Table S1. Summary of Affinity Measurements by Isothermal Titration Calorimetry and Surface Plasmon Resonance, Related to Figures 1 and 2

By ITC		K_D (M)	*N*	Δ*H* (kcal/mol)
SYG-1 D1	SYG-2 D1-D4	$6.02\times10^{-7} \pm 1.62\times10^{-7}$	0.80 ± 0.04	-12.76 ± 1.47
SYG-1 ECD	SYG-2 ECD	$6.69\times10^{-7} \pm 3.78\times10^{-7}$	0.82 ± 0.14	-7.90 ± 0.33

By SPR		K_D (M)
SYG-1 ECD	SYG-2 D1-D4	7.5×10^{-7}
SYG-1 D1	SYG-2 ECD	$5.9\times10^{-7} \pm 0.4\times10^{-7}$
SYG-1 ECD	SYG-2 ECD	$7.6\times10^{-7} \pm 3.1\times10^{-7}$
Rst D1D2	SNS ECD	2.8×10^{-6}
Rst D1	SNS ECD	2.2×10^{-6}
Rst ECD	SNS ECD	3.5×10^{-6}
Rst D1D2	Hbs ECD	1.2×10^{-6}
Rst D1	Hbs ECD	1.1×10^{-6}
Rst ECD	Hbs ECD	1.3×10^{-6}
Duf ECD	SNS ECD	2.5×10^{-6}
Duf ECD	Hbs ECD	3.4×10^{-6}
Rst D1D2	Rst ECD	$\sim7\times10^{-4}$

Reported errors are standard deviations calculated from two to four replicates.

Table S2. Data and Refinement Statistics for X-Ray Crystallography, Related to Figures 1 and 2

	Refolded Se-Met SYG-1 D1D2	Glycosylated SYG-1 D1D2	Glycosylated SYG-1 D1	Glycosylated SYG-1 D1, 2nd form	Rst D1D2	mmNeph1 D1D2	Duf D1	SYG-1/SYG-2 D1D2/D1-D4 N391C	SYG-2 D4	SYG-2 D3D4
Data Collection										
Space Group	$C2$	$P3_221$	$P4_22_12$	$I4_122$	$P2_1$	$C222_1$	$P2_1$	$C2$	$C2$	$P4_32_12$
Cell Dimensions										
a, b, c (Å)	86.54, 32.07, 102.23	92.65, 92.65, 129.01	84.81, 84.81, 74.13	129.18, 129.18, 141.49	59.94, 77.94, 121.10	118.96, 120.01, 119.91	74.33, 84.36, 82.63	286.79, 116.14, 98.03	61.81, 54.13, 63.62	121.24, 121.24, 178.16
α, β, γ (°)	90, 113.84, 90	90, 90, 120	90, 90, 90	90, 90, 90	90, 95.44, 90	90, 90, 90	90, 115.27, 90	90, 107.62, 90	90, 104.61, 90	90, 90, 90
Resolution (Å)	50-2.30 (2.38-2.30)	50-2.50 (2.59-2.50)	50-1.70 (1.76-1.70)	50-2.10 (2.18-2.10)	50-1.90 (1.93-1.90)	50-3.95 (4.09-3.95)	50-2.30 (2.34-2.30)	50-3.30 (3.42-3.30)	50-1.80 (1.83-1.80)	50-3.0 (3.08-3.0)**
R_{sym} (%)	5.3 (23.1)*	5.7 (80.7)	6.4 (68.2)	7.1 (49.5)	6.6 (32.8)	9.2 (88.5)	10.6 (60.8)	9.8 (57.5)	5.1 (51.3)	15.8 (>100)**
$\langle I \rangle / \langle \sigma(I) \rangle$	19.3 (2.3)*	25.1 (2.4)	32.8 (2.3)	25.6 (2.6)	16.2 (2.3)	18.9 (1.8)	12.7 (2.2)	13.4 (1.7)	24.3 (2.6)	13.15 (0.8)**
Completeness (%)	90.7 (41.3)*	99.6 (100.0)	99.5 (95.4)	98.0 (85.1)	88.0 (50.2)	99.7 (98.1)	100 (100)	95.9 (77.7)	100 (100)	99.9 (100.0)
Redundancy	3.5 (1.5)*	7.0 (6.6)	12.7 (7.2)	8.3 (3.8)	3.4 (2.1)	7.0 (6.4)	3.8 (3.7)	3.7 (3.1)	3.8 (3.7)	18.4 (18.6)
Refinement										
Resolution (Å)	50-2.30 (2.40-2.30)	50-2.50 (2.61-2.50)	50-1.70 (1.75-1.70)	50-2.10 (2.16-2.10)	50-1.90 (1.93-1.90)	50-3.94 (4.50-3.94)	50-2.30 (2.35-2.30)	50-3.29 (3.36-3.29)	50-1.80 (1.90-1.80)	50-3.0 (3.11-3.0)
Reflections	11098	22690	30345	34491	77176	7856	41179	44580	18854	27288
R_{cryst} (%)	20.08 (21.66)	19.63 (27.55)	17.48 (24.40)	20.17 (25.41)	17.57 (22.26)	29.13 (31.16)	19.17 (25.89)	25.87 (37.53)	19.13 (23.82)	24.18 (32.21)
R_{free} (%)	24.54 (24.54)	25.25 (35.71)	20.58 (28.65)	22.76 (27.34)	21.10 (29.06)	32.79 (32.65)	24.33 (33.99)	30.61 (41.60)	21.06 (23.80)	28.34 (36.54)
Number of atoms										
Protein	1800	3550	2081	3394	6565	2940	6548	14404	1588	5948
Ligand	0	125	74	62	52	67	116	401	42	84
Water	34	39	273	347	787	0	328	0	143	0
Average B-factors (Å^2)										
All	72.9	81.3	28.2	49.3	46.8	184.2	39.9	95.5	33.0	148.0
Protein	73.4	80.2	25.5	49.1	46.9	183.5	39.6	94.7	31.9	148.1
Solvent	48.5	65.3	35.3	46.1	44.9	N/A	35.7	N/A	38.6	N/A
R.m.s. deviations from ideality										
Bond Lengths (Å)	0.005	0.007	0.011	0.005	0.009	0.004	0.008	0.004	0.005	0.006
Bond Angles (°)	0.808	1.076	1.327	0.942	1.122	0.805	0.716	0.994	1.044	1.055

* These statistics are for Friedel's pairs not merged, for data collected only at the Se peak wavelength.

** The $CC_{1/2}$ value for the highest resolution bin is 32.4%.