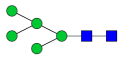
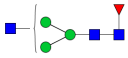
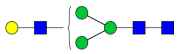
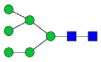
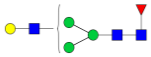
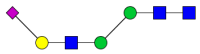
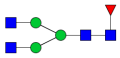
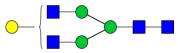
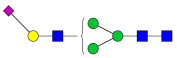
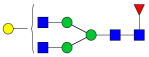
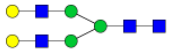
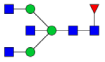
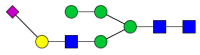
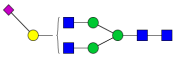
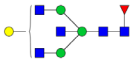
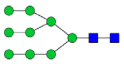
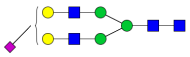
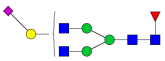
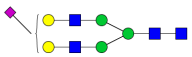
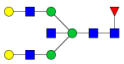
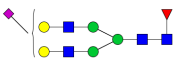
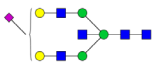
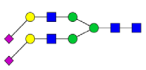
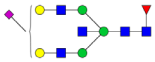
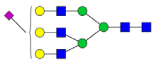
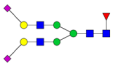
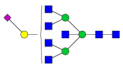
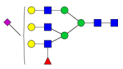
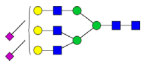
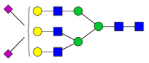
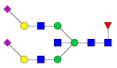
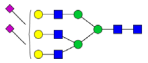
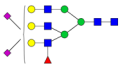
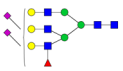
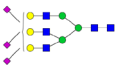
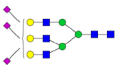
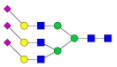
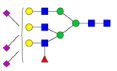
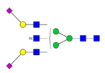
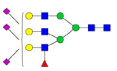
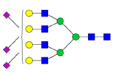
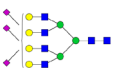
Table S1. The list of N-glycans in human serum used for quantitation

No	Putative structure	MW $(M+Na)^+$		composition	CV
		Sample (light)	Internal Standard (heavy)		
G1		1257.44	1260.45	H5N2	17.40%
G2		1282.47	1285.48	H3N3F1	20.98%
G3		1298.46	1301.49	H4N3	17.48%
G4		1419.48	1422.49	H6N2	20.74%
G5		1444.52	1447.55	H4N3F1	23.88%
G6		1455.53	1458.54	H3N3E1	18.36%
G7		1485.55	1488.57	H3N4F1	7.78%
G8		1501.53	1504.55	H4N4	19.33%
G9		1617.60	1620.61	H4N3E1	7.04%
G10		1647.61	1650.63	H4N4F1	8.82%
G11		1663.59	1666.61	H5N4	15.91%
G12		1688.62	1691.66	H3N5F1	16.16%
G13		1779.70	1782.70	H5N3E1	22.10%
G14		1809.67	1812.69	H5N4F1	8.87%
G15		1820.70	1823.70	H4N4E1	9.29%
G16		1850.69	1853.69	H4N5F1	13.96%
G17		1905.64	1908.68	H9N2	23.73%
G18		1936.69	1939.74	H5N4L1	10.32%
G19		1966.74	1969.75	H4N4F1E1	6.70%
G20		1982.73	1985.76	H5N4E1	3.87%
G21		2012.75	2015.76	H5N5F1	16.32%
G22		2128.78	2131.80	H5N4F1E1	5.72%
G23		2185.78	2188.79	H5N5E1	10.22%
G24		2209.74	2212.79	H5N4L2	11.90%

