The insilico analysis of two targeted proteins (FabG1,Wag31) by molecular docking approach

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***Abstract*- Tuberculosis, also known as TB, It is a bacterial infection that can spread through the lymph nodes and bloodstream to any organ in your body. It is caused by the bacteria Mycobacterium tuberculosis. Among various targeted proteins in this bacteria, FabG1 and Wag31 are playing an important role to cause and survival of TB. So these two proteins are inhibited by an inhibitor called benzothiazinone. The molecular interaction of FabG1, Wag31 with benzothiazinone is predicted through molecular docking approach.**

I. INTRODUCTION

TB is an infectious disease which spreads person to person through air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. India have the highest burden of TB. The World Health Organisation (WHO) in 2014 statistics, 2.2 million cases of TB in India out of the global incidence of 9 million. Both eukaryotic and prokaryotic cells, reversible protein phosphorylation is the most common mechanism by which environmental signals are transmitted to regulate gene expression.

The localization and function of Wag31 and its phosphorylation demonstrating that Wag31 is localized to the cell poles. The homologues suggest that Wag31 may be involved in septum formation, cell wall synthesis or chromosome segregation in mycobacteria. [1] The potential component of the protein FabG1 was over expressed and purified in mycobacterium tuberculosis and other mycobacteria. The enzymological and structural analyses of FabG1 that represent a fundamental step towards the design of inhibitors. Specific structural features of FabG1, interrelated with its substrate specificity, could allow the development of new antibiotics directed against mycobacteria. [2]

The protein FabG1 is a plasma membrane protein and the location of Wag31 is in cytoplasm. Benzothiazinone having PubChem CID 45121705, molecular formula is C_7H_7NOS is known as a good inhibitor for TB [3]. The molecular weight of Benzothiazinone is 153.20158 g/mol.

II. MATERIALS AND METHODS

The tertiary structure of protein FabG1 (PDB ID: 1uzm) is downloaded from Protein Data Bank. But for the protein Wag31, the structure is predicted by Phyre2 tool [4] due to the unavailability of experimental determined 3D structure. Verification of predicted structure is done by using Rampage tool [5]. The protein-protein interaction is analyzed with other proteins by using String database [6]. The inhibitor Benzothiazinone is downloaded from PubChem database [7]. Then both the proteins are taken to study the binding energy, KI value and interacting residues with the inhibitor Benzothiazinone.

