



HOMOLOGY MODELING, DOCKING AND A COMPARATIVE STUDY OF THE SELECTIVITY OF FEW HDAC INHIBITORS ON PFHDAC-1 AND HUMAN HDAC MODELS

NNENNA W. ODOZI^{1*} AND PETER FRISTRUP²

¹University of Ibadan, Nigeria and ²Denmark Technical University

ABSTRACT

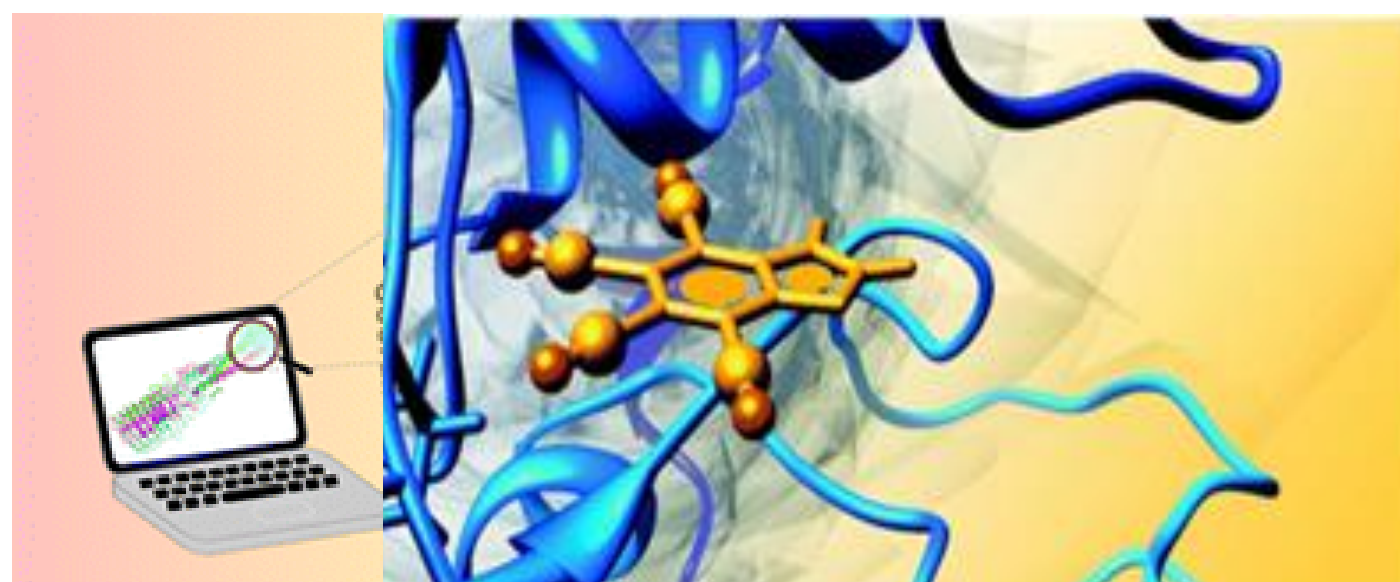
In the light of the dawn of multi-drug resistant malaria parasites, Plasmodium histone deacetylase 1 (PfHDAC-1) was explored as a potential antimalarial enzyme therapeutic target.

OPLS/GBSA potential set up was used to construct the ligand-refined homology model of PfHdac 1 and docking studies revealed that YC-II-88 inhibitor was more selective towards PfHdac 1 than for the human HDAC.

INTRODUCTION



- Malaria a mosquito borne infectious disease caused by plasmodium parasites is widely spread in tropical and subtropical regions of the world.
- The protozoan parasites have become increasingly resistant to drugs in use
- Development of drugs attacking crucial targets in the mechanism of action of the malaria pathogen is imperative.



