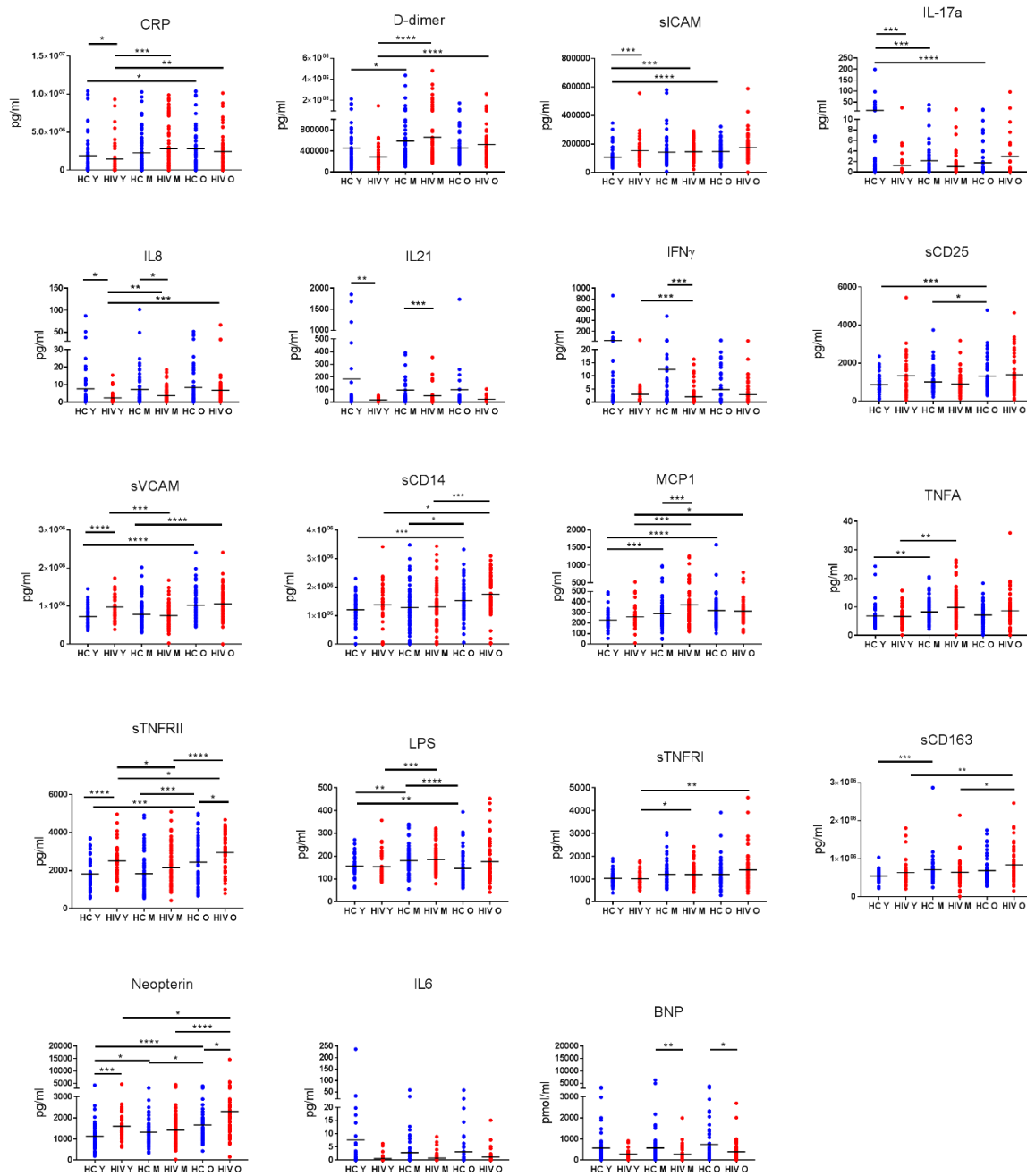
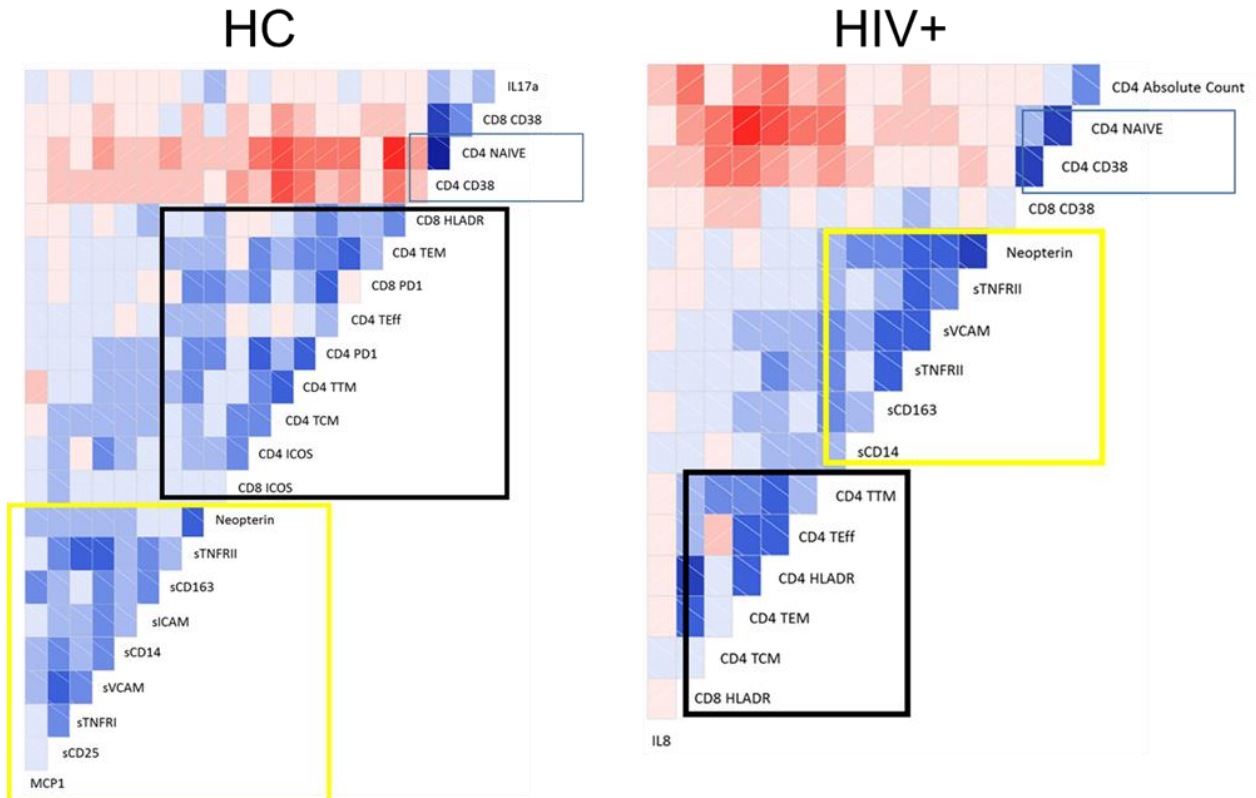