G25		2255.81	2258.83	H5N4L1E1	4.09%
G26		2301.85	2304.88	H5N4E2	2.20%
G27		2331.84	2334.86	H5N5F1E1	7.18%
G28		2347.83	2350.84	H6N5E1	10.85%
G29		2401.83	2404.86	H5N4F1L1E1	7.09%
G30		2429.86	2432. 86	H4N7E1	15.72%
G31		2447.88	2450.90	H5N4F1E2	5.09%
G32		2493.86	2496.93	H6N5F1E1	18.03%
G33		2504.88	2507.89	H5N5E2	13.46%
G34		2574.80	2577.83	H6N5L2	17.64%
G35		2620.90	2623.91	H6N5L1E1	5.91%
G36		2650.95	2653.97	H5N5F1E2	7.49%
G37		2666.93	2669.96	H6N5E2	8.16%
G38		2766.94	2769.95	H6N5F1L1E1	11.02%
G39		2813.09	2816.11	H6N5F1E2	16.75%
G40		2893.96	2897.01	H6N5L2E1	8.91%
G41		2940.05	2943.06	H6N5L1E2	4.06%
G42		2986.07	2989.08	H6N5E3	5.24%
G43		3040.03	2043.07	H6N5F1L2E1	16.93%
G44		3068.16	3071.20	H5N5L1E1	21.48%
G45		3086.09	3089.11	H6N5F1L1E2	5.21%
G46		3259.12	3262.18	H7N6L2E1	21.26%
G47		3305.23	3308.20	H7N6L1E2	22.81%

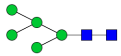
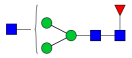
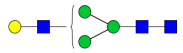
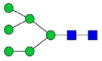
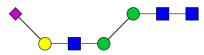
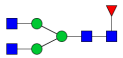
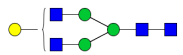
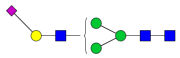
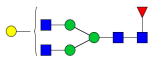
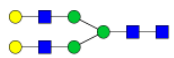
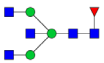
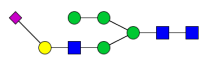
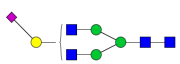
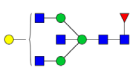
G48		3532.34	3535.34	H7N6L3E1	23.57%
G49		3578.28	3581.30	H7N6L2E2	22.38%

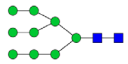
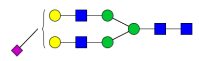
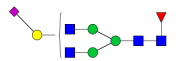
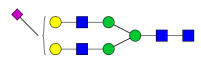
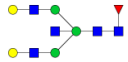
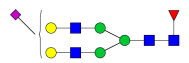
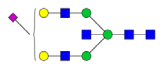
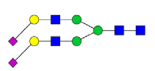
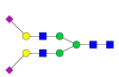
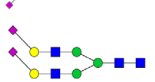
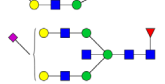
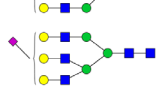
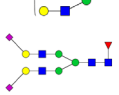
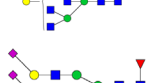
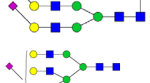
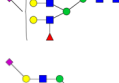
H = hexose, N = N-acetylhexosamine, F = fucose, L = lactonized N-acetylneuraminic acid (α2,3-linked), E = ethyl esterified N-acetylneuraminic acid (α2,6-linked), the number of residues given listed the letter. Green circle, Man; yellow circle, Gal; blue square, GlcNAc; red triangle, Fuc; clockwise purple diamond, α(2,6)-linked sialic acid; anticlockwise purple diamond, α(2,3)-linked sialic acid.

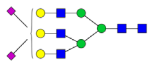
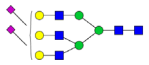
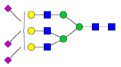
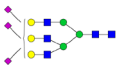
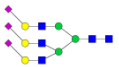
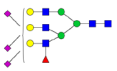
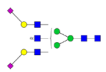
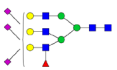
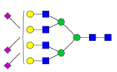
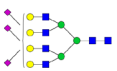
Table S2. Derived trait calculation

