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ORIGINAL ARTICLE

Homology Modeling of Predicted Methyl Transferases (STY 3264): A Protein of Salmonella TYPHI CT18

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ABSTRACT

Background: Salmonella typhi gives rise to typhoid fever which is life threatening illness.It puts end to approximately 600,000 people per annum around the world.Food and water are the leading components through which this disease is passed on and becomes origin of typhoid.It lays out widely where cleanliness is very substandard.
Objective: To construct 3 dimensional structure of protein Methyl Transferase of Salmonella typhi CT18 by homology modeling.
Materials and Methods: Bioinformatic tools and programs like Comprehensive Microbial Resource (CMR), Interproscan, Basic Local Alignment Search Tool (BLAST), Modellor 9.10, Procheck and Prosa were helpful for the complete homology modeling of methyl transferases (STY 3264).The models were visualized by DS Viever.
Results: Homology modeling is an effective method to find structure of methyl transferase protein for future discovery of drugs.
Conclusion: Homology modeling is an effective method to find structure of protein which provides good solution for drug discovery.
Keywords: Methyl transferase ,Homology modeling, Typhoid fever,Salmonella typhi CT18.

INTRODUCTION

The main origin of typhoid fever is Salmonellaentericaservartyphi (S.typhi). It is bacterial infection.which causes death of 16 million human annually all over the world.[1].

Salmonella typhi stain CT18 comprises of thousands of proteins and enzymes in its structure. The data about functions of proteins and enzymes collected through a tool,interproscan. One of the enzymes of Salmonella typhi CT18,methyl transferases is gigantic group of enzymes that detects certain sequence of nucleotide and transfers methyl group in DNA. This process of transferring methyl group is called methylation which is very important in eukaryotic cells. It plays role in transcription of DNA,balances and stabilizes gene and parental imprinting. Chromatin structure is brought about by methylation. Gene transcription is regulated by methylation. Protein-Protein interaction,DNA –protein interaction management is carried out in eukaryotes by methylation process.

In prokaryotes,when foreign DNA attacks on host cell,methyltransferase shields it from forein DNA by restriction enzymes.

One important function of DNA methyl transferases is oncogenic regulation of gene expression helpful in cancer therapy.So methylation plays a crucial role in diverse biological processes and in causing human diseases [2].

Protein lysine methyl transferases and Protein argine methyl transferases are two types of protein methyl transferases [3].

To minimize its gene expression effects of causing disease, structural study of methyl transferases is carried through homology modeling.It is of prime importance.Three dimensional structure of methyl transferases was set up through homology modeling.Homology modeling is quick and authentic method to raise models of proteins. Target protein(methyl transferase) is modeled by using structural template (similar known sequence protein). It consists of many phases.The target sequence is helpful for searching templates in Protein Data Bank(PDB)(4-5).

Sequence alignment between template and target is done in next step[6]. The information retrieved is used to build three dimensional structure of the quarry in the last step.

In another study,Homology modelingis completed in 4 steps (7).In first step,PDB data bank is source for template recognition of known protein.Sequence alignment of the quarry with that template is done in second step.On the basis of alignment,building 10 different models in third step.Clarifying of more accurate and exact model in fourth final step.

So to know and acknowledge biological functions of proteins, three dimensional protein structure is valuable and precious source of information[8].It represents a heart of SWISS –MODEL[9]. Energy calculation and energy minimization to stabilize model is also done inside Model face[10].

MATERIAL AND METHODS

Perfect sequence of Salmonella typhi CT18 was initialized through comprehensive microbial resource.The Comprehensive Microbial Resource or CMR(http://cmr.jcvi.org) delivers freely available central resource for the view,explore and examining of the sequence and explaining the complete and openly available bacterial and archaeal genomes[11].It manifests that Salmonella typhi CT18 carries more than 4000 proteins. Functions of protein were perceived through interproscan. Among these proteins,one protein was methyl transferases (STY 3264).Homology modeling was preferred to build three dimensional structure of predicted methyl transferases(STY 3264).The template was foraged through Basic Local Alignment Search Tool (BLAST) which brings about pairwise alignment between the quarry sequence and template[12].

