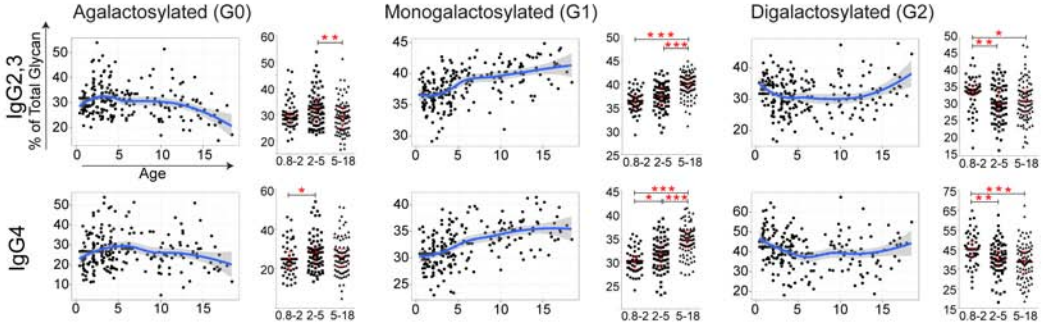
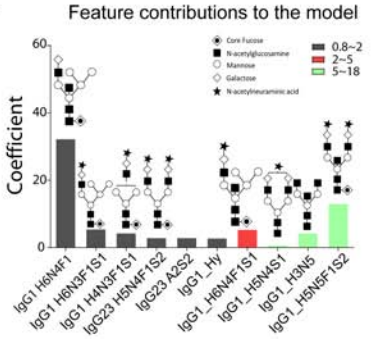
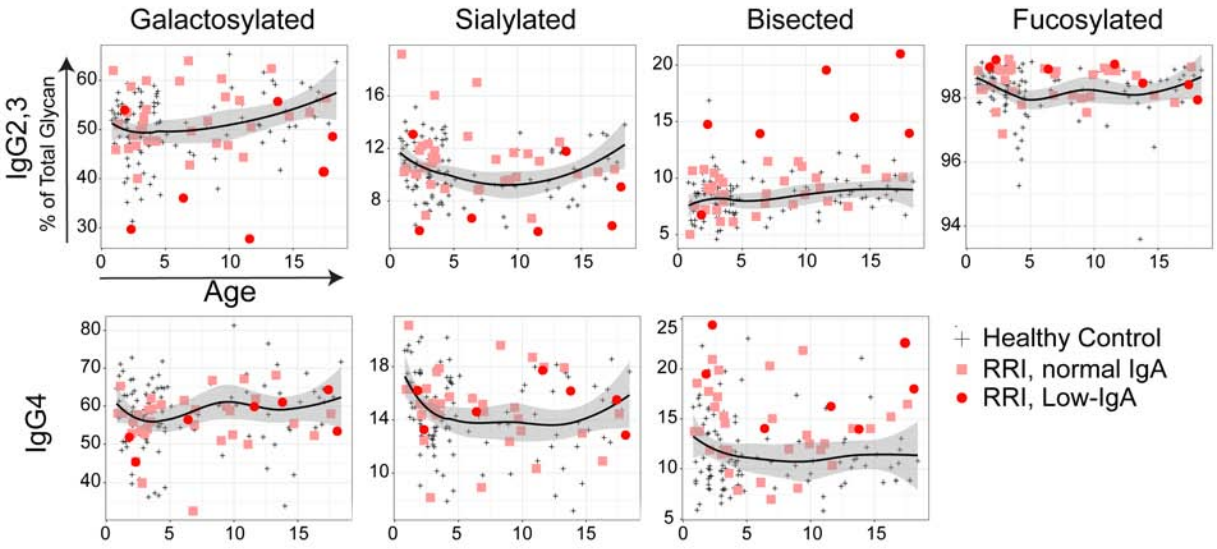
A.



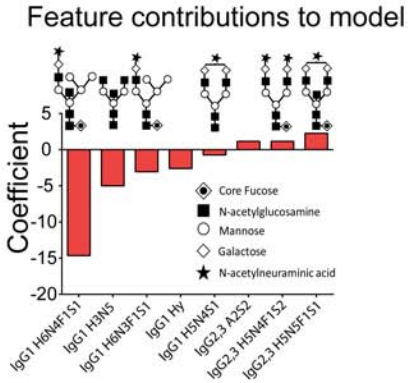
B.

