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Functional Target Mapping in *Plasmodium vivax*P22290 for Vaccine Development using PEST- FIND Bioinformatics Tool

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Abstract:-
The most prominent protein used in an invasion into the surface of the erythrocytes is called Duffy binding protein. The family in which Duffy binding protein (DBP) is included resembles Duffy binding-like erythrocyte binding proteins which are situated on the surface of the micronemes. Plasmodium vivax is a very common available causative agent of malaria disease in this world. These protein can be very helpful for vaccine development. DARC (Duffy binding chemokine receptors) are functional motifs in P.vivax to insert in erythrocytes.These have high content of α-helical secondary structure of protein - typical of chemokine receptors.

This study of PEST FIND of P22290 describes a bioinformatics approach that is used to mark specific antigen of P.vivax which has a great role in attachment of P22290 with erythrocytes. potentially involved in erythrocytes invasion. There are different protein training sets that are highly motif were built and these are tuned in specific structure based on different atmospherics and biological parameters, which are used for experimental evidence of secretion or involvement of high motif in invasion-related processes. A profile-based amino acid sequence of P22290 is used as a methodological process in the bioinformatics tool called as PEST FIND bioinformatics tool. This tool is used to search specific proteins that can be used for targeting erythrocytes. The result of these bioinformatics tools gives us specific protein which has an essential role in the attachment of P.vivax with erythrocytes.

Keywords: *Duffy binding protein (DBP), Duffy binding chemokine receptors ((DARC)), Plasmodium vivax, PEST FIND.*

INTRODUCTION:-

The most prominent protein which is most commonly used in an invasion into the surface of the erythrocytes is called Duffy binding protein (DBP) [1, 2]. Plasmodium.vivax and *Plasmodium .knowlesi* merozoites surface have these micronemes[3]. *P. vivax* the most suitablevaccine candidate Duffy Binding Protein (DBP) is a target protein that is essential for making a connection of *P. vivax* with erythrocytes [4]. The different types of polymorphic nature of DBP induce different types of chain of a gene which has a different immunogenic characteristic featuresthat play a role in the inhibition of the process of making a vaccine for *P.vivax*[5]. This is the greatest protein that is found at the surface of micronemes of *P.vivax* [6]. Duffy binding protein (DBP) has a unique characteristic feature that attracts us and possesses to think about vaccine development for *P.vivax*[7]. P22290 is *P.vivax* Duffy binding protein (DBP) which is situated on the position of N terminals branch of the Duffy binding protein on surface of *P.vivax* merozoites. The basic function of this area is to make an attachment to *P.vivax* within human erythrocytes. The P22290 protein which plays a role in erythrocytes invasion has 70 amino acids in the chain [8,9].

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DARC (Duffy binding chemokine receptors) are functional motifs in *P.vivax*to be inserted in erythrocytes.DARC has a high content of α-helical secondary structure of protein - typical of chemokine receptors. The DARC (Duffy binding chemokine receptors) are found on the surface of erythrocytes which makes a connection on N Terminal area of chain P22290 and gives attachment with DBP. There are presently four types of chain-like A, B, C, D on 4NUV. 4NUV is a combined structure of Duffy binding protein(DBP) with Duffy binding chemokine receptors(DARC)which is used to study this attachment. Chain A and B basically Duffy binding protein found in P22290 of *P.vivax* whereas chain C, D chain of DARC which is part of human erythrocytes. These two types of chain show interaction between *P.vivax* and human erythrocytes. This type of attachment was discovered in 1980. The Duffy binding protein (DBP) is a glycol- protein Fy6 is essential for the attachment of *P.vivax* with erythrocytes[10].

Malaria is an acute periodic infectious disease which is caused by plasmodium protozoa. The causative agents of malaria all over the world are the main three species 1. *Plasmodium vivax*, 2.*Plasmodium falciparum* and 3.*Plasmodium malaria* other two spices (*Plasmodium Yoelli*, Plasmodium knowlesi) infects only in birds but now a day's these can infect human beings also in some case of *Plasmodium knowalsi*. The disease of malaria is transmitted in human beings through the bite of female Anopheles mosquitoes, even though it can be transmitted by transfusion infected blood. [11]

Malaria is the most important and fatal tropical disease all over the world especially in Asia and South Africa. This is presumed that at least 80 million peoples worldwide suffer from malaria *vivax* diseases. [7, 12]

P22290 is an antigen of *P.vivax* which has the ability in invasion in erythrocytes. The antigens of p22290 are a member of Duffy Blood Group of human body System. It has a very common efficiency of involvement in all human beings and also transmits hemolytic disease in the newborn. The attachment of DBP of *P.vivax*with DARC of erythrocytes plays a great role in malaria and so this site is very important to study for a scientist. [13-15]

PEST- FIND bioinformatics tool is used to determine specific antigen which may be a potential antigen and poor antigen in the P22290 amino acid sequence.

PEST FIND tool helps us to find antigen which are potential and most suitable photolytic indentation sites to break the chain of protein of *plasmodium vivax*. The most common breaking site is the erythrocyte binding antigen of Duffy binding protein.[15].

