Supporting Information

Insight into Antagonist Binding and Induced Conformational Dynamics of Class B GPCR Corticotropin-Releasing Factor Receptor 1

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Contents:

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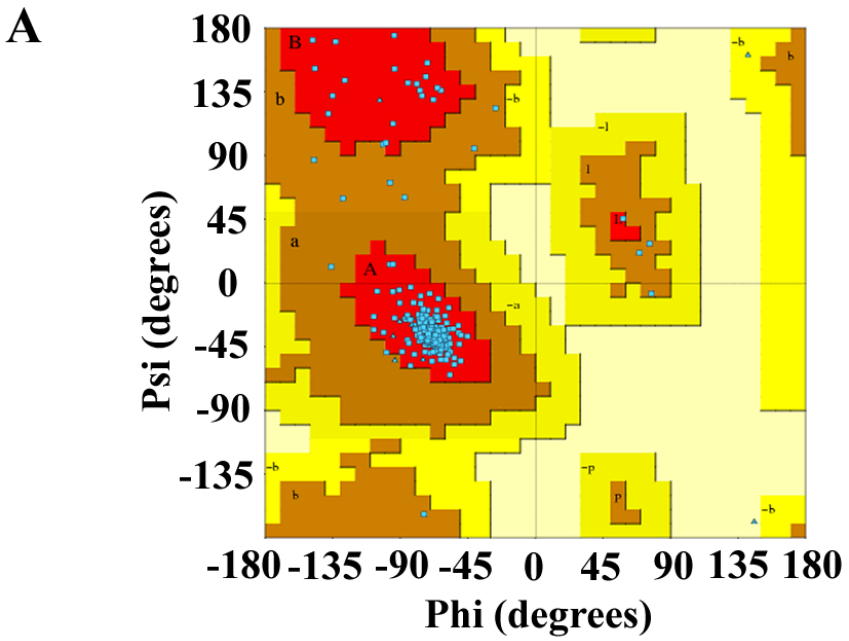
(44) D.A. Case, T.A. Darden, T.E. Cheatham, III, C.L. Simmerling, J. Wang, R.E. Duke, R. Luo, R.C. Walker, W. Zhang, K.M. Merz, B. Roberts, S. Hayik, A. Roitberg, G. Seabra, J. Swails, A.W. Götz, I. Kolossváry, K.F. Wong, F. Paesani, J. Vanicek, R.M. Wolf, J. Liu, X. Wu, S.R. Brozell, T. Steinbrecher, H. Gohlke, Q. Cai, X. Ye, J. Wang, M.-J. Hsieh, G. Cui, D.R. Roe, D.H. Mathews, M.G. Seetin, R. Salomon-Ferrer, C. Sagui, V. Babin, T. Luchko, S. Gusarov, A. Kovalenko, and P.A. Kollman (2012), AMBER 12, University of California, San Francisco.



		No. of residues	Pencentage
Most favoured regions	[A,B,L]	218	95.2%
Additional allowed regions	[a,b,l,p]	11	4.8%
Generously allowed regions	[~a,~b,~l,~p]	0	0.0%
Disallowed regions	[XX]	0	0.0%