Derived glycosylation trait	Formula
Fucosylation	G2+G5+G7+G10+G12+G14+G16+G19+G21+G22+G27+G29+G31+G36
High mannose glycans	G1+G14+G17
Bisection	G12+G16+G21+G23+G27+G30+G33+G36
Monoantennary glycans	G2+G3+G5+G9
Diantennary glycans	G7+G8+G10+G11+G12+G14+G15+G16+G18+G19+G20+G21+G22+G23+G24+G25+G26+G27+G29+G31+G33+G36
Triantennary glycans	G28+G34+G35+G37+G38+G39+G40+G41+G42+G43+G44+G45
Tetraantennary glycans	G30+G46+G47+G49
Multi-antennary glycans	G28+G34+G35+G37+G38+G39+G40+G41+G42+G43+G44+G45+G30+G46+G47+G49
Lewis type glycans	G32+G38+G39+G43+G45
α2,3-sialyation	1/2*(G18+G25+G29)+1/3*(G35+G38+G41+G44+G45)+2/3*(G34+G40+G43)+1/4*G47+2/4*(G46+G49)+G24
α2,6-sialyation	1/2*(G15+G19+G20+G22+G25+G29)+1/3*(G28+G32+G35+G38+G40+G43+G44)+2/3*(G37+G39+G41+G45)+1/4*G46+2/4*(G47+G49)+G26+G31+G42

Table S3. Relative quantitative data of the 49 N-glycans of 186 samples in the training cohort

No	Putative structure	m/z	Composition	Peak area ratio (Mean ± SD)						CRC vs Healthy Control		AA vs Healthy Control		AA vs CRC	
				Healthy Control		AA		CRC							
				Mean	SD	Mean	SD	Mean	SD	*P* value	AUC	*P* value	AUC	*P* value	AUC
1		1257.44	H5N2	2.22	0.76	1.59	0.48	1.84	0.88	0.0026	0.67	8.11E-05	0.75	0.0554	0.61
2		1282.47	H3N3F1	2.96	0.95	2.20	0.83	2.57	1.02	0.0264	0.63	0.0001	0.75	0.0443	0.62
3		1298.46	H4N3	1.80	0.50	1.33	0.31	1.67	0.52	0.2604	0.57	1.92E-06	0.81	9.75E-05	0.73
4		1419.48	H6N2	2.27	0.86	1.89	0.65	2.26	0.73	0.9156	0.51	0.0210	0.65	0.0102	0.65
5		1444.52	H4N3F1	2.46	0.74	1.71	0.45	1.71	0.64	3.84E-09	0.81	7.67E-07	0.82	0.3866	0.55
6		1455.53	H3N3E1	1.42	0.40	1.10	0.30	1.51	0.61	0.8451	0.52	0.0002	0.74	8.23E-05	0.73
7		1485.55	H3N4F1	2.00	0.87	1.51	0.93	2.16	1.21	0.7449	0.53	0.0031	0.69	0.0017	0.68
8		1501.53	H4N4	2.08	1.10	1.28	0.35	1.64	0.82	0.0086	0.65	1.05E-06	0.82	0.0079	0.65
9		1617.60	H4N3E1	1.56	0.34	1.21	0.19	1.65	0.50	0.5091	0.55	1.05E-06	0.82	2.89E-07	0.82
10		1647.61	H4N4F1	1.59	0.50	1.11	0.42	1.27	0.49	0.0023	0.67	1.03E-05	0.78	0.0727	0.60
11		1663.59	H5N4	1.71	0.65	1.13	0.31	1.24	0.42	8.65E-06	0.75	5.12E-07	0.83	0.1977	0.57
12		1688.62	H3N5F1	2.57	0.99	2.22	1.22	2.65	1.38	0.8886	0.51	0.0311	0.64	0.0438	0.62
13		1779.70	H5N3E1	1.77	0.29	1.56	0.34	1.76	0.43	0.7433	0.53	0.0053	0.68	0.0280	0.63
14		1809.67	H5N4F1	1.32	0.46	0.85	0.31	0.78	0.32	3.90E-11	0.85	1.75E-06	0.81	0.2727	0.56
15		1820.70	H4N4E1	0.60	0.13	0.46	0.08	0.60	0.15	0.9223	0.51	3.47E-07	0.85	8.94E-07	0.80
16		1850.69	H4N5F1	1.91	0.57	1.50	0.53	1.73	0.65	0.1035	0.60	0.0014	0.70	0.0769	0.60

