ACCSCIENCE PUBLISHING

INNOSC Theranostics and Pharmacological Sciences

ORIGINAL RESEARCH ARTICLE

Drug repurposing approach for identifying Pfmrk inhibitors as potential antimalarial agents: an *in silico* analysis

Supplementary File

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CLUSTAL O(1.2.4) multiple sequence alignment

sp|P50613|CDK7_HUMAN        MALDVKSRAKRYEKLDFLGEGQFATVYKARDKNTNQIVAIKKIKLGHRSEA--KDGINRT     58
tr|P90584|P90584_PLAFA      --MENNSTERYIFKPNFLGEGSYGKVYKAYDTILKKEVAIKKMKLNEISNYIDDCGINFV     58
                              :: :*  :   * :*****.:..**** *.  :: *****:**.. *:   . *** .

sp|P50613|CDK7_HUMAN        ALREIKLLQELSHPNIIGLLDAFGHKSNISLVFDFMETDLEVIIKDNSLVLTPSHIKAYM     118
tr|P90584|P90584_PLAFA      LLREIKIMKEIKHKNIMSALDLYCEKDYINLVMEIMDYDLSKIINRK-IFLTDSQKKCIL     117
                             *****:::*:.* **:. ** : .*. *.**:::*: **. **: : :.** *: *. :

sp|P50613|CDK7_HUMAN        LMTLQGLEYLHQHWILHRDLKPNNLLLDENGVLKLADFGLAKSFGSP-------------     165
tr|P90584|P90584_PLAFA      LQILNGLNVLHKYYFMHRDLSPANIFINKKGEVKLADFGLCTKYGYDMYSDKLFRDKYKK     177
                            *  *:**: **::::::****.* *:::::* :*******...:*

sp|P50613|CDK7_HUMAN        NRAYTHQVVTRWYRAPELLFGARMYGVGVDMWAVGCILAELLLRVPFLPGDSDLDQLTRI     225
tr|P90584|P90584_PLAFA      NLNLTSKVVTLWYRAPELLLGSNKYNSSIDMWSFGCIFAELLLQKALFPGENEIDQLGKI     237
                            *   * :*** ********:*:. *. .:***:.***:*****:  ::**:.::*** :*

sp|P50613|CDK7_HUMAN        FETLGTPTEEQWPDMCSLPDYVTFKSFPGIPLHHIFSAAGDDLLDLIQGLFLFNPCARIT     285
tr|P90584|P90584_PLAFA      FFLLGTPNENNWPEALCLPLYTEFTKATKKDFKTYFKIDDDDCIDLLTSFLKLNAHERIS     297
                            *  ****.*::**:  .** *. *..     ::  *.  .** :**: .:: :*   **:

sp|P50613|CDK7_HUMAN        ATQALKMKYFSNRPGPTPGCQLPRPNCPVETLKEQSNPALAIKRKRTEALEQGGLPKKLI     345
tr|P90584|P90584_PLAFA      AEDAMKHRYFFNDPLPCDISQLPFNDL--------------------------------     324
                            * :*:* :** * * *   .***  :

sp|P50613|CDK7_HUMAN        F   346
tr|P90584|P90584_PLAFA      -   324
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Figure S1. Multiple sequence alignment analysis between Pfmrk and hCDK7 using CLUSTALO (1.2.4) indicates a sequence identity of 36.28%.

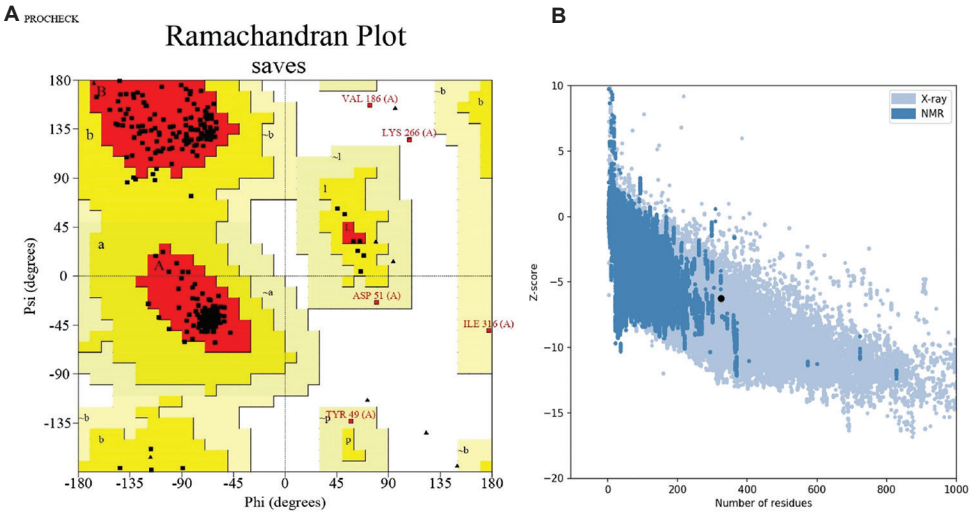

Figure S2. (A) Ramachandran plot for the modeled structure of Pfmrk was assessed using Procheck. 92.3% of residues fall within the most favored regions, while only 0.7% residues are found in disallowed regions. (B) The quality of the modeled structure of Pfmrk was assessed using the QMEAN score through the ProSA web tool, yielding a Z-score of –6.25.

Table S1. Solvent-accessible surface area of model protein in apostate and in complex with various ligands

Model	SASA (nm²)
Apoprotein	184.0569
Alvesco	181.9433
Donovex	178.1943
Lurasidone	181.3419
Orap	183.1197
Vorapaxar	180.9219

Table S2. Hydrogen bond analysis between apoprotein and various ligands used in the study

Ligands	H-bonding	Average H-bonds
Alvesco	Lys100, Ser138, Ala140	~1
Donovex	Met94, Asp154, Ile 93, Ser138, Ala140, Phe143	~1
Lurasidone	Gly22, Lys39, Lys100	~1
Orap	Lys23, Asp154	~2
Vorapaxar	Glu18, Lys26, Tyr96, Lys100	~1

Table S3. Secondary structure analysis of apoprotein and apoprotein in various complexes with different ligands

Ligands	Coil (%)	B-Sheet (%)	B-bridge (%)	Bend (%)	Turn (%)	A-Helix (%)	5-Helix (%)	3-Helix (%)
Apoprotein	28	13	1	15	10	31	0	3
Alvesco	29	12	1	15	12	27	2	1
Donovex	27	12	1	16	12	27	2	2
Lurasidone	28	13	1	14	11	32	0	3
Orap	27	13	1	13	13	31	0	2
Vorapaxar	28	12	2	15	12	28	3	1

Table S4. The original use and year of approval of the FDA-approved drugs

Drug	Original use	Year of approval
Lurasidone	Schizophrenia and bipolar I disorder	2010
Vorapaxar	Myocardial infarction	2014
Donovex	Psoriasis	1999
Alvesco	Nasal symptoms	2008
Orap	Tourette's disorder	1985