Electronic Supplementary Material (ESI) for Molecular BioSystems.

Supporting Information

Understanding the binding of inhibitors of Matrix Metalloproteinases by molecular docking, quantum mechanical calculations, molecular dynamics simulations, and MMGBSA/MMBappl study

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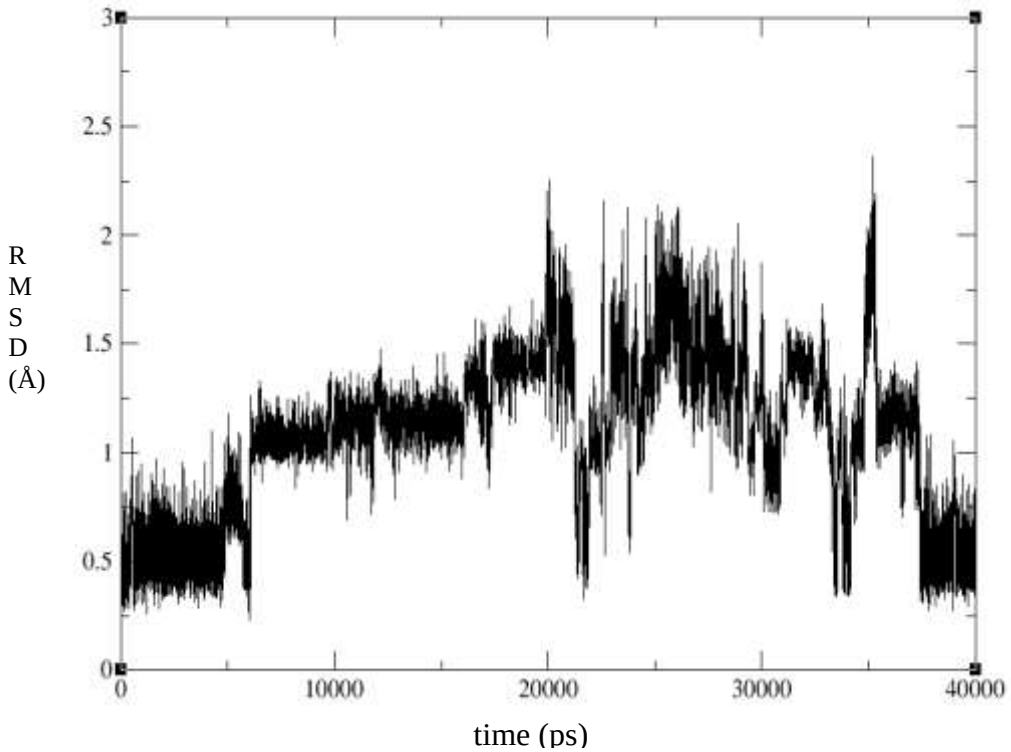


