SUPPORTING INFORMATION

Elucidating the Interaction between Pyridoxine 5′-Phosphate Oxidase and Dopa Decarboxylase: Activation of B6-Dependent Enzyme

Mohammed H. AL Mughram, Mohini S. Ghatge, Glen E. Kellogg and Martin K. Safo *

Department of Medicinal Chemistry and the Institute for Structural Biology, Drug Discovery, and Development, School of Pharmacy, Virginia Commonwealth University, Richmond, VA 23298, USA
* Correspondence: msafo@vcu.edu

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Table S1. Cluspro2.0 docking results for the top 10 clusters of PNPO and apoDDC (PDB: 3RCH) complex, along with calculated HINT scores.

Cluster	Members	%	HINT score	Hydrogen Bond	Acid/Base	Hydrophobic	Acid/Acid	Base/Base	Hydroph./Polar
0	76	7.6	2032.209	8596.166	3226.822	2706.76	-789.2139	-3385.264	-8323.062
1	71	7.1	1152.42	9578.741	2970.288	2839.457	-645.8171	-4312.954	-9277.295
2	43	4.3	6336.489	13193.75	3990.281	2181.616	-904.4463	-4329.23	-7795.483
3	37	3.7	2868.208	6721.397	1398.719	2037.818	-134.4676	-1730.892	-5424.368
4	36	3.6	7867.385	17079.55	4806.177	2496.075	-1252.961	-5930.431	-9331.025
5	35	3.5	7337.191	15509.96	3977.718	3029.297	-1070.994	-4849.986	-9258.809
6	32	3.2	3616.5	10424.32	2387.766	1955.174	-723.9514	-3269.073	-7157.736
7	32	3.2	4732.194	13330.25	4406.887	2810.313	-815.2784	-6449.8	-8550.173
8	29	2.9	5496.712	16148.84	4427.738	3060.189	-1024.375	-5939.218	-11176.46
9	26	2.6	-339.0726	7988.533	2497.652	2166.552	-623.7452	-4173.083	-8194.98

Table S2. Cluspro2.0 docking results for the top 10 clusters of PNPO and apoDDC-AF (model) complex, along with calculated HINT scores.

Cluster	Members	%	HINT score	Hydrogen Bond	Acid/Base	Hydrophobic	Acid/Acid	Base/Base	Hydroph./Polar
0	52	5.2	8649.985	13017.68	1870.801	1606.691	-733.7706	-2387.735	-4723.683
1	45	4.5	1789.329	10401.7	3242.745	2781.445	-505.138	-4667.735	-9463.684
2	44	4.4	549.0074	4843.478	2555.973	2012.546	-557.3123	-2878.877	-5426.8
3	43	4.3	3389.987	9625.224	2650.935	2134.361	-565.8962	-4081.872	-6372.764
4	40	4	745.7246	5119.332	1937.121	2381.634	-291.5302	-3445.69	-4955.142
5	36	3.6	2669.604	9728.706	2697.509	2230.926	-206.4271	-5673.592	-6107.517
6	34	3.4	668.2127	3655.788	1401.505	1523.839	-217.4465	-1175.301	-4520.171
7	30	3	5486.292	13080.61	3581.48	2238.726	-556.8046	-4326.55	-8531.171
8	29	2.9	2146.309	6029.135	1373.44	1534.223	-240.0219	-1718.776	-4831.691
9	29	2.9	348.5145	8042.262	2605.485	2045.279	-559.587	-4772.616	-7012.308

Table S3. Cluspro2.0 docking results for the top 10 clusters of PNPO and holoDDC complex (PDB 1JS3), along with calculated HINT scores.

Cluster	Members	%	HINT score	Hydrogen Bond	Acid/Base	Hydrophobic	Acid/Acid	Base/Base	Hydroph./Polar
0	58	5.8	2222.017	5653.545	1865.784	1384.034	-698.7088	-1508.832	-4473.805
1	55	5.5	2401.835	5388.355	2648.495	1539.826	-533.5378	-2249.115	-4392.188
2	52	5.2	2085.665	5640.911	2166.836	1396.976	-759.2861	-2337.534	-4022.238
3	47	4.7	11061.66	21090.79	4964.848	1864.776	-1026.855	-6830.125	-9001.772
4	45	4.5	859.9533	4174.195	2288.513	1464.489	-802.5218	-2194.99	-4069.731
5	44	4.4	11544.62	19866.46	4463.452	1803.829	-778.8778	-5986.074	-7824.172
6	44	4.4	13924.61	24358.32	5873.867	1794.173	-1151.033	-7894.123	-9056.592
7	33	3.3	9606.528	18262.32	5231.149	1945.587	-838.3188	-6069.647	-8924.565
8	29	2.9	-2173.584	5026.435	2564.959	1957.44	-817.2881	-3772.891	-7132.24
9	26	2.6	3512.605	11744.63	3275.028	1964.022	-1030.814	-4382.392	-8057.873