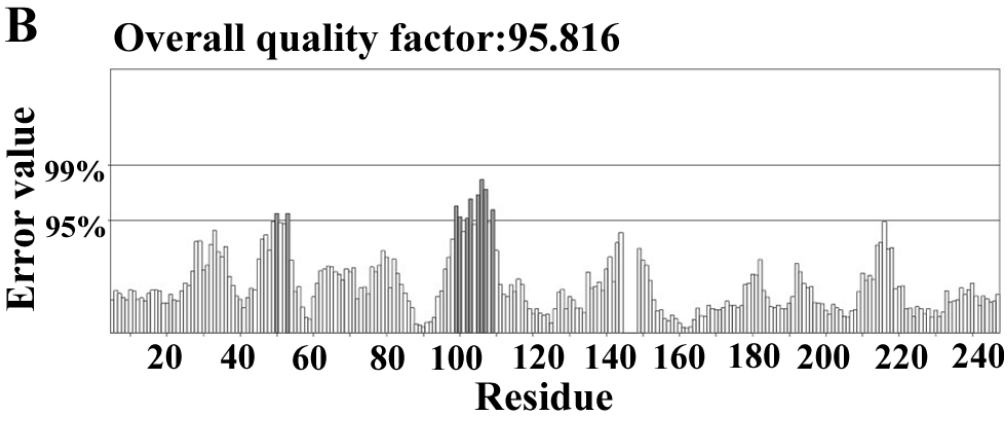


Fig. S1. Quality of the constructed CP-376395-CRF$_1$R model checked by PROCHECK and ERRAT. (A) The Ramachandran plot made by PROCHECK, the most favoured regions (A, B, L) was in red, the additional allowed regions (a, b, l, p) was in brown, the generously allowed regions (~a, ~b, ~c, ~p) was in yellow and the disallowed regions (XX) was in light yellow. (B) The overall quality factor checked by ERRAT.

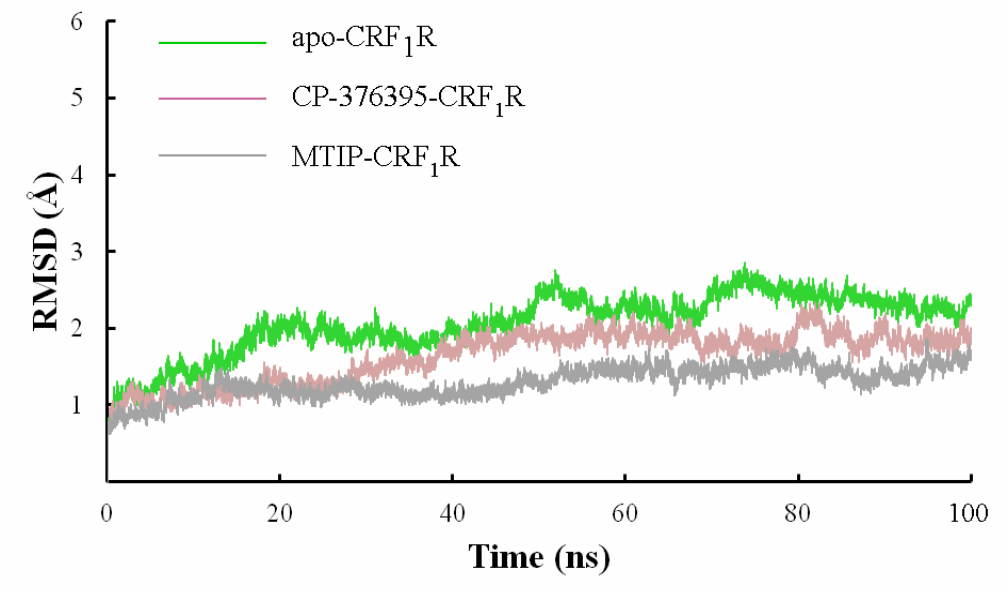


Fig. S2. The root-mean-square deviation (RMSD) of the simulated positions of the protein backbone atoms from those in the initial structure vs. simulation time for apo-CRF1R, CP-376395-CRF1R complex and MTIP-CRF1R complex.

Table S1. Binding free energy decompositions of CP-376395-CRF_1R and MTIP-CRF_1R.

