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Genomic Insights into the Biology of Digenetic Fluke, *Explanatum explanatum* Infecting Domestic Water Buffalo, *Bubalus bubalis* from India: New Targets for Drug Designing

Tyagi Anju[1], Chauhan Bhumika[1], Sharma Bindu[1]* and Sharma Akshat[2]

[1]Laboratory of Molecular Parasitology, Department of Zoology, Chaudhary Charan Singh University, Meerut 250004, India
[2]Department of Computer Science, Florida State University, Tallahassee FL 32304, USA

**Corresponding Author*

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Abstract: *Explanatum explanatum* is a digenetic trematode mostly found parasitizing bile duct and the gall bladder of domestic buffaloes in India .The parasite fabricates productivity loss and occasionally turns out as severe clinical disease leading to granulomatous nodules in the bile duct mucosa, glandular hyperplasia and thickening of the blood vessels. Ribosomes are macromolecular machinery for cell protein synthesis in all organisms. The present study deals with the identification of different DNA motif in 5.8S rDNA to block the activity of ribosome translocation, thereby hindering the process of protein synthesis within the parasite and thus serving as a novel tool for controlling its growth. Moreover, this segment of gene remains evolutionary conserved thus, enhancing the rate of success in designing potent drug molecules for these identified motifs in the genome of *E. explanatum*. This is first report of the identification of position of DNA motifs in 5.8S rDNA of *E. explanatum* from India and an attempt to provide new insights for further designing of new potent drugs for its efficient treatment as the parasite has developed tolerance power for already available drugs and the significant loss caused by it to the livestock and economy. Our study will form the foundation for future in-depth analysis of the parasite biology and development, immune evasion strategies, virulence and long-term survival within the definitive host. Our findings aim to provide a better understanding of the parasite genome, the search for new drug design research and thus, can prove as a vital tool for improving animal health that would ultimately succor to meet the ever increasing demand for food.

Keywords: *Explanatum explanatum,* Motif, DNA, *In silico*, Phosphorylation, Myristoylation, Genome

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Introduction

Livestock plays a key role in Indian economy constituting 16% of the income of the poor farmers and people living in rural areas. About 20.5 million people are dependent upon livestock for their livelihood and buffaloes have been of great economic importance as they are closely associated with the life activities of resource-poor rural farmer and cater to their demands of milk,

meat, skin, manure and traction. Buffaloes usually graze in the open natural external environment, and due to regular natural calamities such as drought or flood they are susceptible to many diseases. Mortality and infections in the livestock has been continuously increasing due to parasitic infections as the parasite be it ecto- or endoparasite linger onto the host for its survival and causes mild to severe infections to the host body. *Explanatum explanatum* is a very common digenetic trematode parasite, a subgenus of *Paramphistomum* which is found in the liver of water buffalo and has a wide geographical distribution in India and neighbouring countries (Rajabloo *et al*., 2014). This parasite causes mortality as well as reduction in the production of meat and milk. *Explanatum explanatum* migrates and matures in the bile duct and gall bladder of cattle and buffaloes. Studies reveal that this parasite forms granulomatous nodules in the bile duct mucosa, glandular hyperplasia and thickened blood vessels in the body of host (Chaudhry *et al*., 2017). The present study focuses on the identification of DNA motif and its analysis in the rDNA of *E. explanatum* using *in silico* computational tools.

Amphistomiasis, a trematode infection of ruminants has long been neglected, but it has recently gained attention due to its significant losses to the livestock and economy. Computational tools are coming up as a technology with the potential to successfully address these issues and complement the mass spectrometry-based techniques (Wright and Sieber, 2016). These tools have provided new insights for parasite management that aims to provide optimal parasite control by parasite monitoring , designing potent target drug molecules using docking, genomic analysis, understanding the proteins functionality, transcriptome analysis, metagenomics, determining the physiochemical properties of the proteins and also to study the host-parasite relationship. Despite of the great hazards caused by *E. explanatum* to the ruminants, lesser attempts have been made till date for its control and treatment.

