

Supplementary Table S1. Immune phenotype characterization.		
Phenotype	Comment or Defining Markers	Parent Population
T cells	CD3+	Live Lymphs
T helper cells	CD4+	CD3+
Naïve-type CD4 cell	CD4+CD45RA+	CD4+
Memory CD4 cell	CD4+CD45RO+	CD4+
CD4+CD28-	senescent cell	CD4+
CD4+CD57+	senescent cell	CD4+
CD4+CD95+		CD4+
CD4+CD127+	long-lived memory CD4 cell	CD4+
CD4+CD137+		CD4+
CD4+CD27-		CD4+
CD4+PD1+	Immune checkpoint marker	CD4+
CD4+CD28-CD57+	senescent cell	CD4+
CD4+CD28-CD27-	senescent cell	CD4+
CD4 NAÏVE	CD4+CD45RA+CD27+CD28+CD57-	CD4+
CD4 ED (early differentiated)	CD4+CD45RA-CD27+CD28+CD57-	CD4+
CD4 ID (intermediate differentiated)	CD4+CD45RA-CD27+CD28-CD57+	CD4+
CD4 LD (late differentiated)	CD4+CD45RA+CD27-CD28-CD57+	CD4+
CD4+ TEMRA	CD4+CD45RA+CD28-CD57+	CD4+
CD4 Tn (True naïve)	CD4+CD45RO-CCR7+CD27+	CD4+
CD4 Tint (intermediate memory)	CD4+CD45RO-CCR7-CD27+	CD4+
CD4 Teff (effector)	CD4+CD45RO-CCR7-CD27-	CD4+
CD4 Tcm (central memory)	CD4+CD45RO+CCR7+CD27+	CD4+
CD4 Ttm (transitional memory)	CD4+CD45RO+CCR7-CD27+	CD4+
CD4 Tem (effector memory)	CD4+CD45RO+CCR7+CD27-	CD4+
Cytotoxic T cells	CD8+	CD3+
Naïve-type CD8 cells	CD8+CD45RA+	CD8+
Memory CD8 cell	CD8+CD45RO+	CD8+
CD8+CD28-		CD8+
CD8+CD57+		CD8+
CD8+CD95+		CD8+
CD8+CD127+		CD8+
CD8+CD137+		CD8+
CD8+CD27-		CD8+
CD8+PD1+	Cancer marker	CD8+
CD8+CD28-CD57+	senescent cell	CD8+
CD8+CD28-CD27-	senescent cell	CD8+
CD8 NAÏVE	CD8+CD45RA+CD27+CD28+CD57-	CD8+

CD8 ED	CD8+CD45RA-CD27+CD28+CD57-	CD8+
CD8 ID	CD8+CD45RA-CD27+CD28- CD57+	CD8+
CD8 LD	CD8+CD45RA+CD27-CD28-CD57+	CD8+
CD8+ TEMRA	CD8+CD45RA+CD28-CD57+	CD8+
CD8 Tn	CD8+CD45RO-CCR7+CD27+	CD8+
CD8 Tint	CD8+CD45RO-CCR7-CD27+	CD8+
CD8 Teff	CD8+CD45RO-CCR7-CD27-	CD8+
CD8 Tcm	CD8+CD45RO+CCR7+CD27+	CD8+
CD8 Ttm	CD8+CD45RO+CCR7-CD27+	CD8+
CD8 Tem	CD8+CD45RO+CCR7+CD27-	CD8+
T cells	CD3+	Live Lymphs
B cells	CD19+	Live Lymphs
gd T cells	gamma delta T cells	CD3+
NK cells	CD3-CD56+CD16+	Live Lymphs
CD38+ T cells	broad activation marker	CD3+
HLA-DR+ T cells	broad activation marker	CD3+
CD38+HLADR+ T cells	Activated T cells	CD3+
IgD B cells		B cells
IgM B cells		B cells
IgDIgM Bcells		B cells
CD43+ B cells		B cells
CD27+ B cells		B cells
CD43+CD27+ B1	B1 cells	B cells
CD43-CD27+ Bmem	memory B cells	B cells
IgD B1cell		B1 cells
IgM B1cell		B1 cells
IgD IgM B1cell		B1 cells
IgD Bmem		B mem Cells
IgM Bmem		B mem Cells
IgD IgM Bmem		B mem Cells
CD3_ICS	T cells	Live Lymphs
CD4_ICS	T helper cells	CD3+
CD8_ICS	Cytotoxic T cells	CD3+
TH1	CD4+IFNg+	CD4+
TH2	CD4+IL4+	CD4+
TH17	CD4+IL17+	CD4+
CD4+TNFa+		CD4+
GRANZYME B + CD4		CD4+
PERFORIN+ CD4		CD4+
TNFa+IFNg+ CD4		CD4+