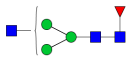
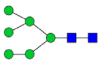
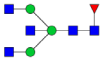
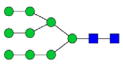
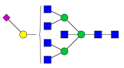
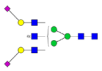
17		1905.64	H9N2	2.39	0.62	2.60	0.72	2.64	0.72	0.0965	0.60	0.2172	0.58	0.7838	0.49
18		1936.69	H5N4L1	0.71	0.19	0.56	0.12	0.78	0.27	0.1619	0.58	8.11E-05	0.75	2.88E-06	0.78
19		1966.74	H4N4F1E1	1.94	0.39	1.52	0.28	1.92	0.47	0.9223	0.51	1.75E-06	0.81	2.70E-06	0.78
20		1982.73	H5N4E1	1.07	0.20	0.85	0.12	1.11	0.29	0.5944	0.54	5.12E-07	0.83	2.89E-07	0.82
21		2012.75	H5N5F1	1.18	0.21	1.02	0.23	1.14	0.25	0.5300	0.54	0.0019	0.70	0.0078	0.66
22		2128.78	H5N4F1E1	1.17	0.29	0.83	0.22	0.93	0.28	8.83E-06	0.74	5.12E-07	0.83	0.0632	0.61
23		2185.78	H5N5E1	1.88	0.55	1.41	0.33	1.82	0.57	0.8886	0.49	8.33E-06	0.79	2.91E-05	0.75
24		2209.74	H5N4L2	0.99	0.20	0.84	0.14	1.03	0.26	0.5091	0.55	0.0002	0.74	2.44E-05	0.75
25		2255.81	H5N4L1E1	1.07	0.21	0.89	0.15	1.14	0.32	0.2604	0.57	0.0001	0.75	1.36E-05	0.76
26		2301.85	H5N4E2	1.30	0.19	1.12	0.13	1.38	0.29	0.1493	0.59	1.18E-05	0.78	2.89E-07	0.81
27		2331.84	H5N5F1E1	1.68	0.55	1.36	0.42	1.65	0.53	0.9256	0.50	0.0053	0.68	0.0040	0.67
28		2347.83	H6N5E1	1.51	0.36	1.26	0.34	1.65	0.52	0.3158	0.56	0.0032	0.69	0.0003	0.71
29		2401.83	H5N4F1L1E1	1.78	0.52	1.34	0.46	2.16	1.00	0.1110	0.59	7.16E-05	0.76	2.36E-06	0.78
30		2429.86	H4N7E1	2.34	0.52	2.49	0.59	2.48	0.84	0.7950	0.52	0.4034	0.55	0.7484	0.52
31		2447.88	H5N4F1E2	1.28	0.37	0.94	0.27	1.20	0.35	0.3508	0.56	7.16E-05	0.76	0.0006	0.70
32		2493.86	H6N5F1E1	1.01	0.18	0.85	0.17	1.03	0.27	0.8886	0.51	0.0003	0.73	0.0005	0.70
33		2504.88	H5N5E2	2.17	0.96	1.62	0.32	2.31	0.71	0.0899	0.60	1.51E-05	0.78	6.62E-07	0.80
34		2574.80	H6N5L2	0.98	0.23	0.89	0.20	1.05	0.34	0.5330	0.54	0.0815	0.61	0.0251	0.63

