Supplementary Materials

Figure S1

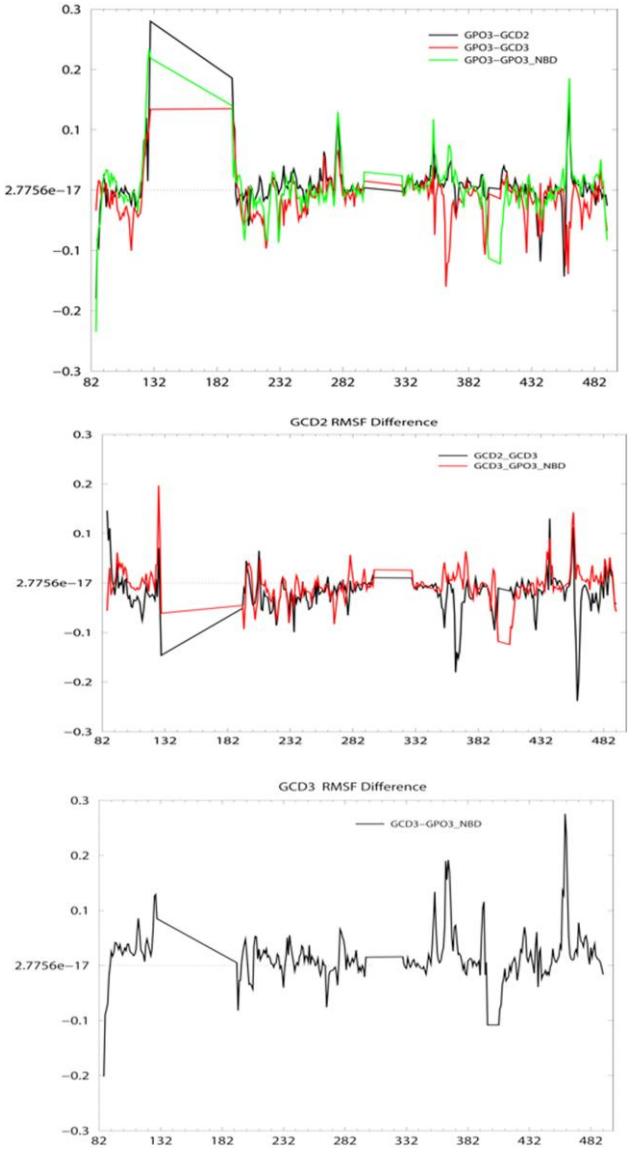
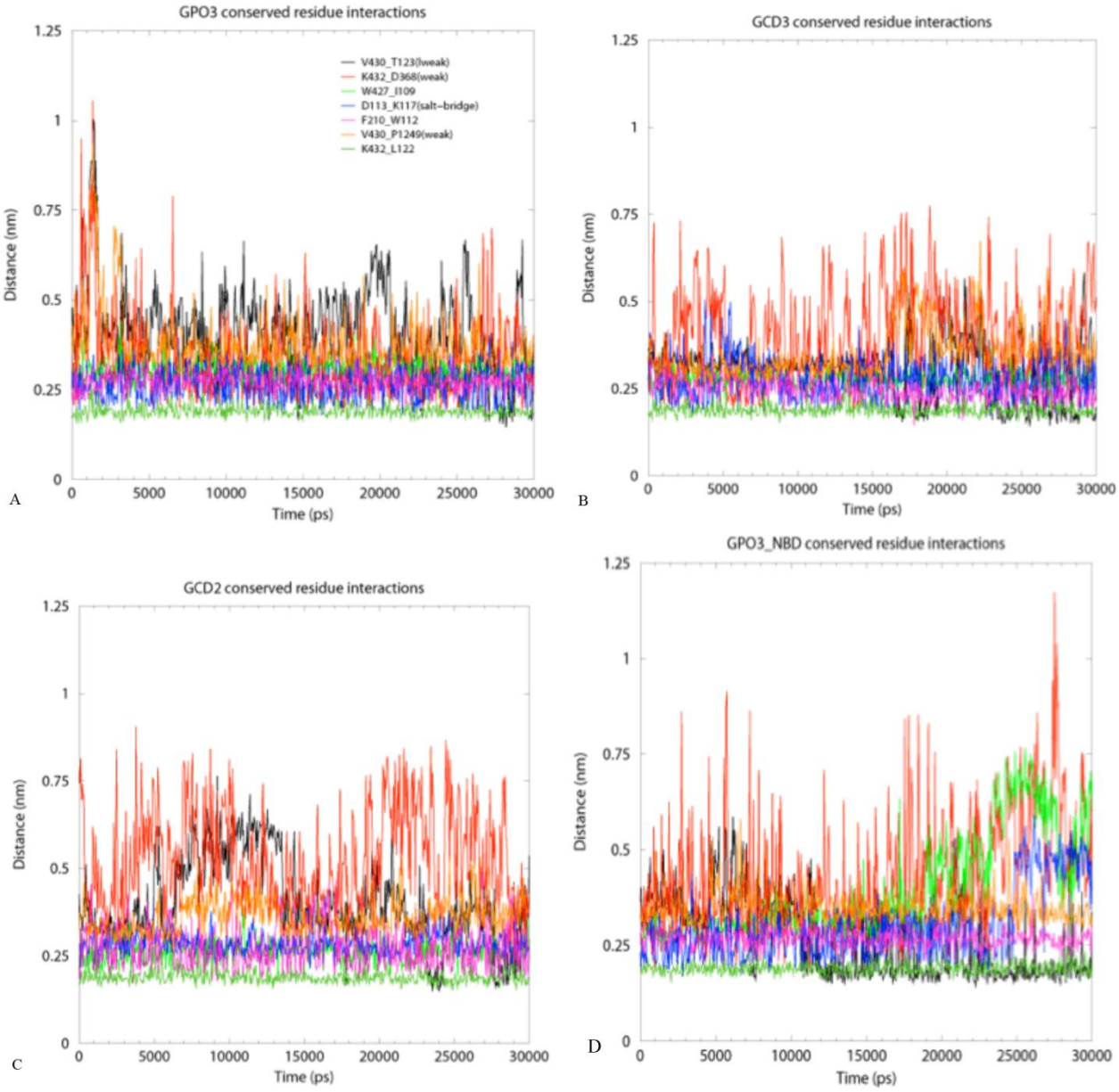