IL17+IFNγ+ CD4		CD4+
IL17+IFNγ+ TH1		Th1
Tc1	CD8+IFN γ +	CD8+
Tc2	CD8+IL4+	CD8+
Tc17	CD8+IL17+	CD8+
CD8+TNFα+		CD8+
Granzyme B+ CD8		CD8+
PERFORIN+ CD8		CD8+
TNFα+IFNγ+ CD8		CD8+
IL17+IFNγ+ CD8		CD8+
IL17+IFNγ+ Tc1		Tc1
CD3_reg	T cells	Live Lymphs
CD4_reg	T helper cells	CD3+
CD8_reg	Cytotoxic T cells	CD3+
CD4+CD25+	Broad regulatory cell	CD4+
CD4+CD25+CD127-	CD4+ REGULATORY T CELL	CD4+
CD4+CD25+CD127-FoxP3+		CD4+
CD4+CD25+CD127-Tbet+		CD4+
CD4+CD25+CD127-FoxP3+Tbet+		CD4+
CD4+CD25+CD127-Rorgt+		CD4+
CD4+CD25+CD127-FoxP3+Rorgt+		CD4+
CD4+FoxP3+		CD4+
CD4+CD25+FoxP3+	FoxP3 CD4 TREGS	CD4+
CD4+Tbet+		CD4+
CD4+Rorgt+		CD4+
CD4+Tbet+Rorgt+		CD4+
CD8+CD25+		CD4+
CD8+CD25+CD127-		CD4+
CD8+CD25+CD127-FoxP3+		CD4+
CD8+CD25+CD127-Tbet+		CD4+
CD8+CD25+CD127-FoxP3+Tbet+		CD4+
CD8+CD25+CD127-Rorgt+		CD4+
CD8+CD25+CD127-FoxP3+Rorgt+		CD4+
CD8+FoxP3+		CD4+
CD8+CD25+FoxP3+		CD4+
CD8+Tbet+		CD4+
CD8+rORGT+		CD4+
CD8+Tbet+Rorgt+		CD4+

CD14 total		Gated monos
CLASSICAL MONOCYTES (CM)	CD14++CD16-	CD14
INTERMEDIATE MONOCYTES (IM)	CD14+CD16+	CD14
NONCLASSICAL MONOCYTES (NCM)	CD14dimCD16+	CD14
HLADR+ CM		CM
TREM2+ CM		CM
CD87+ CM		CM
CCR2+ CM		CM
Slan+ CM		CM
CD33+ CM		CM
CD163+ CM		CM
HLADR+ IM		IM
TREM2+ IM		IM
CD87+ IM		IM
CCR2+ IM		IM
Slan+ IM		IM
CD33+ IM		IM
CD163+ IM		IM
HLADR+ NCM		ncm
TREM2+ NCM		NCM
CD87+ NCM		NCM
CCR2+ NCM		NCM
Slan+ NCM		NCM
CD33+ NCM		NCM
CD163+ NCM		NCM

Supplemental Table S2. Association of sickle cell trait with immune cell phenotypes, adjusting for age, sex, and genetic ancestry

Phenotype	Not accounting for relatedness			Accounting for relatedness		
	Beta	SE	p-value	Beta	SE	p-value
cd8cd28cd57	-0.612	0.122	5.68E-07	-0.586	0.123	1.88E-06
cd8cd57	-0.591	0.121	1.29E-06	-0.556	0.123	5.78E-06
cd8temra	-0.575	0.122	2.91E-06	-0.546	0.124	1.00E-05
cd8cd28	-0.563	0.122	4.14E-06	-0.547	0.123	8.31E-06
cd8cd28cd27	-0.540	0.120	7.13E-06	-0.517	0.121	1.93E-05
cd8ld	-0.535	0.122	1.33E-05	-0.512	0.124	3.46E-05