35		2620.90	H6N5L1E1	0.84	0.30	0.67	0.23	1.03	0.48	0.0271	0.63	0.0077	0.67	2.94E-05	0.75
36		2650.95	H5N5F1E2	1.89	0.58	1.37	0.44	1.84	0.70	0.8597	0.48	7.45E-05	0.75	0.0004	0.71
37		2666.93	H6N5E2	0.96	0.34	0.73	0.22	1.25	0.63	0.0157	0.64	0.0027	0.69	3.43E-06	0.77
38		2766.94	H6N5F1L1E1	1.17	0.50	0.89	0.30	1.71	0.97	0.0026	0.67	0.0159	0.65	1.92E-06	0.78
39		2813.09	H6N5F1E2	0.95	0.42	0.73	0.27	1.11	0.60	0.2690	0.57	0.0210	0.65	0.0002	0.72
40		2893.96	H6N5L2E1	0.92	0.37	0.77	0.29	1.15	0.61	0.0499	0.61	0.0660	0.62	0.0004	0.71
41		2940.05	H6N5L1E2	0.92	0.26	0.81	0.24	1.04	0.38	0.0965	0.60	0.0403	0.63	0.0011	0.69
42		2986.07	H6N5E3	1.22	0.37	1.02	0.30	1.70	0.71	0.0003	0.71	0.0213	0.65	4.02E-07	0.81
43		3040.03	H6N5F1L2E1	1.24	0.50	1.01	0.44	1.89	1.02	0.0004	0.70	0.0225	0.64	1.30E-06	0.79
44		3068.16	H5N5L1E1	2.02	0.79	1.83	0.86	2.72	1.31	0.0036	0.66	0.2164	0.58	0.0002	0.72
45		3086.09	H6N5F1L1E2	0.86	0.42	0.67	0.38	1.25	0.66	0.0026	0.67	0.0268	0.64	3.43E-06	0.77
46		3259.12	H7N6L2E1	0.71	0.30	0.62	0.29	0.97	0.60	0.0164	0.64	0.1014	0.60	0.0004	0.71
47		3305.23	H7N6L1E2	0.93	0.35	0.91	0.37	1.33	0.74	0.0004	0.70	0.7883	0.48	0.0006	0.70
48		3532.34	H7N6L3E1	0.75	0.40	0.69	0.33	0.98	0.59	0.0264	0.63	0.6958	0.53	0.0061	0.66
49		3578.28	H7N6L2E2	0.70	0.33	0.74	0.30	1.04	0.61	0.0006	0.69	0.4941	0.54	0.0064	0.66

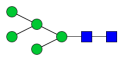
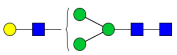
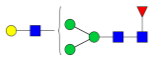
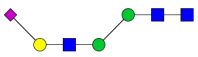
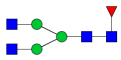
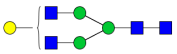
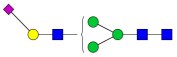
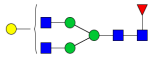
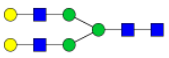
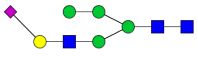
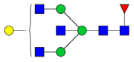
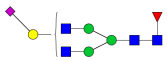
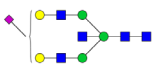
CRC, colorectal cancer; AA, advanced adenomas; H = hexose, N = N-acetylhexosamine, F = fucose, L = lactonized N-acetylneuraminic acid (α2,3-linked), E = ethyl esterified N-acetyl-neuraminic acid (α2,6-linked), the number of residues given listed the letter. Green circle, Man; yellow circle, Gal; blue square, GlcNAc; red triangle, Fuc; clockwise purple diamond, α(2,6)-linked sialic acid; anticlockwise purple diamond, α(2,3)-linked sialic acid.

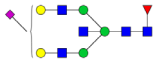
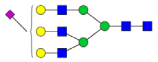
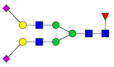
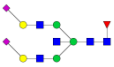
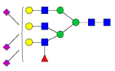
Table S4. Results of the *K-means* classifier

Cluster 1:

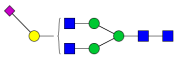
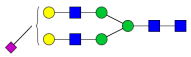
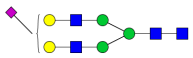
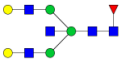
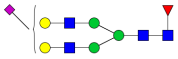
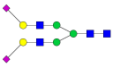
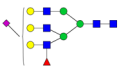
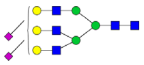
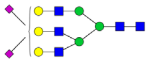
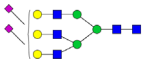
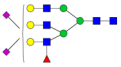
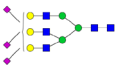
No	Putative structure	MW (M+Na)$^+$		composition
		Sample (light)	Internal Standard (heavy)	
G2		1282.47	1285.48	H3N3F1
G4		1419.48	1422.49	H6N2
G12		1688.62	1691.66	H3N5F1
G17		1905.64	1908.68	H9N2
G30		2429.86	2432. 86	H4N7E1
G33		2504.88	2507.89	H5N5E2
G44		3068.16	3071.20	H5N5L1E1