Table S4. Cluspro2.0 docking results for the top 10 clusters of PNPO and holoDDC (model) complex, along with calculated HINT scores.

Cluster	Members	%	HINT score	Hydrogen Bond	Acid/Base	Hydrophobic	Acid/Acid	Base/Base	Hydroph./Polar
0	78	7.8	4745.655	11350.68	3113.448	2308.501	-660.892	-4317.154	-7048.932
1	74	7.4	4755.787	11107.45	3106.383	2093.718	-882.9797	-3577.388	-7091.4
2	32	3.2	181.1883	4154.712	1557.112	1461.816	-168.1234	-2036.553	-4787.775
3	30	3	8928.14	14843.65	3738.476	1728.813	-807.2473	-3650.755	-6924.799
4	30	3	7503.392	14103.93	3613.991	1741.297	-585.3145	-4067.964	-7302.544
5	28	2.8	5248.711	10989.66	2477.844	1664.984	-412.624	-4168.736	-5302.421
6	26	2.6	3973.426	9907.376	2247.175	1939.506	-331.0345	-3082.377	-6707.22
7	23	2.3	4787.83	10147.88	2238.768	1874.134	-267.4978	-3531.957	-5673.502
8	19	1.9	3520.338	8087.063	2091.333	1954.558	-432.3741	-3062.331	-5117.911
9	19	1.9	2944.349	7515.712	2115.851	1722.862	-265.2529	-2371.483	-5773.34

Table S5. Key interactions at the domain interface for the PNPO•apoDDC complex model as predicted by MD simulations.

Donor	Acceptor	Occupancy
ARG88-sc	GLU421-sc	69.30%
ARG88-sc	ASP442-sc	67.93%
GLU114-sc	LYS207-sc	53.60%
TYR183-sc	GLU181-sc	47.62%
HIS439-sc	ARG88-sc	41.23%
TYR332-sc	GLN214-sc	36.13%
ARG197-sc	THR238-bb	36.10%
GLU181-sc	LYS187-sc	27.66%
ARG228-sc	GLU114-sc	20.30%
GLU480-sc	LYS119-sc	14.61%
GLU227-sc	LYS204-sc	13.70%

