Supplemental Table 3: CD1 crystal structure summary, including calculated antigen binding pocket volumes and bound lipid tail lengths, related to Figure 6

PDB	Antigen	Structure	Volume (Å^3)	Antigen (C)	Spacer/Scaffold (C)	Total (C)
	CD1a					
1ONQ-A	Sulfatide	CD1	1780	34	0	34
1ONQ-B	Sulfatide	CD1	1640	34	0	34
1XZ0	Lipopeptide	CD1	1870	16	0	16
4X6C	Lysophosphatidylcholine	CD1-TCR	1380	18	0	18
4X6D	Oleic acid (endogenous)	CD1-TCR	1380	16	0	16
4X6E	Lysophosphatidylcholine	CD1	1610	18	0	18
4X6F	Sphingomyelin 42:2	CD1	1580	42	0	42
5J1A	Urushiol	CD1	1920	15	0	15
6NUX	Farnesol	CD1	1750	15	0	15
7KOZ	Sphingomyelin 36:2	CD1	1630	36	0	36
7KP0	Sphingomyelin 42:1	CD1	1680	42	0	42
7KP1	Sphingomyelin 42:2	CD1	1950	42	0	42
7RYO	Dideoxymycobactin	CD1-TCR	1960	20	0	20
7RYN	Sulfatide	CD1-TCR	1690	40	0	40
7RYM	Empty	CD1-TCR	1750	-	-	-
7SH4	Phosphatidylglycerol	CD1	1550	36	0	36
CD1a Average			**1690 ± 180**	**16.7/38.3**	**-**	**16.7/38.3**
	CD1b					
1GZP	Ganglioside GM2	CD1	2350	36	34	60
1GZQ	Phosphatidylinositol	CD1	2310	33	34	67
1UQS	C54 Glucose Monomycolate	CD1	2320	60*	0*	60
2H26	Phosphatidylcholine (endogenous)	CD1	2270	34	41	75
3T8X	Sulfoglycolipid	CD1	2020	42	40	82
5L2J	C32 Glucose Monomycolate	CD1	2070	36	25	61
5L2K	C32 Glucose Monomycolate	CD1-TCR	2120	36	25	61
5WKE	Phosphatidylserine	CD1	2220	34	34	68
5WKG	Phosphatidic Acid	CD1	2190	34	35	68
5WL1	Phosphatidylglycerol	CD1	2190	32	34	65
5WKI	Phosphatidylglycerol	CD1-TCR	2190	32	22	54
6CUG	Phosphatidylcholine	CD1-TCR	2250	34	35	69
6D64	Phosphatidylcholine POPC	CD1	2380	34	31	65
8DV3	Phosphatidylinositol C34:1	CD1	2361	34	31	65
8DV4	Phosphatidylinositol C34:1	CD1-TCR	2348	34	36	70
8GLE	Lysosulfatide	CD1	2220	18*	32	50*
8GLF	Sphingomyelin	CD1	2190	34	31	65
8GLG	Phosphatidylethanolamine	CD1	2360	34	25	59
8GLH	Phosphatidylcholine (endogenous)	CD1	2120	40	16*	56
8GLI	C85 Glucose Monomycolate	CD1	2010	71*	-	71
CD1b Average			**2220 ± 110**	**34.9**	**32.1**	**65.3**
	CD1c					
3OV6	Mannosyl phosphomycoketide	CD1	2340	32	12	44
4ONO	Phosphomycoketide	CD1	2470	32	0*	32
5C9J	Spacer Lipids	CD1	1920	18	24	42
6C09	Monoacylglycerol	CD1-TCR	2030	16	20	36
6C15	Phosphatidylcholine (endogenous)	CD1	1900	32	12	44
7MX4	Mannosyl phosphomycoketides analog 1	CD1	1980	32	28	60
7MXF	Mannosyl phosphomycoketides analog 2	CD1	1840	32	28	60
7MXH	Mannosyl phosphomycoketides analog 3	CD1	2010	32	28	60
CD1c Average			**2060 ± 220**	**28.3**	**21.7**	**47.3**
	CD1d					
1ZHN	Phosphatidylcholine	CD1	1700	37	0	37
1ZT4	α-Galactosyl ceramide	CD1	1750	41	0	41
1ZT4	Empty	CD1	1830	-	-	-
2PO6	α-Galactosyl ceramide	CD1-TCR	1590	41	0	41
3AU1	Ganglioside GD3	CD1	2050	35	0	35
3HUJ	α-Galactosyl ceramide	CD1-TCR	1550	41	0	41
3QI9	Phosphatidylinositol	CD1-TCR	1650	33	0	33
3SCM	iGB3	CD1-TCR	1730	40	0	40
3SDD	β-lactosyl ceramide	CD1-TCR	1810	38	0	38
3SDX	β-galactosyl ceramide	CD1-TCR	1940	40	0	40
3TZV	Lysophosphatidylcholine	CD1-TCR	2000	18	18	36
3U0P	Lysophosphatidylcholine	CD1	1920	18	0/17	35

