Silverman - IgA deficiency destabilizes immune homeostasis towards intestinal microbiota and increases the risk of systemic immune dysregulation

Ceylan Tanes - PennCHOP Microbiome Program

May 4, 2023

Contents

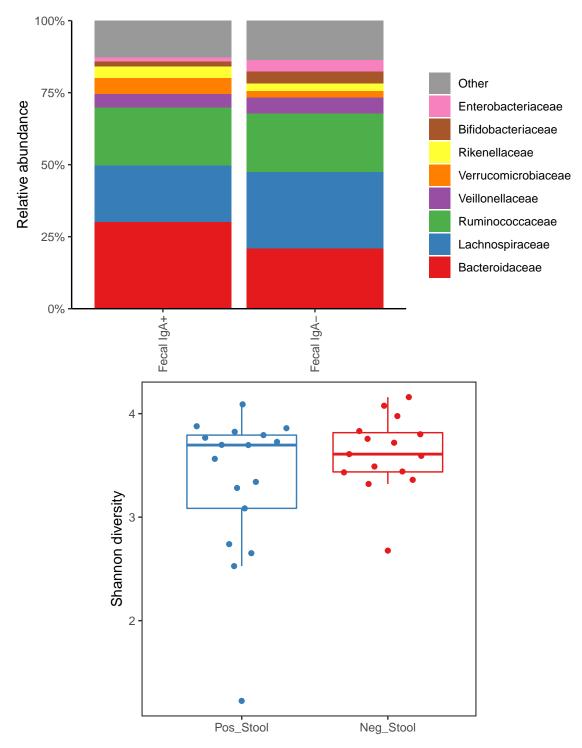
Unsorted fecal analysis	1
FACS samples - stool only IgA and IgM sorted	9
Looking at healthy population only	4
What are the changes in the SigAD group?	٤
FACS samples - stool only IgG and IgM sorted	6
What are the changes in the SigAD group?	7

Unsorted fecal analysis

Number of samples in each study group and study day.

Table 1: Number of subjects in each household.

F03	F11	F14	F33	F36	F46	F47	F48	F49	F50	F51	F52	F54	F59	F63
2	2	2	2	2	2	2	2	3	2	2	3	2	2	2

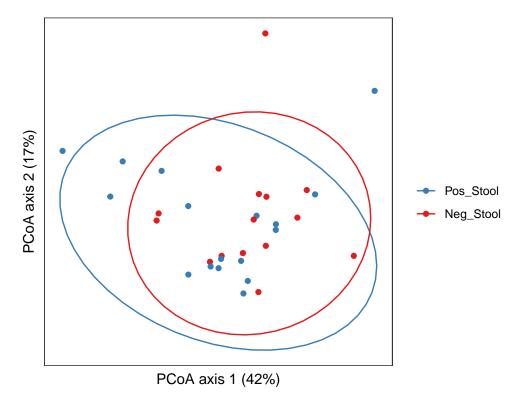


Linear models were used to estimate the difference between cases and controls for each categorization.

term	estimate	std.error	statistic	p.value
Pos - Neg Stool	0.28	0.21	1.4	0.19

Linear mixed effects models were used to estimate the difference between cases and controls for each categorization. Family IDs were used as random effects.

term	Value	Std.Error	DF	t.value	p.value
Pos - Neg Stool	0.25	0.18	16	1.4	0.19



PERMANOVA test on weighted UniFrac distances to test if the centroids of the study groups can be distinguished from each other.

Term	Df	F.Model	R2	p.value
Analysis4	1	1.4	0.044	0.2

${\rm FACS}$ samples - stool only ${\rm IgA}$ and ${\rm IgM}$ sorted

Table 5: Sampled populations from each subject.

	IgA- IgM - IgG -	IgA+IgM-	IgM+IgA-	IgM+IgA+
F1-1	1	1	1	1
F1-2	1	0	1	0
F10-1	1	1	1	1
F10-2	1	1	1	1
F11-1	1	0	1	0
F11-2	1	1	1	1
F12-1	1	0	1	0
F12-2	1	1	1	1
F12-3	1	1	1	1
F13-1	1	0	1	0
F13-2	1	1	1	1
F14-1	1	0	1	0

	IgA-IgM-IgG-	IgA+IgM-	IgM+IgA-	IgM+IgA+
F14-2	1	0	1	0
F15-1	1	0	1	0
F15-2	1	1	1	1
F2-1	1	0	1	0
F2-2	1	1	1	1
F4-1	1	0	1	0
F4-2	1	1	1	1
F5-1	1	0	1	0
F5-2	1	1	1	1
F6-1	1	0	1	0
F6-2	1	1	1	1
F7-1	1	0	1	0
F7-2	1	1	1	1
F8-1	1	0	1	0
F8-2	1	1	1	1
F9-1	1	0	1	0
F9-2	1	1	1	1
F9-3	1	1	1	1

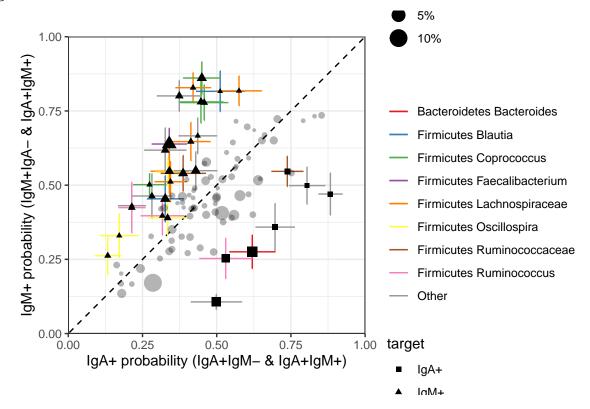
Table 6: Total number of populations sequenced.