DDC chainA
DDC chainB
PNPO chainA
PNPO chainB

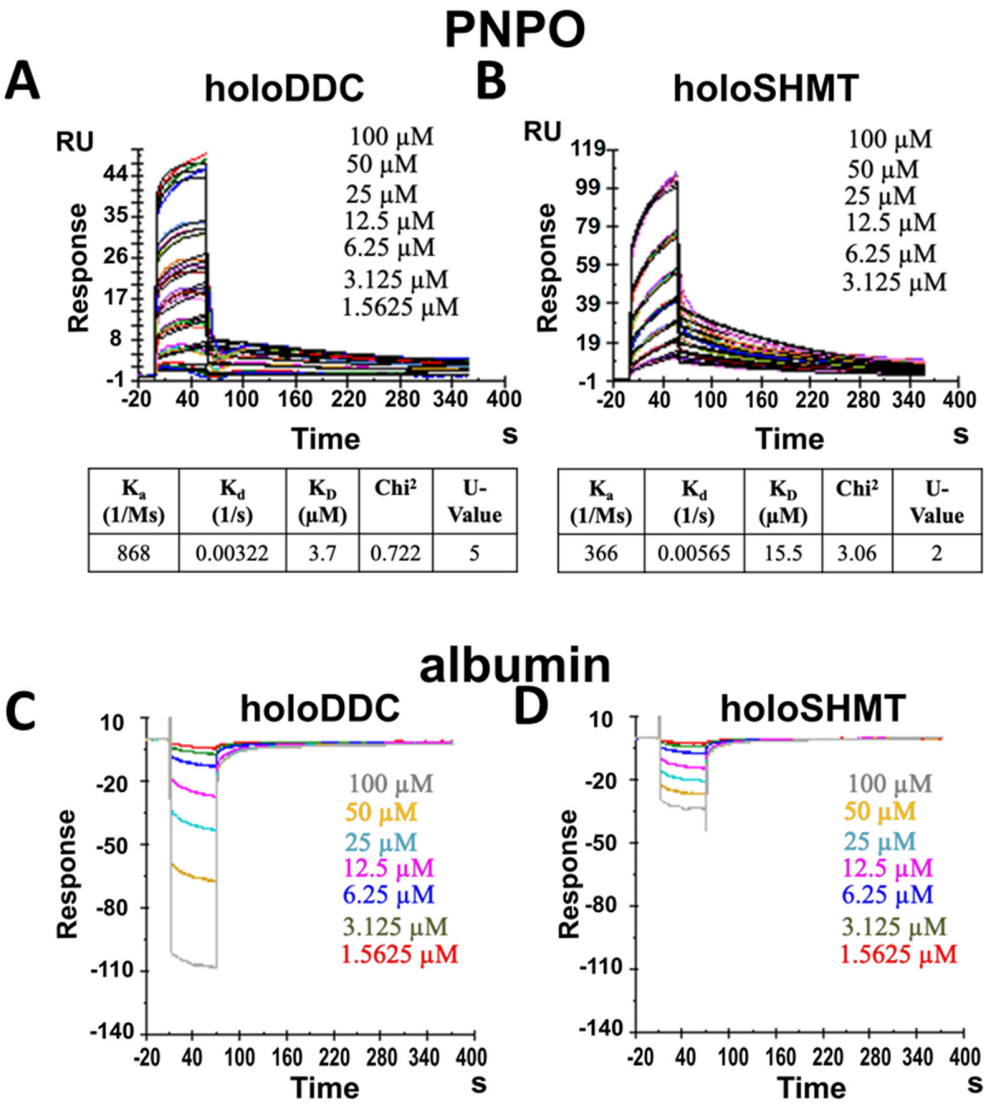
Table S6. Key interactions at the domain interface for the PNPO•holoDDC complex model as predicted by MD simulations.

Donor	Acceptor	Occupancy
THR246-sc	ASP240-sc	66.14%
SER193-sc	ASP240-sc	59.64%
THR238-sc	SER104-sc	58.89%
LYS91-sc	GLU425-sc	43.82%
SER193-bb	ASP240-sc	35.91%
THR54-sc	TYR332-bb	35.48%
ARG258-sc	ASP228-sc	35.35%
ARG426-sc	ASP89-sc	32.66%
TYR332-bb	LEU53-bb	28.24%
LYS327-sc	GLU251-sc	26.41%
ARG439-sc	GLU257-sc	17.26%
ARG347-sc	ASP253-sc	13.01%

DDC chainA
DDC chainB
PNPO chainA
PNPO chainB

Table S7. *In silico* alanine scanning of the PNPO•apoDDC-AF complex model obtained by hierarchical clustering of MD trajectories. Binding energy changes ($\Delta\Delta G = \Delta G_{wild\text{-}type} - \Delta G_{ALA}$) for key interacting amino acid residues at the interface with respect to clusters as predicted by Robetta server, where negative $\Delta\Delta G$ values (kcal mol^{-1}) indicate unfavorable replacement.