granzymebcd8	-0.518	0.119	1.47E-05	-0.481	0.121	6.63E-05
cd8teff	-0.513	0.120	1.97E-05	-0.484	0.121	6.46E-05
cd4cd28cd57	-0.513	0.123	3.18E-05	-0.475	0.124	1.31E-04
cd4cd28cd27	-0.495	0.123	5.91E-05	-0.471	0.124	1.38E-04
cd4teff	-0.470	0.126	1.94E-04	-0.438	0.127	5.45E-04
cdld	-0.454	0.124	2.53E-04	-0.422	0.125	7.13E-04
cd8cd25cd127tbet	-0.437	0.122	3.60E-04	-0.394	0.124	1.47E-03
cdid	-0.415	0.119	5.32E-04	-0.412	0.121	6.43E-04
cd4cd57	-0.408	0.123	9.72E-04	-0.358	0.125	4.06E-03
cd4temra	-0.411	0.125	1.01E-03	-0.368	0.126	3.51E-03
perforincd8	-0.387	0.121	1.43E-03	-0.336	0.121	5.35E-03
trem2cm	0.444	0.141	1.67E-03	0.396	0.143	5.66E-03
cd4t	-0.393	0.125	1.69E-03	-0.391	0.126	1.89E-03
tc1	-0.359	0.117	2.10E-03	-0.338	0.117	4.01E-03
il17ifngth1	0.374	0.123	2.43E-03	0.353	0.124	4.54E-03
cd4cd28	-0.377	0.125	2.60E-03	-0.348	0.126	5.73E-03
cd8cd127	0.371	0.124	2.80E-03	0.344	0.125	6.12E-03
trem2im	0.410	0.140	3.46E-03	0.392	0.142	5.73E-03
cd4tem	-0.356	0.122	3.70E-03	-0.374	0.124	2.44E-03
th17	0.364	0.125	3.73E-03	0.351	0.127	5.70E-03
cd8cd27	-0.330	0.115	4.15E-03	-0.307	0.116	8.46E-03
cd8tn	0.310	0.112	5.68E-03	0.289	0.113	1.08E-02
tnfaifngcd8	-0.322	0.116	5.70E-03	-0.299	0.117	1.09E-02
trem2ncm	0.374	0.139	7.14E-03	0.388	0.142	6.15E-03
cd8id	-0.308	0.114	7.21E-03	-0.322	0.115	5.35E-03
cd4cd27	-0.326	0.124	8.56E-03	-0.310	0.125	1.30E-02
th1	-0.326	0.124	8.69E-03	-0.300	0.125	1.67E-02
cd43cd27bmem	-0.329	0.127	9.54E-03	-0.276	0.125	2.74E-02
granzymebcd4	-0.315	0.122	9.72E-03	-0.299	0.123	1.53E-02
cd4cd127	0.313	0.126	1.31E-02	0.297	0.127	1.94E-02
cd8naive	0.265	0.113	1.94E-02	0.255	0.115	2.64E-02
cd163im	0.314	0.141	2.64E-02	0.286	0.144	4.73E-02
il17ifngtc1	0.325	0.146	2.66E-02	0.311	0.147	3.44E-02
cd27bcells	-0.267	0.127	3.56E-02	-0.212	0.126	9.13E-02
cd8cd25cd127foxp3tbet	-0.217	0.105	3.86E-02	-0.192	0.107	7.23E-02
icscd3	-0.255	0.125	4.07E-02	-0.238	0.126	5.96E-02
cd8tbet	-0.255	0.125	4.19E-02	-0.226	0.127	7.49E-02
il17ifngcd4	0.251	0.124	4.22E-02	0.239	0.125	5.62E-02
cd87im	-0.124	0.063	4.80E-02	-0.128	0.063	4.32E-02
cd8tcm	0.228	0.124	6.68E-02	0.203	0.126	1.07E-01
th2	0.228	0.125	6.80E-02	0.247	0.126	5.00E-02