Fig S1. RMSD (ordinate) versus time (abscissa) plot for MMP-1-Batimastat complex

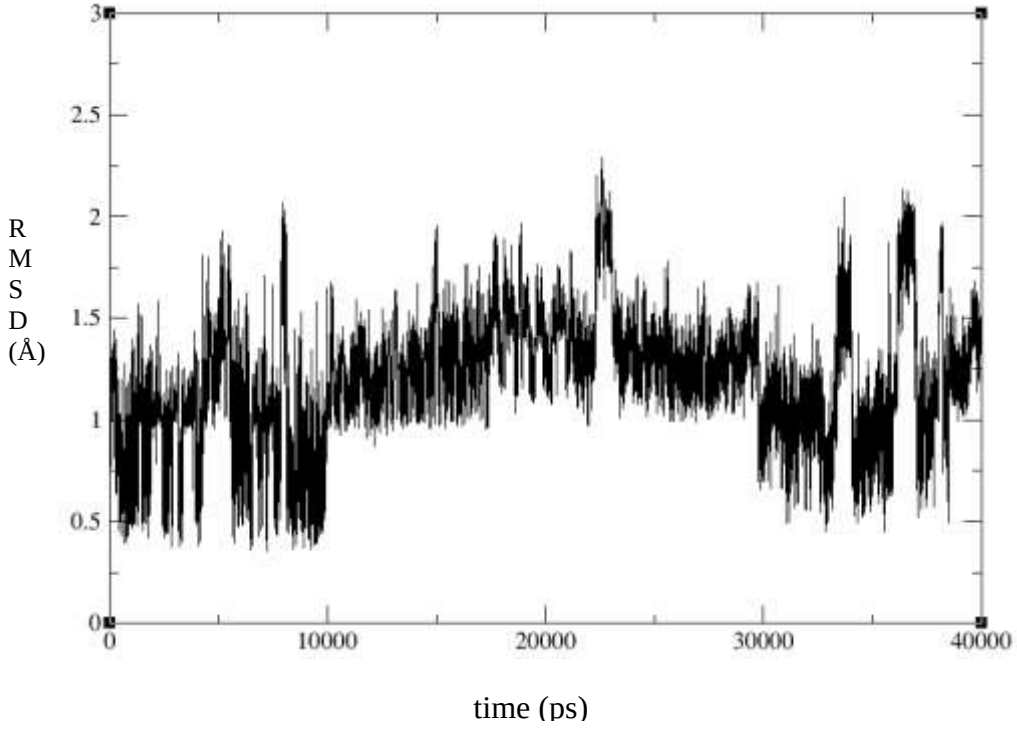


Fig S2. RMSD (ordinate) versus time (abscissa) plot for MMP-2-Batimastat complex

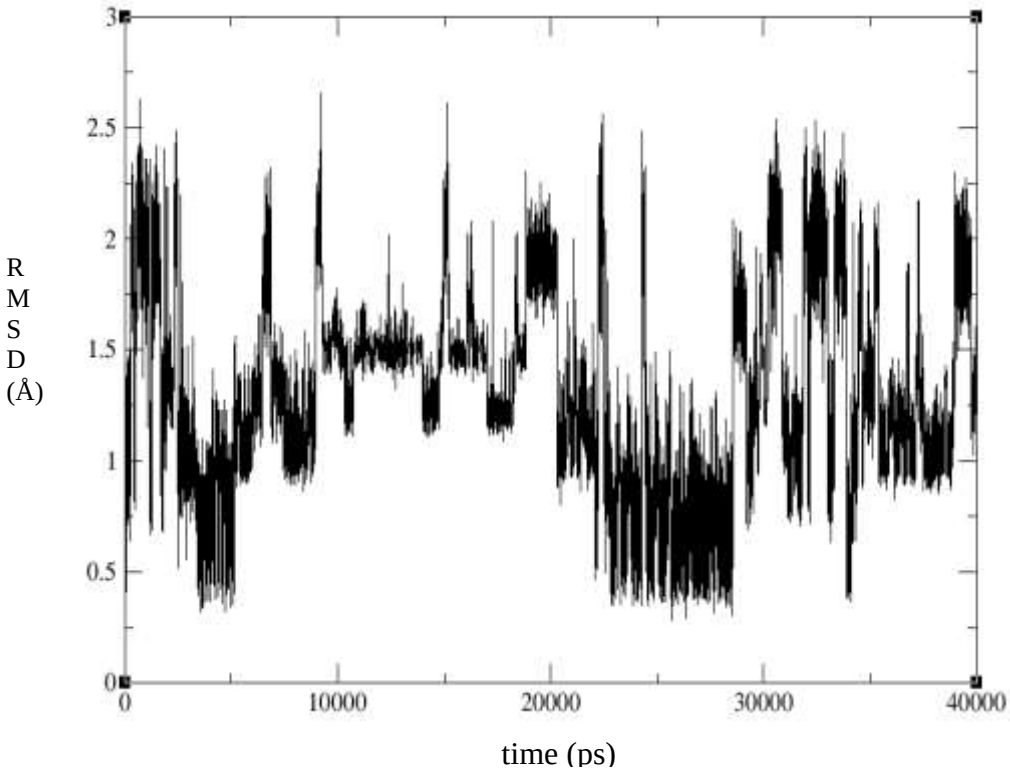


Fig S3. RMSD (ordinate) versus time (abscissa) plot for MMP-3-Batimastat complex

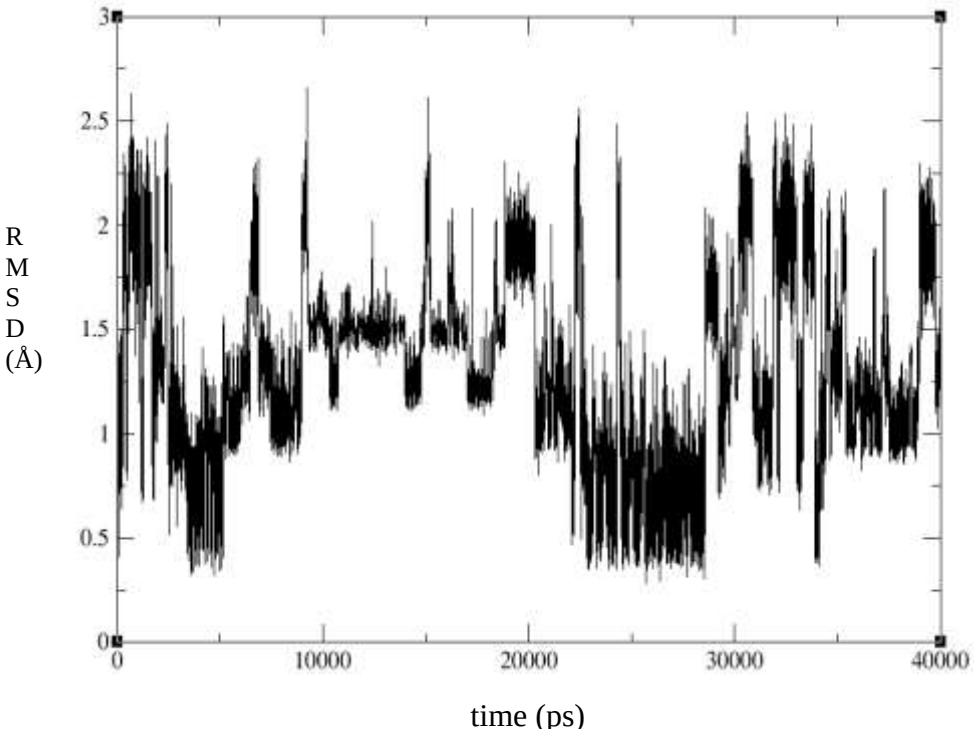


Fig S4. RMSD (ordinate) versus time (abscissa) plot for MMP-8-Batimastat complex