III. RESULTS

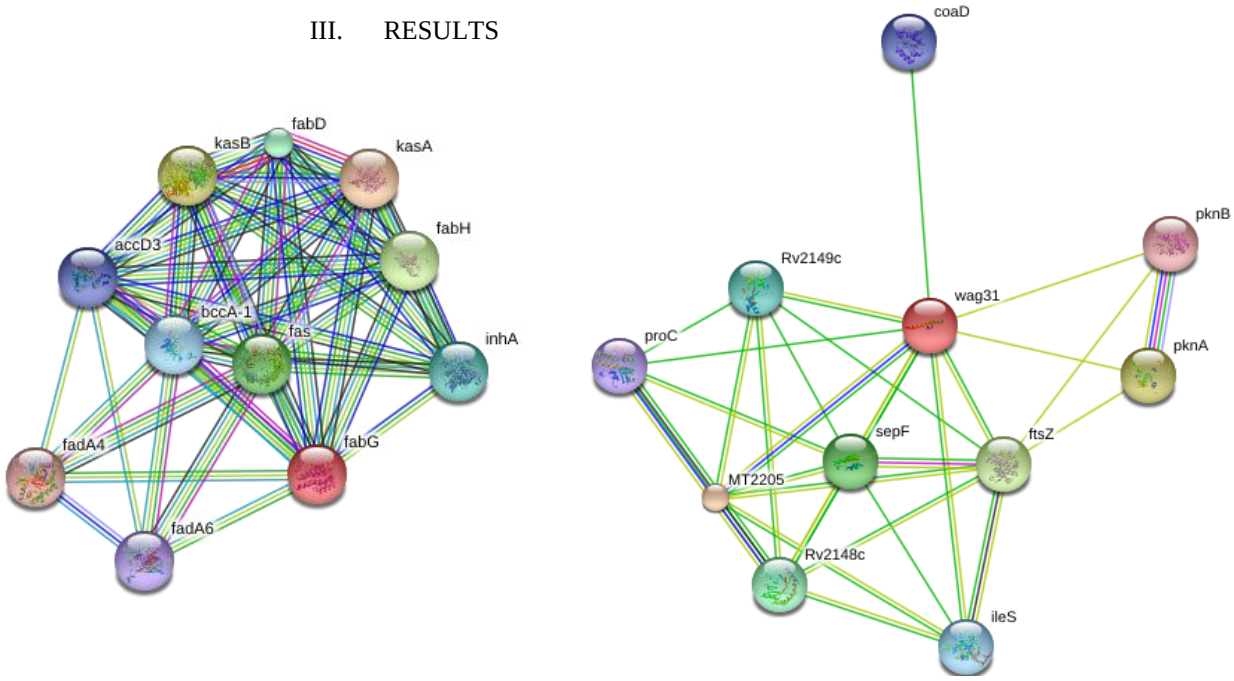

Fig1: Interaction of FabG1 and Wag31 with other proteins.

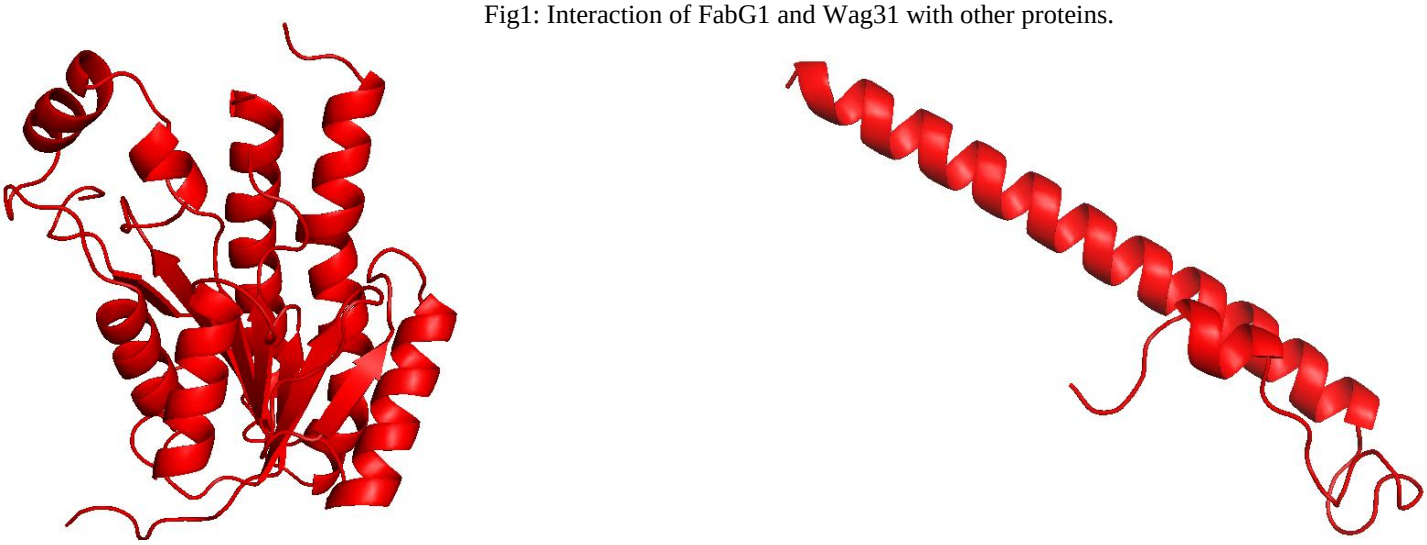

Fig2: protein structure of FabG1 (left) and Wag31 (right).

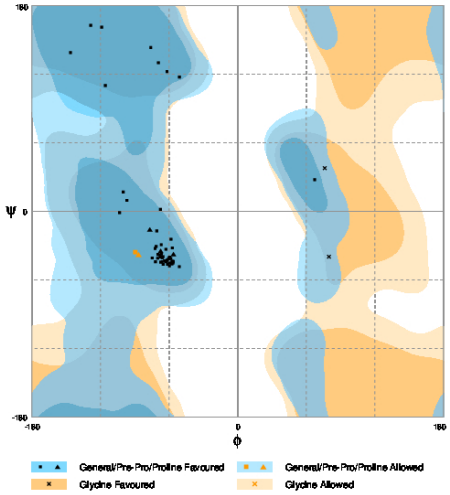

Fig 3: structure validation of predicted Wag31 protein.