COMPUTATIONAL DETAILS

Identification of Related Template Structure from Data base

Selection of Templates (1C3R from HDLP and 1TC4 from hHDAC)

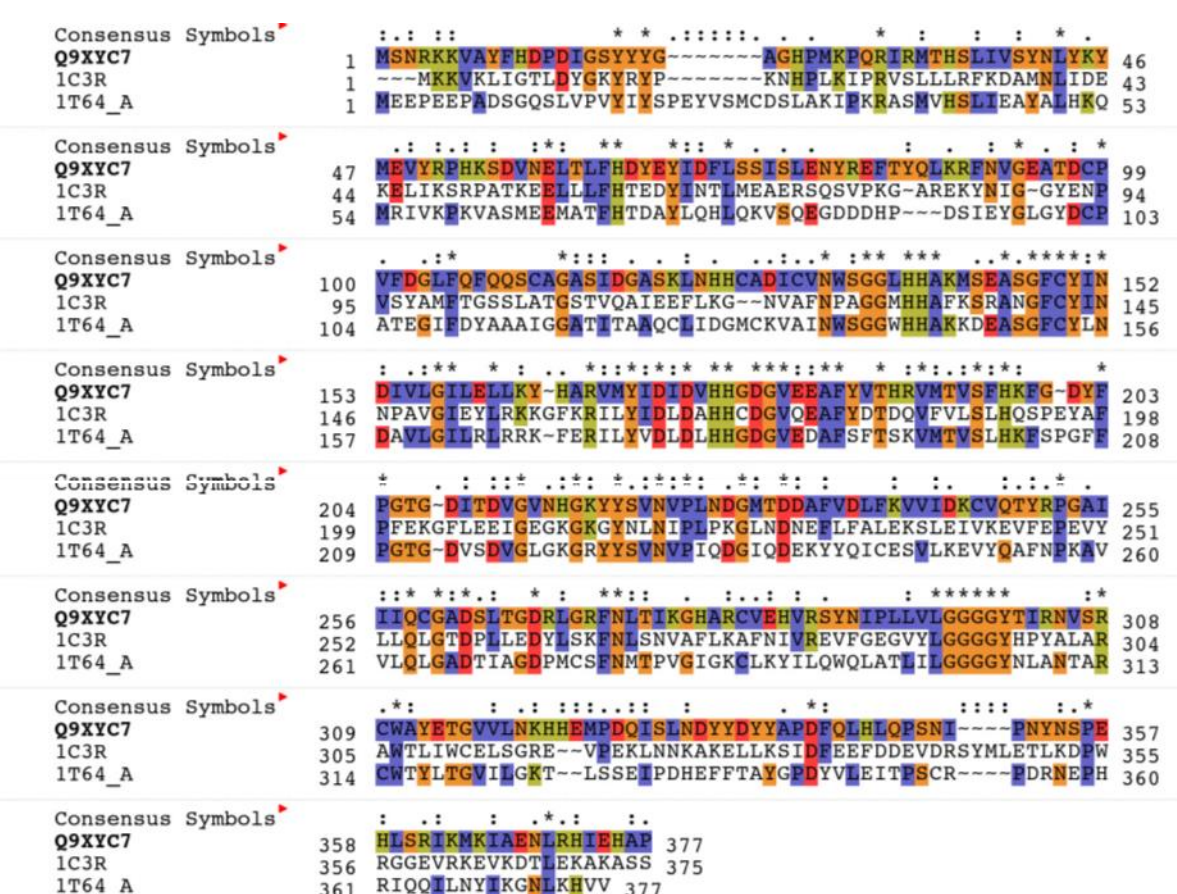
Extraction and Alignment of Sequence