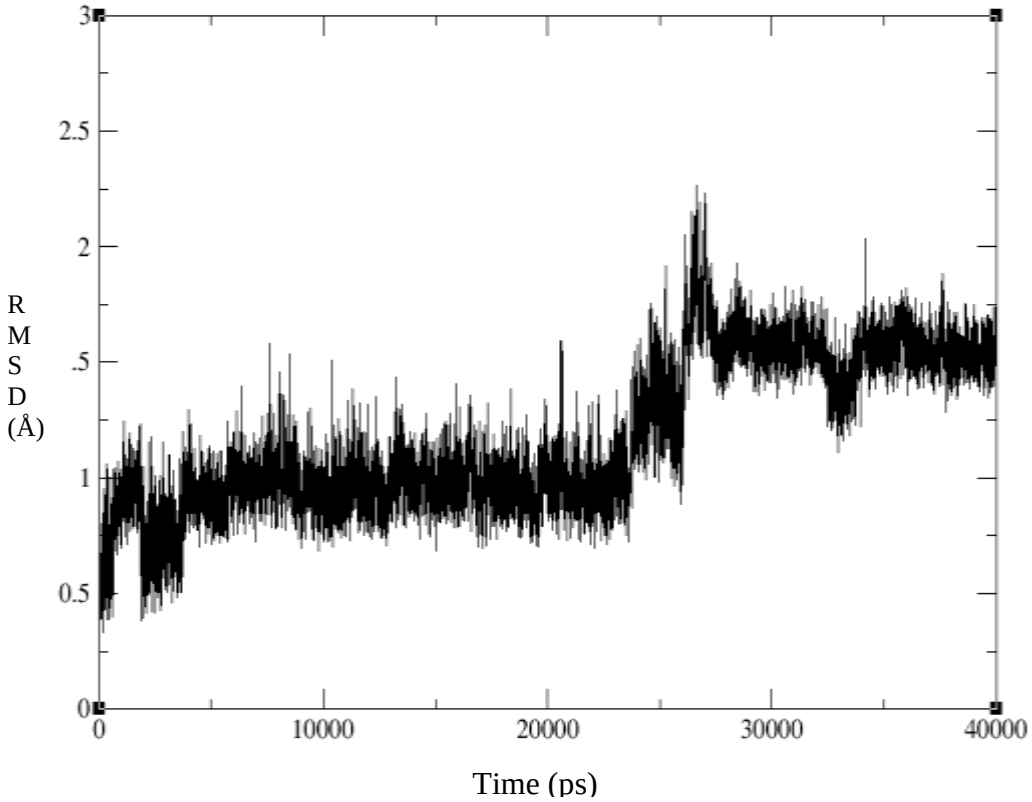


Fig S5. RMSD (ordinate) versus time (abscissa) plot for MMP-9-Batimastat complex

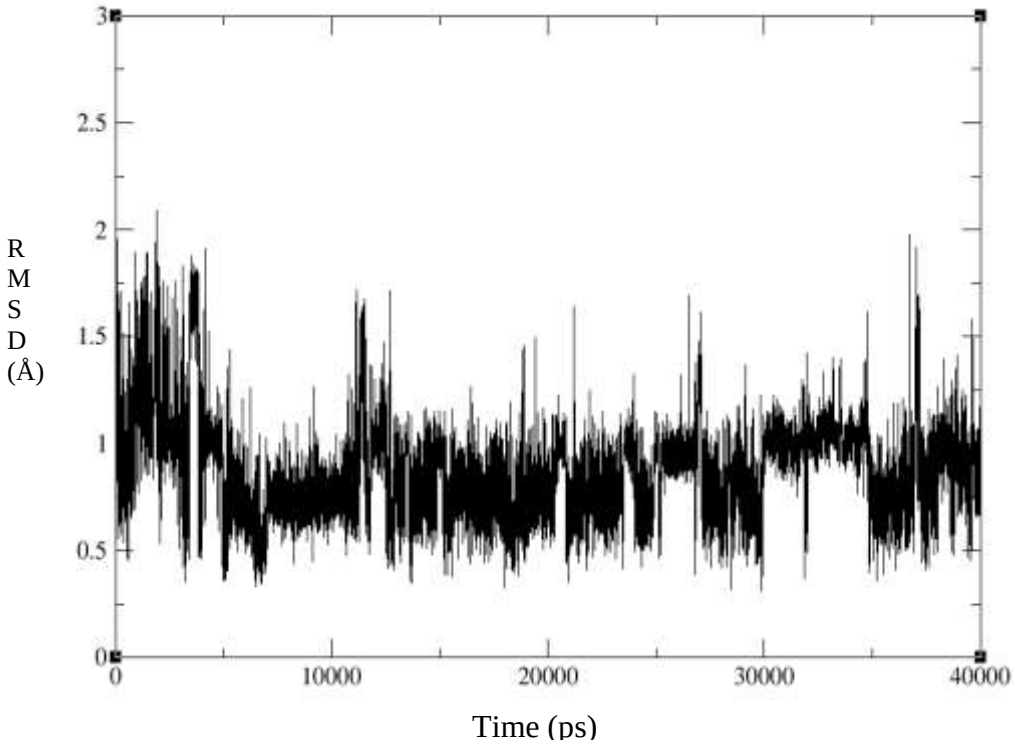


Fig S6. RMSD (ordinate) versus time (abscissa) plot for MMP-13-Batimastat complex

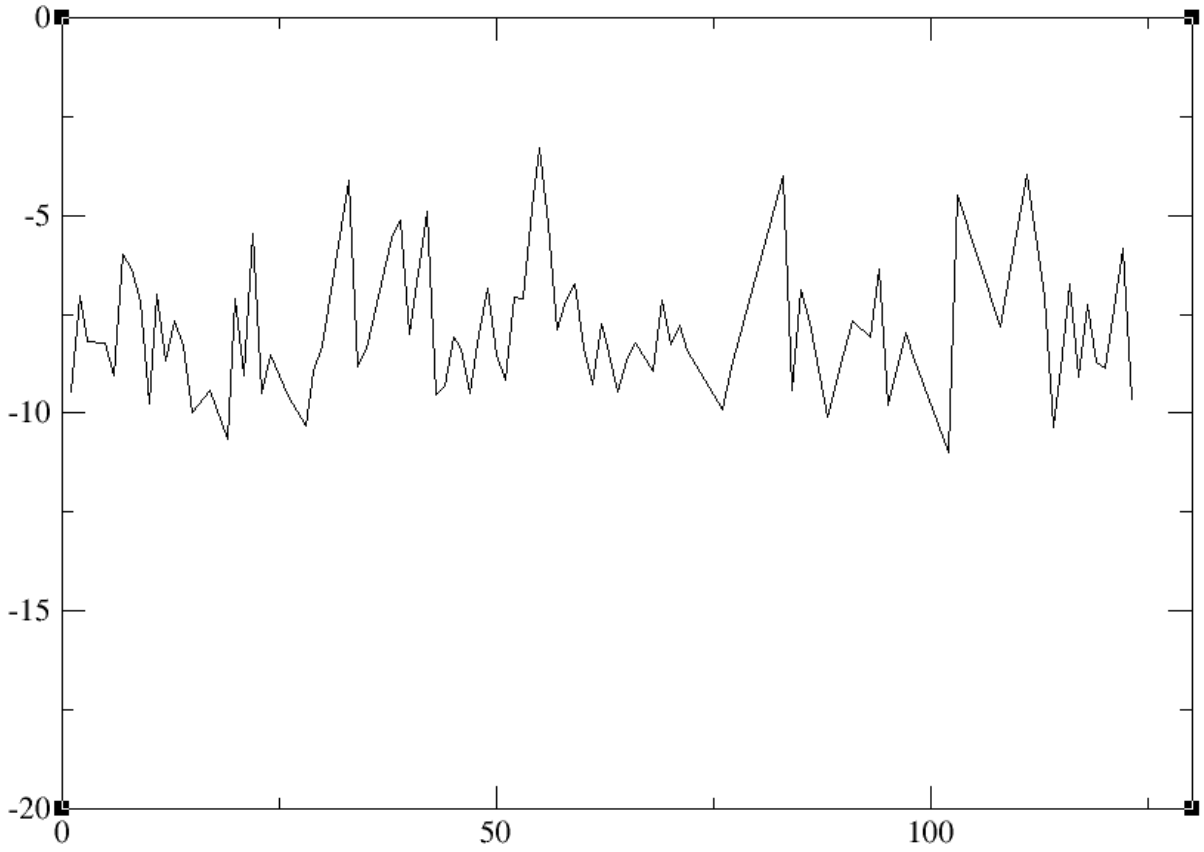


Figure S7. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-1 complex.

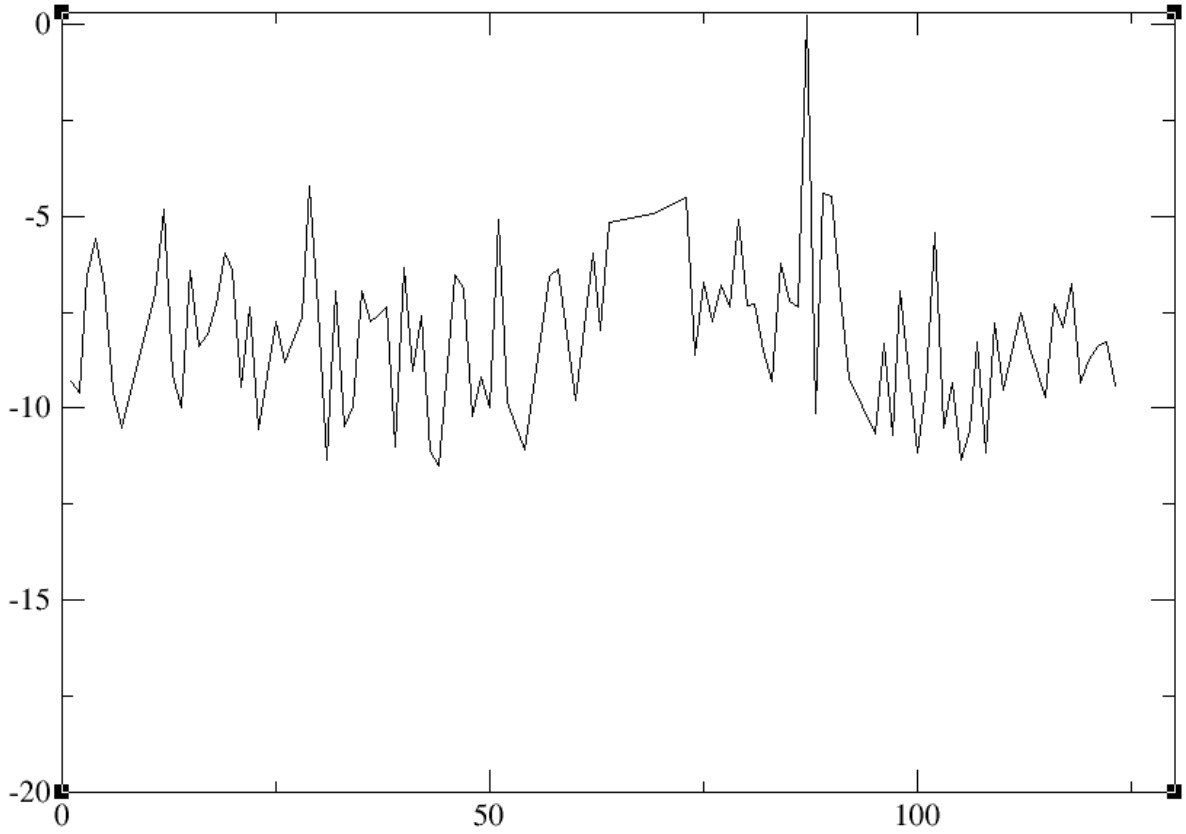


Figure S8. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-2 complex.

