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In silico Modeling of *Beta*-lactamase Protein *Acinetobacter baumannii*

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Abstract: The most common mechanism of resistance to *β*-lactam antibiotics in gram-negative bacteria is the production of *β*-lactamases that hydrolyze the drug. Results that have been obtained from some servers that have been used in this study were gave a poor quality and prediction. SWISS MODEL server results gave more promising result as it had 92% query coverage. Validated was done for the model study by using QMEAN score, Ramachandran plot and ProSA server. 3D Refine and Mod Refiner were used for model refinement. Finally, ProSA server have been used in order to revalidate the model.

Keywords: *In silico*, Modeling, *beta*-lactamase, *Acinetobacter baumannii* .

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Introduction:

A. baumannii is a non-motile, Gramnegative, coccobacilli, opportunistic, extracellular human pathogen (1). It is emerging as an important nosocomial pathogen causing a variety of infections mostly acquired in the hospital. It is increasingly associated with serious infections among patients on these life-support systems. *A. baumannii* have become resistant to almost all currently available antibacterial agents multidrug resistant (MDR), extensive drug resistant (XDR). MDR strains of *A. baumannii* are notorious in their ability to spread among hospitalized, patients and cause outbreaks, which have been reported worldwide (2, 3).

Bioinformatics is the combination of biology and information technology are can be defined as computational molecular biology(4).

This study aims was to the structure function analysis of the 3D-Structure of *β*-lactamases protein and designing a drug to inhibit.

Materials and Methods:

The amino acids sequence of *β*-lactamases of *A. baumannii* with accession numberWP_000027057.1

PSIPREDhttp://bioinf.cs.ucl.ac.uk/psipred/,(5) predict protein, Phyre2 http://www.sbg.bio.ic.ac.uk/~phyre2/html/page.cgi?id=index, (6) Raptor X http://raptorx.uchicago.edu/andSOPMhttps://npsa-prabi.ibcp.fr/cgi-bin/npsa_automat.pl?page=/NPSA/npsa_sopma.html (7,8,9). A were used to predict the secondary structure calculations data. (helix, sheets, and coils) of the default protein. First of all,

the protein secondary structure was predicted by SOPMA server online(10). It have been found that the alpha helix was the most predominant (46.50%), this result followed by random coil (35.31%) and Extended strand (12.24%). Also Beta turn was found as (5.94%). Second, different results were obtained from the rest servers. Figure(1) represent *β*-lactamases secondary structure of obtained from SOPMA servers online.

Results and Discussion:

FASTA format of amino acids sequence of *β*-lactamases of with accession retrieved from NCBI as a target sequence which consist of 286.amino acids identify conserved domains feature at NCBI revealed that the protein sequence include one domain(11).

Secondary structure analysis:

The PSIPRED, predict protein, Phyre2, Raptor X and SOPMA were applied for secondary structure calculations (helix, sheets, and coils) of the hypothetical protein. First, the secondary structure of the protein remained predicted by SOPMA server. The alpha helix was found to be the most predominant (46.50%), followed by random coil (35.31%) and Extended strand (12.24%).likewise Beta turn was found as (5.94%). Second, different results were obtained from the rest servers. Figure (1) represent the secondary structure of *β*-lactamases obtained from SOPMA servers.

