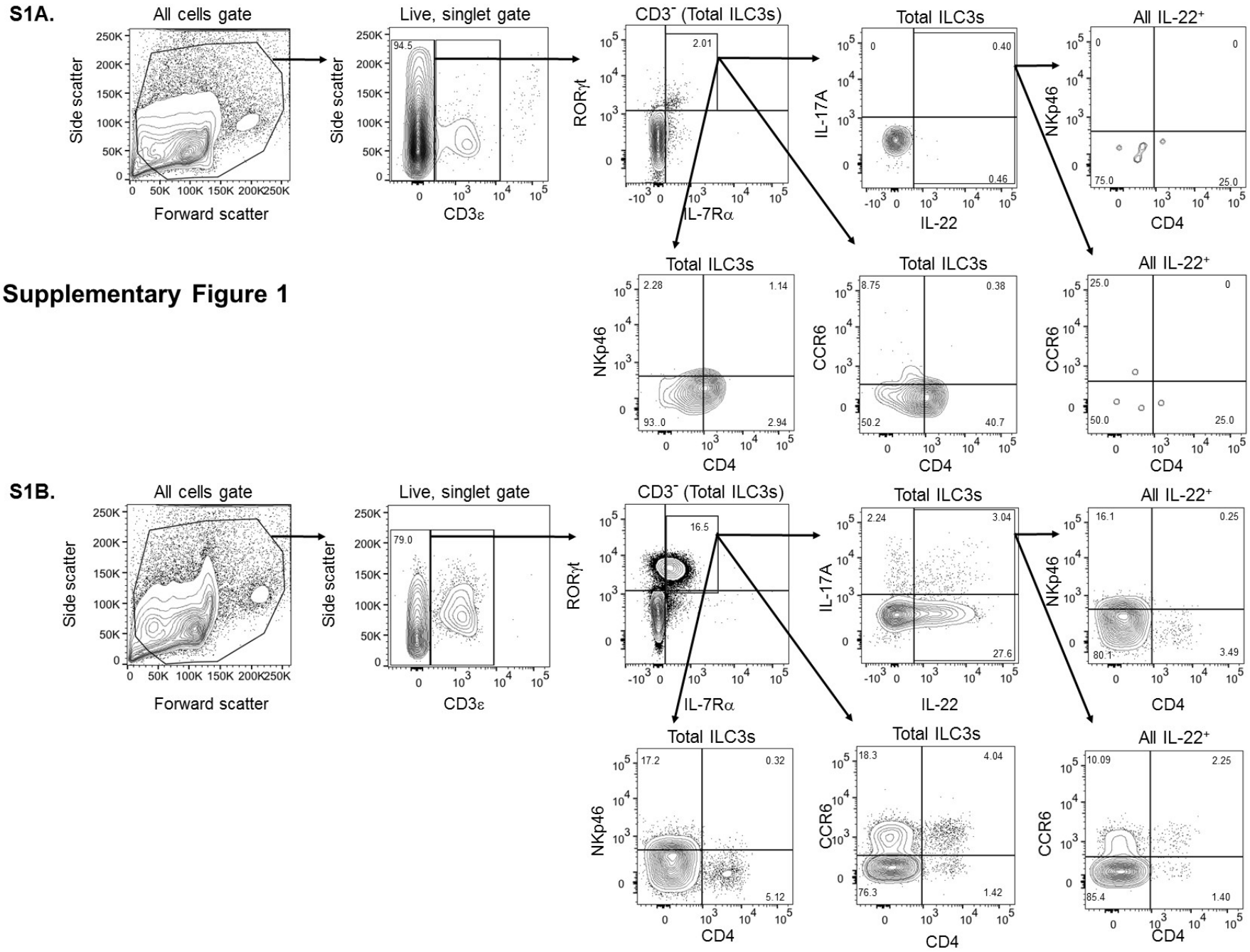
List of Supplementary Figures:

Figure S1. Flow cytometry gating strategy for ILC3s

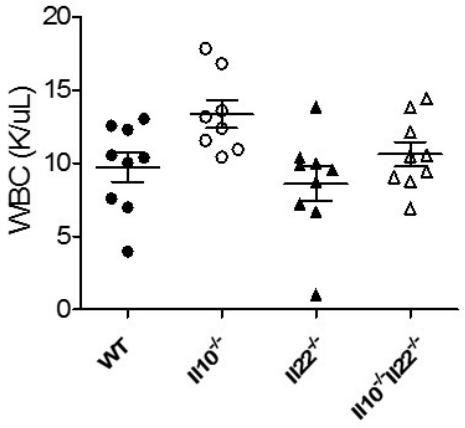
Figure S2. Complete blood count (CBC) analysis



Supplementary Figure 1

Supplementary Figure 2

S2A.