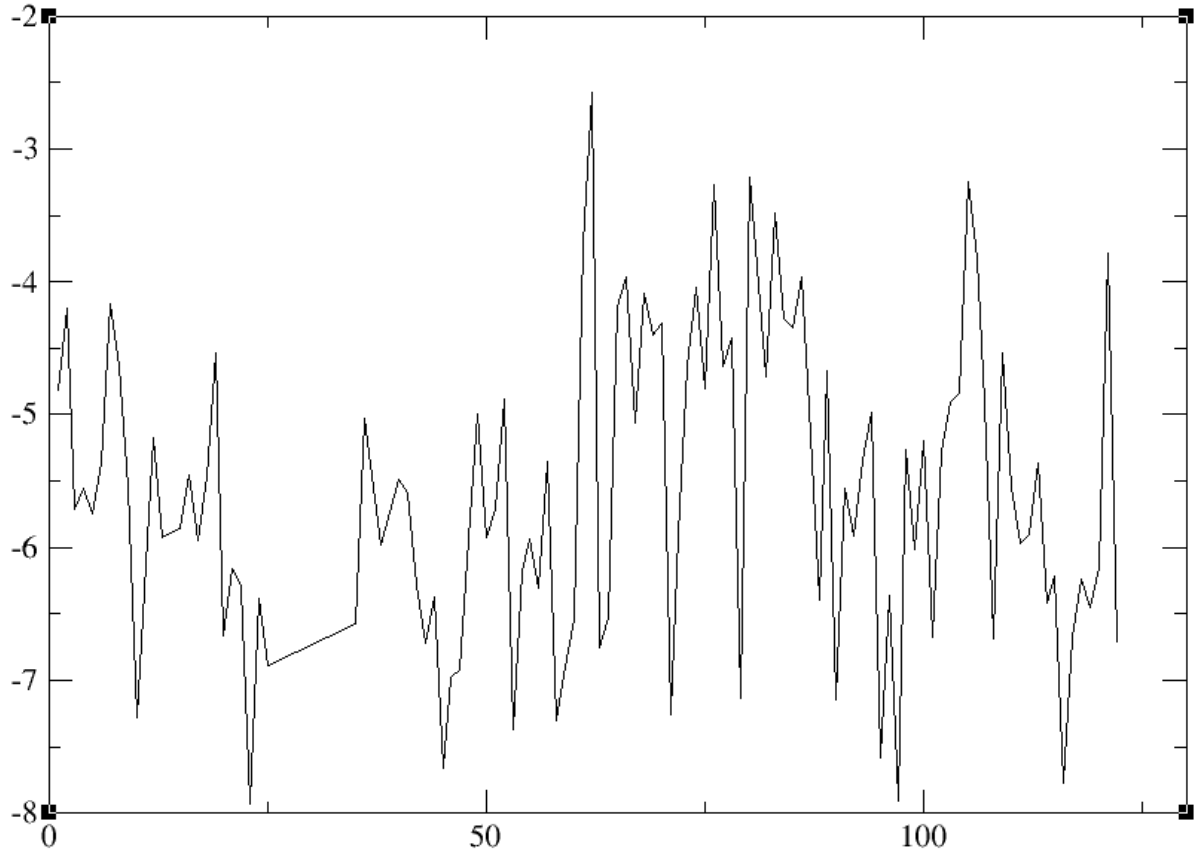


Figure S9. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-3 complex.

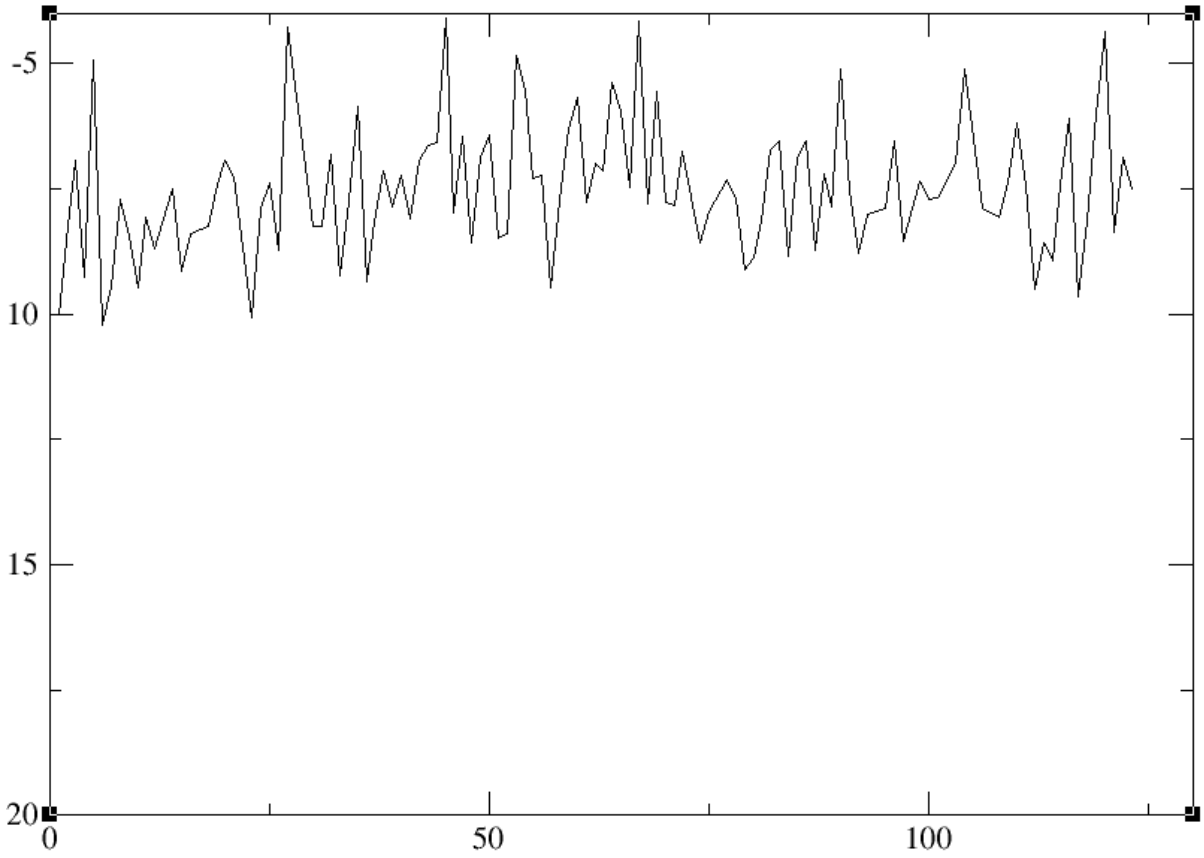


Figure S10. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-8 complex.