Supplementary Material



Supplemental Figure 1. Plasma biomarker levels by age group in HIV negative (HC) and HIV participants. Blue = HC, Red = HIV. Mann-Whitney test was performed to determine significant differences between participant groups as labeled; * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001.



Supplemental Figure 2. Correlation matrix of immune activation and plasma biomarkers with significant correlations with age for HIV negative (HC) (left) and HIV (right). Pairwise correlations were performed between each of the variables shown, blue squares represent positive correlation and red squares represent negative correlation. Color saturation of individual squares indicate stronger correlations. Unfilled boxes show clustering of similar parameters between HC and HIV. In the blue box are parameters that showed negative correlations with age and therefore show positive correlations with each other. In yellow, clusters of plasma biomarkers and in black, flow cytometry parameters which all showed positive correlations with age (shown in tables 2 and 3).

Supplemental Table 1. Mean HAI titers for participant groups: Absolute responders, Non-responders, and Other at timepoints before (T0) and after vaccination (T2).

HC	(n)	H1N1		H3N2		B	
		T0	T2	T0	T2	T0	T2
Young R	15	101	1899	136	747	171	2475
Young Other	13	492	929	114	348	271	1034
Young NR	14	680	949	320	389	549	777
Middle R	22	75	1884	69	560	168	1476
Middle Other	24	120	894	177	337	287	993
Middle NR	10	240	416	132	208	312	440
Old R	12	64	813	179	1347	102	1147
Old Other	18	156	602	222	556	230	680
Old NR	12	133	164	143	183	598	593

HIV	(n)	T0	T2	T0	T2	T0	T2
		Young R	4	200	1280	150	760
Young Other	13	207	789	155	326	140	998
Young NR	11	360	574	156	189	735	575
Middle R	3	87	1280	93	747	107	1173
Middle Other	38	340	845	198	459	203	749
Middle NR	26	412	628	180	268	457	566
Old R	9	66	667	42	338	269	518
Old Other	17	279	652	208	593	269	518
Old NR	18	358	469	208	311	456	551