Figure S1. The difference plots of the Root Mean Square Fluctuations (RMSF) between the respective simulations. **A**. Difference plot of GPO3 and GCD2 (black curve), GCD3 (red curve) and GPO3_NBD (green curve). Negative values indicate the motions in GPO3 are reduced relative to the structure to which it is being compared. **B**. Difference plot of GCD2 and GCD3 (black curve) and GPO3_NBD (red curve). **C**. Difference plot of GCD3 and GPO3_NBD.

Figure S2


GPO3 conserved residue interactions
V430_T123(lweak)
K432_D368(weak)
W427_I109
D113_K117(salt−bridge)
F210_W112
V430_P1249(weak)
K432_L122
Distance (nm)
Time (ps)
A
GCD3 conserved residue interactions
Distance (nm)
Time (ps)
B
GCD2 conserved residue interactions
Distance (nm)
Time (ps)
C
GPO3_NBD conserved residue interactions
Distance (nm)
Time (ps)
D

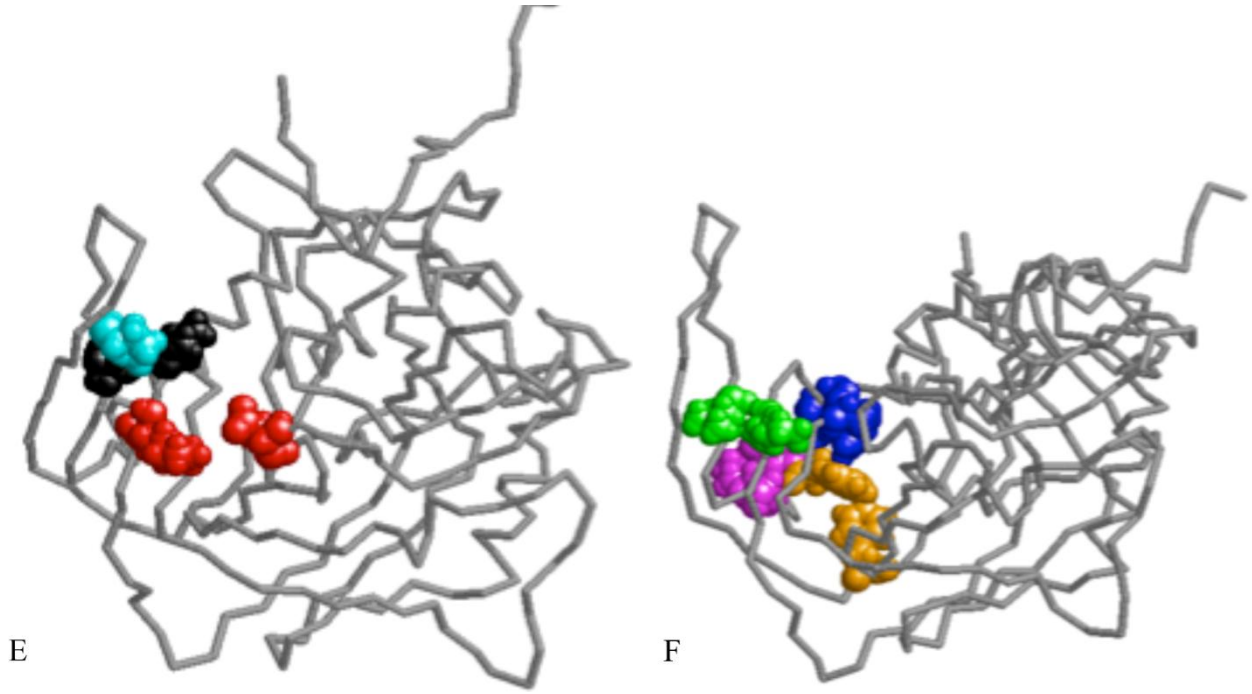


Figure S3. Intra-residues distances (nm) of interacting residues pairs for the residues conserved in the gp120 amino-acid sequence. V430 to T123 (black), K432-D368 (pink), W427-I109 (light green), D113-K117 (blue), F210-W112 (magenta), V320-P124 (orange) and K432-L122 (dark green) for the four constructs, GPO3 (**A**), GCD2 (**B**), GCD3 (**C**) and GPO3_NBD (**D**). Loose Interactions (**E**) are observed for V430-T123, K432-D368, V430-P124, while tight interactions (**F**) are seen for F210-W112, W427-I109, D113-K117 and K432-L122

