

Modeling Of Beta-Lactamase Protein In *Klebsiella pneumoniae*: In Silico Study

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ABSTRACT

Background: *Klebsiella pneumoniae* is a bacterium that normally lives inside human intestines, where it doesn't cause disease. But if *K. pneumoniae* gets into other areas of the body, it can lead to a range of illnesses, including pneumonia, bloodstream infections, meningitis, and urinary tract infections. The results that have been obtained from some servers that have been used in this study were gave a poor and good quality of prediction. SWISS MODEL server gave more promising results. Validation was done for the model study by using QMEAN score 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.

Conclusion: SwissMODEL is a three-dimensional structure of an assumed protein sequence that was predicted via homology modeling, and this three-dimensional structure is based mostly on alignments to one or more proteins with known structures. Following construction of the model, it was evaluated and enhanced using 3D-Structure modeling software, which was developed by the University of California, San Francisco (UCSF).

Keywords: In silico; Modeling; Beta-lactamase; *Klebsiella pneumoniae*

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INTRODUCTION

Microbial resistance, especially resistance to cephalosporins, is an ever increasing public health problem worldwide among pathogenic *Enterobacteriaceae*, namely, *Escherichia coli* and *Klebsiella pneumoniae*. The mechanisms that bacterial pathogens have developed to fight antibiotics are many, one of them being production of enzymes degrading particular antibacterial agents. In case of β -lactam antibiotics, the enzymes are β -lactamases. To date, more than 7000 β -lactamases have been described in the Beta-Lactamase DataBase (BLDB) [1] which have different characteristics in terms of their substrate specificities.

Klebsiella pneumoniae is a Gram negative, non motile, encapsulated, facultative anaerobic, lactose fermenting, rod shaped bacterium. The range of clinical diseases caused by this includes pneumonia, thrombophlebitis, urinary tract infection (UTI), bacteremia and septicemia. Indiscriminate antibiotic use is a major factor that often result in multi drug resistant strains [2]. The production of broad-spectrum β -lactamases (TEM-1, TEM-2, SHV-1, OXA-1) results in resistance to ampicillin, ticarcillin, piperacillin and

cephalosporins. Three enzymatic mechanisms have been described for resistance to inhibitor penicillin combinations: i.) production of class C chromosomal β -lactamase. are can be defined as computational molecular biology[3]. 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 Bap of *klebsiella pneumoniae* with accession number M59181.1. Various physicochemical parameters of *Beta* lactamase predict protein, Phyre2 [http://www.sbg.bio.ic.ac.uk/~phyre2/html/page.cgi?id=index,or\[4\]RaptX](http://www.sbg.bio.ic.ac.uk/~phyre2/html/page.cgi?id=index,or[4]RaptX) <http://raptorx.uchicago.edu/andSOPM> https://npsaprabi.ibcp.fr/cgi-bin/npsa_automat.pl?page=/NPSA/npsa_sopma.html [5,6,7].

RESULTS AND DISCUSSION

The PSIPRED, predict protein, Phyre2, Raptor X and SOPMA were applied for secondary structure calculations (helix, sheets, and coils) of the hypothetical protein. were used to predict the secondary structure calculations data. (helix, sheets, and coils) are of the default protein. First of all, the protein secondary structure was predicted by SOPMA server

online [8]. It has been found that the alpha helix was the most predominant was the most predominant (48.95%), this result followed by random coil (31.47%) and Extended strand (12.94%). Also Beta turn was found as (6.64%). Second, different results were obtained from the rest servers. Figure(1) represent β -lactamases secondary structure of obtained from SOPMA servers online. While, the protein secondary structure was predicted by SOPMA server online phyre2 as shown in Figure (2).

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

Figure (2): β -lactamases secondary structure of β -lactamases. (Phyre2 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[9,10]. Hypothetical protein sequence 3D structure predict by using homology

modeling and this 3D as shown in Figure (2) SWISSMODEL<https://swissmodel.expasy.org/> [11], Phyre2<http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index>[12], was used to perform the homology modeling. The model was obtained visualized under UCSF Chimera software [15] and then submitted to 3D-Structure validation and refinement. The 3D-Structure of Phyre2 is given in Figure (3 A&B).