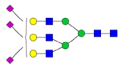
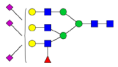
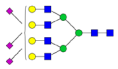
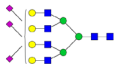
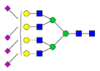
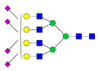
Cluster 2:

No	Putative structure	MW (M+Na)$^+$		composition
		Sample (light)	Internal Standard (heavy)	
G1		1257.44	1260.45	H5N2
G3		1298.46	1301.49	H4N3
G5		1444.52	1447.55	H4N3F1
G6		1455.53	1458.54	H3N3E1
G7		1485.55	1488.57	H3N4F1
G8		1501.53	1504.55	H4N4
G9		1617.60	1620.61	H4N3E1
G10		1647.61	1650.63	H4N4F1
G11		1663.59	1666.61	H5N4
G13		1779.70	1782.70	H5N3E1
G16		1850.69	1853.69	H4N5F1
G19		1966.74	1969.75	H4N4F1E1
G23		2185.78	2188.79	H5N5E1
G26		2301.85	2304.88	H5N4E2

G27		2331.84	2334.86	H5N5F1E1
G28		2347.83	2350.84	H6N5E1
G29		2401.83	2404.86	H5N4F1L1E1
G36		2650.95	2653.97	H5N5F1E2
G42		2986.07	2989.08	H6N5E3
G43		3040.03	2043.07	H6N5F1L2E1

Cluster 3:

No	Putative structure	MW $(M+Na)^+$		composition
		Sample (light)	Internal Standard (heavy)	
G14		1809.67	1812.69	H5N4F1
G15		1820.70	1823.70	H4N4E1
G18		1936.69	1939.74	H5N4L1
G20		1982.73	1985.76	H5N4E1
G21		2012.75	2015.76	H5N5F1
G22		2128.78	2131.80	H5N4F1E1
G24		2209.74	2212.79	H5N4L2
G25		2255.81	2258.83	H5N4L1E1
G31		2447.88	2450.90	H5N4F1E2
G32		2493.86	2496.93	H6N5F1E1
G34		2574.80	2577.83	H6N5L2
G35		2620.90	2623.91	H6N5L1E1
G37		2666.93	2669.96	H6N5E2
G38		2766.94	2769.95	H6N5F1L1E1
G39		2813.09	2816.11	H6N5F1E2
G40		2893.96	2897.01	H6N5L2E1

G41		2940.05	2943.06	H6N5L1E2
G45		3086.09	3089.11	H6N5F1L1E2
G46		3259.12	3262.18	H7N6L2E1
G47		3305.23	3308.20	H7N6L1E2
G48		3532.34	3535.34	H7N6L3E1
G49		3578.28	3581.30	H7N6L2E2

H = hexose, N = N-acetylhexosamine, F = fucose, L = lactonized N-acetylneuraminic acid (α2,3-linked), E = ethyl esterified N-acetylneuraminic acid (α2,6-linked), the number of residues given listed the letter. Green circle, Man; yellow circle, Gal; blue square, GlcNAc; red triangle, Fuc; clockwise purple diamond, α(2,6)-linked sialic acid; anticlockwise purple diamond, α(2,3)-linked sialic acid.