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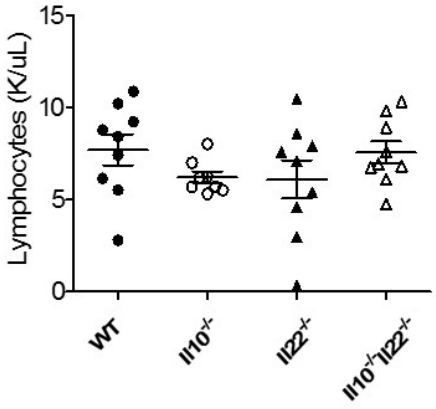

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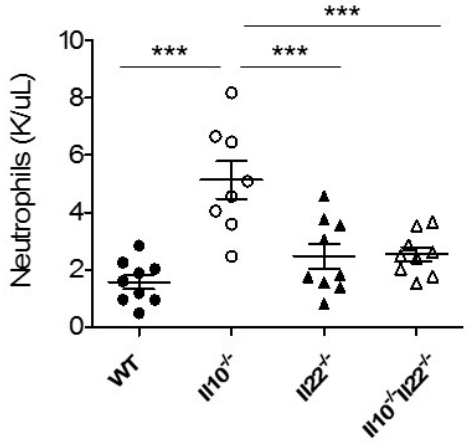

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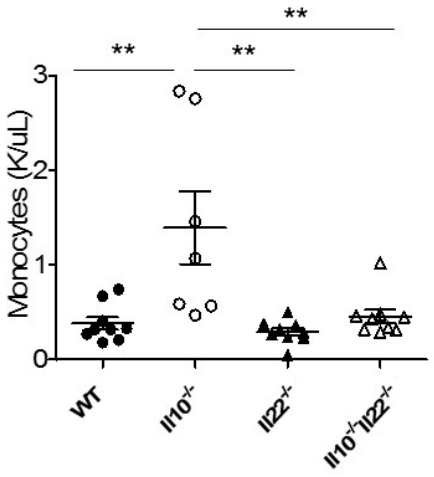

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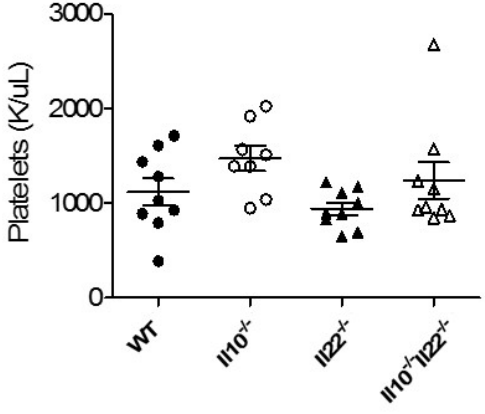

Supplementary Figure Legends:

Supplemental Figure S1. Flow cytometry gating strategy for ILC3s. Representative flow cytometry plots showing gating strategy for ILC3s in sLPL from (**A**) WT and (**B**) *Il10*$^{-/-}$ mice. Gates were established on single, live, CD45^{+} CD3^{-} cells. Cells in this gate that were RORγt^{+} IL-7Rα^{+} were considered ILC3s (Total ILC3s). The Total ILC3s population was examined for IL-17A and IL-22 expression. A sub-gate on IL-22^{+} ILC3s (All IL-22^{+}) was used to determine the percentages of IL-22-producing ILC3 subsets based on NKp46 or CCR6 (+/ CD4). Also, the Total ILC3s gate was examined to determine the percentages of ILC3 subsets based on NKp46 or CCR6 (+/- CD4).