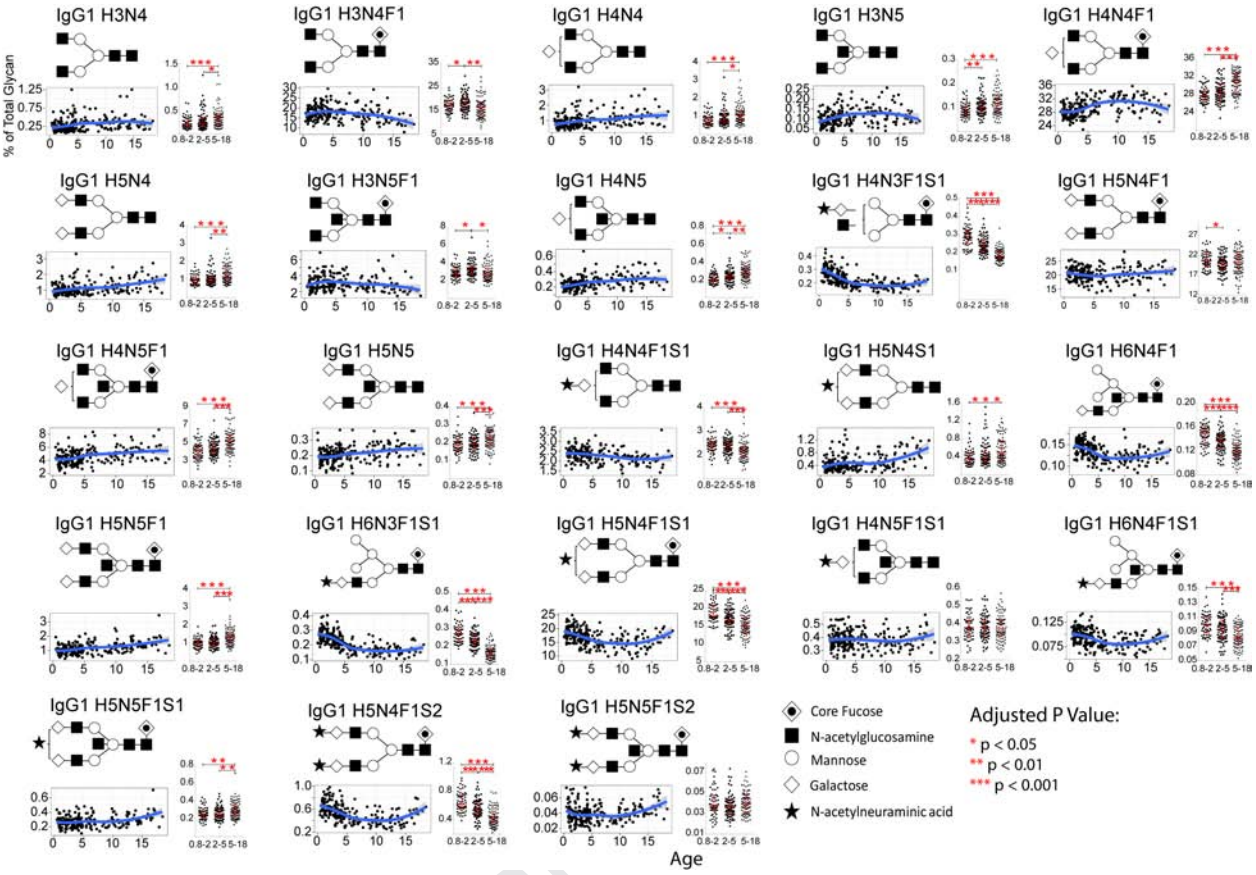


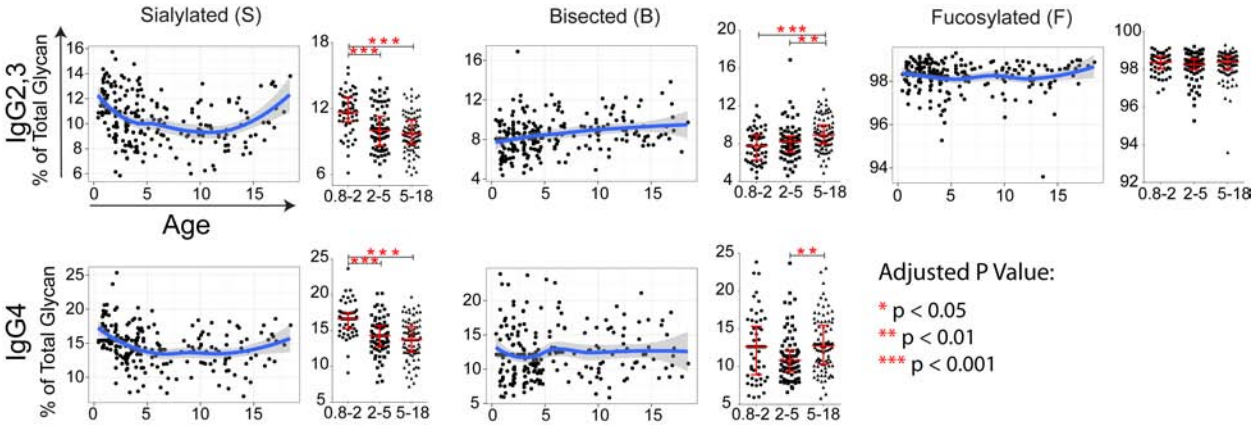
A.

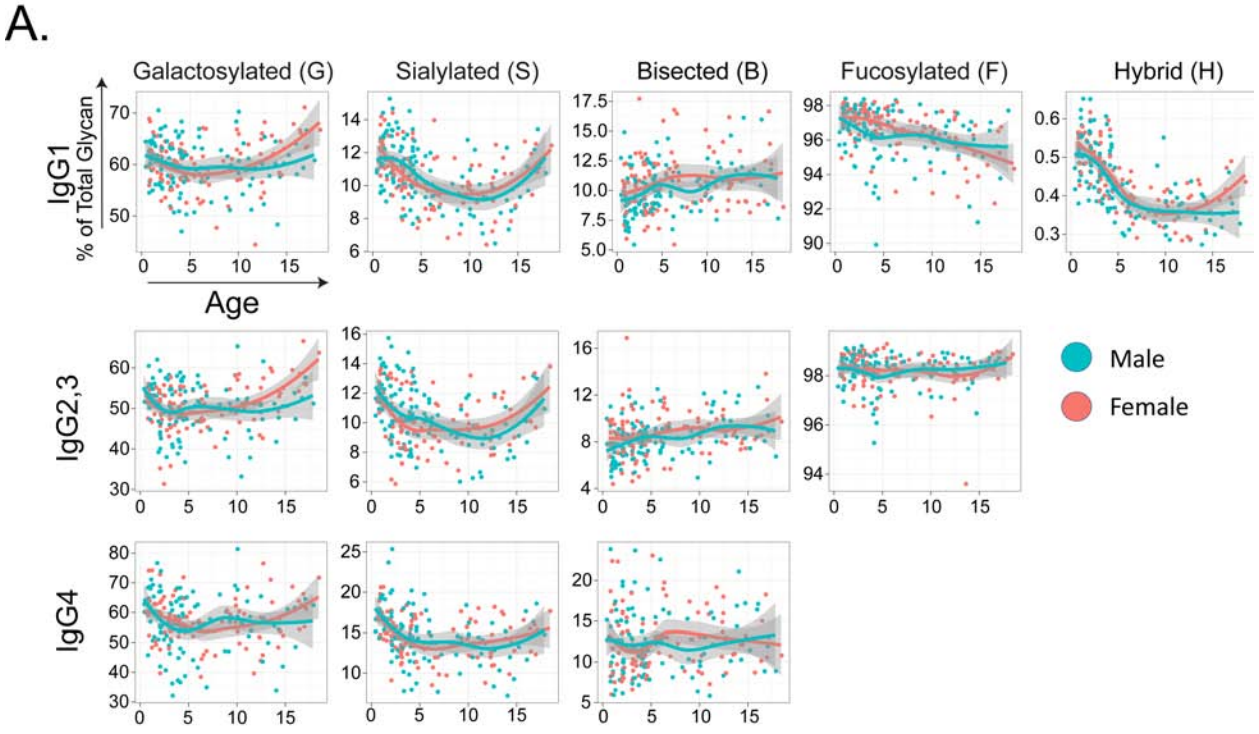

Galactosylated
Sialylated
Bisected
Fucosylated
IgG2,3
% of Total Glycan
Age
IgG4
Healthy Control
RRI, normal IgA
RRI, Low-IgA