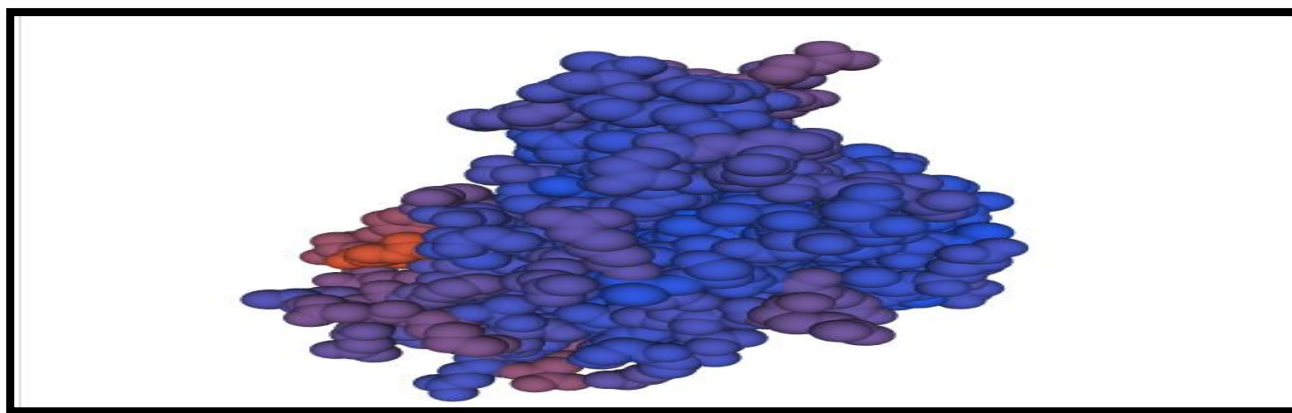


Figure (3.A): 3D-Structure of SWISS MODEL.

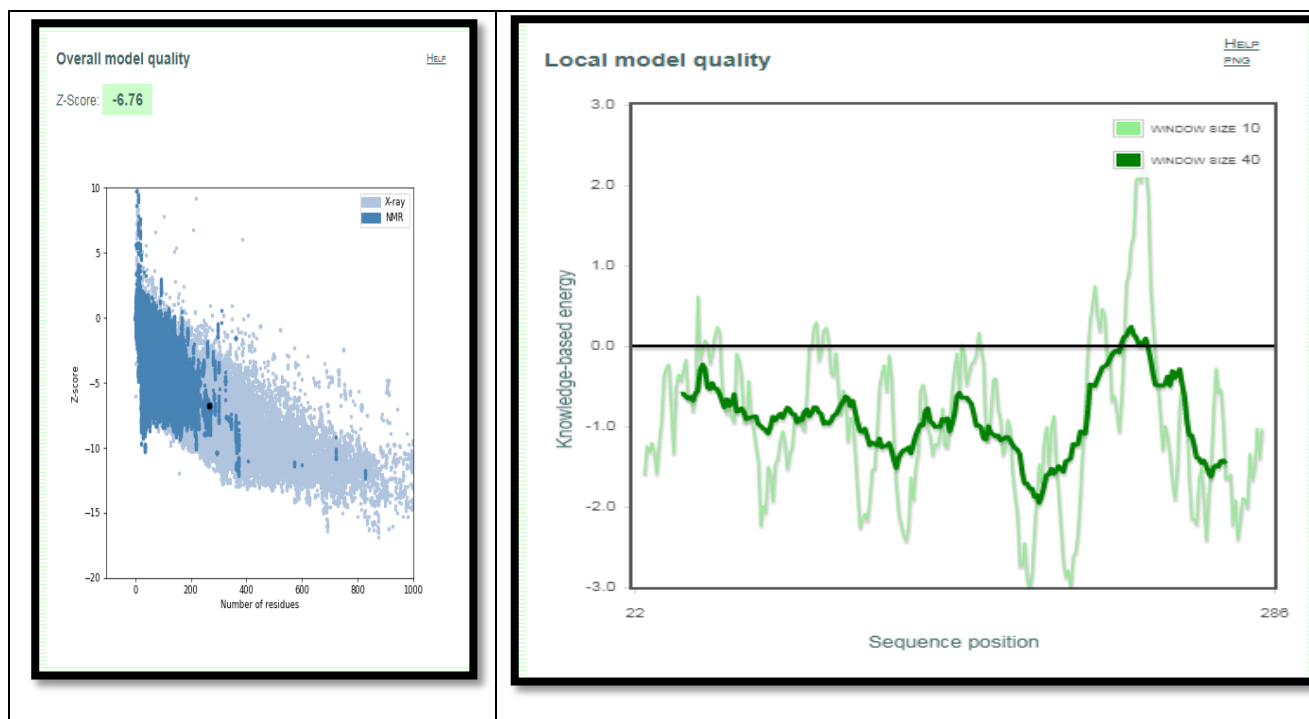


Figure: (3.B): Validation result (A) Overall model quality , (B): Local model quality from (Raptor-x)

CONCLUSION

Understanding the three-dimensional structure of proteins enables the exploration of protein function and active sites, as well as the expedited development of drugs. After doing a search in the protein data bank, it is revealed that no protein structures that correspond to the amino acid sequence of the protein are currently accessible for download (PDB). SwissMODEL is a three-dimensional structure

of an assumed protein sequence that was predicted via homology modeling, and this three-dimensional structure is based mostly on alignments to one or more proteins with known structures. Following construction of the model, it was evaluated and enhanced using 3D-Structure modeling software, which was developed by the University of California, San Francisco (UCSF).

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