CP-376395-CRF_1R										
Residue	**VDW (SD)**		**ELE (SD)**		**POLAR (SD)**		**NONPOLAR (SD)**		**TOT (SD)**	
Asn283	-2.42	0.60	-5.34	0.62	3.27	0.49	-0.23	0.02	-4.72	0.70
Phe203	-2.69	0.45	-0.10	0.11	-0.74	0.29	-0.21	0.03	-3.74	0.58
Met206	-3.54	0.41	0.28	0.31	0.03	0.30	-0.31	0.03	-3.54	0.52
Leu280	-2.14	0.33	0.26	0.10	-0.15	0.11	-0.21	0.05	-2.24	0.38
Thr316	-1.47	0.23	-0.14	0.39	0.48	0.46	-0.28	0.04	-1.40	0.29
Leu323	-1.15	0.32	-0.03	0.06	0.23	0.09	-0.25	0.05	-1.19	0.33
Leu287	-1.10	0.26	-0.04	0.04	0.21	0.11	-0.09	0.02	-1.03	0.31
Phe284	-1.08	0.24	0.02	0.07	0.28	0.09	-0.04	0.02	-0.81	0.29
Phe207	-0.72	0.17	0.14	0.06	-0.15	0.11	-0.01	0.00	-0.74	0.19
Gly210	-0.69	0.21	-0.47	0.11	0.58	0.14	-0.07	0.02	-0.65	0.26
Glu209	-0.71	0.15	0.15	0.16	0.03	0.39	-0.08	0.02	-0.61	0.35
Val279	-0.56	0.11	0.43	0.08	-0.45	0.09	-0.01	0.01	-0.60	0.11
Phe160	-0.46	0.18	-0.002	0.04	-0.05	0.08	-0.07	0.03	-0.58	0.23
Leu319	-0.52	0.14	-0.15	0.05	0.15	0.09	-0.05	0.02	-0.56	0.14
Phe362	-0.48	0.14	-0.02	0.04	0.03	0.06	-0.05	0.02	-0.51	0.16
MTIP-CRF_1R										
Residue	**VDW (SD)**		**ELE (SD)**		**POLAR (SD)**		**NONPOLAR (SD)**		**TOT (SD)**	
Phe203	-2.69	0.34	-0.40	0.12	-1.04	0.27	-0.19	0.02	-4.32	0.38
Met206	-3.83	0.40	-0.27	0.33	0.89	0.34	-0.34	0.03	-3.54	0.48
Asn283	-2.91	0.55	-2.96	0.76	3.36	0.55	-0.20	0.02	-2.72	0.94
Leu287	-2.00	0.38	-0.67	0.19	0.21	0.13	-0.12	0.03	-2.57	0.54
Thr316	-1.70	0.37	-0.47	0.23	-0.17	0.42	-0.20	0.04	-2.54	0.60
Leu280	-2.09	0.35	0.61	0.12	-0.50	0.10	-0.17	0.03	-2.15	0.41
Leu320	-1.40	0.65	-0.05	0.07	-0.09	0.12	-0.12	0.06	-1.66	0.65
Leu323	-1.19	0.32	-0.08	0.05	0.16	0.09	-0.20	0.04	-1.31	0.34
Leu213	-0.64	0.22	-0.29	0.13	-0.17	0.08	-0.05	0.02	-1.16	0.27
Phe362	-0.66	0.20	-0.04	0.05	-0.18	0.09	-0.04	0.02	-0.92	0.30
Phe284	-1.02	0.27	0.16	0.21	0.17	0.16	-0.03	0.01	-0.72	0.23
Ile290	-0.50	0.24	-0.05	0.06	-0.11	0.05	-0.03	0.01	-0.69	0.26
Phe162	-0.53	0.15	-0.01	0.02	-0.04	0.08	-0.09	0.03	-0.67	0.21
Val313	-0.54	0.20	-0.08	0.09	-0.01	0.09	-0.03	0.01	-0.66	0.26
Gly210	-0.77	0.29	-0.03	0.21	0.26	0.14	-0.07	0.02	-0.62	0.40
Phe207	-0.72	0.13	0.19	0.07	-0.05	0.10	-0.01	0.00	-0.58	0.15
Val279	-0.59	0.11	0.44	0.09	-0.40	0.08	-0.01	0.00	-0.56	0.13
Leu319	-0.53	0.17	0.21	0.06	-0.16	0.08	-0.04	0.02	-0.52	0.18