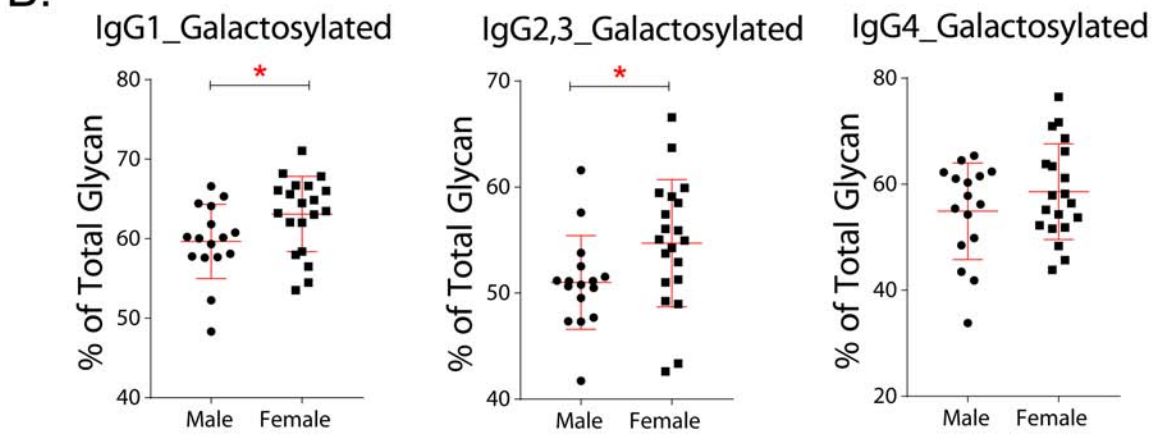
B.


Feature contributions to model
Coefficient
Core Fucose
N-acetylglucosamine
Mannose
Galactose
N-acetylneuraminic acid
IgG1 H6N4F1S1
IgG1 H3N5
IgG1 H6N3F1S1
IgG1 Hy
IgG1 H5N4S1
IgG2,3 A2S2
IgG2,3 H5N4F1S2
IgG2,3 H5N5F1S1


IgG1 H3N4
IgG1 H3N4F1
IgG1 H4N4
IgG1 H3N5
IgG1 H4N4F1
% of Total Glycan
IgG1 H5N4
IgG1 H3N5F1
IgG1 H4N5
IgG1 H4N3F1S1
IgG1 H5N4F1
IgG1 H4N5F1
IgG1 H5N5
IgG1 H4N4F1S1
IgG1 H5N4S1
IgG1 H6N4F1
IgG1 H5N5F1
IgG1 H6N3F1S1
IgG1 H5N4F1S1
IgG1 H4N5F1S1
IgG1 H6N4F1S1
IgG1 H5N5F1S1
IgG1 H5N4F1S2
IgG1 H5N5F1S2
0.8-2 2-5 5-18
Age
Core Fucose
N-acetylglucosamine
Mannose
Galactose
N-acetylneuraminic acid
Adjusted P Value:
* p < 0.05
** p < 0.01
*** p < 0.001




A.
Galactosylated (G)
Sialylated (S)
Bisected (B)
Fucosylated (F)
Hybrid (H)
IgG1
IgG2,3
IgG4
% of Total Glycan
Age
Male
Female