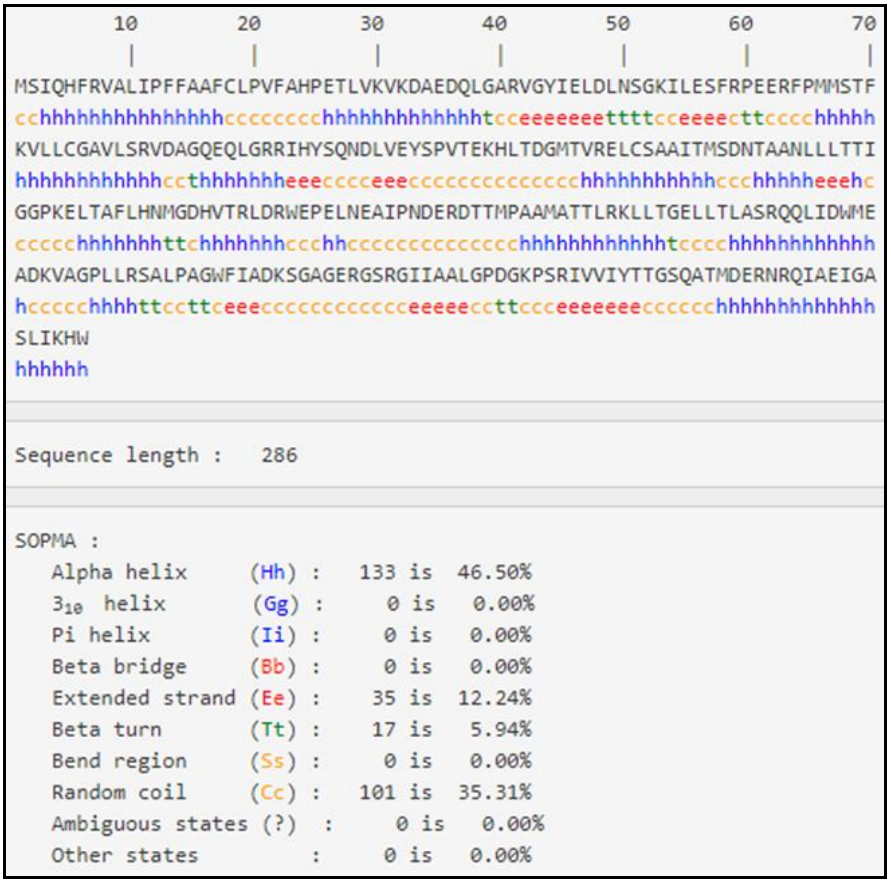

Figure (1): *β*-lactamases secondary structure of *β*-lactamases. (SOPMA Server).

Homology modeling:

The 3 Dimension structures of the detected target that are not found in its natural formula was computationally was predicted with the aid computational method homology modeling. the biological functions of such un-characterized proteins can be determine with aid the *In silico* analysis, and so such circumstances where the experimental structure of target protein is unavailable, computational method can be helpful(12,13). Hypothetical protein sequence 3D structure predict by using homology modeling and this 3D structure an assumed protein sequence build principally by respect of its alignments to one or more proteins of known structure. SWISS MODEL https://swissmodel.expasy.org/(14), RaptorX(15,16), Phyre 2(17), I-TASSERhttps://zhanglab.ccmb.med.umich.edu/I-TASSER/ and LOMETS https://zhanglab.ccmb.med.umich.edu/LOMETS/FAQ.html(18)was used perform the homology modeling. Thirteen models were obtained visualized under UCSF Chimera software and then submitted(19).

To 3D-Structure validation and refinement. The 3D-Structure of SWISS MODEL is given below Figure (2).

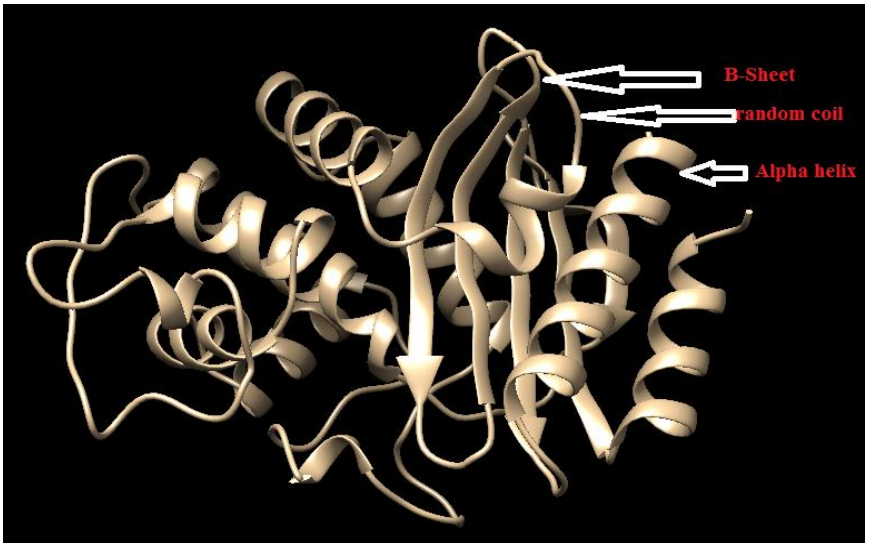

Figure (2): 3D-Structure of SWISS MODEL (19).

Model refinement and validation:

The protein model created need to be evaluated for quality. Ramachandran plots were resolved for the further checked of the model. PROSAweb(20) has been used for checking Z-score of the query model, and in order to estimate the quality of model using structured solved proteins as reference, Z-score have been used. 3D Refiner server was used to refine the selected models to increase the quality of these models. Higher QMEAN Z-score value means better acceptation with the detected features. QMEANS value was (1.57), Torsion of Phi and Psi was (0.31), secondary structure agreement (SS Agree) was (0.97) and finally solvent accessibility agreement (ACC Agree) was (2.06) by QMEAN server(21) as shown in Figure (3).