METHODOLOGY:-

PEST FIND bioinformatics tool is used for determining a highly potential motif in Plasmodium vivax. I have used the extasy bioinformatics resource portal for the online EPEST FIND bioinformatics toolepestfind tool that allows find rapid and fastobjective motif identification of PEST motifs in P22290 sequences. Those proteins in P22290 have highly motif concentrations of amino acids. Here Pstands for proline (P), Estands for glutamic acid (E), Stands for serine (S), threonine (T) and to a lesser extent aspartic acid (D). It seems that PEST motifs of P22290 reduce the half-lives of proteins dramatically and hence, that they target proteins for photolytic degradation of P22290.In the PEST-FIND bioinformatics tool PEST word is defined as rich in amino acid P stand for proline,E stands for glutamic acid, S stands for stanserine and T stand for threonine amino acid.

It basically represents the proteins that have a short intracellular half-life; therefore, it is hypothesized that the PEST sequence acts as a signal peptide for protein degradation and can

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help to find invading process between *P.vivax* and erythrocytes.

P22290 have 1070 amino acid which is used for PEST FIND tool.
1 mkgknrslfv llvllllhkv nnvllertie tlleckneyv kgengyklak ghhcveednl

61 erwlqgtner rseenikyky gvtelkikya qmngkrssri lkesiygahn fggnsymegk

121 dggdktgeek dgehktdskt dngkgannlv mldyetssng qpagtldnvl efvtghegns

181 rknssnggnp ydidhkktis saiinhaflq ntvmkncnyk rkrrerdwdc ntkkdvcipd

241 rryqlcmkel tnlvnntdtn fhrditfrkl ylkrkliyda avegdlllkl nnyrynkdfc

301 kdirwslgdf gdiimgtdme gigyskvven nlrsifgtde kaqqrrkqww neskaqiwta

361 mmysvkkrlk gnfiwickln vavniepqiy rwirewgrdy vselptevqk lkekcdgkin

421 ytdkkvckvp pcqnacksyd qwitrkknqw dvlsnkfisv knaekvqtag ivtpydilkq

481 eldefnevaf eneinkrdga yielcvcsve eakkntqevv tnvdnaaksq atnsnpisqp

541 vdsskaekvp gdsthgnvns gqdssttgka vtgdgqngnq tpaesdvqrs diaesvsakn

601 vdpqksvskr sddtasvtgi aeagkenlga snsrpsestv eanspgddtv nsasipvvsg

661 enplvtpyng lrhskdnsds dgpaesmanp dsnskgetgk gqdndmakat kdssnssdgt

721 ssatgdttda vdreinkgvp edrdktvgsk dgggednsan kdaatvvged rirensaggs

781 tndrskndte kngastpdsk qsedatalsk teslestesg drttndttns lenknggkek

841 dlqkhdfksn dtpneepnsd qttdaeghdr dsikndkaer rkhmnkdtft kntnshhlns

901 nnnlsngkld ikeykyrdvk atrediilms svrkcnnnis leycnsvedk issntcsrek

961 sknlccsisd fclnyfdvys yeylscmkke fedpsykcft kggfkdktyf aaagallill

1021 lliasrkmik ndseeatfne feeycdnihr iplmpnnieh mqpstpldys

P22290 M.W. is 119683.1, amino acids present in P222290: 1070. P22290 Theoretical pI: 5.79.PEST result:- 12.63
We found 19 Potential PEST genes find between in-between position 675 and 695.
675 KDNSDSDGPAESMANPDSNSK 695
DPEST RESULT of this area: 47.14 % (w/w). HPindex of this area: 26.60. PEST result in this area: 12.63

Table-1 Presence of Potential PEST genes finds in-between position 675 and 695.

Presence of Potential PEST genes finds in-between position 675 and 695.	19

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22290 DEPST result of this area	7.14%(w/w)
Pindex of this area:	6.60
PESTRESULT in this area:	2.63

We found 19 Potential PEST genes find between in-between position 848 and 868.
848 KSNDTPNEEPNSDQTTDAEGH 868
DEPST RESULT of this area : 53.77 % (w/w). HP index of this area: 21.11
PEST RESULT of this area: 19.02

Table-2: Presence ofPotential PEST genes find between in-between position 848 and 868.

Presence of Potential PEST genes in-between positions848and 868.	19
22290 DPEST result of this area	3.77%(w/w)
HPindex of this area :	1.11
ESTRESULT of this area:	9.02

PEST is basically used for searching highly potential motifs as potential photolytic cleavage sites for insertion in erythrocytes. We found the Gene area with 31 amino acids was very poor which are situated in between position 848-868 with PEST score result is -9.38.We found 9 PEST gene area in P22290 situated in positions of 1 to 1070.We found 37 amino acid Poor PEST gene area of P22290 situated between position 634 and 672.