B.
IgG1_Galactosylated
IgG2,3_Galactosylated
IgG4_Galactosylated
% of Total Glycan
Male
Female
*

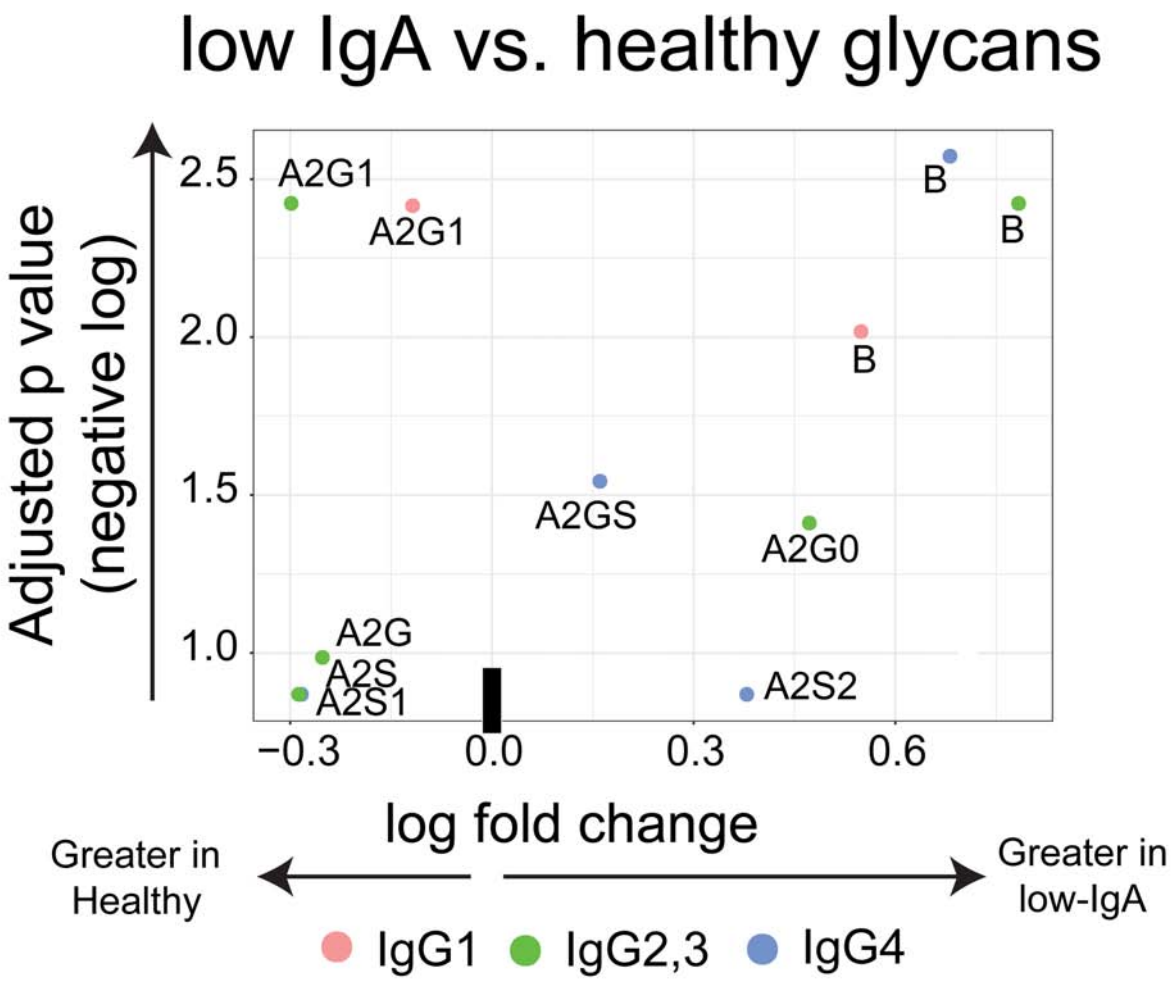

low IgA vs. healthy glycans
Adjusted p value
(negative log)
2.5
2.0
1.5
1.0
A2G1
A2G1
B
B
B
A2GS
A2G0
A2G
A2S
A2S1
A2S2
−0.3
0.0
0.3
0.6
log fold change
Greater in
Healthy
Greater in
low-IgA
IgG1
IgG2,3
IgG4

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Table E1. Recurrent respiratory infection subjects