Supplemental Figure S2: Complete blood count (CBC) analysis. (**A**) WBC, (**B**) lymphocyte (**C**) monocyte (**D**) neutrophil and (**E**) platelet frequencies in peripheral blood of WT, *Il10*$^{-/-}$, *Il22*$^{-/-}$, and *Il10*$^{-/-}$ *Il22*$^{-/-}$ mice (n= 9-10 per group) (***, $p<0.001$, **, $p<0.01$, using the Mann–Whitney *U* test (error bars represent SD).

List of Supplementary Tables:

Table S1. Genes differentially expressed in both *Il10*$^{-/-}$ and *Il10*$^{-/-}$*Il22*$^{-/-}$ mice compared to WT (Group 1)

Table S2. Genes differentially expressed in *Il10*$^{-/-}$*Il22*$^{-/-}$ mice only compared to WT (Group 2)

Table S3. Genes differentially expressed in *Il10*$^{-/-}$ mice only compared to WT (Group 3)

Table S4. (**a**) Chao1 Statistics and (**b**) Shannon Statistics from fecal microbiome analysis

Table S5. List of significantly different taxa in fecal microbiome

Supplementary Table 1: Genes differentially expressed in both *Il10*$^{-/-}$ and *Il10*$^{-/-}$*Il22*$^{-/-}$ mice compared to WT (Group 1)

	Il10$^{-/-}$ (compared to WT)		*Il10*$^{-/-}$*Il22*$^{-/-}$ (compared to WT)	
Gene	**p-value**	**Fold-difference**	**p-value**	**Fold-difference**
Abcb1a	0.00238447	-2.9	0.00106374	-3.3
Alox5	0.00292459	-2.2	2.09E-05	-4.4
Aoah	1.02E-07	3.2	5.68E-06	2.2
Aoc3	0.00628964	-2.4	0.0094028	-2.3
B2m	2.04E-06	5.7	3.62E-06	5.2
Bdkrb1	0.0081094	2.6	0.00864262	2.6
Bmp3	0.0061224	-2.8	0.00206836	-3.4
C2	6.62E-07	11.6	1.82E-05	5.9
C3	5.03E-05	5.2	0.0106775	2.2
Ccl1	0.00670074	932.6	0.00871763	693.3
Ccl2	0.00200778	3.9	0.009145	2.9
Ccl20	0.00161736	3.9	0.000276811	5.5
Ccl22	0.00195491	8.1	0.000141201	18.3
Ccl5	2.04E-05	31.5	6.16E-05	21.5
Ccl5	0.00011631	18.2	0.000193779	15.5
Ccl7	0.000495421	5.5	0.0015497	4.3
Ccl8	4.53E-05	5.4	0.000111651	4.6
Ccr1	0.00493682	2.0	0.00159636	2.3
Ccr5	2.13E-05	7.3	3.87E-05	6.4
Cd14	7.41E-06	3.5	0.000524014	2.2
Cd274	5.28E-05	6.9	2.04E-05	8.5
Cd4	0.00528985	4.1	0.000902417	6.3
Cd74	1.47E-09	16.2	1.44E-09	16.2
Chrna7	0.00575245	-2.8	0.00548288	-2.8
Cmtm5	0.0014076	-3.8	0.00865433	-2.7
Csf2	0.0013231	400.9	0.000847815	576.3
Csf2rb	0.00793234	3.1	0.00358386	3.6
Ctla4	0.000165893	17.4	0.000127399	19.0
Cxcl1	0.000250708	17.2	0.00246616	8.3
Cxcl1	0.000808265	10.6	0.0050476	6.2
Cxcl10	0.00711367	11.6	0.00180348	20.5
Cxcl3	0.00219792	2905.3	0.00430579	1363.1
Cxcl5	0.00102204	7.4	0.0105547	4.0
Cxcl9	0.00155534	529.7	0.000529753	1363.6
Cxcr3	0.00102082	4.5	0.00823312	3.0
Cybb	0.00546101	2.5	0.00145411	3.1
Fasl	0.00163608	1305.3	0.00218593	981.4
Fpr1	5.11E-05	2961.2	0.000324966	654.3
H2-Q10	0.00186128	2.5	0.000200172	3.4