Supplemental Table 2. Variables included in LASSO analysis

1	AgeEntry	45	TFH/CD38+HLADR+ICOS-KI67-PD1+ (%)	89	CD4/CD38+HLADR+ICOS-KI67+PD1- (%)
2	IFNg	46	TFH/CD38+HLADR+ICOS-KI67-PD1- (%)	90	CD4/CD38+HLADR+ICOS-KI67-PD1+ (%)
3	IL17a	47	TFH/CD38+HLADR+ICOS+KI67+PD1+ (%)	91	CD4/CD38+HLADR+ICOS-KI67-PD1- (%)
4	IL6	48	TFH/CD38+HLADR-ICOS+KI67+PD1- (%)	92	CD4/CD38+HLADR-ICOS+KI67+PD1+ (%)
5	IL8	49	TFH/CD38+HLADR-ICOS+KI67+PD1+ (%)	93	CD4/CD38+HLADR-ICOS+KI67+PD1- (%)
6	MCP1	50	TFH/CD38+HLADR+ICOS+KI67-PD1- (%)	94	CD4/CD38+HLADR-ICOS+KI67+PD1+ (%)
7	TNFA	51	TFH/CD38+HLADR-ICOS-KI67+PD1+ (%)	95	CD4/CD38+HLADR-ICOS+KI67-PD1- (%)
8	sICAM	52	TFH/CD38+HLADR-ICOS-KI67+PD1- (%)	96	CD4/CD38+HLADR-ICOS-KI67+PD1+ (%)
9	sVCAM	53	TFH/CD38+HLADR-ICOS-KI67-PD1+ (%)	97	CD4/CD38+HLADR-ICOS-KI67+PD1- (%)
10	BNP	54	TFH/CD38+HLADR-ICOS-KI67-PD1- (%)	98	CD4/CD38+HLADR-ICOS-KI67-PD1+ (%)
11	CRP	55	TFH/CD38-HLADR+ICOS+KI67+PD1+ (%)	99	CD4/CD38+HLADR-ICOS+KI67-PD1- (%)
12	IL21	56	TFH/CD38-HLADR+ICOS+KI67+PD1- (%)	100	CD4/CD38-HLADR+ICOS+KI67+PD1+ (%)
13	neopterin	57	TFH/CD38-HLADR+ICOS+KI67-PD1+ (%)	101	CD4/CD38-HLADR+ICOS+KI67+PD1- (%)
14	sCD14	58	TFH/CD38-HLADR+ICOS+KI67-PD1- (%)	102	CD4/CD38-HLADR+ICOS+KI67+PD1+ (%)
15	CXCL13	59	TFH/CD38-HLADR+ICOS-KI67+PD1+ (%)	103	CD4/CD38-HLADR+ICOS+KI67-PD1- (%)
16	sCD25	60	TFH/CD38-HLADR+ICOS-KI67+PD1- (%)	104	CD4/CD38-HLADR+ICOS-KI67+PD1+ (%)
17	sCD163	61	TFH/CD38-HLADR+ICOS-KI67-PD1+ (%)	105	CD4/CD38-HLADR+ICOS-KI67+PD1- (%)
18	sTNF α	62	TFH/CD38-HLADR+ICOS-KI67-PD1- (%)	106	CD4/CD38-HLADR+ICOS-KI67-PD1+ (%)
19	sTNFR II	63	TFH/CD38-HLADR-ICOS+KI67+PD1+ (%)	107	CD4/CD38-HLADR+ICOS-KI67-PD1- (%)
20	D-Dimer	64	TFH/CD38-HLADR-ICOS+KI67+PD1- (%)	108	CD4/CD38-HLADR-ICOS+KI67+PD1+ (%)