Age (y)	M/F	Infections	WBC Kcells/ul	ALC Kcells/ul	IgG mg/dl	IgA mg/dl	IgM mg/dl	IgE unit/ml	IgG subclasses	IgG1 mg/dl	IgG2 mg/dl	IgG3 mg/dl	IgG4 mg/dl	Pneumococal titer	CH50 (60-144)
0.9	M	rec otitis	14.89	8.79	512	67	74	1	Low IgG4	330	70	114 H	<1 L	Good	Normal
1.0	M	rec sinusitis	7.25	5.18	469	36	59		Low IgG4	322	53	74	<1 L	Good	Not done
1.1	M	rec otitis, rec sinusitis	8.28	4.65	390	47	76	26	Normal	256	52	26	2	Not done	Normal
1.8	M	rec otitis	11.41	3.65	481	66	87		Low IgG4	295	113	85	<1L	Good	156H
2.1	M	rec otitis, rec pneumonia, rec sinusitis	7.73	3.32	617	79	46	14	Normal	392	99	30	2	Good	57L
2.3	F	rec ear otitis, rec pneumonia	10.14	4.85	649	65	88	18	Normal	412	81	42	7	Good	Not done
2.6	F	rec otitis, rec pneumonia	18.59	8.88	468	41	64	4	Normal	340	63	35	2	Good	Not done
2.6	F	rec otitis, rec pneumonia	17.35	8.88	527	63	57	4	Normal	363	56	27	6	Good	Not done
2.8	M	rec otitis	5.27	1.94	665	81	37	52	Normal	459	51	22	14	Low	Not done
3.0	M	rec sinusitis	8.44	6.08	746	180	48	12	High IgG3	516	134	83H	17	Good	Normal
3.1	M	rec pneumonia	13.19	4.91	733	61	82	13	Normal	509	83	24	2	Good	Not done
3.2	M	rec otitis	9.86	4.28	567	49	52	21	Normal	377	89	36	4	Good	Normal
3.4	M	rec otitis	9.84	4.1	881	110	107	6	Normal	525	114	61	9	Not done	Not done
3.6	M	rec sinusitis	9.23	4.85	1171	78	89	3	High IgG3	762	133	130H	24	Good	Not done
4.3	F	rec otitis, rec pneumonia	5.58	2.42	848	75	108	153	Normal	573	159	44	1	Good	Not done
4.3	M	rec otitis			680	91	54	14	Normal	441	88	33	8	Good	Not done
4.3	M	rec otitis, rec pneumonia	5.85	2.52	1188	172	147	76	High IgG4	720	207	43	125H	Good	Normal
5.5	M	rec otitis, rec pneumonia, rec sinusitis	6.11	3.2	898	79	60	9	Normal	575	215	22	36	Good	Not done
5.9	M	rec pneumonia	6.3	2.86	705	125	69	108	Normal	384	205	27	7	Good	Not done
6.0	F	rec sinusitis	5.61	2.7	1142	132	153	145	Normal	705	302	47	30	Good	Normal
6.1	F	rec pneumonia	10.47	4.46	791	124	96	715 H	Normal	422	272	81	64	Good	Normal
6.8	M	rec otitis	6.71	3.03	675	186	61	90	Normal	357	212	64	96	Not done	Not done
7.0	F	rec otitis	6.43	3.57	667	82	110	21	Normal	462	107	44	13	Good	Not done
9.1	M	rec sinusitis, rec pneumonia	9.58	2.32	779	91	57	42	Normal	429	196	68	70	Low	Normal
9.5	M	rec otitis, rec pneumonia, rec sinusitis	5.33	2.14	764	112	87	25	Normal	519	143	33	11	Good	Normal
9.5	M	rec sinusitis	9.7	2.84	927	96	119	11	Normal	482	236	156	34	Good	Normal
10.0	F	rec sinusitis	7.89	2.35	1,139	128	166	51	High IgG3	700	277	131H	17	Good	Normal
10.7	M	rec sinusitis	7.34	3.54	711	154	113	125	Normal	401	212	67	10	Good	Normal
11.1	M	rec otitis, rec sinusitis	6.51	1.17	1023	306	99	145	Normal	477	357	72	26	Good	Normal
13.2	M	rec pneumonia, rec sinusitis			866			9	Normal	386	282	76	11	Good	Not done
14.7	F	rec otitis	6.92	2.41	857	64	246	13	Normal	496	178	42	12	Not done	56L
16.3	M	rec sinusitis	6.97	2.12	1104	149	173	311H	High IgG4	640	256	80	111H	Good	Normal
17.7	M	rec sinusitis, rec pneumonia	5.7	1.77	965	149	88	317H	Normal	534	264	24	13	Good	Not done