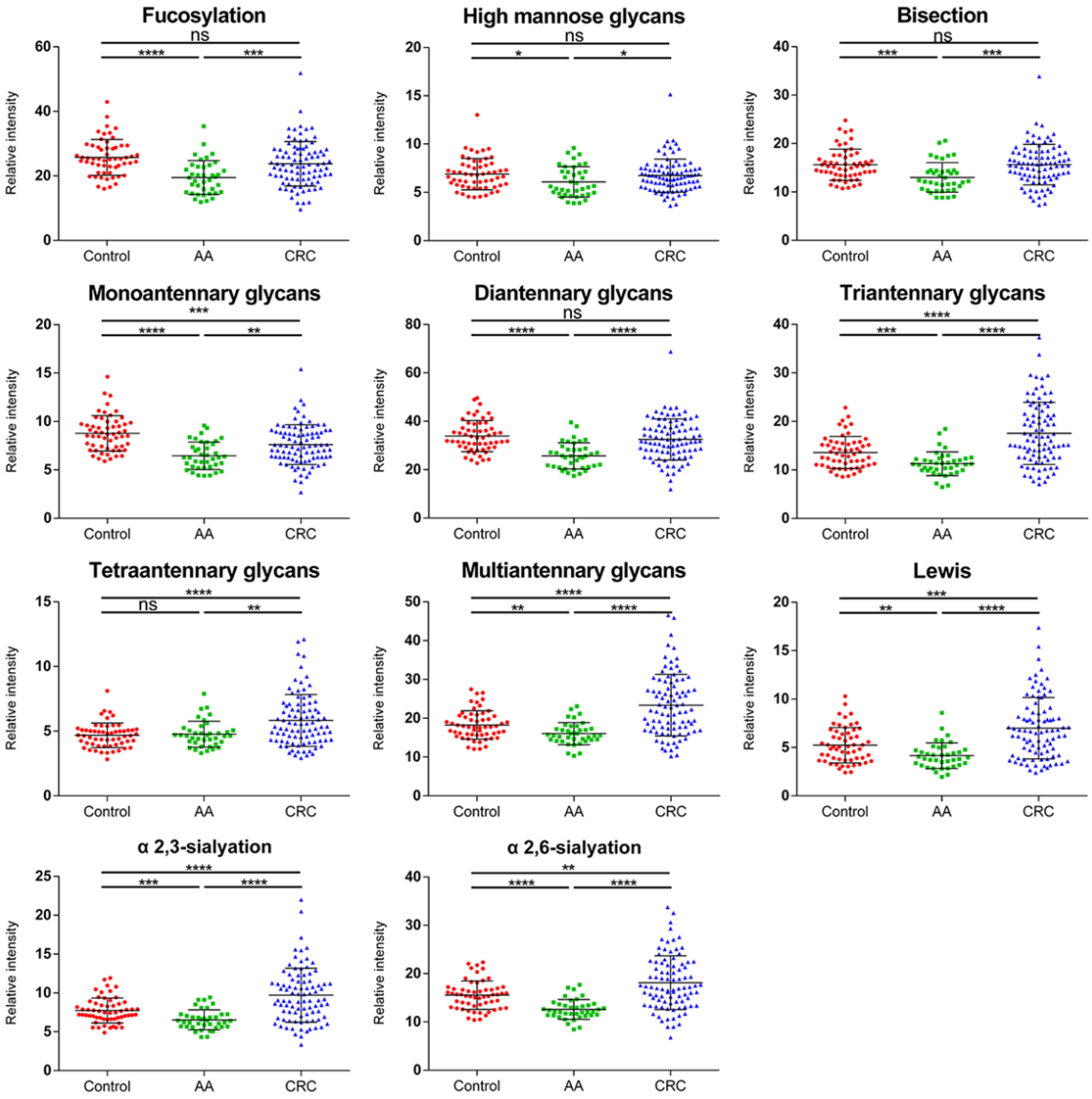


Figure S1. Scatter plot depicting the different relative intensity of derived glycosylation traits in the three groups. The N-glycans were grouped according to their structural features: fucosylation; high mannose glycans; bisecting type N-glycans; monoantennary; diantennary; triantennnary; tetraantennary; α2,3-sialyation; α2,6-sialyation. * The equivalent of P<0.05, ** the equivalent of P<0.01, *** the equivalent of P<0.001, **** the equivalent of P<0.0001.

Table S5. N-glycan summary of the AUC above 0.8

Number	Group	Composition	AUC
G3	AA/Control	H4N3	0.8061
G5	AA/Control	H4N3F1	0.8241
G8	AA/Control	H4N4	0.8169
G9	AA/Control	H4N3E1	0.8187
G11	AA/Control	H5N4	0.8309
G14	AA/Control	H5N4F1	0.8088
G15	AA/Control	H4N4E1	0.8493
G19	AA/Control	H4N4F1E1	0.8084
G20	AA/Control	H5N4E1	0.8313
G22	AA/Control	H5N4F1E1	0.834
G5	CRC/Control	H4N3F1	0.8138
G14	CRC/Control	H5N4F1	0.8513
G9	AA/CRC	H4N3E1	0.8203
G20	AA/CRC	H5N4E1	0.8186
G26	AA/CRC	H5N4E2	0.8164
G33	AA/CRC	H5N5E2	0.8017
G42	AA/CRC	H6N5E3	0.8119