IgA-IgM-IgG-	IgA+IgM-	IgM+IgA-	IgM+IgA+
30	16	30	16

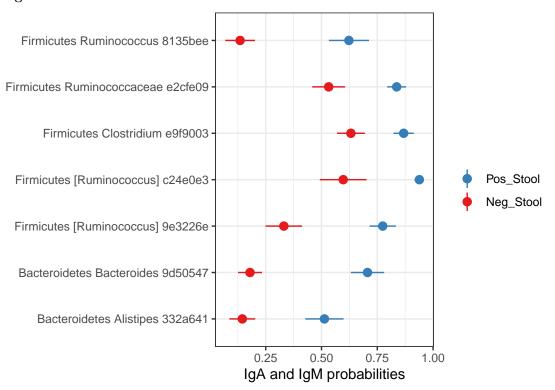
Looking at healthy population only

The angle of the vector defining the probability of binding to IgM and probability of binding to IgA are calculated for each subject. M targeted SNVs are defined as having an angle greater than 45 degrees. A targeted SNVs are defined as having an angle less than 45 degrees.

Fig 1C



What are the changes in the SigAD group? Supp Fig 5D



Taxa	p.value	fdr
Bacteroidetes Alistipes	0.0015	0.0027
332a6411ff00b4010ac2397f504c4695		
Bacteroidetes Bacteroides	5.2e-06	3.7e-05
9d5054752ed33d6a22bd0f96b5618b1c		
Firmicutes [Ruminococcus]	0.00022	0.00051
9e3226efaf559eb14a478f880462cb8a		
Firmicutes [Ruminococcus]	0.0071	0.0071
c24e0e391aa836b5eae25567c7eb89ee		
Firmicutes Clostridium	0.0056	0.0065
e9f900358bb9297e10b9fbb1321b1e6e		
Firmicutes Ruminococcaceae	0.0019	0.0027
e2cfe099d4a73a03ac5f80d4f8369dbc		
Firmicutes Ruminococcus	0.00018	0.00051
8135 beec 331 a 8 d 5580 70 c 38 b 580 e 4 b 8 e		

Results of Wilcoxon rank sum test

Taxa	p.value	fdr
Bacteroidetes Alistipes	0.0027	0.0037
332a6411ff00b4010ac2397f504c4695		
Bacteroidetes Bacteroides	0.00014	0.001
9d5054752ed33d6a22bd0f96b5618b1c		
Firmicutes [Ruminococcus]	0.0012	0.0029
$9 \mathrm{e} 3226 \mathrm{e} \mathrm{fa} 559 \mathrm{e} \mathrm{b} 14 \mathrm{a} 478 \mathrm{f} 880462 \mathrm{c} \mathrm{b} 8 \mathrm{a}$		
Firmicutes [Ruminococcus]	0.008	0.008
c24e0e391aa836b5eae25567c7eb89ee		
Firmicutes Clostridium	0.0069	0.008
e9f900358bb9297e10b9fbb1321b1e6e		
Firmicutes Ruminococcaceae	0.002	0.0035
e2cfe099d4a73a03ac5f80d4f8369dbc		
Firmicutes Ruminococcus	0.00066	0.0023
8135 beec 331 a 8 d 558070 c 38 b 580 e 4 b 8 e		

FACS samples - stool only IgG and IgM sorted

Table 9: Sampled populations from each subject.

	IgA-IgM-IgG-	IgG+IgM-	IgG+IgM+	IgM+IgG-
F1-1	1	1	1	1
$\mathbf{F1-2}$	1	1	1	1
F10-1	1	0	1	1
F10-2	1	1	1	1
F11-1	1	1	1	1
F11-2	1	0	1	1
F12-1	1	0	1	1
F12-2	1	1	1	1
F12-3	1	1	1	1

	IgA-IgM-IgG-	IgG+IgM-	IgG+IgM+	IgM+IgG-
	1871-18101-18-0-	IgO IgW-	1gO 1gW	IgM IgO-
F13-1	1	1	1	1
F13-2	1	0	1	1
F14-1	1	0	1	1
F14-2	1	0	1	1
F15-1	1	1	1	1
F15-2	1	0	1	1
F2-1	1	0	1	1
F2-2	1	0	1	1
F4-1	1	1	1	1
F4-2	1	0	1	1
F5-1	1	1	1	1
F5-2	1	0	1	1
F6-1	1	1	1	1
F6-2	1	0	1	1
F7-1	1	1	1	1
F7-2	1	1	1	1
F8-1	1	1	1	1
F8-2	1	0	1	1
F9-1	1	1	1	1
F9-2	1	1	1	1
F9-3	1	1	1	1

Table 10: Total number of populations sequenced.

IgA-IgM-IgG-	IgG+IgM-	IgG+IgM+	IgM+IgG-
30	17	30	30

Analysis4	num_subjects	
Pos_Stool	17	
Neg_Stool	13	

What are the changes in the SigAD group?

Supp Fig 9A

