Supplementary Information

Binding Structures and Energies of Human Neonatal Fc Receptor with Human Fc and Its Mutants by Molecular Modeling and Dynamics Simulations

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Running title: Human FcRn-Fc Binding Structure

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Table S1. Calculated Fc mutation-caused shifts ($\Delta\Delta E_{calc}$, kcal/mol) of human FcRn-Fc binding energy based on the implicit solvent model,[1, 2] in comparison with the corresponding experimental data ($\Delta\Delta G_{expt}$, kcal/mol).

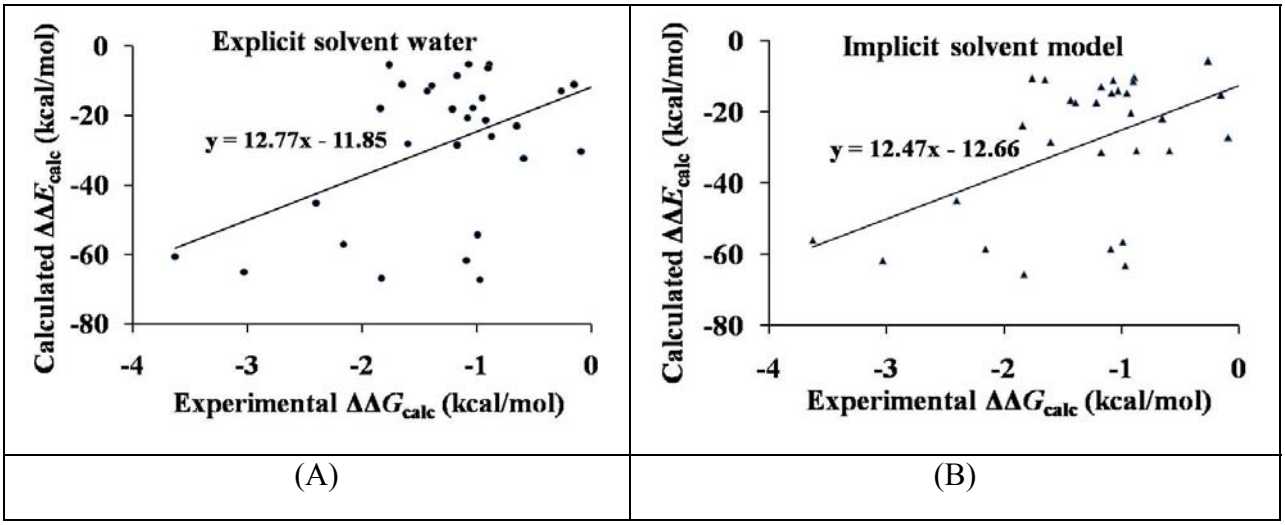
Fc and its mutants	$\Delta\Delta E_{calc}$[a]	$\Delta\Delta G_{expt}$[b]	K_d (nM)[c]	Ref.
Human IgG1-Fc	0.00	0.00	2527±117	3
I39A	+36.25		N.D.[d]	3
M38Y	-20.40	-0.92	532±37	3
M38W	-14.72	-1.08	408±24	3
M38F/T42D	-30.92	-0.59	933±170	3
M38Y/T42Q	-10.33	-0.89	560±102	3
N220F/Y222H	-63.13	-0.97	493±7	3
M38Y/S40T/T42E	-16.82	-1.43	225±10	3
V94T/L95P/Q97S	-15.27	-0.15	1964±84	3
G171D/Q172P/N175S	-27.23	-0.09	2164±331	3
H219R/N220Y/Y222H	-56.50	-0.99	472±61	3
H219K/N220F/Y222H	-58.41	-1.09	399±47	3
G171R/Q172T/P173R/N175P	-5.71	-0.26	1620±61	3
M38Y/S40T/T42E/H219K/N220F/Y222H	-44.94	-2.40	44±3	3
M38Y/S40T/T42E/G171R/Q172T/P173R/N175P	-17.38	-1.39	243±48	3
Human Fc	0.00	0.00	1700±20	4
N220A	-21.90	-0.65	570±30	4
N220H	-11.39	-0.90	370±30	4
N220Y	-65.57	-1.83	78±12	4
N220W	-58.55	-2.16	44±5	4
A164V/N220A	-30.86	-0.87	390±40	4
N220A/Y222I	-14.74	-0.95	340±80	4
M38Y/N220A	-17.51	-1.21	220±20	4
M214L/N220A	-14.17	-1.03	300±40	4
V94P/N220Y	-61.88	-3.03	10.2±1.8	4
T93Q/N220A	-12.92	-1.17	235±20	4
T36Q/M214L	-31.34	-1.17	234±22	4
V94P/N220A	-23.93	-1.84	76±10	4
T93Q/E166A/N220A	-11.20	-1.07	280±10	4
M38Y/V94P/N220Y	-56.02	-3.63	3.7±1.0	4
Human Fc	0.00	0.00	37±5	5
D162V/N220H	-28.56	-1.60	2.5±1.4	5
P43I/Q97I	-10.58	-1.76	1.9±0.4	5
P43I/N220H	-10.87	-1.65	2.3±0.2	5

[a]Directly calculated binding free energy shift from human FcRn binding with wild-type human Fc to human FcRn binding with the mutant of human Fc.

[b]The binding free energy shift (from human FcRn binding with wild-type human Fc to human FcRn binding with the mutant of human Fc) derived from the experimentally measured dissociation constant (K_d) change as according to equation $\Delta\Delta G=RT\ln K_{d(mutant)}/K_{d(wild\text{-}type)}$.

[c]The experimental dissociation constant for the FcRn-Fc binding reported in literature cited.

[d]No detectable binding.



(A) (B)

Figure S1. Plots of the calculated Fc mutation-caused shifts ($\Delta\Delta E_{calc}$, kcal/mol) of human FcRn-Fc binding energy (Table 2 in the text) *vs* the shifts of binding free energy ($\Delta\Delta G_{expt}$, kcal/mol) derived from experimentally measured K_d values based on the relationship of $\Delta\Delta G=RT\ln K_{d(mutant)}/K_{d(wild\text{-}type)}$. (A) The calculated results based on the explicit solvent water; and (B) the calculated results based on implicit solvent model, *i.e.* generalized born (GB)[1,2] model.

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