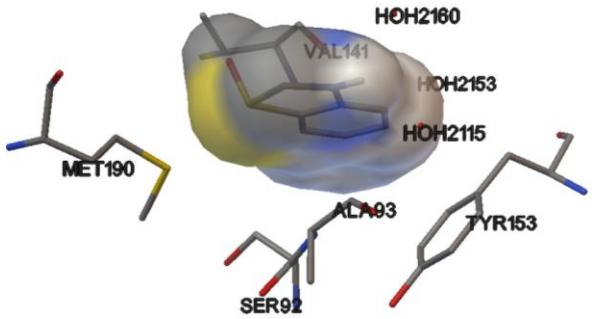

Fig 4: Interaction of FabG1 protein with Benzothiazinone.

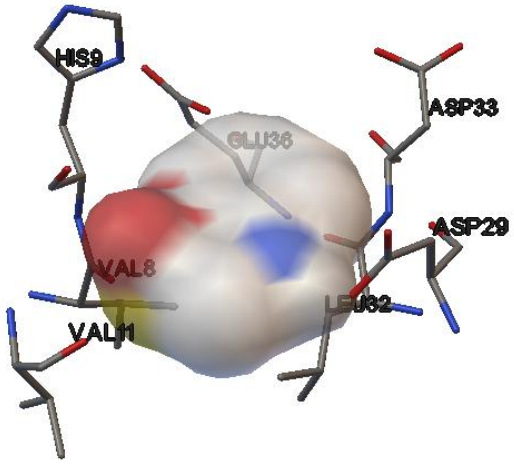

Fig 5: Interaction of Wag31 protein with Benzothiazinone.

IV. DISCUSSION

The above protein Wag31 is modelled and validation of structure is done by using Rampage. Model structure had 99.6% confidence in modelling and 96.7% residues are found in favoured region which shows the good quality of the predicted structure. The interacting residues are analysed by docking of FabG1 and Wag31 protein with Benzothiazinone. In case of FabG1 protein, the interacting residues are MET190, SER92, TYR153, ILA93, and VAL141. Similarly in Wag31 protein, HIS9, ASP33, GLU36, ASP29, LEU62, VAL8, VAL11 are the interacting residues. The docking energy of Benzothiazinone

with the protein FabG1 is -4.97 and KI value is 227.9 u.M . For the protein Wag31, -4.33 is the binding energy and 668.63u.M is the KI value.

V. CONCLUSION

This over all study is about the protein structure prediction, the validation of predicted structure and interacting residues study of these two targeted proteins with the inhibitor Benzothiazinone. From this work we have determined that wag31 and FabG1 was an essential gene which can localize the cell poles. The FabG1 protein from mycobacterium tuberculosis was produced from e-coli and purified. From the docked energy, KI value and interacting residues like insilico study, the process of drug discovery against TB might be more helpful.

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REFERENCES

1. Hedia Marrakchi, Steiphanie Ducasse, Gilles Labesse, Henri Montrozier, Emmanuel Margeat, Laurent Emorine, Xavier Charpentier, Mamadou Daffe and Annaısk Queimard. MabA (FabG1), a *Mycobacterium tuberculosis* protein involved in the long-chain fatty acid elongation system FAS-II. *Microbiology* (2002), 148, 951–960.
2. Choong-Min Kang, Seeta Nyayapathy, Jung-Yeon Lee, Joo-Won Suh, and Robert N. Husson. Wag31, a homologue of the cell division protein DivIVA, regulates growth, morphology and polar cell wall synthesis in mycobacteria. Microbiology (2008), 154, 725–735.
3. Batt SM, Jabeen T, Bhowruth V, Quill L, Lund PA, Eggeling L, Alderwick LJ, Fütterer K, Besra GS. Structural basis of inhibition of Mycobacterium tuberculosis DprE1 by benzothiazinone inhibitors. Proc Natl Acad Sci U S A. 2012 Jul 10; 109(28):11354-9.
4. http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index
5. http://mordred.bioc.cam.ac.uk/~rapper/rampage.php
6. http://string-db.org/
7. http://ncbi.nlm.nih.gov/pccompound