One of the modellors,Modellor 9.10 was made use of building models.10 different models had been put up .Among them,one finest model had been chosen.The reliability of models was reviewed and examined by PROCHECK. The PROCHECK comes up with a particular examine on the stereochemistry of a protein structure[13].The PROCHECK gives rise to distinct files.One of the important file was Ramachandran Plot.The Ramachandran Plot is among the most central abstraction in structural biology.Neverthless,with the increasing numbers of known protein structures and considerable validity of ultra-high resolution protein structures,we are still studying further about the chief principles of protein structure [14].The energy of methyl transferases enzymes was calculated through Prosa.A great complication in structural biology is the identification of inaccuracy in experimental and theoretical models of protein.The Prosa program (protein structure analysis)is an initiated tool which possesses a wide support and is regularly operated and serviced in proof reading and refinement of protein structure and models[15].

RESULTS AND DISCUSSION

Allignment was followed with BLAST(Figure 2).Template like Ectmb (protein) having accession number 3DXX was picked out having greater resemblance with the target protein.Allignment was accomplished as shown in figure 2.

Figure 1: Result of Blast of methyl transferases (STY 3264)

Figure- 2: Alignment of methyl transferase (STY3264) sequence with template (3DXX)

One best model was chosen among 10 different models.The model was viewed by DS viewer.Red coiled structure was helices which were 8 in numbers and blue sheets were beta sheets (Figure 3) which were 7 in numbers.

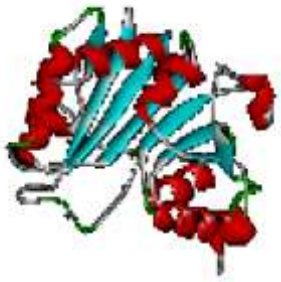

Figure 3: 3D model of methyl transferase showing helices and beta sheets

Procheck was run to examine the reliability of models. The Procheck set up 10 files.Ramachandran Plot was valuable accent among them.It is spaced apart into 4 regions namely maximum accommudationpart, fewer allowed region,inadequately allowed region and disallowed region.Model no.4 was considered to be the finest model because it showed greatest percentage of leftovers than that of other models.

This plot showed that 94.9% debris were present in most accomudatingparts,4.5% were in fewer allowed parts,0.6% waspresent in inadequate allowed part and no particle was found in disallowed part.(Figure 5).

Regions	Number of residues	Percentage of residues
particlesin most accomudatingparts[A,B,L]	167 8	94.9% 4.5%
particlesin fewer allowed parts[a,b,l,p]	1	0.6%
particles in inadequate allowed parts[a, b, l, p]	0	0%
particlesin disallowed parts		

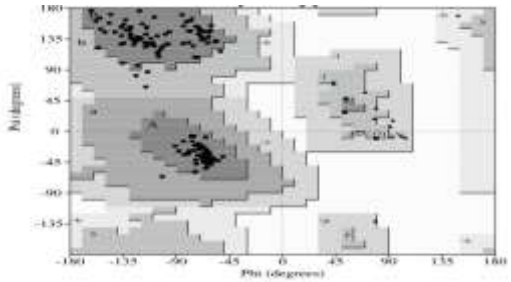

Figure 4: Ramachandran plot (Z value: -7.26)

Prosa was run to assess the energy of methyl tyransferases which displayed the stable structure. The Z-score of methyl transferase presented hugely negative value(-7.26) which termed that model was balanced and stable.(Figure 5).

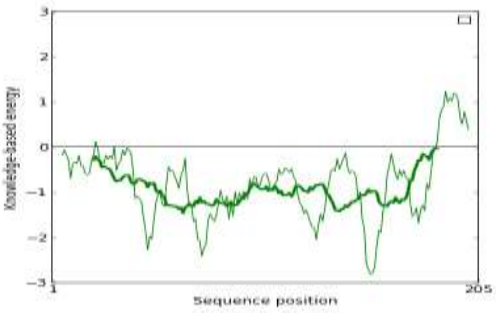

Figure 5: Graphenergy of methyl transferases obtained through Prosa-web

CONCLUSION

Salmonella typhi accounts long term and severe disease around the world.Comprehensive Microbial Resource assisted in attaining the protein sequence.4000 proteins of salmonella typhi were sequenced. Among these proteins, methyl transferase was selected and structure was modeled by homology modeling which provides adequate information for drug discovery to control its gene expression in causing further infection.By knowing the 3D structure of methyl transferase, we can design a drug to inhibit its function to stop the virulent effect of Salmonella typhi CT18.

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