bcells	-0.226	0.125	7.09E-02	-0.244	0.126	5.19E-02
tc17	0.221	0.123	7.36E-02	0.225	0.124	7.02E-02
im	-0.251	0.141	7.60E-02	-0.221	0.142	1.21E-01
cd4n	0.213	0.121	7.84E-02	0.222	0.122	6.95E-02
cd4pd1	-0.220	0.127	8.20E-02	-0.253	0.128	4.76E-02
cd33	-0.244	0.141	8.38E-02	-0.190	0.141	1.77E-01
igdbcells	0.217	0.126	8.58E-02	0.162	0.128	2.06E-01
cd163ncm	0.239	0.140	8.87E-02	0.241	0.141	8.72E-02
cd3	-0.206	0.125	9.89E-02	-0.177	0.126	1.62E-01
cd4naive	0.197	0.121	1.04E-01	0.206	0.123	9.34E-02
slanim	0.225	0.139	1.07E-01	0.220	0.142	1.20E-01
cd8cd25cd127foxp3rorgt	-0.174	0.109	1.11E-01	-0.203	0.111	6.75E-02
cd8cd25cd127foxp3	-0.176	0.111	1.13E-01	-0.194	0.112	8.43E-02
slancm	0.222	0.141	1.16E-01	0.206	0.144	1.51E-01
tnfaifngcd4	-0.195	0.124	1.16E-01	-0.165	0.126	1.89E-01
cd43bcells	0.196	0.125	1.18E-01	0.178	0.126	1.59E-01
cd8cd25cd127	-0.194	0.126	1.23E-01	-0.195	0.127	1.26E-01
tregscd8	-0.195	0.127	1.25E-01	-0.211	0.129	1.02E-01
cd8cd137	-0.192	0.127	1.30E-01	-0.206	0.124	9.73E-02
ccr2ncm	0.204	0.138	1.40E-01	0.115	0.141	4.15E-01
tcells	-0.180	0.125	1.50E-01	-0.126	0.126	3.18E-01
cd8tnfa	-0.162	0.112	1.50E-01	-0.152	0.113	1.79E-01
icscd8	-0.179	0.125	1.53E-01	-0.194	0.127	1.26E-01
cd8ed	0.179	0.126	1.54E-01	0.153	0.127	2.27E-01
ccr2cm	-0.193	0.140	1.67E-01	-0.208	0.143	1.44E-01
cd33cm	-0.191	0.142	1.78E-01	-0.180	0.143	2.09E-01
cd31	-0.167	0.124	1.80E-01	-0.141	0.126	2.63E-01
cd8tem	-0.163	0.122	1.81E-01	-0.170	0.123	1.67E-01
cd8tbetrorgt	-0.164	0.124	1.87E-01	-0.119	0.126	3.43E-01
gdtcells	-0.163	0.125	1.90E-01	-0.137	0.126	2.76E-01
cd87ncm	0.167	0.128	1.93E-01	0.090	0.130	4.89E-01
cd33ncm	-0.176	0.141	2.10E-01	-0.153	0.142	2.83E-01
tregscd3	-0.159	0.127	2.13E-01	-0.116	0.129	3.69E-01
perforincd4	-0.153	0.124	2.18E-01	-0.117	0.125	3.49E-01
icscd4	0.149	0.124	2.31E-01	0.153	0.125	2.23E-01
cm	0.167	0.141	2.38E-01	0.120	0.144	4.02E-01
cd4cd25cd127	0.146	0.127	2.51E-01	0.091	0.129	4.78E-01
hladrncm	0.144	0.125	2.51E-01	0.084	0.128	5.13E-01
cd8cd25cd127rorgt	-0.140	0.125	2.64E-01	-0.145	0.127	2.54E-01
cd4tbet	-0.138	0.126	2.74E-01	-0.115	0.128	3.69E-01
cd4cd137	-0.139	0.127	2.75E-01	-0.151	0.127	2.37E-01