Residue no.	chainID	ΔΔG (kcal/mol)								AV	STDDEV
		cluster1	cluster2	cluster3	cluster4	cluster5	cluster6	cluster7	cluster8		
103	DDC_B	0.38		0.63	0.67	0.63				0.5775	0.13301
176	DDC_B	0.96	1.1	0.4		1.14	0.22			0.764	0.42459
326	DDC_B		0.34				0.23	0.24		0.27	0.06083
327	DDC_B	0.29	1.6	1.47	0.28	0.22	0.3	0.38	0.66	0.65	0.56338
328	DDC_B	0.66	0.99	0.83		0.62	0.65	0.82	0.6	0.7386	0.14462
331	DDC_B	0.4	0.49	0.31	0.21	0.46	0.3	0.13	0.36	0.3325	0.12186
332	DDC_B	2.42	2.29	2.68	2.47	2.72	2.47	2.42	2.56	2.5038	0.14292
333	DDC_B	0.36	0.27	0.33			0.27			0.3075	0.045
353	DDC_B	0.61		0.69	1.27	1.2	1.06	0.92	0.83	0.94	0.24993
181	DDC_A		0.7	1.27	0.97	0.17	-0.07			0.608	0.55436
197	DDC_A	3.69	2.95	2.32	2.66	3.37	2.8	2.29	2.95	2.8788	0.48144
200	DDC_A	0.95	0.97	0.66	0.68	2.4	0.83	1.04	0.64	1.0213	0.57791
201	DDC_A	0.34	0.52					0.54		0.4667	0.11015
207	DDC_A	0.51	1.51	1.83	2.4		0.98	2.65	0.77	1.5214	0.81871
228	DDC_A	1.14	0.33		0.96	1.08	1.18	2.11	0.31	1.0157	0.60764
417	DDC_A	1.03	0.61	0.93	0.98	0.65	3	1.92	0.54	1.2075	0.84468
421	DDC_A	0.77	4.15	0.59	1.47	1.05	1.45	2.7	3.14	1.915	1.27286
441	DDC_A		0.11	0.1	0.06	0.12	0.01	0.03	0.12	0.0786	0.04525
442	DDC_A	0.57	-0.48	0.66	0.6	0.99	1.3	0.58	0.41	0.5788	0.51352
51	PNPO_B	0.08		0.23		0.36				0.2233	0.14012
56	PNPO_B		1.06	1.11		0.43				0.8667	0.37899
88	PNPO_B	1.37	4.59	1.06	1.95	1.49	1.79	3.02	3.49	2.345	1.23077
119	PNPO_B	0.13			0.4		0.67	0.51	0.05	0.352	0.25927
212	PNPO_B	1.09	0.67	1.18		0.96	1.05	1.06	0.78	0.97	0.18221
214	PNPO_B	0.21	0.76	0.83	0.68	0.92	0.43	0.52	0.71	0.6325	0.23249
234	PNPO_B	0.33	0.39	0.38	0.41	0.51	0.34	0.39	0.47	0.4025	0.06112
236	PNPO_B	0.48	0.67	0.72	0.75	0.23	0.79	0.52	0.32	0.56	0.20743
238	PNPO_B	0.23			0.35	0.39				0.3233	0.08327
240	PNPO_B	0.99	0.52	-0.21	-0.14		0.24	-0.11	-0.18	0.1586	0.45466
241	PNPO_B		0.96	-0.01	-0.03	-0.08	-0.05	-0.05		0.1233	0.41054
249	PNPO_B		1.34	0.72	-0.11	0.15	0.91		0.21	0.5367	0.54639
252	PNPO_B	-0.07		-0.08	0.28			0.42		0.1375	0.25198
253	PNPO_B	0.2	-0.17		0.34	0.15	0.49	-0.09	0.82	0.2486	0.34036
88	PNPO_A	1.31	0.33	1.34	1.18	1.74	2.12	1.53	1.57	1.39	0.51879
114	PNPO_A	0.98	0.27	0.03	1.44	1.71	1.55	2.32	0.52	1.1025	0.7895
119	PNPO_A	0.54	0.08	0.24	0.69		0.73	-0.43	0.32	0.31	0.40398
183	PNPO_A		0.84	0.64	1.18	-0.04	0.22			0.568	0.48592
187	PNPO_A		-0.15	0.45		0.2				0.1667	0.30139
204	PNPO_A	0.95	0.77	0	0	0.57	0.13	0.16	1.02	0.45	0.42815



K_a (1/Ms)	K_d (1/s)	K_D (µM)	Chi²	U-Value
868	0.00322	3.7	0.722	5

K_a (1/Ms)	K_d (1/s)	K_D (µM)	Chi²	U-Value
366	0.00565	15.5	3.06	2

Figure S1. SPR results for the binding of PNPO to immobilized holoDDC and holoSHMT. (A) SPR sensorgram binding of PNPO to holoDDC; (B) SPR sensorgram binding of PNPO to holoSHMT (positive control); and (C-D) Negative control, binding of albumin to holoDDC and holoSHMT, respectively. Flow rate of all analytes were maintained at 50 µL/min, and injections of 100 µM to 1.5625 µM (from top to bottom) were made. The contact and dissociation times used for all analytes were 60 s and 300 s, respectively. One 15 s pulse of 1 M NaCl was injected for surface regeneration. All analytes were injected in triplicate.