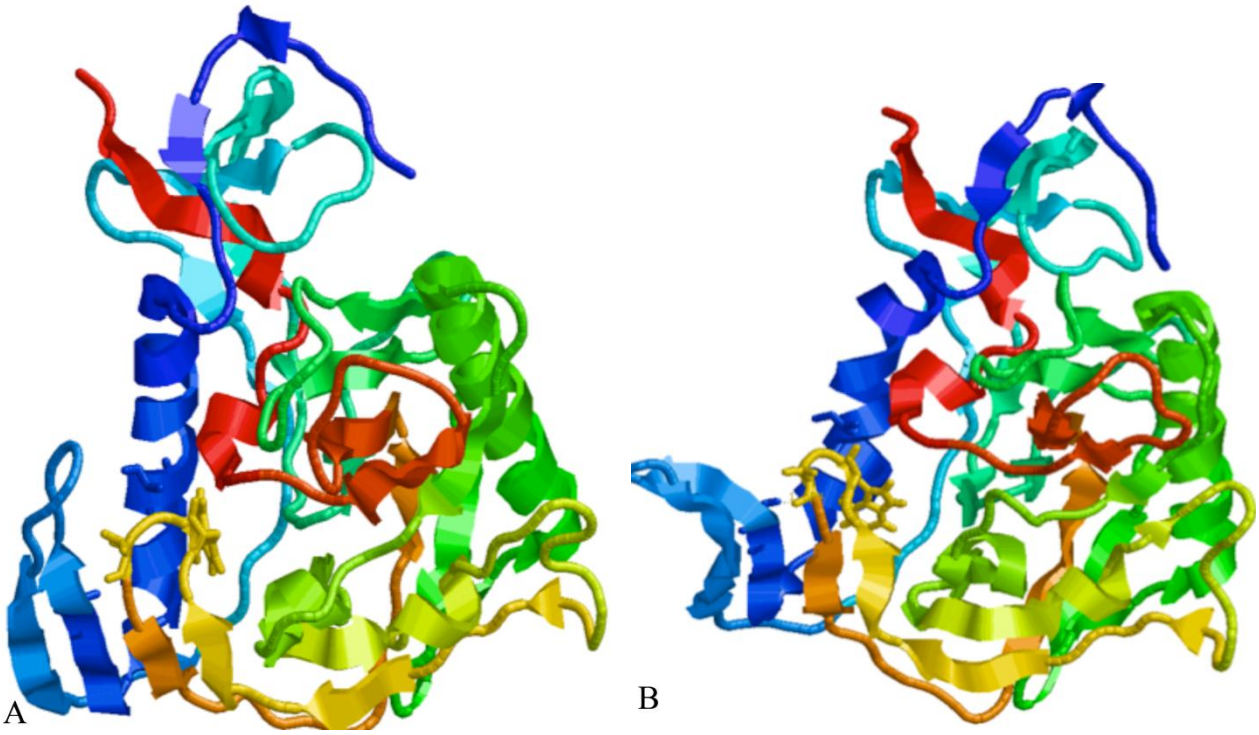


Figure S2. A) Ribbon diagram of snapshots of GPO3_NBD simulation showing W427 and I109 on the bridging sheet β-20/β-21 at (A) t=10 ns and (**B**) t = 2ns. The increase in distance between W427 and I 109 seen in the simulation is a consequence of the movement of W427 away from the Phe 43 cavity.

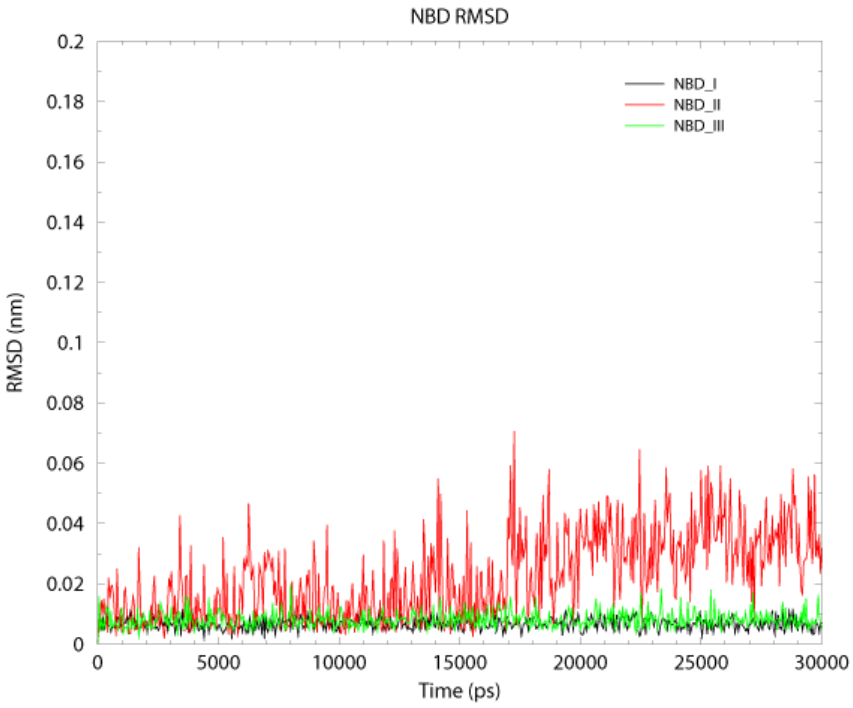


Figure S4. RMSDs plotted for the three NBD-556 Region I (black), Region II (red) and Region III (green).