cd4ra	0.132	0.121	2.78E-01	0.157	0.122	1.97E-01
tc2	0.129	0.125	3.05E-01	0.150	0.126	2.37E-01
cd163cm	0.141	0.138	3.07E-01	0.107	0.139	4.44E-01
cd4cd25cd127rorgt	0.126	0.126	3.18E-01	0.084	0.127	5.12E-01
igdbmem	0.122	0.127	3.34E-01	0.069	0.128	5.90E-01
cd8	-0.121	0.126	3.36E-01	-0.119	0.127	3.48E-01
nkcells	0.116	0.121	3.41E-01	0.117	0.123	3.42E-01
cd4ro	-0.116	0.122	3.42E-01	-0.140	0.123	2.54E-01
cd4tnfa	-0.112	0.122	3.58E-01	-0.123	0.124	3.20E-01
cd87cm	-0.118	0.139	3.96E-01	-0.110	0.141	4.34E-01
cd4cd25foxp3	-0.105	0.125	4.01E-01	-0.116	0.126	3.57E-01
cd8t	-0.104	0.126	4.09E-01	-0.084	0.127	5.09E-01
il17ifngcd8	0.118	0.146	4.18E-01	0.109	0.147	4.56E-01
cd4ttm	-0.100	0.126	4.26E-01	-0.152	0.127	2.34E-01
cd8cd95	0.090	0.119	4.50E-01	0.086	0.121	4.76E-01
cd4tbetrorgt	-0.083	0.126	5.06E-01	-0.056	0.127	6.62E-01
igdb1	0.085	0.128	5.07E-01	0.074	0.129	5.66E-01
slanncm	0.088	0.139	5.29E-01	0.099	0.140	4.80E-01
cd14total	0.086	0.141	5.41E-01	0.060	0.143	6.75E-01
igdigmbcells	0.075	0.126	5.48E-01	0.029	0.126	8.20E-01
cd38tcells	-0.071	0.125	5.69E-01	0.015	0.126	9.08E-01
cd4rorgt	0.071	0.126	5.74E-01	0.062	0.129	6.32E-01
cd8foxp3	-0.066	0.121	5.83E-01	-0.064	0.123	6.03E-01
hladrcm	0.074	0.140	5.98E-01	0.105	0.143	4.65E-01
cd8cd25foxp3	0.063	0.125	6.12E-01	0.023	0.126	8.57E-01
cd4cd25	0.064	0.128	6.18E-01	0.038	0.130	7.68E-01
cd4cd25cd127foxp3tbet	-0.052	0.111	6.40E-01	-0.057	0.113	6.13E-01
cd4cd25cd127tbet	-0.059	0.126	6.41E-01	-0.059	0.128	6.44E-01
cd4	0.058	0.125	6.43E-01	0.057	0.126	6.50E-01
cd43cd27b1	0.053	0.125	6.71E-01	0.061	0.126	6.27E-01
cd8pd1	-0.044	0.127	7.32E-01	-0.086	0.128	4.98E-01
igmbcells	0.041	0.126	7.48E-01	-0.007	0.127	9.57E-01
ccr2im	-0.037	0.128	7.74E-01	-0.078	0.130	5.52E-01
cd8rorgt	0.035	0.126	7.80E-01	0.018	0.129	8.88E-01
cd8ro	-0.034	0.122	7.82E-01	-0.055	0.123	6.57E-01
igmb1	0.034	0.128	7.92E-01	-0.001	0.130	9.93E-01
tregscd4	0.033	0.127	7.95E-01	0.026	0.129	8.42E-01
igdigmbmem	0.031	0.126	8.08E-01	-0.022	0.127	8.62E-01
cd8cd25	0.029	0.127	8.21E-01	0.007	0.129	9.59E-01
cd8ra	0.027	0.122	8.25E-01	0.039	0.123	7.49E-01
igdigmb1	0.026	0.126	8.35E-01	0.003	0.127	9.80E-01

cd38hladrtcells	0.025	0.121	8.36E-01	0.067	0.119	5.73E-01
igmbmem	0.019	0.127	8.78E-01	-0.028	0.127	8.27E-01
cd4cd95	0.017	0.123	8.89E-01	-0.005	0.125	9.65E-01
cd4cd25cd127foxp3	0.017	0.122	8.92E-01	0.001	0.123	9.94E-01
hladrtcells	0.016	0.120	8.96E-01	0.002	0.118	9.86E-01
hladrim	0.014	0.120	9.04E-01	0.019	0.122	8.74E-01
cd4foxp3	-0.014	0.127	9.14E-01	-0.033	0.129	8.01E-01
cded	-0.008	0.124	9.51E-01	-0.040	0.126	7.51E-01
cd8ttm	0.007	0.126	9.53E-01	-0.012	0.127	9.23E-01
cd4tcm	-0.007	0.123	9.57E-01	-0.018	0.125	8.84E-01
ncm	0.007	0.141	9.60E-01	0.011	0.142	9.38E-01
cd4cd25cd127foxp3rorgt	-0.003	0.120	9.81E-01	-0.049	0.122	6.88E-01