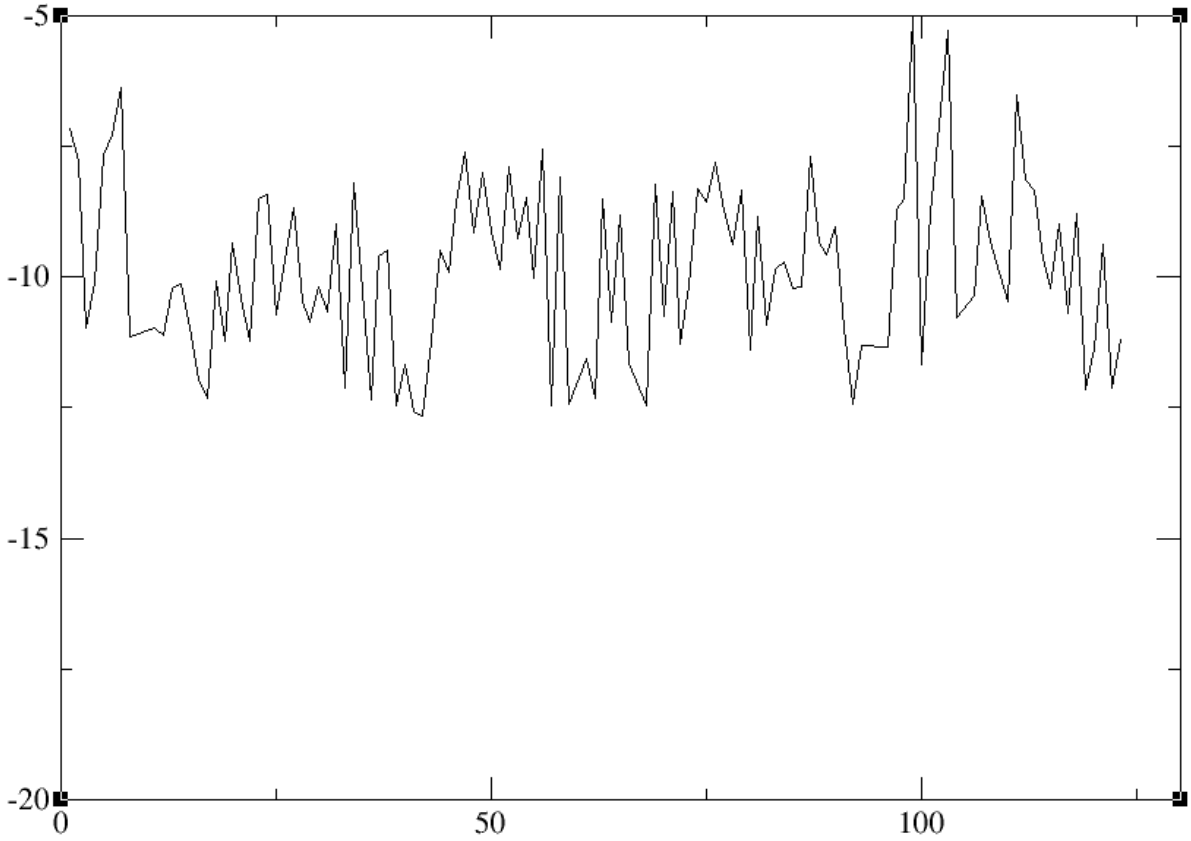


Figure S11. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-9 complex.

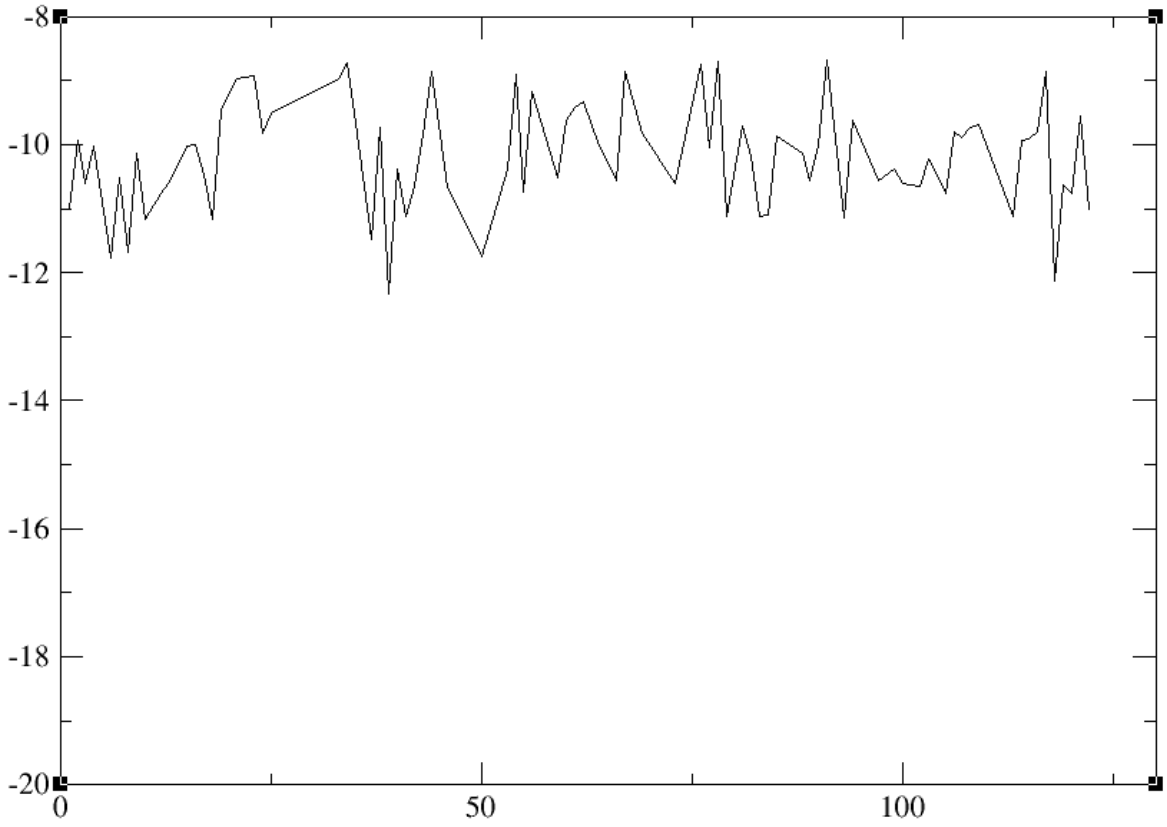


Figure S12. Predicted binding free energy (in kcal/mol on the ordinate) versus time (in ns on the abscissa) for Batimastat-MMP-1 complex.