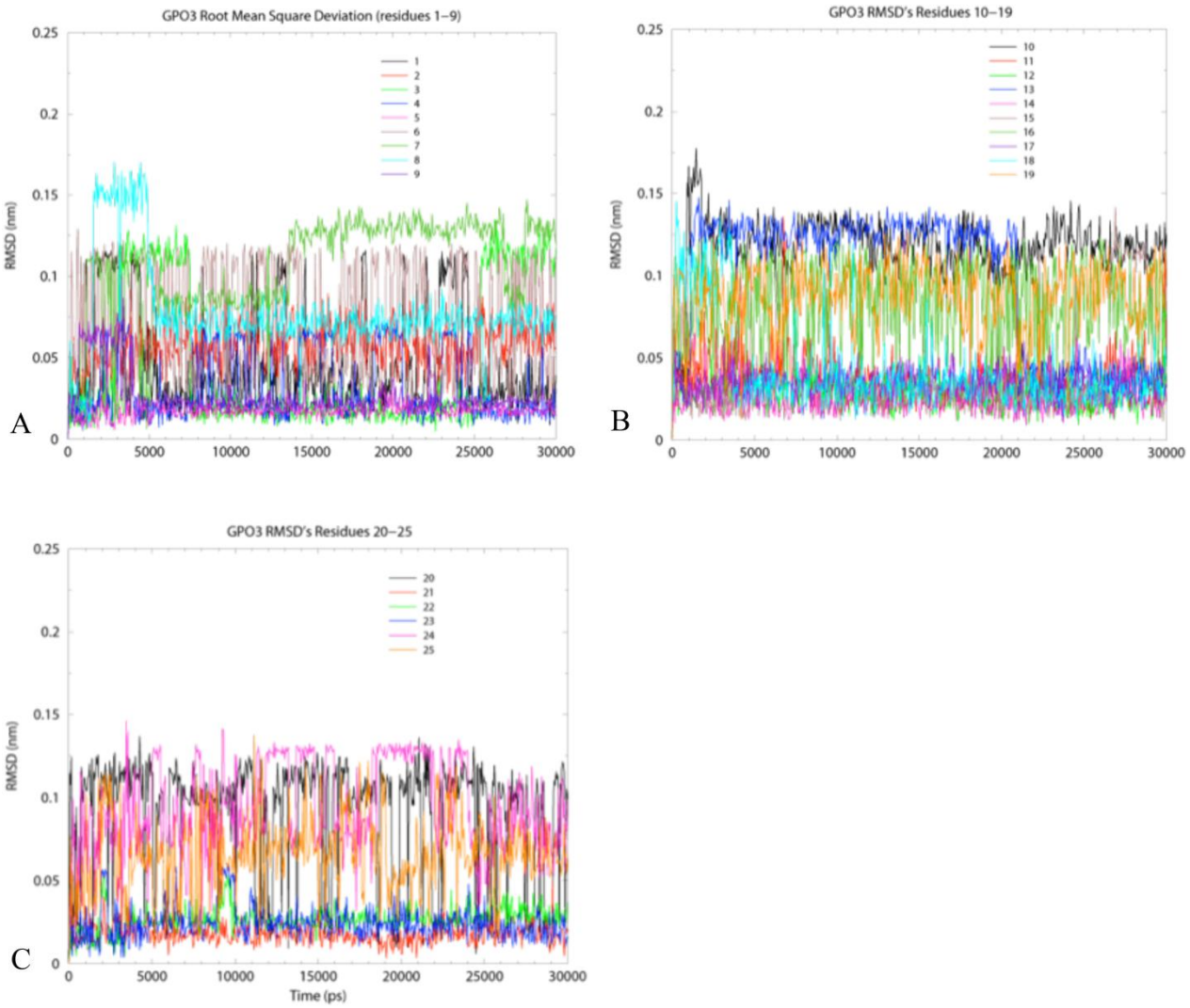


Figure S5. RMSDs for the 25 residues that form the Phe 43 cavity of GPO3 and are within 4.5 Å of NBD-556 as predicted by docking. **A)** Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 **B)** Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 **C)** Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475.