Model Building/ Structure validation

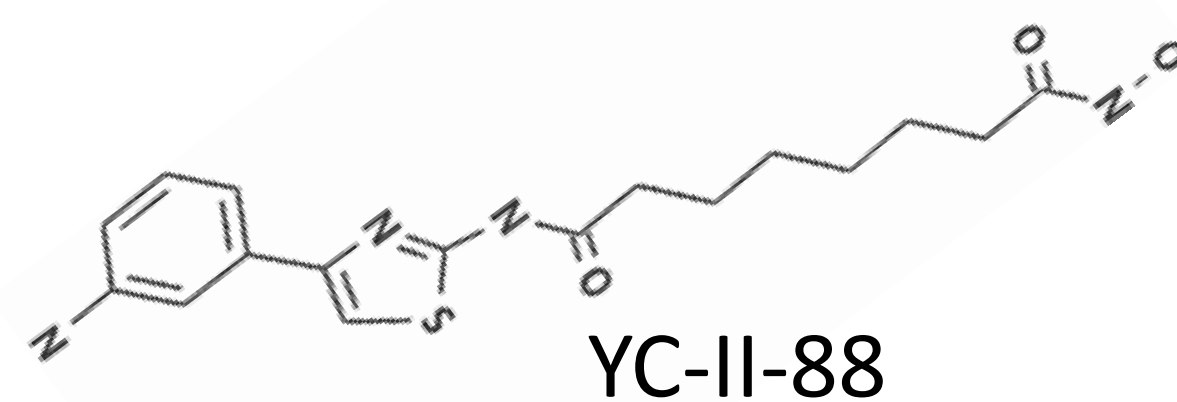
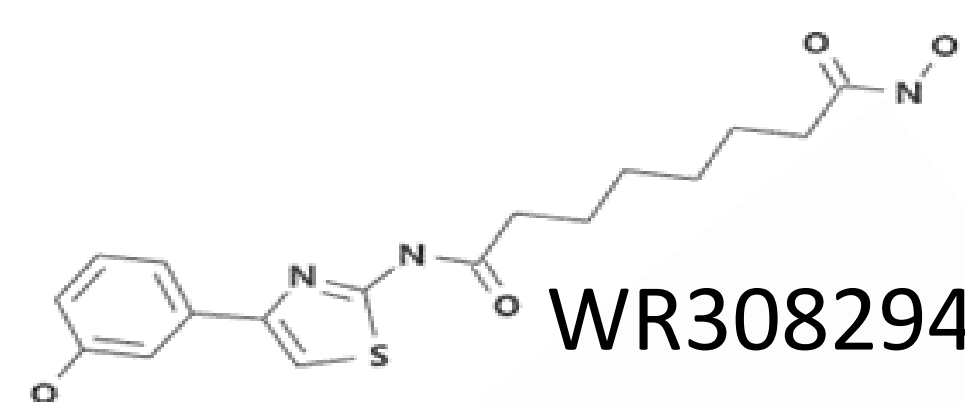
Identification of Target Binding Site on Model / Ligand preparation