Icos	0.00548041	3.9	0.000307301	7.5
Ifng	8.58E-06	20944.0	1.25E-05	14427.2
Il12b	0.00129804	1004.3	0.00161049	822.2
Il12rb1	0.000417435	6.1	0.000538028	5.8
Il12rb2	0.00405627	731.5	0.00442055	670.5
Il15	0.000423708	-2.6	0.000807622	-2.4
Il17a	1.19E-05	4274.3	5.01E-06	9099.0
Il18bp	3.62E-08	15.7	2.14E-06	6.6
Il1a	0.00614955	12.7	0.00502956	13.8
Il1b	0.0020318	24.5	0.00348555	19.2
Il1b	0.002002	21.0	0.00178113	22.1
Il1f9	0.0020701	1090.1	0.00128751	1749.8
Il2rg	0.00566712	3.0	0.0052451	3.1
Il7r	0.001827	3.4	0.00151092	3.5
Itgb2	0.00153147	2.6	0.00182944	2.6
Lilrb3	1.89E-05	3.5	0.000369535	2.4
Ltf	0.000943918	24.8	0.00188895	18.6
Lyn	1.97E-05	2.5	4.24E-05	2.3
Mefv	0.00104442	4.5	0.00021368	6.2
Nlrp3	0.00496957	5.3	0.00401091	5.6
Nod2	0.00112751	3.3	0.00171035	3.1
Nos2	1.69E-07	186.2	3.68E-07	129.8
Pglyrp1	7.15E-05	3.1	0.000130999	2.9
Prg2	0.000127271	6.9	0.000163568	6.5
S100a8	2.59E-05	195.8	0.000635859	39.1
S100a8	1.52E-05	166.0	0.000285891	40.8
S100a9	0.000199177	50.4	0.000778043	27.7
S1pr3	0.000105757	-2.7	0.000456266	-2.3
Saa3	0.000355516	970.9	0.00032095	1057.1
Socs1	0.00154115	7.9	0.00401311	6.0
Tlr11	0.00697523	3.1	0.00642618	3.1
Tlr13	8.70E-05	2.6	0.000187492	2.4
Tlr9	0.0069402	2.0	0.00253182	2.3
Tnf	8.18E-07	21.4	2.83E-06	15.2
Tnfrsf8	0.000306257	27.0	8.58E-05	45.3
Tnfrsf9	0.00347227	6.8	0.000956495	10.0
Tnfsf10	2.25E-06	4.8	4.29E-06	4.3
Unc13d	0.00405847	2.3	0.00846253	2.1

Supplementary Table 2: Genes differentially expressed in *Il10*$^{-/-}$*Il22*$^{-/-}$ mice only compared to WT (Group 2)

Gene	p-value	Fold-difference
Alox5	0.00479949	-3.7
Bmp3	0.000629089	-3.9
C8g	0.00138908	-2.9
Cav1	0.00342036	-2.3
Ccl17	0.000851116	7.0
Cd163	0.00818285	-5.5
Cd180	0.00735117	2.1
Cd40	0.00673335	3.2
Cd40lg	0.00908089	216.8
Cebpa	4.26E-08	-83.5
Cebpb	5.92E-07	-19914.1
Cftr	0.000168215	-2.1
Cmtm4	0.0044312	-2.0
Cntnap1	0.00613507	-2.4
Ctf1	0.00392415	-5.3
Cxcl14	0.00522238	2.0
Cxcl16	0.00186368	2.1
Fpr3	0.00709804	8732.9
Gdf15	0.00744193	-2.3
Il12b	0.00908872	531.3
Il17d	0.000267927	-2.8
Il18	3.79E-06	-5.6
Il18rap	0.00923122	55.8
Il1rl2	0.00559334	-2.3
Kit	0.00434982	-2.5
P2rx1	0.00328103	-4.4
Ptn	0.0073677	-2.4
Tgfb2	0.000915831	-2.0
Tnfrsf11b	0.00528023	3.0
Tnfrsf4	0.00211631	2.8
Tnfsf12;Tnfsf12-tnfsf13	0.0022568	-2.4
Tpst1	0.00142718	-2.1
Xcr1	0.00416754	4.8