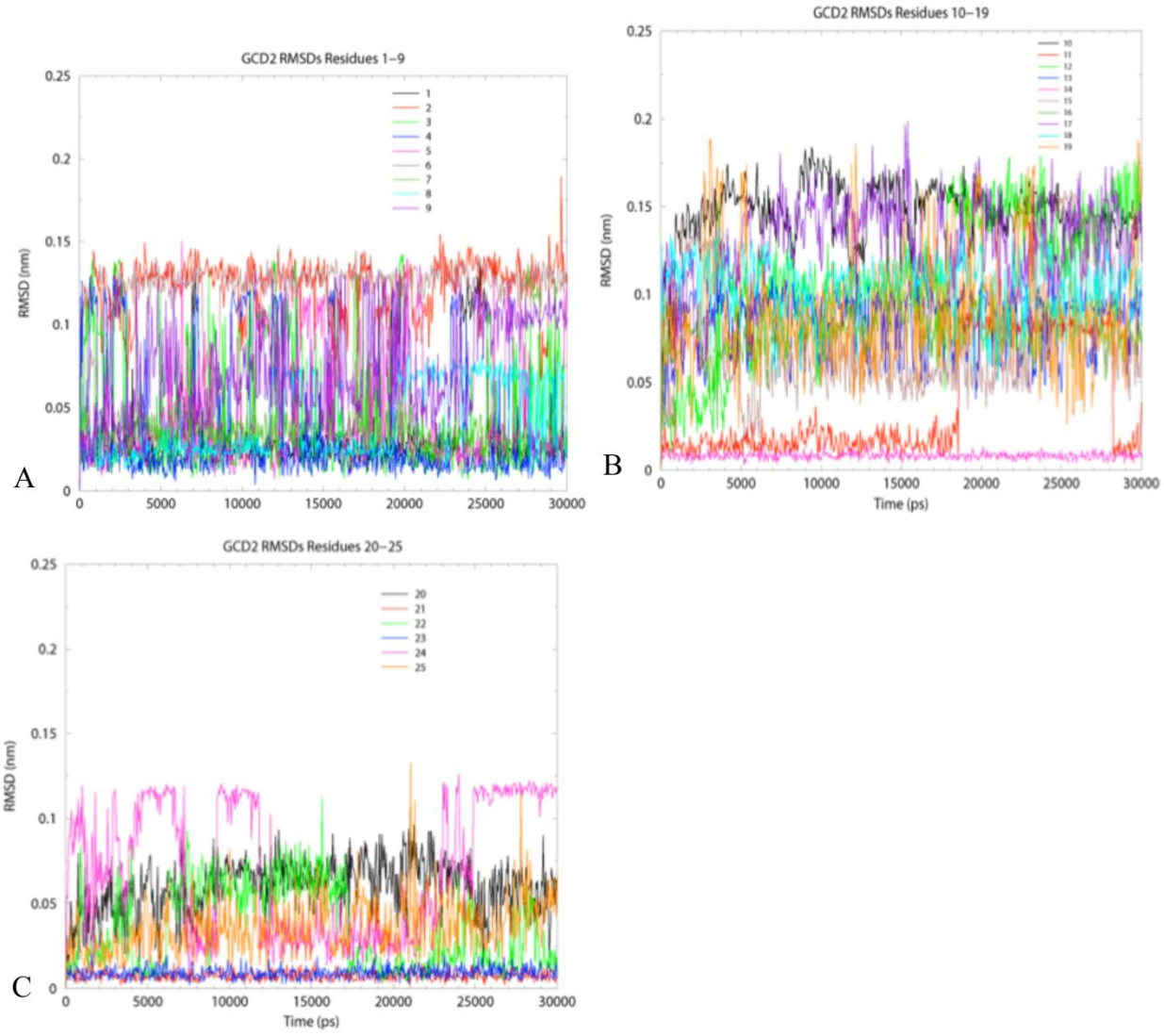


Figure S6. RMSDs for the 25 residues that form the Phe 43 cavity of GCD2 and are within 4.5 Å of NBD-556 as predicted by docking. A) Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 B) Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 C) Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475.