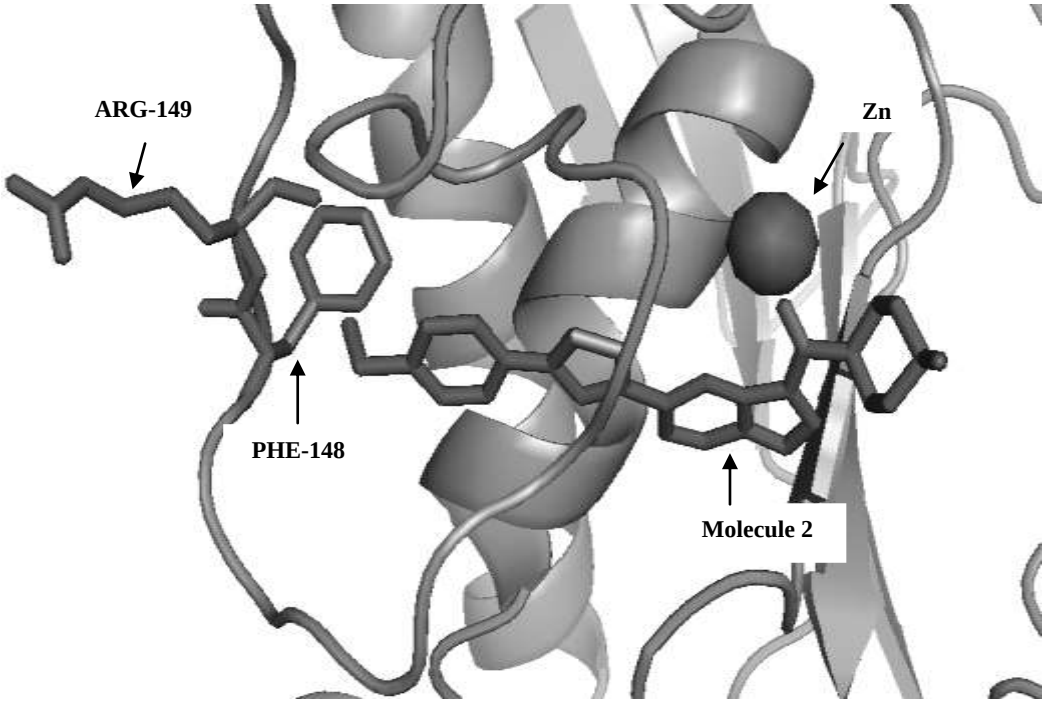


Figure S13 A cross sectional view of the catalytic and the S1' region of the final snapshots from a 10ns MD trajectory on the designed Molecule2-MMP2 complex.

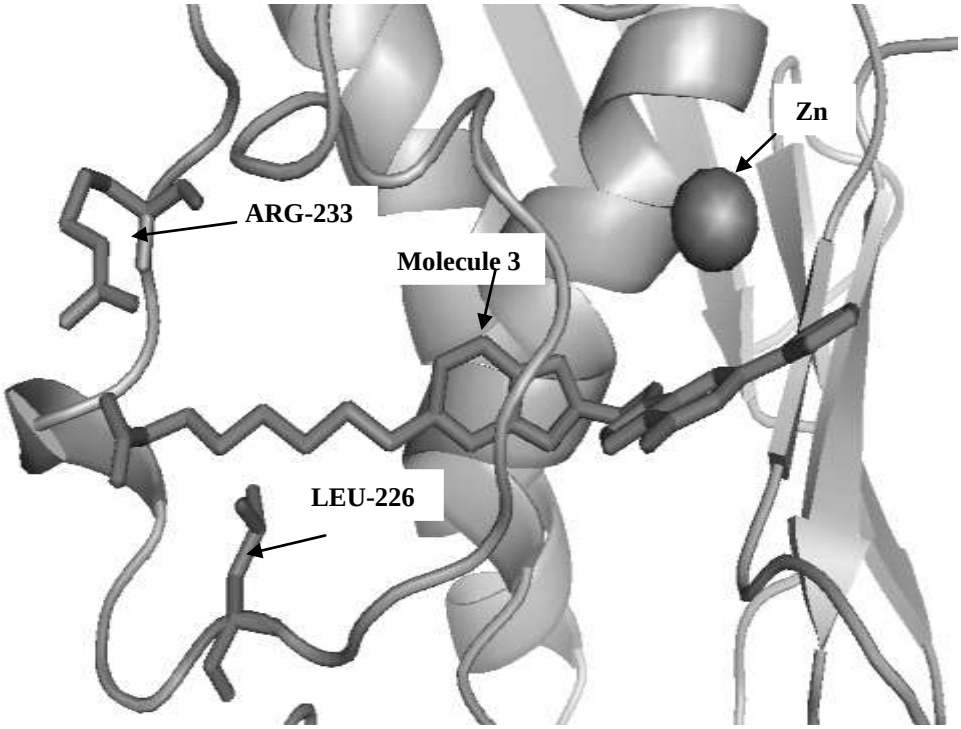


Figure S14 A cross sectional view of the catalytic and the S1' region of the final snapshot from a 10ns MD trajectory on the designed Molecule3-MMP3 complex.

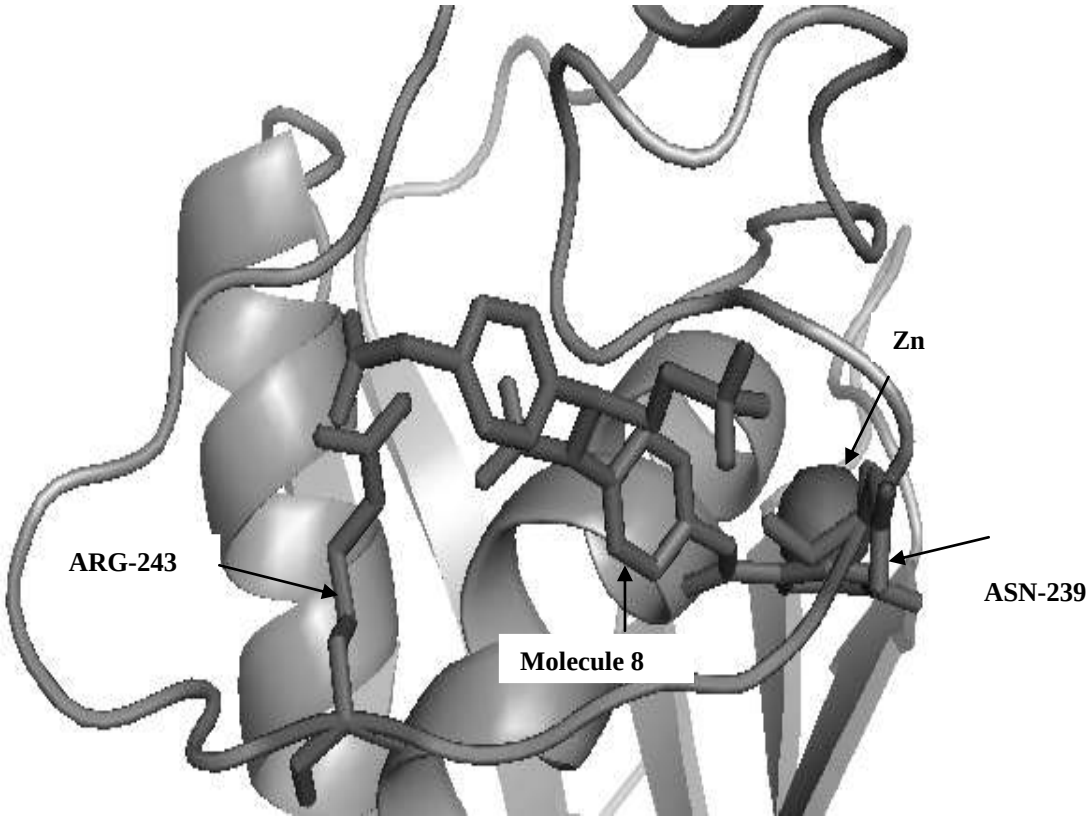


Figure S15 A cross sectional view of the catalytic and the S1' region of the final snapshot from a 10ns MD trajectory on the designed Molecule8-MMP8 complex.

