***A. baumannii* histone acetyl transferase Hpa2: Optimization of homology modeling, analysis of protein–protein interaction and virtual screening**

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ELECTRONIC SUPPLEMENTARY INFORMATION

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Figure S1 **A)** Multiple sequence alignment of Hpa2 sequence with its templates having sequence similarity up to 29%, **B)** Multiple sequence alignment of Hpa2 sequence with 1XEB and 1QSM protein templates, (the area highlighted in red represents the residues conserved between all the aligned proteins, and that in yellow represents the residues similar between at least two of the aligned proteins, purple box is showing the motif residues of GNAT superfamily), figures are generated using *ESPrpt*.

Table S1. Summary of structural validation programs and parameters values for Hpa2 monomer model generated by the Swiss-model/Modeller programs and optimized model using *FoldX*.

Server	Parameters	Hpa2 Model (Swiss-model)	Hpa2 Model (Modeller)	Repaired Hpa2 Model
<i>PROCHECK</i>	Residues in core, Allowed	85.1%, 11.1%	82.8%, 12.6%	85.4%, 10.7%
	Generously allowed and	2.5%	3.4%	2.5%
	Disallowed regions	1.4%	1.2%	1.4%
<i>PROSA</i>	PROSA Z-score	-5.75	-5.70	-5.75
<i>Verify3D</i>	Residues having averaged 3D-1D score > 0.2	75.01%	66.13%	88.24%
<i>Errat</i>	Overall quality factor	64.84%	50.38%	85.29%

Figure S2. Docked pose of acetyl-CoA (magenta) superimposed on the experimental pose (from yeast Hpa2 *i.e.*, 1QSM Red) showing interactions with motif residues (Blue coloured) *Q**R-X-X-G-X-G**A* of GNAT superfamily.

Table S2. PDB files, residues involved in the formation of experimental dimer interface and rmsd values for redocked experimental dimers calculated using experimental structure as reference.

PDB/ MODEL	Interface residues	RMSD value
1XEB-AC	A-Chain: H72, E73, G74, Q75, V77, Y114, V133, T134, Y137 and R148. C-Chain: V70, E73, G74, Q75, V77, Y114, V133, T134, and R148.	3.02
1J4J-AB	A-Chain: Q16, L17, Q121, D124, E125, E127, Q128, K182 and L184. B-Chain: Q16, L17, R18, T21, E23, H27, Y28, A79 and D81.	2.35
1GHE-AB	A-Chain: H30, G31, P100, S101, R103, R105 and V136. B-Chain: H19, Q23, D42, M43, Q44 and Y47.	3.23
2DXQ-AB	A-Chain: L16, Q27, D30, P31, L33, A38, V41, A44, M45, P49, L51, V71, P72, N73, L74, T75, R76, A77, A78, R79, Y81, F83, F111, C115, Y116, V118, M119, L121, T122, Y133, F138, V139, K142, T143, F145, Q146, I147, R148 and G149. B-Chain: L16, Q27, D30, P31, L33, A38, V41, G48, P49, P72, N73, L74, R76, A77, A78, R79, Y81, F83, N86, R104, Y116, K117, V118, M119, L120, L121, T122, Q140, V139, N141, K142, T143, F145, Q146, I147, and R148.	6.80
1QSM-AB	A-Chain: Y29, Y33, V35, F37, P38, D40, L41, F44, A45, R48, F49, I54, K55, M56, N74, F76, M79, T80, T81, W82, D83, F84, K85, D86, K87, Y89, N91, D92, Q110, Y113, D114, A116, D117, P122, S123, V124, Y125, W126, C127, T128, D129, E130, S131, Q136, Y139, V140, K141, V142, Y144, K145, A146, P147, K148, I149, L150, Y151, K152, R153, K154 and Y156. B-Chain: W26, Y29, Y33, V35, F37, P38, D40, L41, F44, N45, R48, F49, I54, K55, M56, N74, F76, N77, M79, T80, T81, W82, D83, F84, K85, D86, K87, Y89, N91, D92, Q110, Y113, D114, A116, D117, P122, S123, V124, Y125, W126, C127, T128, D129, E130, Q136, Y139, V140, K141, V142, Y144, K145, A146, P147, K148, I149, Y151, K152, R153, K154 and Y156.	4.79
Dimer-Hpa2	A-Chain: Q63, H64, P98, Y99, G121, D122, V123, Y124 and D133. B-Chain: D38, F39, T42, L61, P62, Q63, H64, V123, Y124, Q125 and D126.	4.41

Table S3. ZINC_ID and binding affinities of the best ten compounds with monomer as well as dimer obtained through virtual screening (out of 760 which are obtained from ZINC database through substrate structure based search). The compounds in Red exhibit good binding affinity at both the binding sites.

Compounds binding at interface of dimer	Binding energy (kcal/mol)	Compounds binding at active site of monomer	Binding energy (kcal/mol)
ZINC65731330	-12.10	ZINC43411693	-10.20
ZINC08215434	-12.10	ZINC85629877	-10.10
ZINC85564657	-12.00	ZINC94303217	-09.90
ZINC85629877	-11.90	ZINC43411702	-09.90
ZINC85564663	-11.80	ZINC08551088	-09.90
ZINC08551088	-11.70	ZINC85574911	-09.80
ZINC85534368	-11.60	ZINC44559643	-09.80
ZINC94303217	-11.60	ZINC43411699	-09.80
ZINC87515504	-11.50	ZINC13829348	-09.80
ZINC85564649	-11.50	ZINC13829346	-09.80

Figure S4. A) Experimental pose of acetyl-CoA (magenta: 1GHE) superimposed on the experimental pose (blue: 1QSM), showing differences in the conformation having optimal binding interactions. 1GHE protein is represented as cyan colour cartoon. B) Redocked pose of acetyl-CoA (magenta) superimposed on the experimental pose (blue: 1QSM) of yeast Hpa2.

Figure S5A. Structures of best ten compounds showing good binding with monomer in virtual screening.

ZINC43411693

ZINC85629877

ZINC94303217

ZINC43411702

ZINC08551088

ZINC85574911

ZINC44559643

ZINC43411699

ZINC13829348

ZINC13829346

Figure S5B. Structures of best ten compounds showing good binding with dimer in virtual screening.

Figure S6. Redocked pose of acetyl-CoA (magenta) superimposed on inhibitors docked pose (blue: ZINC08215434, green: ZINC85629887, cyan: ZINC65731330 and marine: ZINC85564657) at the model active site (green cartoon) to depict the similarity in binding interactions.