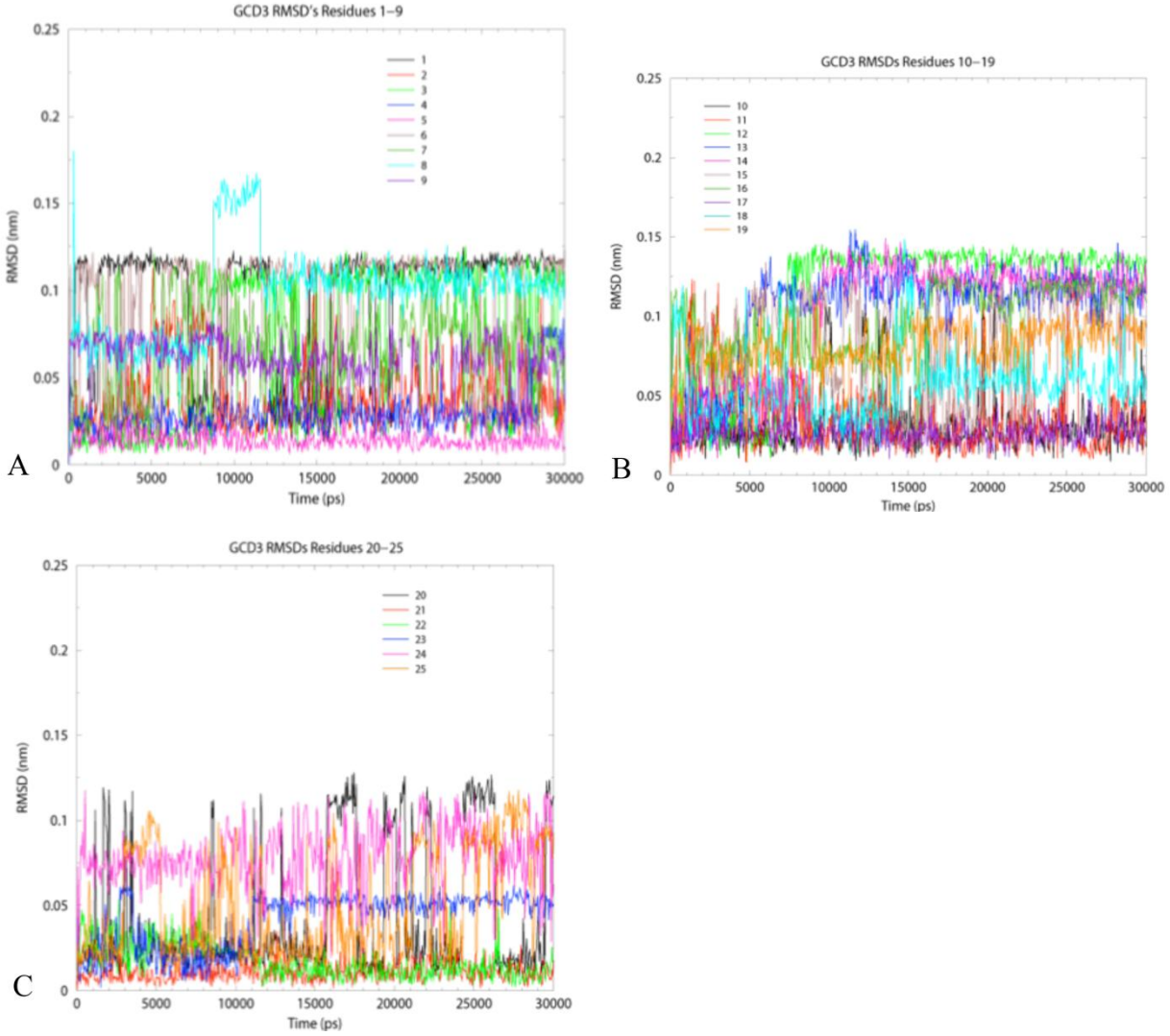


Figure S7. RMSDs for the 25 residues that form the Phe 43 cavity of GCD3 and are within 4.5 Å of NBD-556 as predicted by docking. A) Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 B) Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 C) Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475

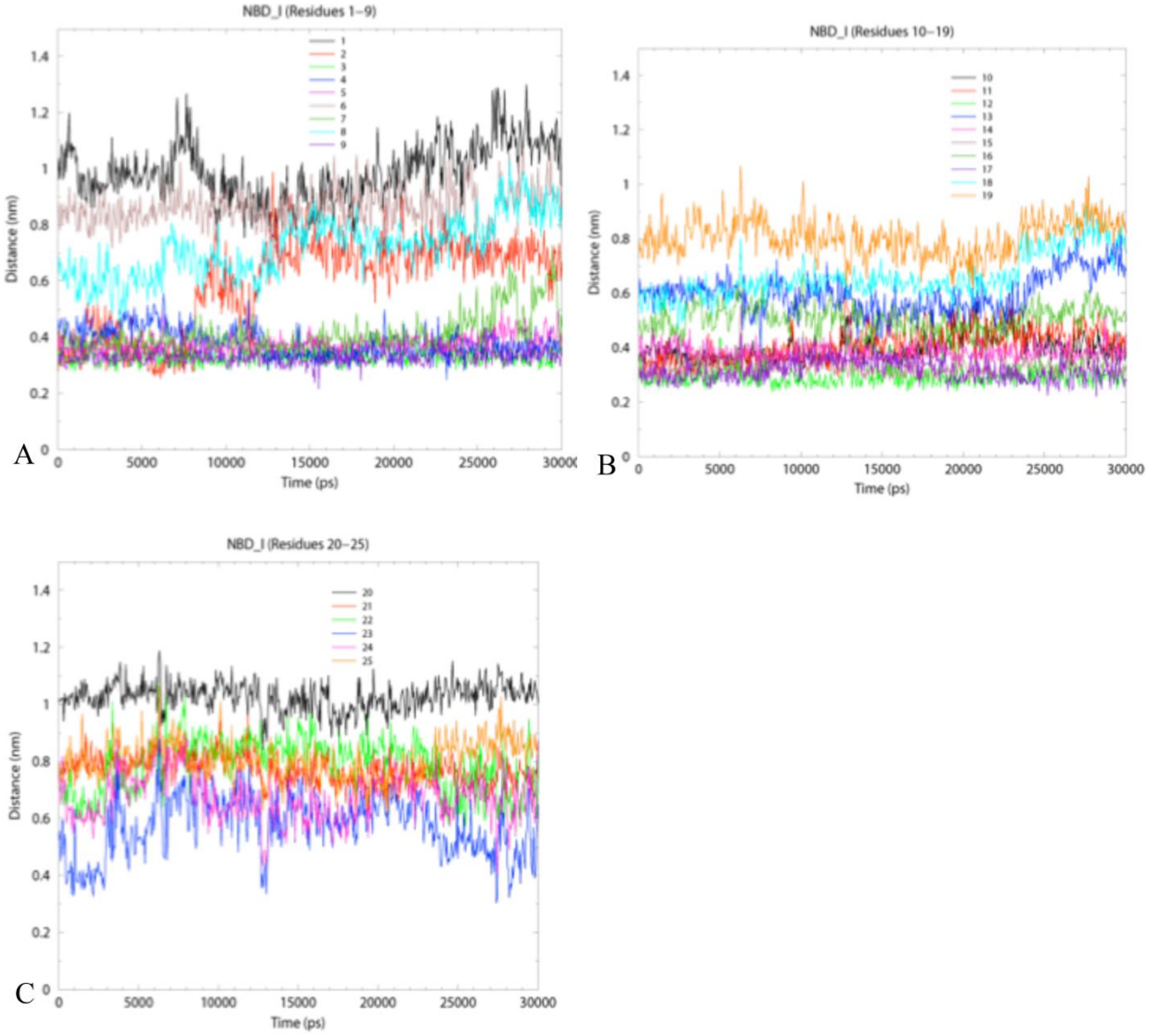
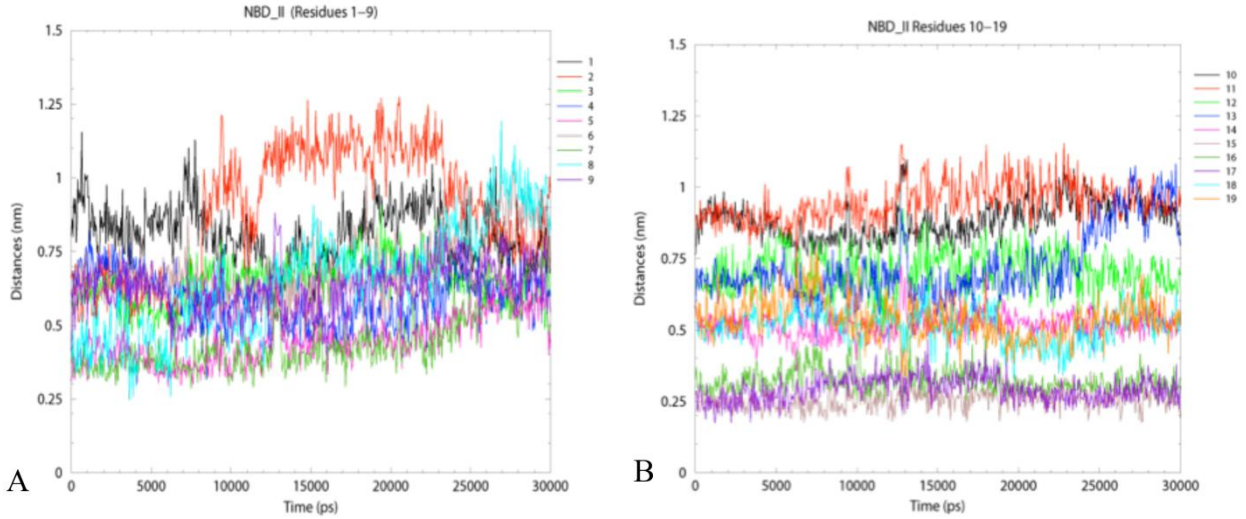