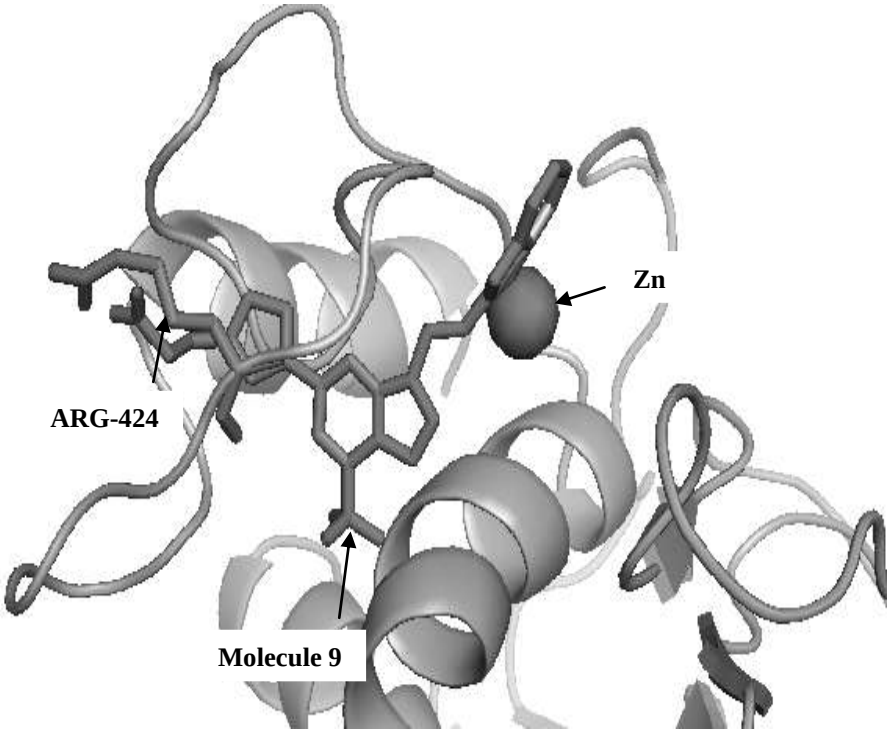


Figure S16 A cross sectional view of the catalytic and the S1' region of the final snapshot from a 10ns MD trajectory on designed Molecule9-MMP9 complex.

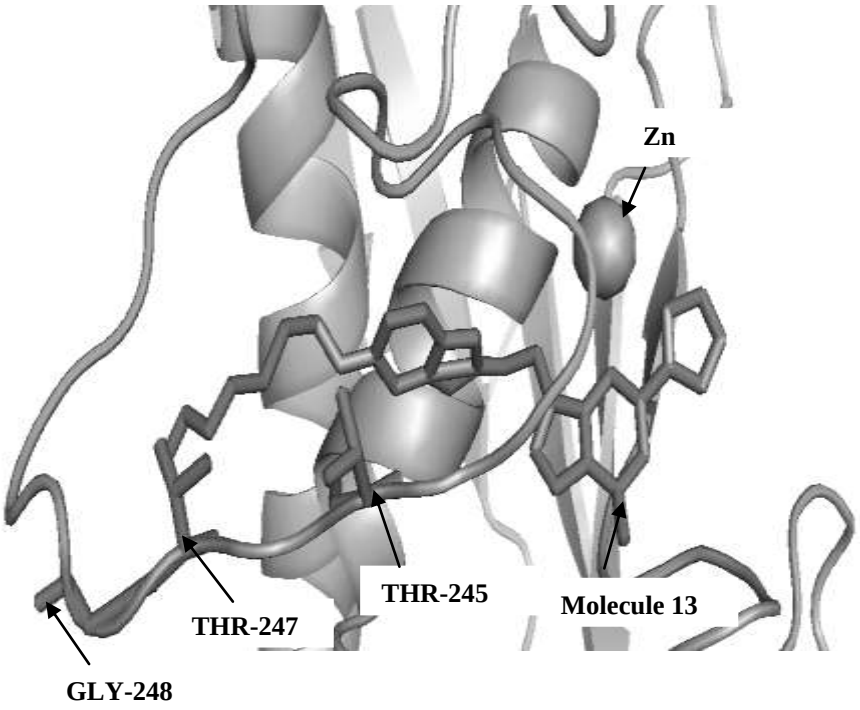
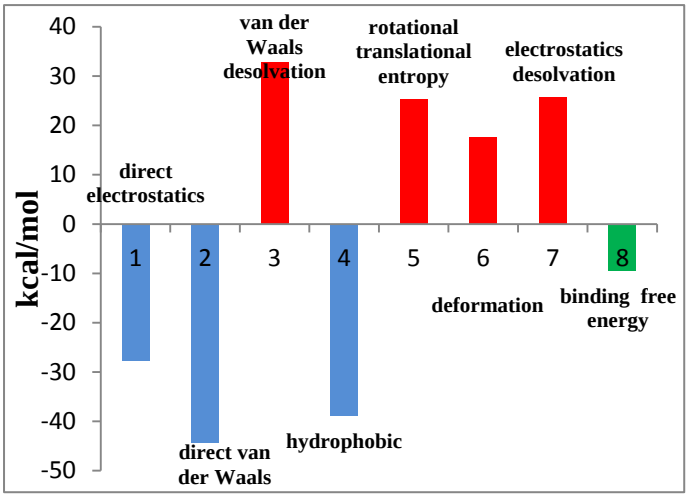
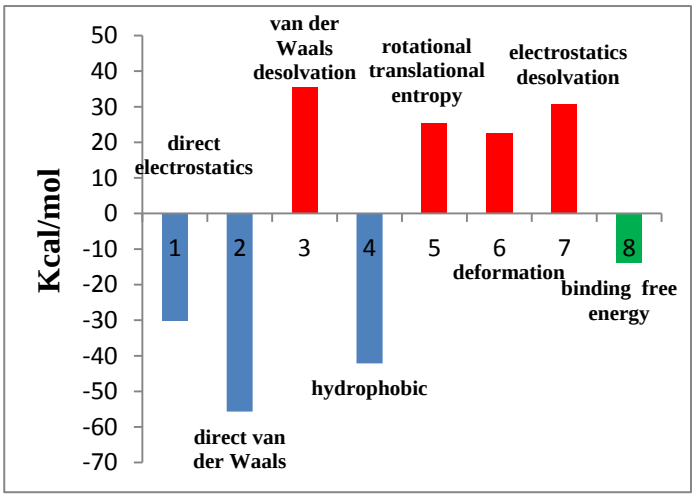


Figure S17 A cross sectional view of the catalytic and the S1' region of the final snapshot from a 10ns MD trajectory on the designed Molecule13-MMP13 complex.



A.