Supplementary Table 3: Genes differentially expressed in *Il10*$^{-/-}$ mice only compared to WT (Group 3)

Gene	p-value	Fold-difference
A2m	0.00957883	718.3
Adora1	0.00407501	3.6
Aif1	3.52E-05	2.7
C6	0.00909242	70.2
Ccl11	0.00819481	2.1
Ccr2	4.24E-05	2.5
Cfb	0.00028884	2.3
Cfh	1.26E-05	3.7
Cxcl2	0.00932489	397.7
Ebi3	0.0081765	2.3
Fam3b	2.80E-05	3.0
Fcer1g	0.0104187	2.0
Fgf23	0.0102809	976.1
Foxp3	0.0105366	373.5
Ghrl	0.00764176	4.8
Grem1	0.00014261	2.2
Il21	0.00195555	1991.6
Il22	0.00126662	168.7
Il27ra	0.00687286	6.1
Il3ra	0.000225822	2.1
Il4ra	0.00182328	2.4
Irf7	0.000510782	2.2
Jak3	0.00500189	2.6
Klrg1	0.00639306	3.8
Lbp	0.000143654	4.5
Ltb	0.0092582	3.8
Ly75	1.95E-05	2.3
Ly86	0.000461109	2.9
Muc1	1.49E-06	7.0
Muc4	0.000305016	3.1
Pla2g2e	0.0082277	2.6
Pla2g4c	0.00461715	2.7
Pxdn	0.00130812	-2.0
Reg3g	0.000488335	4861.7
Saa1	0.00129597	3.2
Socs2	0.000726173	-3.2
Tfrc	5.84E-05	2.8
Thpo	0.000263784	2.6
Tlr3	0.000782639	2.1
Tnfrsf18	0.00466065	2.2
Tnfrsf1b	0.00068281	3.2
Twist1	0.00709812	-2.6

Supplementary Table 4: Alpha diversity statistics from fecal microbiome analysis

Table 4a. Chao1 index: statistics from fecal microbiome analysis				
Group 1	**Group 2**	**Group 1 mean**	**Group 2 mean**	**p-value**
Il10$^{-/-}$	WT	474.4122	527.8155	0.102
WT	*Il22*$^{-/-}$	527.8155	586.4659	0.03
Il10$^{-/-}$*Il22*$^{-/-}$	WT	566.3712	527.8155	0.192
Il10$^{-/-}$	*Il22*$^{-/-}$	474.4122	586.4659	0.006
Il10$^{-/-}$	*Il10*$^{-/-}$*Il22*$^{-/-}$	474.4122	566.3712	0.012
Il10$^{-/-}$*Il22*$^{-/-}$	*Il22*$^{-/-}$	566.3712	586.4659	1
Table 4b. Shannon diversity: statistics from fecal microbiome analysis				
Group 1	**Group 2**	**Group 1 mean**	**Group 2 mean**	**p-value**
Il10$^{-/-}$	WT	6.339657	6.044052	0.15
WT	*Il22*$^{-/-}$	6.044052	6.375445	0.12
Il10$^{-/-}$*Il22*$^{-/-}$	WT	5.684859	6.044052	0.528
Il10$^{-/-}$	*Il22*$^{-/-}$	5.684859	6.375445	0.006
Il10$^{-/-}$	*Il10*$^{-/-}$*Il22*$^{-/-}$	5.684859	6.339657	0.018
Il10$^{-/-}$*Il22*$^{-/-}$	*Il22*$^{-/-}$	6.339657	6.375445	1

Supplementary Table 5: Significantly different taxa in fecal microbiome identified by LEfSe analysis