Figure S8. The pair wise residue (c-α) distances between NBD Region I plotted for the 25 residues of the Phe-43 cavity for GPO3_NBD. **A)** Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 **B)** Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 **C)** Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475.



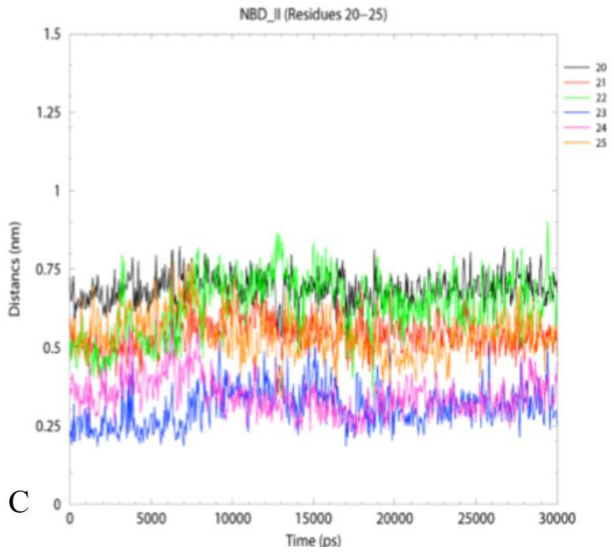
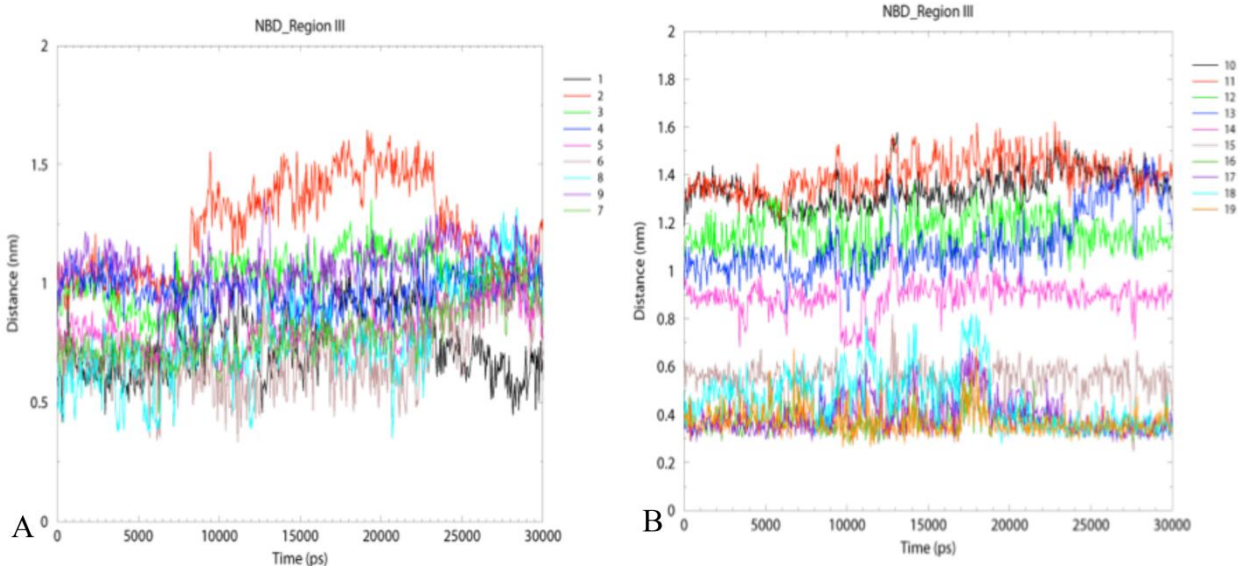


Figure S9 The pair wise residue (C-α) distances between NBD Region II plotted for the 25 residues of the Phe-43 cavity for GPO3_NBD. **A)** Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 **B)** Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 **C)** Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475.