21	LPS	65	TFH/CD38-HLADR-ICOS+KI67-PD1+ (%)	109	CD4/CD38-HLADR-ICOS+KI67+PD1- (%)
22	CD8_absolute count	66	TFH/CD38-HLADR-ICOS+KI67-PD1- (%)	110	CD4/CD38-HLADR-ICOS+KI67+PD1+ (%)
23	CD4_absolute count	67	TFH/CD38-HLADR-ICOS-KI67+PD1+ (%)	111	CD4/CD38-HLADR-ICOS+KI67-PD1- (%)
24	CD4_CD8 Ratio	68	TFH/CD38-HLADR-ICOS-KI67+PD1- (%)	112	CD4/CD38-HLADR-ICOS-KI67+PD1+ (%)
25	CD4/CD38 (%)	69	TFH/CD38-HLADR-ICOS-KI67-PD1+ (%)	113	CD4/CD38-HLADR-ICOS-KI67+PD1- (%)
26	CD4/HLADR (%)	70	TFH/CD38-HLADR-ICOS-KI67-PD1- (%)	114	CD4/CD38-HLADR-ICOS-KI67-PD1+ (%)
27	CD4/ICOS (%)	71	CD4/TTM (%)	115	CD4/CD38-HLADR-ICOS-KI67-PD1- (%)
28	CD4/KI67 (%)	72	CD4/CD38-, HLADR+ (%)	116	CD8/CD38 (%)
29	CD4/PD1 (%)	73	CD4/CD38+, HLADR+ (%)	117	CD8/HLADR (%)
30	CD4/PD1 high (%)	74	CD4/CD38+, HLADR- (%)	118	CD8/ICOS (%)
31	CD4/PD1 low (%)	75	CD4/CD38-, HLADR- (%)	119	CD8/KI67 (%)
32	CD4/TCM (%)	76	CD4/T NAIVE (%)	120	CD8/PD1 (%)
33	CD4/TFH (%)	77	CD4/TEFF (%)	121	CD8/PD1 high (%)
34	TFH/CD38- (%)	78	CD4/TEM (%)	122	CD8/PD1 low (%)
35	TFH/HLADR- (%)	79	CD4/CD38- (%)	123	CD8/TCM (%)
36	TFH/ICOS- (%)	80	CD4/HLADR- (%)	124	CD8/TTM (%)
37	TFH/KI67- (%)	81	CD4/ICOS- (%)	125	CD8/CD38-, HLADR+ (%)
38	TFH/PD1- (%)	82	CD4/KI67- (%)	126	CD8/CD38+, HLADR+ (%)
39	TFH/CD38+HLADR+ICOS+KI67+PD1+ (%)	83	CD4/PD1- (%)	127	CD8/CD38+, HLADR- (%)
40	TFH/CD38+HLADR+ICOS+KI67+PD1- (%)	84	CD4/CD38+HLADR+ICOS+KI67+PD1+ (%)	128	CD8/CD38-, HLADR- (%)
41	TFH/CD38+HLADR+ICOS+KI67-PD1+ (%)	85	CD4/CD38+HLADR+ICOS+KI67+PD1- (%)	129	CD8/T NAIVE (%)
42	TFH/CD38+HLADR+ICOS+KI67-PD1- (%)	86	CD4/CD38+HLADR+ICOS+KI67-PD1+ (%)	130	CD8/TEFF (%)
43	TFH/CD38+HLADR+ICOS-KI67+PD1+ (%)	87	CD4/CD38+HLADR+ICOS+KI67-PD1- (%)	131	CD8/TEM (%)
44	TFH/CD38+HLADR+ICOS-KI67+PD1- (%)	88	CD4/CD38+HLADR+ICOS-KI67+PD1+ (%)		