CRC, colorectal cancer; AA, advanced adenomas; Control, healthy controls; H = hexose, N = N-acetylhexosamine, F = fucose, L = lactonized N-acetylneuraminic acid (α2,3-linked), E = ethyl esterified N-acetylneuraminic acid (α2,6-linked), the number of residues given listed the letter. Green circle, Man; yellow circle, Gal; blue square, GlcNAc; red triangle, Fuc; clockwise purple diamond, α(2,6)-linked sialic acid; anticlockwise purple diamond, α(2,3)-linked sialic acid.

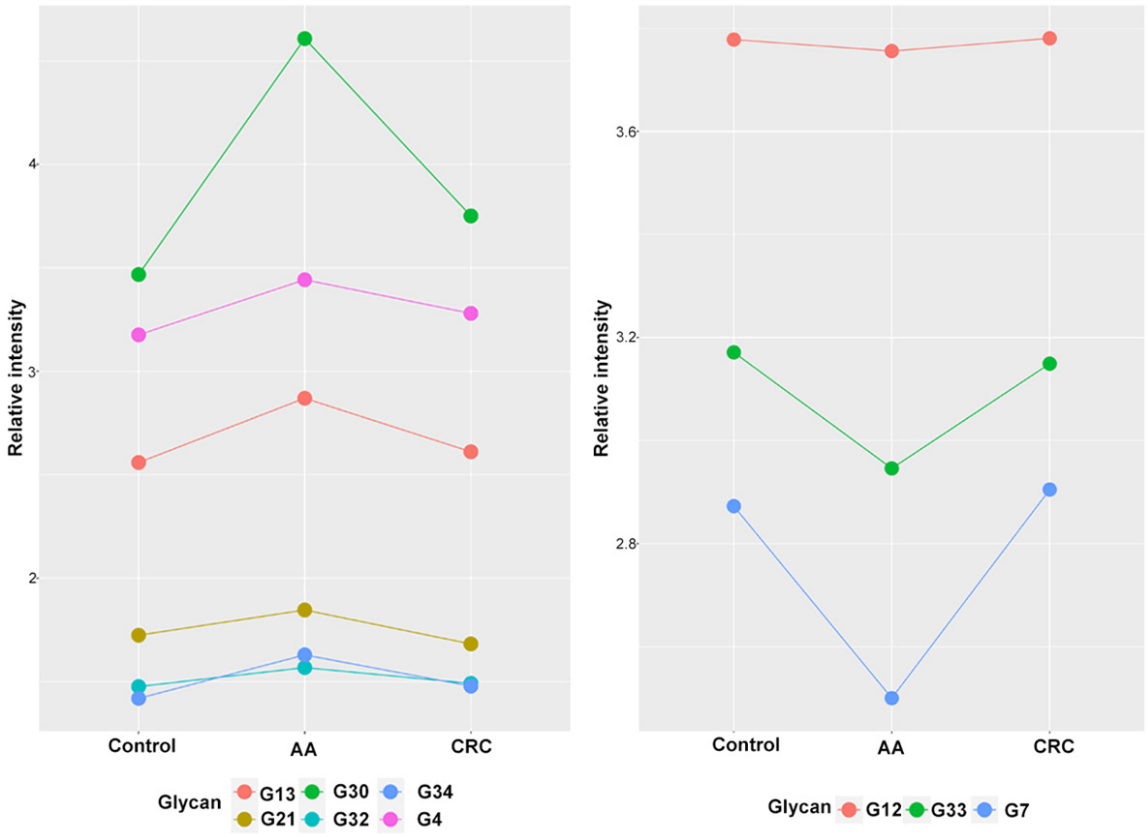


Figure S2. The N-glycans whose relative contents are not linearly correlated with the progression of the CRC.