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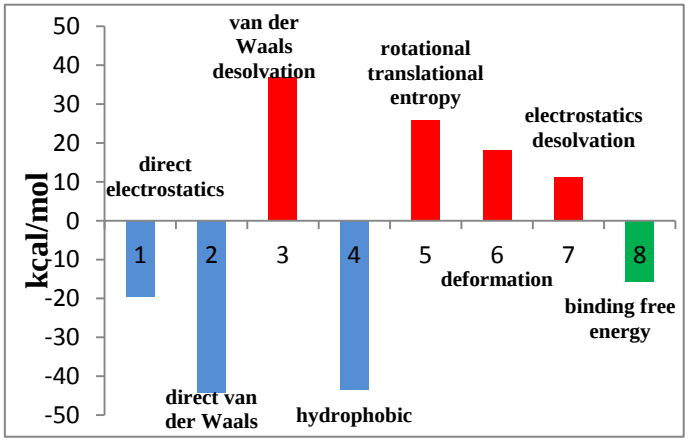

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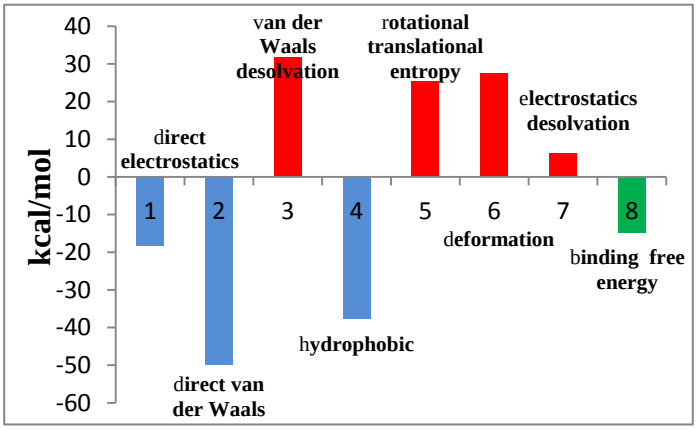

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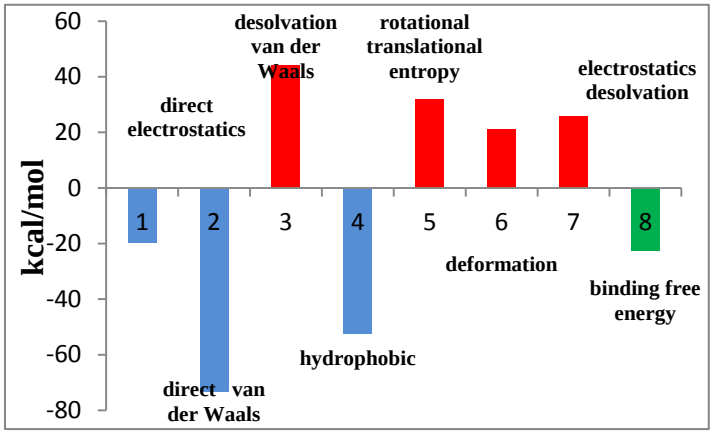

E.

Figure S18. A histogram of the calculated primary contributions to the binding free energy for A.) Molecule2-MMP-2, B.) Molecule3-MMP-3, C.) Molecule8-MMP-8, D.) Molecule9-MMP-9 and E.) Molecule13-MMP-13 docked complexes. The negative values (blue color) are favorable and the positive values (red color) are unfavorable to binding. The net binding free energy (green color) represents a sum of the seven bars viz. the direct electrostatics, the direct van der Waals, the hydrophobic, the rotational translational entropy, the deformation expense and the electrostatics desolvation term to obtain the net binding free energy.

Table S1. Docking and scoring study on some known MMP inhibitors.

Sl. No.	PDBID[a]	EBFE[b] (kcal/mol)	PBFE[c] (kcal/mol)	RMSD[d] (Å)
1	1g4k	-7.87	-7.97	0.94
2	1jj9	-7.97	-5.45	0.76
3	1ciz	-10.28	-9	3.77
4	1sln	-9.06	-9.95	0.55
5	1mmp	-8.51	-8.72	1.62
6	1hy7	-8.44	-7.84	1.015
7	1c3i	-8.01	-8.01	0.63
8	1c8t	-8.01	-9	0.72
9	1jao	-6.8	-5.32	0.53
10	2tcl	-11.12	-10.61	0.42
11	966c	-10.56	-7.49	0.9
12	456c	-13.5	-12.89	0.89
13	830c	-12.82	-11.8	0.9
14	1d8m	-11.76	-8.11	1.08
15	1bqo	-10.7	-10.07	1.19
16	1d8f	-10.7	-8.7	0.97
17	1b3d	-10.52	-8.83	0.45
18	1mmq	-10.26	-9.73	1.48
19	1jap	-6.52	-5.5	2.64
20	1caq	-10.67	-10.26	0.52
21	1mmr	-8.03	-6.18	1.64
22	1b8y	-10.85	-9.12	0.76
23	1a85	-10.49	-9.92	0.66
24	1-Jan	-6.52	-6.19	0.46
25	1jaq	-6.19	-7.14	0.54
27	1cxv	-13.5	-11.43	0.8
28	1a86	-5.52	-6.59	0.61
29	1hv5	-10.98	-13.03	1.2
30	1hfs	-11.87	-11.4	0.80

[a]Protein Data Bank ID
[b]Experimental Binding Free Energies of the known MMP inhibitors in kcal/mol
[c]Predicted Binding Free Energies in kcal/mol of the top ranked docked structure given as an output by *Sanjeevini* software
[d]Root Mean Square Deviation in Å of the crystal structure and the top ranked docked structure.

Table S2. A comparison of binding free energies of 16 known MMP inhibitors estimated by *Sanjeevini and Autodock* softwares versus experiment.

Sl. No.	PDBID[a]	EBFE[b] (kcal/mol)	PBFE[c] (kcal/mol) *Sanjeevini*	PBFE[d] (kcal/mol) *Autodock*
1	966c	-10.56	-7.49	-11.75
2	1b8y	-10.85	-9.12	-12.27
3	1caq	-10.67	-10.26	-13.98
4	1ciz	-10.28	-9	-15.78
5	1hfs	-11.87	-11.4	-14.52
6	1mmp	-8.51	-8.72	-11.95
7	1mmq	-10.26	-9.73	-11.48
8	1mmr	-8.03	-6.18	-8.75
9	1a85	-10.49	-9.92	-8.78
10	1a86	-5.52	-6.59	-9.32
11	1jao	-6.8	-5.32	-11.46
12	1jaq	-6.19	-7.14	-9.57
13	456c	-13.5	-12.89	-12.45
14	830c	-12.82	-11.8	-11.68
15	1jap	-6.52	-5.5	-8.31
16	1hv5	-10.98	-13.03	-14.45

[a]Protein Data Bank ID
[b]Experimental Binding Free Energies of the known MMP inhibitors in kcal/mol
[c]Predicted Binding Free Energies in kcal/mol of the top ranked docked structure given as an output by *Sanjeevini* software
[d] Predicted Binding Free Energies in kcal/mol of the top ranked docked structure given as an output by *Autodock* software

Table S3. Molecular properties of the Molecules designed against different MMPs

Molecular Properties / Molecules Designed	Molecular Mass (Daltons)	Number of Hydrogen Bond Donors	Number of Hydrogen Bond Acceptors	Log P
Molecule2	418	2	6	0.39
Molecule3	487	2	8	2.88
Molecule8	512	1	7	2.28
Molecule9	472	4	8	1.11
Molecule13	459	3	7	5.18