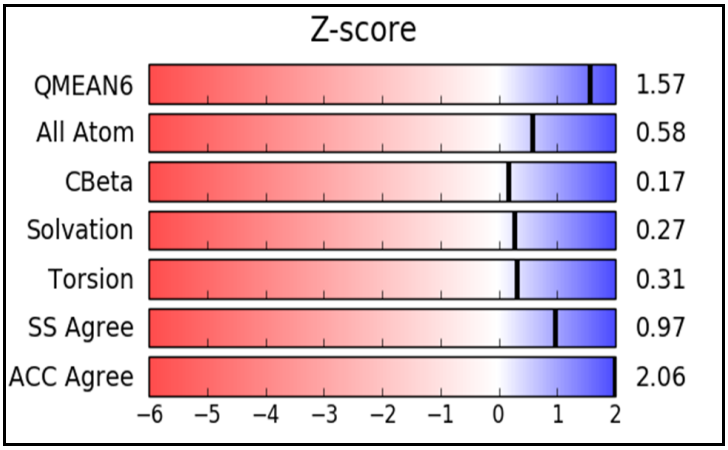

Figure (3): Total of Z-score for the reliable *β*-lactamases protein model (21).

The best model for *β*-lactamases protein was SWISS MODEL because it has the higher z-score (-7.93), and best local model quality with 92% covering of the protein sequence as shown in Figure (4) meanwhile with Raptor-x it has the lower z-score (-7.35) as shown in Figure (5).

Result of validation after refinement were appeared in Table (1) and the best predicted protein structure was selected according to the rules Refinement (-7.88) and qmean6 (1.89) .But in comparison with the Mod Refiner lower predicted protein structure was selected according to the rules Refinement (-7.93) and qmeann6 (1.57).

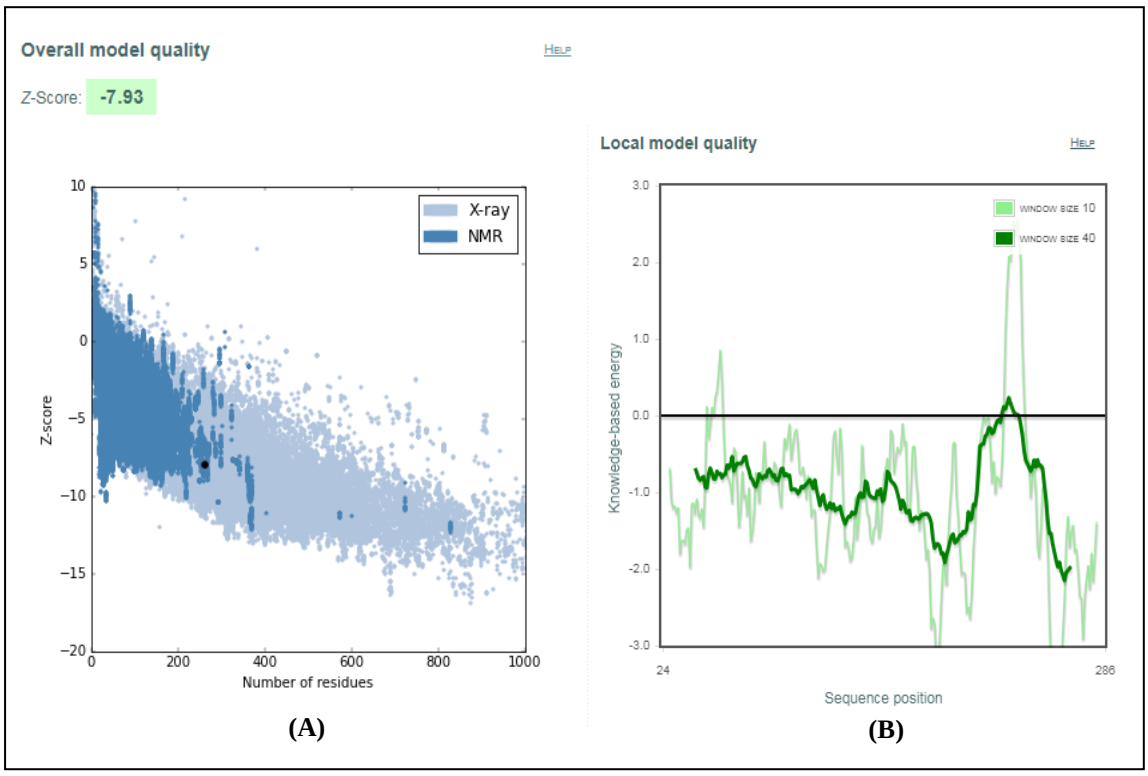

Figure (4): Validation result (A) Overall model quality , (B): Local model quality from (Raptor-x) (20).