Table E2. Low IgA subjects

Subject	1	2	3	4	5	6	7
Age	1.7	2.2	6.3	9.8	11.5	13.7	17.3
M/F	M	F	F	F	M	F	F
Infections	rec otitis	rec otitis	rec otitis	rec otitis, rec sinusitis	rec otitis, rec pneuminia, rec sinusitis	rec sinusitis	rec sinusitis
WBC Kcells/ul	11.52	6.56	9.9	6.94	5.35	5.6	6.3
ALC Kcells/ul	4.69	3.74	4.67	3.29	1.69	2.39	1.97
IgG mg/dl	432	524	1096	894	1115	693	1204
IgA mg/dl	13	10	<7	54	<7	53	<7
IgM mg/dl	Not done	64	130	164	185	114	131
IgE unit/ml	56H	Not done	42	30	49	3	4
IgG subclasses	Normal	Normal	Normal	Normal	Normal	Normal	Normal
IgG1 mg/dl	309	367	633	532	650	385	745
IgG2 mg/dl	52	74	367	259	369	209	354
IgG3 mg/dl	42	16	24	78	35	35	37
IgG4 mg/dl	1	1	8	31	12	40	10
Pneumoccocal titer	Low	Good	Good	Good	Good	Good	Good
CH50 (60-144)	45L	Not done	Not done	Not done	Not done	Normal	Not done

Figure E1. IgG2,3 and Ig4 Fc glycans in healthy children. (A) Levels of galactosylated IgG2,3 and IgG4 glycans in 145 healthy children, as defined by LC-ESI-MS, plotted by age. (B) Glycan feature contributions to the age category classification model, colored by respective contribution to each age group. P values (adjusted in A for multiple comparisons): * <0.05, **<0.01, ***, <0.001

Figure E2. IgG2,3 and IgG4 Fc glycans in healthy children and immunodeficient subjects. (A) Scatterplots of galactosylated, sialylated, bisected, fucosylated and hybrid glycans by age in IgG2,3 and Ig4 from healthy children (black LOESS line, 95% confidence interval indicated in gray), RRI with normal IgA, and RRI with low IgA. (B) Glycan feature contributions to the RRI vs. HC classification model

Figure E3. Individual IgG1 Fc glycans in healthy children. Levels of individual IgG1 Fc glycans in 145 healthy children, as defined by LC-ESI-MS, plotted by age. (Left) Scatterplots of glycan prevalence versus age (black LOESS line, 95% confidence interval indicated in gray). P values adjusted for multiple comparisons: *<0.05, ** <0.01, *** < 0.001.

Figure E4. Summary IgG2,3 and IgG4 Fc glycans in healthy children. Level of sialylated, bisected, and fucosylated IgG2,3 and IgG4 Fc glycans in 145 healthy children, as defined by LC-ESI-MS, plotted by age (black LOESS line, 95% confidence interval indicated in gray). P values adjusted for multiple comparisons: *<0.05, ** <0.01, *** < 0.001

Figure E5. Summary IgG Fc glycans in healthy male versus female children. A. Levels of summary IgG1 (top), IgG2,3 (middle), and IgG4 (bottom) glycans including galactosylated, sialylated, bisected, fucosylated and hybrid species in healthy male (blue) and female (red) children, as defined by LC-ESI MS, plotted by age. (black LOESS line, 95% confidence interval indicated in gray) B. IgG Galactosylation in age 12 or older in males n=16 vs. females n=20, mean +/- SD IgG1 60.0+/-4.7% vs. 63.1+/-4.7%, p=0.035; IgG2/3 51.0+/-4.1% vs. 54.7+/-6.0%, p=0.047, IgG4 54.9+/-9.1% vs. 58.6+/-9.0%, p=0.24.

Figure E6. Comparison of IgG Fc glycans in healthy children versusIgA low children. Volcano plot depicting differences between healthy and RRI subjects with low-IgA. A2=biantennary, G = galactosylation (0, 1 or 2), S=sialylated (0, 1 or 2), B=bisected, Hy=hybrid.