Taxa	Strain	LDA Score (log 10)	P value
Proteobacteria	WT	4.276	1.50E-04
Proteobacteria|Epsilonproteobacteria	WT	4.214	1.29E-06
Proteobacteria|Epsilonproteobacteria|Campylobacterales	WT	4.214	1.29E-06
Proteobacteria|Epsilonproteobacteria|Campylobacterales|Helicobacteraceae	WT	4.214	1.29E-06
Proteobacteria|Epsilonproteobacteria|Campylobacterales|Helicobacteraceae|Helicobacter	WT	4.214	1.29E-06
Firmicutes|Clostridia|	WT	3.599	1.93E-02
Firmicutes|Clostridia||	WT	3.599	1.93E-02
Firmicutes|Clostridia|||	WT	3.599	1.93E-02
Firmicutes|Bacilli|Bacillales|Staphylococcaceae	WT	3.233	7.77E-04
Firmicutes|Bacilli|Bacillales	WT	3.227	4.45E-04
Firmicutes|Bacilli|Bacillales|Planococcaceae	WT	3.080	2.79E-02
Firmicutes|Bacilli|Bacillales|Planococcaceae|Sporosarcina	WT	3.038	2.79E-02
Firmicutes|Clostridia|Clostridiales|Dehalobacteriaceae	WT	2.824	2.87E-04
Firmicutes|Clostridia|Clostridiales|Dehalobacteriaceae|Dehalobacterium	WT	2.822	2.87E-04
Firmicutes|Bacilli|Bacillales|Staphylococcaceae|	WT	2.167	5.06E-07
Bacteroidetes|Bacteroidia|Bacteroidales|Bacteroidaceae	*Il10*$^{-/-}$	4.711	7.42E-06
Bacteroidetes|Bacteroidia|Bacteroidales|Bacteroidaceae|	*Il10*$^{-/-}$	4.482	2.75E-08
Bacteroidetes|Bacteroidia|Bacteroidales|	*Il10*$^{-/-}$	4.198	7.38E-06
Bacteroidetes|Bacteroidia|Bacteroidales||	*Il10*$^{-/-}$	4.198	7.38E-06
*Firmicutes|Erysipelotrichi|Erysipelotrichales|_Coprobacillaceae_*	*Il10*$^{-/-}$	3.997	1.67E-07
Firmicutes|Erysipelotrichi|Erysipelotrichales|_Coprobacillaceae_|Coprobacillus	*Il10*$^{-/-}$	3.827	8.65E-07
Proteobacteria|Deltaproteobacteria|Desulfovibrionales|Desulfovibrionaceae|Desulfovibrio	*Il10*$^{-/-}$	3.675	1.16E-02
Firmicutes|Erysipelotrichi|Erysipelotrichales|_Coprobacillaceae_|	*Il10*$^{-/-}$	3.507	4.86E-05
Proteobacteria|Betaproteobacteria|Burkholderiales	*Il10*$^{-/-}$	3.440	4.44E-06
Proteobacteria|Betaproteobacteria|Burkholderiales|Alcaligenaceae	*Il10*$^{-/-}$	3.440	4.44E-06
Proteobacteria|Betaproteobacteria|Burkholderiales|Alcaligenaceae|Sutterella	*Il10*$^{-/-}$	3.440	4.44E-06
Proteobacteria|Betaproteobacteria	*Il10*$^{-/-}$	3.440	4.57E-06
Proteobacteria|Gammaproteobacteria|Pasteurellales|Pasteurellaceae|Aggregatibacter	*Il10*$^{-/-}$	3.253	7.48E-06
Proteobacteria|Gammaproteobacteria|Pasteurellales	*Il10*$^{-/-}$	2.983	2.58E-05
Proteobacteria|Deltaproteobacteria|Desulfovibrionales|Desulfovibrionaceae|Bilophila	*Il10*$^{-/-}$	2.822	3.95E-05
Proteobacteria|Gammaproteobacteria|Pasteurellales|Pasteurellaceae	*Il10*$^{-/-}$	2.745	2.58E-05
Firmicutes|Bacilli|Lactobacillales|Carnobacteriaceae	*Il10*$^{-/-}$	2.634	2.71E-05
Firmicutes|Bacilli|Lactobacillales|Carnobacteriaceae|Granulicatella	*Il10*$^{-/-}$	2.633	2.71E-05
Firmicutes|Bacilli|Lactobacillales|Streptococcaceae|Streptococcus	*Il10*$^{-/-}$	2.379	1.19E-04
Bacteroidetes|Bacteroidia|Bacteroidales|S24_7	*Il22*$^{-/-}$	4.954	7.55E-03
Bacteroidetes|Bacteroidia|Bacteroidales|S24_7|	*Il22*$^{-/-}$	4.954	7.55E-03
Firmicutes|Bacilli|Turicibacterales	*Il22*$^{-/-}$	3.952	2.43E-08
Firmicutes|Bacilli|Turicibacterales|Turicibacteraceae	*Il22*$^{-/-}$	3.952	2.43E-08
Firmicutes|Bacilli|Turicibacterales|Turicibacteraceae|Turicibacter	*Il22*$^{-/-}$	3.952	2.43E-08
Actinobacteria|Actinobacteria|Bifidobacteriales	*Il22*$^{-/-}$	3.756	1.38E-05
Actinobacteria|Actinobacteria|Bifidobacteriales|Bifidobacteriaceae	*Il22*$^{-/-}$	3.756	1.38E-05
Actinobacteria|Actinobacteria|Bifidobacteriales|Bifidobacteriaceae|Bifidobacterium	*Il22*$^{-/-}$	3.756	1.38E-05
Actinobacteria	*Il22*$^{-/-}$	3.756	7.22E-05
Actinobacteria|Actinobacteria	*Il22*$^{-/-}$	3.756	7.22E-05
Cyanobacteria	*Il22*$^{-/-}$	3.306	1.26E-09
Cyanobacteria|4C0d_2	*Il22*$^{-/-}$	3.305	1.26E-09
Cyanobacteria|4C0d_2|YS2|	*Il22*$^{-/-}$	3.305	1.26E-09
Cyanobacteria|4C0d_2|YS2	*Il22*$^{-/-}$	3.305	1.26E-09
Cyanobacteria|4C0d_2|YS2||	*Il22*$^{-/-}$	3.305	1.26E-09
Firmicutes|Erysipelotrichi|Erysipelotrichales|Erysipelotrichaceae|	*Il22*$^{-/-}$	2.640	1.22E-02
Proteobacteria|Alphaproteobacteria	*Il22*$^{-/-}$	2.066	4.66E-03
Bacteroidetes|Bacteroidia|Bacteroidales|Bacteroidaceae|Bacteroides	*Il10*$^{-/-}$*Il22*$^{-/-}$	4.616	1.45E-05
Bacteroidetes|Bacteroidia|Bacteroidales|Rikenellaceae	*Il10*$^{-/-}$*Il22*$^{-/-}$	4.237	1.53E-06