Ribosomes are highly conserved macromolecular machines for protein synthesis in all living organisms. Work published in the past shows that changes to the ribosome core can affect the mechanism of translation initiation that is favored in the cell, potentially leading to specific changes in the relative efficiencies with which different proteins are made (Gilbert *et al*., 2011). The role of 5.8S subunit has been widely studied in translocation activity during translation process. Thus, the present study was designed with an idea of creating new drug molecules that would target these motif sites of 5.8S subunit of the parasite and hinder its activity and stop its growth within the host body. Drug development has become the Holy Grail of structural bioinformatics groups. The explosion of information about protein structures, ligand-binding affinity, parasite genome projects, and biological activity of millions of molecules has unlocked the possibility to correlate this scattered information for designing small-molecule drug. Computational methods have shown their potential in drug discovery and development allied with *in vitro* and *in vivo* methodologies (Azevedo *et al*., 2009). The use of *in silico* biology has provided an excellent framework for the initial identification of key genes and gene clusters and disease control. Motif plays a crucial role in genome as it not only depicts the functionality of the specific gene but can also be used as a novel drug target for disease control. The utilization of *in silico* approaches for the functional prediction of gene functioning has been successfully used in several parasites such as *Plasmodium falciparum*, *Plasmodium vivax, Toxoplasma gondii, Leishmania donovani ,Entamobea nutalli* and *Schistosoma manosi* and also in plants like *Arabidopsis thaliana, Oryza sativa, Lycopersicon esculentum, Cucurbita pepo* and *Solanum tuberosum*.

The aim of the present work was to analyze the motif in 5.8S rDNA of *E. explanatum* for the

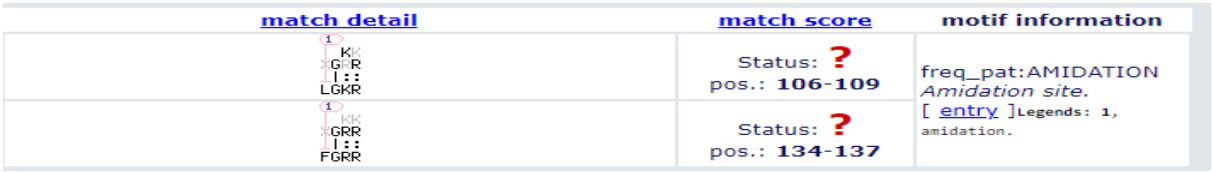

Fig.1: AMIDATION motif in the sequence.

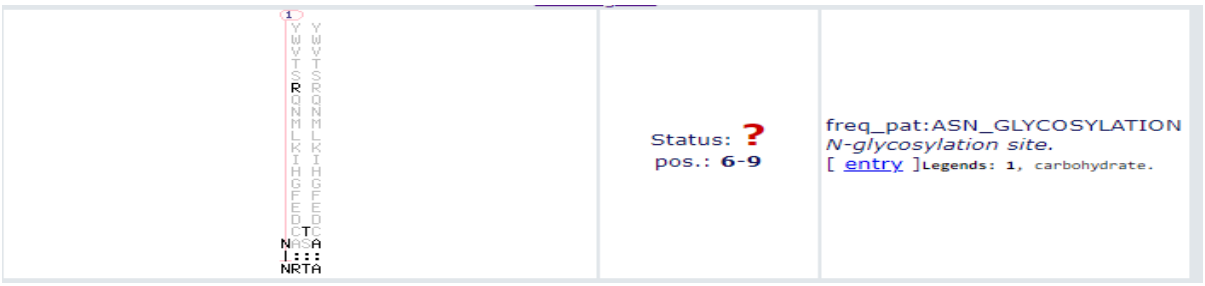

Fig. 2: ASN_GLYCOSYLATION motif in the desired sequence.

Fig. 3: CAMP_PHOSPHO_SITE motif in the sequence.

inventive process of finding new medications based on the knowledge of biological targets for drug repurposing.

Materials and Methods

Retrieval of the Sequence :

In this work, rDNA sequence of gene of *Explanatum explanatum* was retrieved from NCBI (National Centre of Biotechnology Information) database (http://www.ncbi.nlm.nih.gov) under accession number MZ068119.