3VWJ	α-Galactosyl ceramide C20:2	CD1-TCR	1870	35	0	35
3VWK	4-deoxy α-Galactosyl ceramide	CD1-TCR	1750	42	0	42
4EN3	α-Galactosyl ceramide	CD1-TCR	1580	41	0	41
4IRS	α-Galactosyl ceramide	CD1-TCR	1680	41	0	41
4LHU	PBS-44 α-Galactosyl ceramide	CD1-TCR	1510	39	0	39
4MQ7	Sulfatide	CD1	1740	40	0	40
4WO4	PBS-44 α-Galactosyl ceramide	CD1-TCR	1780	39	0	39
4WW2	PBS-44 α-Galactosyl ceramide	CD1-TCR	1560	39	0	39
4WWK	PBS-44 α-Galactosyl ceramide	CD1-TCR	1730	39	0	39
6CYW	Sphingomyelin	CD1	1890	42	0	42
CD1d Average			**1760 ± 150**	**37.1**	**17.5**	**38.8**

* Outlier: Excluded from calculations

Supplemental Table 4. Data collection and refinement statistics, related to Figure 6 and 7

Highest resolution shell is shown in parenthesis

	CD1b-endogenous PC	CD1b-SM	CD1b-PE	CD1b-Lysosulfatide	CD1b-C85-GMM
Data Collection statistics					
Space group	P 21 21 21	P 21 21 21	P 21 21 21	P 21 21 21	P 21 21 21
Resolution Range (Å)	46.05 – 1.83 (1.87 – 1.83)	48.70 – 2.0 (2.05 – 2.0)	46.49 – 1.60 (1.63 – 1.60)	49.16 – 1.85 (1.92 – 1.85)	46.22 – 2.10 (2.16 – 2.10)
Cell dimensions (Å, °)	a = 57.45, b = 77.05, c = 91.44, α/β/γ = 90	a = 57.57, b = 77.98, c = 91.32, α/β/γ = 90	a = 58.10, b = 80.50, c = 93.00, α/β/γ = 90	a = 57.90, b = 79.50, c = 93.20, α/β/γ = 90	a = 57.23, b = 76.60, c = 92.45, α/β/γ = 90
Total No. of Reflections	2666560 (15290)	308374 (19017)	852936 (41118)	75763 (7340)	325323 (26636)
No. of Unique Reflections	36495 (2143)	27135 (1897)	57434 (2741)	37383 (3670)	24370 (2400)
Multiplicity	7.3 (7.1)	11.4 (10.0)	14.9 (15.0)	2.0 (2.0)	13.3 (13.6)
Completeness (%)	99.7 (95.7)	95.7 (92.2)	98.8 (97.3)	99.6 (98.5)	99.6 (100.00)
CC (1/2)	0.99 (0.78)	0.99 (0.720)	0.99 (0.73)	0.99 (0.84)	1.00 (0.62)
R_{pim} (%) [a]	3.7 (46.9)	7.7 (48.9)	4.1 (54.1)	3.0 (24.5)	7.5 (75.3)
Mean *I*/ ∫(*I*) [b]	19.5 (2.3)	9.3 (2.1)	17.2 (2.2)	8.51 (2.65)	10.0 (2.40)
Refinement Statistics					
R_{factor}/R_{free} [c]	17.0/22.4	17.6/23.0	18.4/20.9	18.8/22.9	20.6/26.7
Non-hydrogen atoms	3660	3490	3852	3544	3342
Macromolecule atoms	3020	3058	3074	3048	2943
Ligand atoms	238	198	236	208	186
Solvent atoms	402	234	542	288	213
Total No. Protein Residues	393	380	380	397	379
R.M.S.D. from Ideality					
Bond Lengths (Å)	0.007	0.008	0.009	0.007	0.087
Bond Angles (°)	1.00	0.99	1.01	0.92	0.94
Ramachandran Plot					
Favoured Region (%)	98.67	98.67	99.47	98.14	97.33
Allowed Region (%)	1.33	1.33	0.53	1.86	2.67
Outliers (%)	0.00	0.00	0.00	0.00	0.00
B-factors (Å^2)					
Average B-factors	30.48	31.39	25.89	35.98	32.47
Average Macromolecule	27.52	30.05	23.24	34.78	31.52
Average Ligand	51.32	47.85	35.54	47.79	40.41
Average Solvent	40.38	35.00	36.72	40.16	38.59
PDB Code Accession	8GLH	8GLF	8GLG	8GLE	8GLI

[a] R_{pim} = ∑hkl [1/(N - 1)]1/2 ∑i | Ihkl, i - |/∑hkl ,

[b] σ(*I*) is the estimated standard deviation of the integrated intensity (*I*).