Docking of Ligands on PfHdac 1 and hHdac model

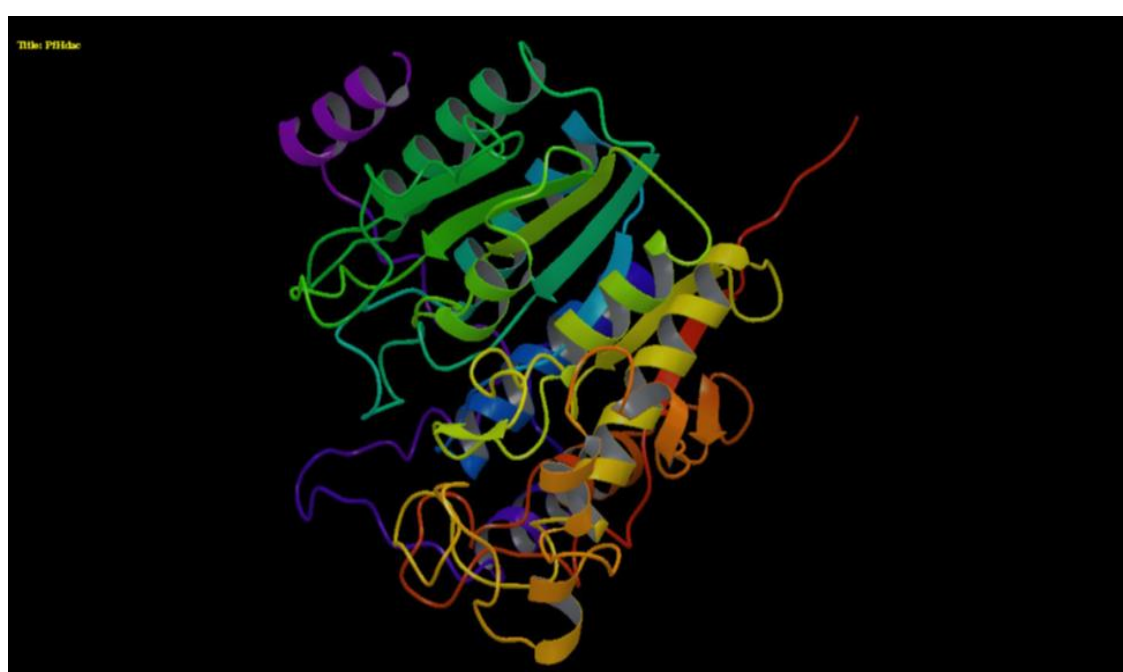
RESULTS/DISCUSSION



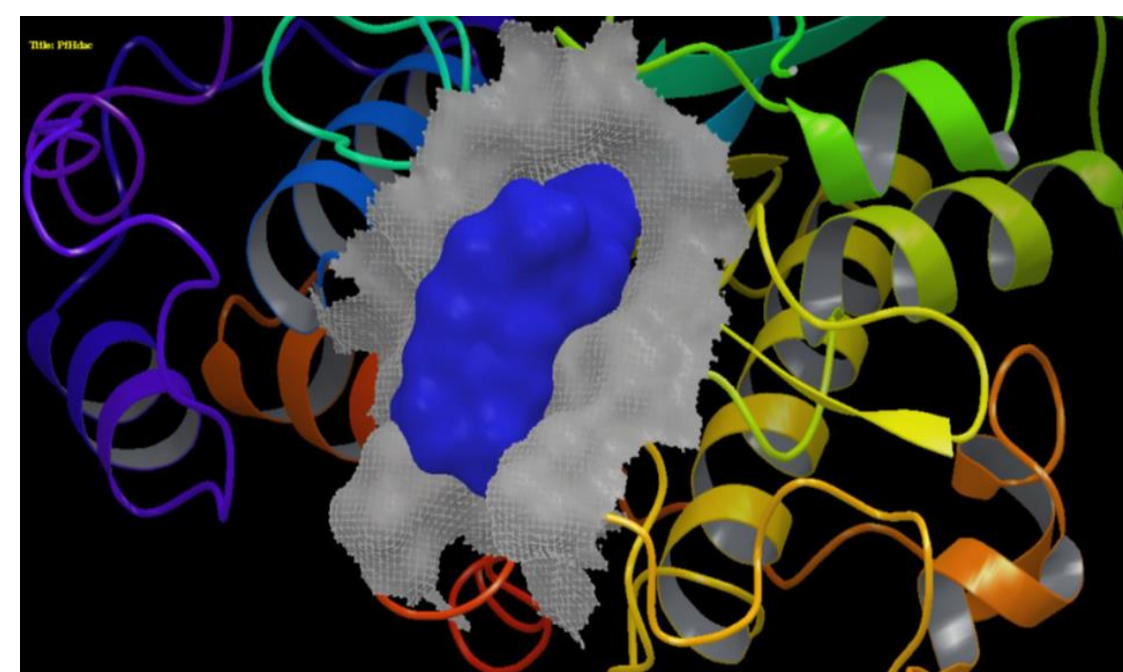
Sequence Alignment of 1C3R and 1T64



Molecular Structure of Some Ligands



Homology Model of PfHDAC 1



Receptor Binding Surface of PfHDAC Model

Summary of Docking Score of PfHDAC 1 and hHDAC 8 Models

Ligand	Docking Score	
	PfHDAC 1	hHDAC 8
WR308294	-12.320	-7.760
WR308298	-12.934	-7.400
YC-II-88	-11.924	-
AG-THAI-01	-11.504	-

CONCLUSION

The 3D structure of PfHDAC 1 was constructed, nine ligands were docked on the PfHDAC 1 and hHDAC 8 models. YC-II-88 ligand showed high selectivity for the plasmodium cell than the human cell, hence on further investigation could be incorporated in the development of new antimalaria drugs.

ACKNOLEDGEMENT

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