Motifs Study of the Parasite:

From the retrieved sequence , the motifs were studied using GLAM2 Web tool and TRANSFAC.

Results and Discussion

Six different motifs namely AMIDATION, ASN-GLYCOSYLATION, CAMP_PHOSPHORYLATION, CK2_PHOSPHORYLATION, N-MYRISTOYLATION and PKC_PHOSPHORYLATION were found in the 5.8S rDNA of *E. explanatum*. The position of these motifs were from position 106-109 and 134-137 (Fig. 1), 6-9 (Fig. 2), 120-123 (Fig. 3), 26-29, 72-75, 149-152, 193-196 and 339-342 (Fig. 4), 19-24,113-118 and 147-152 (Fig. 5) and 96-98,114-116 and 150-152 (Fig. 6), respectively. The role of these motifs have been widely studied in coding DNA.

The process of hunt of a lead molecule is a long and a tedious process and one has to search through endless possibilities. Computational tools undoubtedly have played a pivotal role in rationalizing the path to drug discovery. Of all techniques, molecular docking has played a crucial role in computer aided drug design in the modern scenario of structure-based drug design. Parasite motif information can provide opportunities for *in silico* mining of novel drug designing candidates which has the potential to progress towards

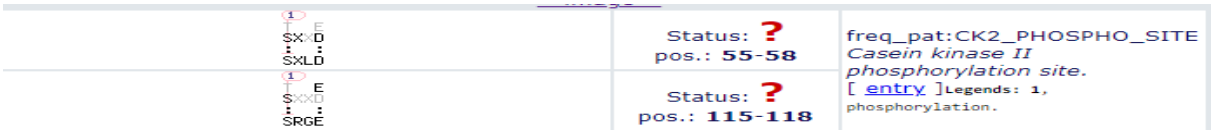

Fig. 4: CK2_PHOSPHO_SITE motif in the sequence.

