

**Table S1** The ten lowest RMSD predicted loop configurations of GART, CYP119, and enolase. The ranked position of each loop configuration is shown after scoring with the DFIRE, single snapshot MM/GBSA, trajectory MM/GBSA, and the Optimized MM/GBSA-dsr scoring functions (with and without co-crystallized ligand).

Protein System	RMSD <sup>a</sup>	Without co-crystallized ligand			With co-crystallized ligand			
		DFIRE <sup>b</sup>	Snapshot MM/GBSA <sup>c</sup>	Traj MM/GBSA <sup>d</sup>	Optimized MM/GBSA-dsr <sup>e</sup>	Snapshot MM/GBSA <sup>c</sup>	Traj MM/GBSA <sup>d</sup>	Optimized MM/GBSA-dsr <sup>e</sup>
GART	0.57	31	3	9	87	5	10	40
	0.74	19	46	74	68	26	30	44
	1.02	45	91	69	18	36	23	47
	1.12	62	64	20	49	4	41	86
	1.20	47	96	57	13	10	27	84
	1.29	34	48	16	41	72	15	24
	1.31	56	29	49	82	15	29	76
	1.35	73	14	31	98	31	36	64
	1.37	59	24	26	94	32	25	65
	1.38	69	23	1	80	11	40	68
CYP119	1.61	50	6	37	87	2	12	74
	1.79	54	9	10	64	8	14	39
	1.80	81	50	87	96	29	25	62
	2.02	69	24	66	33	31	52	72
	2.18	88	11	8	68	96	100	86
	2.25	91	91	29	81	93	84	81
	2.31	99	42	92	72	100	92	92
	2.39	59	56	27	82	36	97	73

	2.41	33	81	30	91	81	79	91
	2.43	66	16	56	78	26	48	55
Enolase	1.43	81	6	18	97	62	66	10
	1.70	12	9	38	83	59	41	32
	1.75	39	25	77	29	29	19	12
	1.79	50	15	59	98	3	59	96
	2.02	31	17	11	89	25	37	90
	2.05	13	91	4	23	97	95	2
	2.07	70	51	97	53	77	93	7
	2.07	30	10	43	100	11	2	47
	2.09	23	60	57	40	7	90	58
	2.10	71	30	20	76	4	83	93

<sup>a</sup> RMSD in Å to known X-ray loop configuration, backbone atoms only

<sup>b</sup> DFIRE scoring function was used to rank predicted loop configurations

<sup>c</sup> a single minimized structure was used to calculate a MM/GBSA score and rank loop configurations

<sup>d</sup> 20 snapshots from an MD trajectory was used to calculate a MM/GBSA score and rank loop configurations

<sup>e</sup> Optimized MM/GBSA-dsr scoring function used to score and rank loop configurations