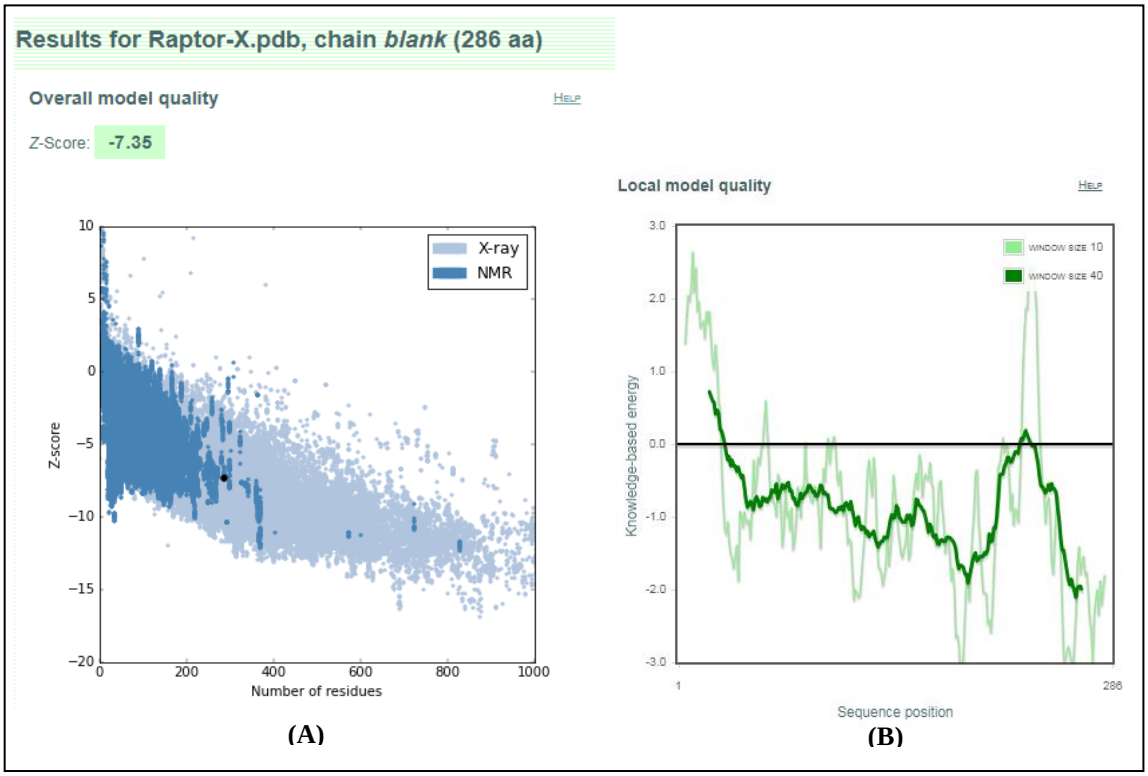

Figure: (5): Validation result (A) Overall model quality , (B): Local model quality from (Raptor-x)(20).

Table (1): Result of validation after refinement.

Program	*Z*-Score	Qmean 6
Mod Refiner	-7.93	1.57
3D refine 1	-7.88	1.89
3Drefine 2	-7.8	1.84
3Drefine 3	-7.83	1.87
3Drefine 4	-7.72	1.83
3Drefine 5	-7.74	1.79

Conclusion:

The purpose of this study was to minimize the gap between *In silico* and wet lab prediction of 3D-Structure of a protein by molecular modeling. The 3D-Structure model of *β*-lactamases protein was stable proved reliable using the ProSA server and the QMEAN server. The overall results provided the evidences that the predicted 3D-Structure of *β*-lactamases by SWISS MODEL is acceptable and of good quality. The predicted structure for *β*-lactamases will give an idea of its active site and the activesite residues which can be farther analyzed for designing inhibitors to inactive one of the most important virulence factor of ***Acinetobacter baumannii*** (result have not being published yet).

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