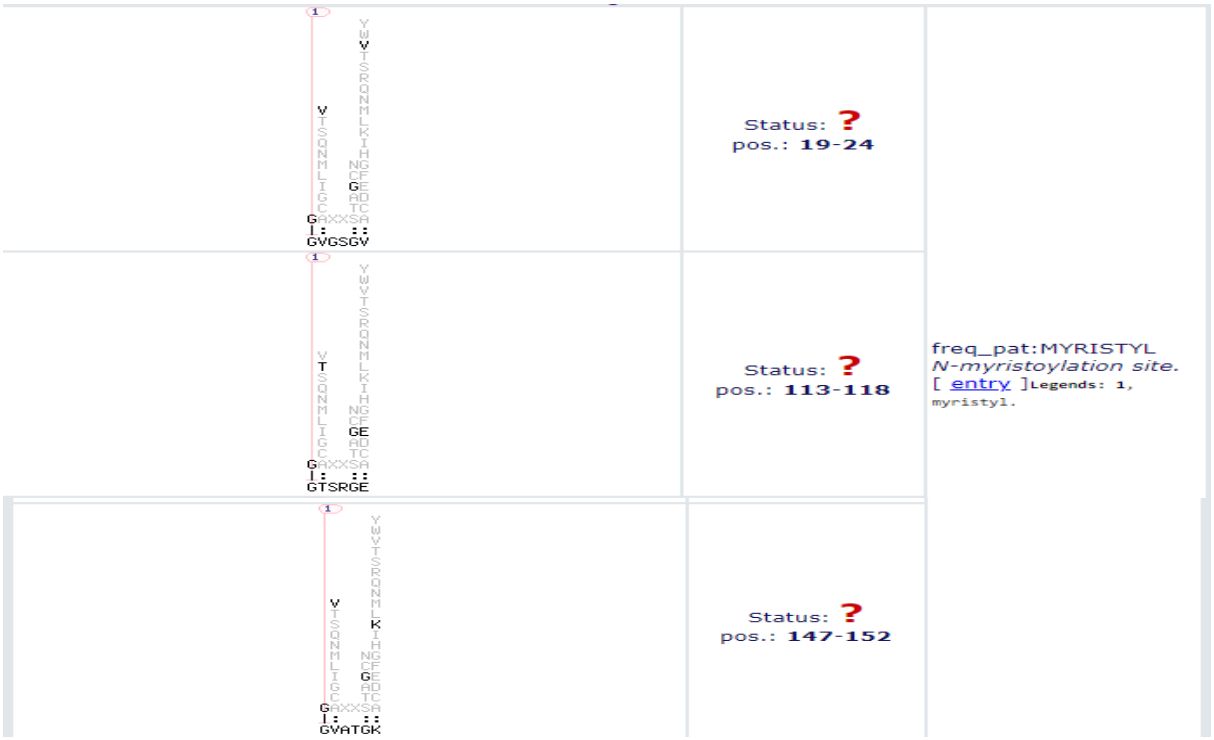

Fig. 5: MYRISTYL motif in the sequence.

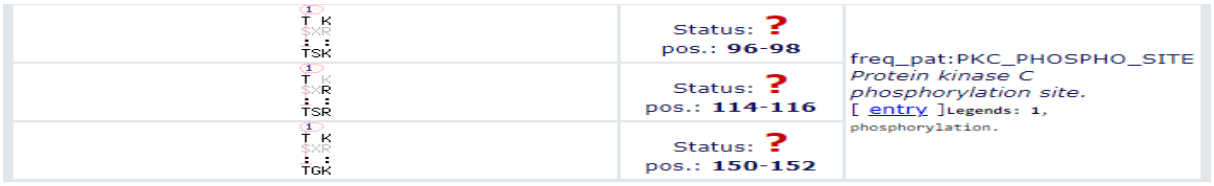

Fig.6: PKC_PHOSPHO_SITE motif in the sequence.

advanced phases of vaccine development for various diseases caused by helminthes. The authors will further carry research for drug molecules and this study will lay a basic pillar for the same.

Conclusion

In the present study, *in silico* analysis predicted the motif of rDNA from genome of commonly found subspecies of Paramphistomum, *Explanatum explanatum* . The study identifies the presence of six important motifs that upon translation in coding DNA has functionality role in protein folding and conformational stability, intracellular transport, antibiotic resistance and homeostasis processes, resistance to digestion by proteases, interaction with cell-surfaces, extracellular matrix proteins and other ligands,

sexual commitment, inducing chemotaxis, DNA repair, cell cycle control, regulating the circadian rhythm and other cellular -processes, providing innate immune response, phosphorylation sites on human lamin and in nuclear lamina structural dynamics. The authors believe that the identification of these motifs might serve an important role in disease control by docking as these sites of motif could be an attractive target of intervention for the treatment of Amphistomiasis by blocking the gene functionality of the parasite and hindering its host-parasite interactions. We also believe that the information gathered may provide new leads for designing inhibitors useful for manipulating the various AMIDATION, ASN-GLYCOSYLATION, CAMP_PHOSPHORYLATION, CK2_PHOSPHORYLATION, N-MYRISTOYLATION and PKC_PHOSPHORYLATION sites and thus, open possibilities for better investigation of this parasite for disease diagnostics in the field of parasitology.

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References

Azevedo WF Jr, Dias R, Timmers LF, Pauli I, Caceres RA and Soares MB. (2009) Bioinformatics tools for screening of antiparasitic drugs. Curr Drug Targets 10: 232-239. doi: 10.2174/138945009787581122.

Chaudhry U, Paridon B, Lejeune M, Shabbir Z, Rashid IM, Ashraf K, Gilleard J and Sargison N. (2017) Morpholgical and molecular identification of *Explanatum explanatum* in domestic water buffalo in Pakistan. Vet Parasitol Regional Stud Rep. 8: 54-59.

Gilbert WV. (2011) Functional specialization of ribosomes?. Trends Biochem Sci. *36*(3):127-132. https://doi.org/10.1016/j.tibs.2010. 2.002.

Rajabloo M, Namazi F, Shayegh H and Alavi A. (2014). *Explanatum explanatum* : an emerging liver fluke in cattle and sheep. Onl J Vet Res. 18(8): 657-661 .

Wright MH and Seiber SA. (2016) Chemical proteomics approaches for identifying the cellular targets of natural products. Nat Prod Rep. 33(5): 681-708.