[c] R_{factor} = ∑hkl||Fo | - |Fc ||/∑hkl|Fo | for all data except 5%, which were used for R_{free} calculation.

Supplemental Table 5: Contacts between CD1b and lipid antigen, related to Figure 7

CD1b	PE C34:1	Bond Type	Pocket
Phe10	C43	VDW	A′
His38	C47	VDW	A′
Val63	C49	VDW	A′
Leu66	C46	VDW	A′
Glu68	**N29**	VDW	-
Ile69	**C20, C21, O22, O25**, **C27**	VDW	-
Val72	C18, C19, **C28**	VDW	-
Tyr73	C09, **O18, C19, C20**, C33	VDW	A′/T′
Gly76	C13, C14	VDW	A′
Phe77	C09, C12, C14	VDW	C′
Glu80	C13	VDW	C′
Ala100	C38, C40	VDW	A′
Val126	C02, C03, C04	VDW	C′
Ala129	C01	VDW	C′
Cys131	C03	VDW	C′
Phe144	C08, C10	VDW	C′
Ile148	C10, C11	VDW	C′
Ile154	C11, C13, C15, C16, **O17**	VDW	C′
Met155	C01	VDW	C′
Thr157	**C31**, **O32**	VDW	-
Ile161	C38	VDW	A′
Tyr169	C46, C47, C48	VDW	A′
CD1b	**SM C34:1**	**Bond Type**	**Pocket**
Phe10	C02	VDW	A′
Leu66	C01	VDW	A′
Val72	C37	VDW	C′
Tyr73	C13, C44	VDW	A′/C′
Gly76	C40	VDW	C′
Phe77	C40, C42	VDW	C′
Ala100	C06, C07, C08	VDW	A′
Ile148	C43, C45	VDW	C′
Tyr151	C35	VDW	C′
Gln152-Nϵ2	**O24**	HB	-
Gln152	**O24, O24, P22**	VDW	-
Gly153	**O24**	VDW	-
Ile154	C41, C46, **O17**	VDW	C′
Thr157	C14, C20	VDW	A′
Val158	C12	VDW	A′
Cys166	C04	VDW	A′
CD1b	**Lysosulfatide**	**Bond Type**	**Pocket**
Phe10	C11, C13	VDW	A′
His38	C15, C16	VDW	A′
Val63	C17	VDW	A′
Leu66	C14	VDW	A′

Ile69	**O4**	VDW	-
Val72	**C46**	VDW	-
Tyr73	C2, **C47, O1**	VDW	A′
Ala100	C5, C7	VDW	A′
Leu114	C5	VDW	A′
Ile154	**N, O, C43, C44, C47, C48, O6**	VDW	-
Thr157	**O3**	VDW	-
Thr157-O©1	**O3**	HB	-
Val158	**N, C1**	VDW	-
Leu161	C4, C6, C8	VDW	A′
Cys166	C11	VDW	A′
Tyr169	C14	VDW	A′
CD1b	**Endogenous C40:5**	**Bond Type**	**Pocket**
Phe10	C30	VDW	A′
Val12	C39	VDW	T′
Ile13	C4128	VDW	T′
Gln14	C43	VDW	T′
Gly28	C40	VDW	T′
Ser29	C38, C40	VDW	T′
His38	C32, C37	VDW	A′/T′
Ala47	C35	VDW	T′
Leu66	C31	VDW	A′
Glu68	**C09**	VDW	-
Ile69	**C11, O62**	VDW	-
Phe70	C20, C36, C42	VDW	A′/T′
Val72	**C04, C09, C45, O10, O46**	VDW	-
Tyr73	C12, C16, C48, C53, C54, O46	VDW	A′/C′/T′
Gly76	C49	VDW	C′
Phe77	C51	VDW	C′
Glu80	C49	VDW	C′
Ala100	C22, C24	VDW	A′
Val126	C58	VDW	C′
Ile148	C52, C53	VDW	C′
Ile154	C50	VDW	C′
Met155	C58	VDW	C′
Thr157	C14, C15, **O44, O62**	VDW	A′
Val158	C17	VDW	A′
Leu161	C22, C23	VDW	A′
Leu162	C22	VDW	A′
Cys166	C25, C27	VDW	A′
Tyr169	C30	VDW	A′

VDW: Van der Waals interaction (cut-off of 4.0 Å), HB: Hydrogen Bond (Cut-off of 3.5 Å), SB: Salt Bridge (cut-off of 3.5 Å). Atoms in bold represent lipid headgroup.