Bacteroidetes|Bacteroidia|Bacteroidales|Rikenellaceae|	*Il10*$^{-/-}$*Il22*$^{-/-}$	4.141	5.31E-06
Bacteroidetes|Bacteroidia|Bacteroidales|Porphyromonadaceae	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.772	4.54E-04
Bacteroidetes|Bacteroidia|Bacteroidales|Porphyromonadaceae|Parabacteroides	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.772	4.54E-04
Bacteroidetes|Bacteroidia|Bacteroidales|Rikenellaceae|AF12	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.535	6.47E-08
Tenericutes	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.261	1.25E-07
Tenericutes|Mollicutes	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.261	1.25E-07
Tenericutes|Mollicutes|Anaeroplasmatales	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.095	4.24E-09
Tenericutes|Mollicutes|Anaeroplasmatales|Anaeroplasmataceae	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.093	4.24E-09
Tenericutes|Mollicutes|Anaeroplasmatales|Anaeroplasmataceae|Anaeroplasma	*Il10*$^{-/-}$*Il22*$^{-/-}$	3.092	4.24E-09
TM7	*Il10*$^{-/-}$*Il22*$^{-/-}$	2.825	2.69E-04
TM7|TM7_3	*Il10*$^{-/-}$*Il22*$^{-/-}$	2.825	2.69E-04
TM7|TM7_3|CW040	*Il10*$^{-/-}$*Il22*$^{-/-}$	2.825	2.69E-04
TM7|TM7_3|CW040|F16	*Il10*$^{-/-}$*Il22*$^{-/-}$	2.825	2.69E-04
TM7|TM7_3|CW040|F16|	*Il10*$^{-/-}$*Il22*$^{-/-}$	2.825	2.69E-04