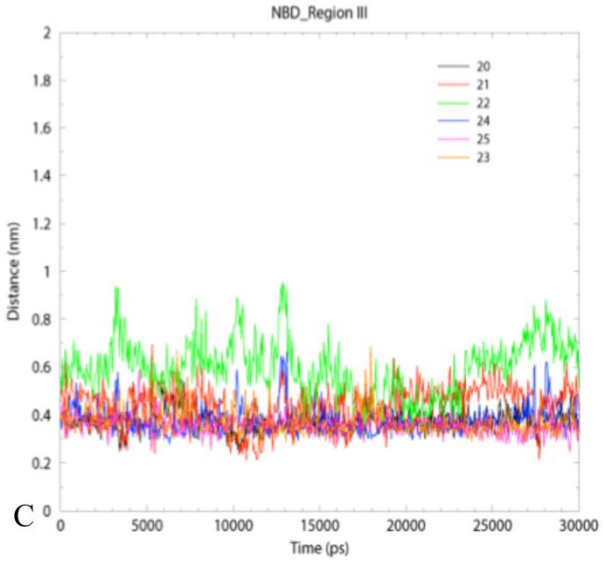


Figure S10. The pair wise residue (C-α) distances between NBD Region III plotted for the 25 residues of the Phe-43 cavity for GPO3_NBD. **A)** Residues are: 1-H105, 2-W112, 3-V255, 4-S256, 5-T257, 6 -D368 , 7-E370, 8-I371, 9-S375 **B)** Residues are: 10-F376, 11-N377, 12 -F382, 13-Y384, 14-I424, 15-N425, 16-M426, 17-W427, 18-Q428, 19-E429 **C)** Residues are: 20-V430, 21-G431, 22-G472, 23-G473, 24-D474, 25- M475.

Tables

Table S1

Res. Num.	Res. Name	RMSD Mean	RMSD Std	Reg. I Mean	Reg. I STD	Reg. II Mean	Reg. II STD	Reg. III Mean	Reg. III STD
1	H105	0.11	0.02	0.99	0.10	0.80	0.10	0.75	0.14
2	W112	0.06	0.02	0.59	0.16	0.89	0.21	1.24	0.20
3	V255	0.08	0.05	0.33	0.02	0.65	0.08	1.03	0.10
4	S256	0.04	0.03	0.38	0.05	0.60	0.09	0.97	0.07
5	T257	0.06	0.02	0.38	0.03	0.45	0.08	0.81	0.09
6	D368	0.08	0.04	0.86	0.07	0.69	0.11	0.70	0.16
7	E370	0.08	0.04	0.41	0.07	0.44	0.11	0.78	0.20
8	I371	0.12	0.06	0.72	0.10	0.66	0.18	1.07	0.09
9	S375	0.07	0.00	0.33	0.03	0.63	0.09	0.79	0.12
10	F376	0.10	0.05	0.40	0.05	0.89	0.07	1.34	0.08
11	N377	0.03	0.01	0.41	0.06	0.95	0.07	1.40	0.07
12	F383	0.10	0.05	0.30	0.03	0.71	0.07	1.16	0.08
13	Y384	0.06	0.03	0.60	0.07	0.72	0.12	1.11	0.13
14	I424	0.04	0.02	0.38	0.03	0.52	0.04	0.89	0.06
15	N425	0.04	0.03	0.33	0.03	0.26	0.04	0.53	0.08
16	M426	0.07	0.03	0.51	0.05	0.32	0.04	0.37	0.05
17	W427	0.07	0.05	0.32	0.04	0.29	0.04	0.39	0.08
18	Q428	0.07	0.04	0.66	0.08	0.51	0.06	0.46	0.12
19	E429	0.09	0.02	0.81	0.07	0.54	0.07	0.37	0.05
20	V430	0.07	0.04	1.03	0.05	0.69	0.05	0.38	0.05
21	G431	0.01	0.01	0.77	0.05	0.54	0.05	0.45	0.08
22	G472	0.03	0.01	0.79	0.10	0.63	0.10	0.59	0.12
23	G473	0.03	0.01	0.57	0.11	0.31	0.06	0.37	0.06
24	D474	0.09	0.03	0.67	0.09	0.35	0.06	0.36	0.04
25	M475	0.07	0.04	0.81	0.07	0.54	0.07	0.37	0.05

Mean and standard deviation of residue interactions with Regions I, II and III over 30 ns trajectory for GPO3_NBD measured in nm from the center of mass of the residue and the center of mass of NBD region I, II or III. Interaction distances < 0.40 and with low standard deviations reflect tight interactions. Residues with tight interaction for Region I are S375, F376, F382, I424, N425, W427; for Region II are N425, M426, and W427 and Region III are M426, W427, E429, V430, G473, D474 and M475.