634 RPSESTVEANSPGDDTVNSASIPVVSGENPLVTPYNGLR 672. PEST score this area: 3.21

We found 31 amino acid Poor PEST gene area of P22290 situated between positions 144 and 176.
144 KGANNLVMLDYETSSNGQPAGTLDNVLEFVTGH 176. PEST score of this area: -9.38

We found 19 amino acids Poor PEST gene areaof P22290 withsituated between position 569 and 589.
569 KAVTGDGQNGNQTPAESDVQR 589. PEST score of this area: -2.82

We found 16 amino acids Poor PEST gene area of P22290 with situated between position 528 and 545.
528 KSQATNSNPISQPVDSSK 545. PEST score of this area: 0.81

We found 13 amino acids Poor PEST motif of P22290 with situated between position 465 and 479.
465 KVQTAGIVTPYDILK 479. PEST score this area: -24.25

We found 12 amino acids Poor PEST gene area of P22290 with situated between positions 182 and 195.
182 KNSSNGGNPYDIDH 195. PEST score of this area: -8.10

We found 11 amino acids Poor PEST gene area of P22290 with situated between position 398 and 410.
398 RDYVSELPTEVQK 410. PEST score of this area: -5.69

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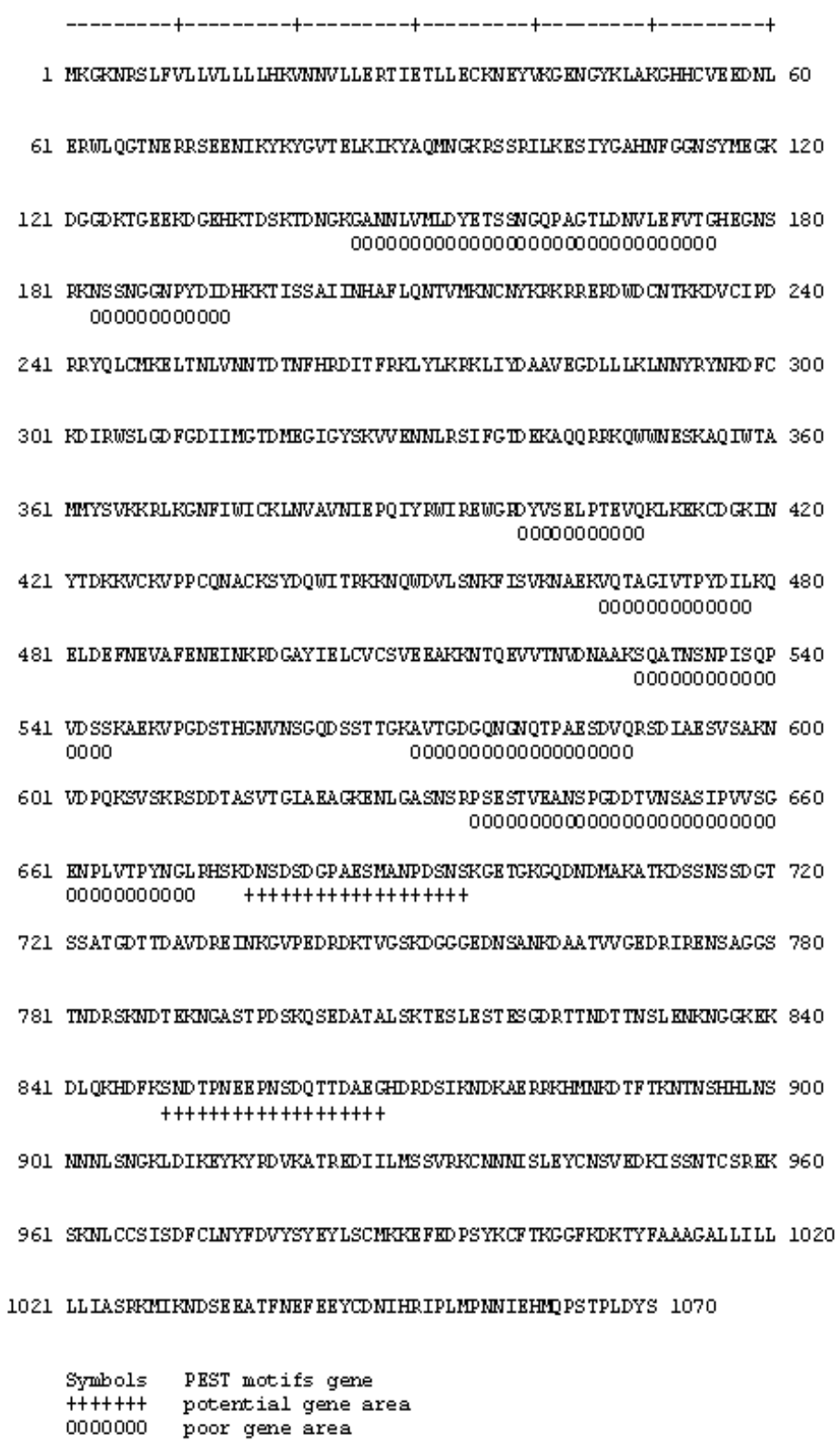

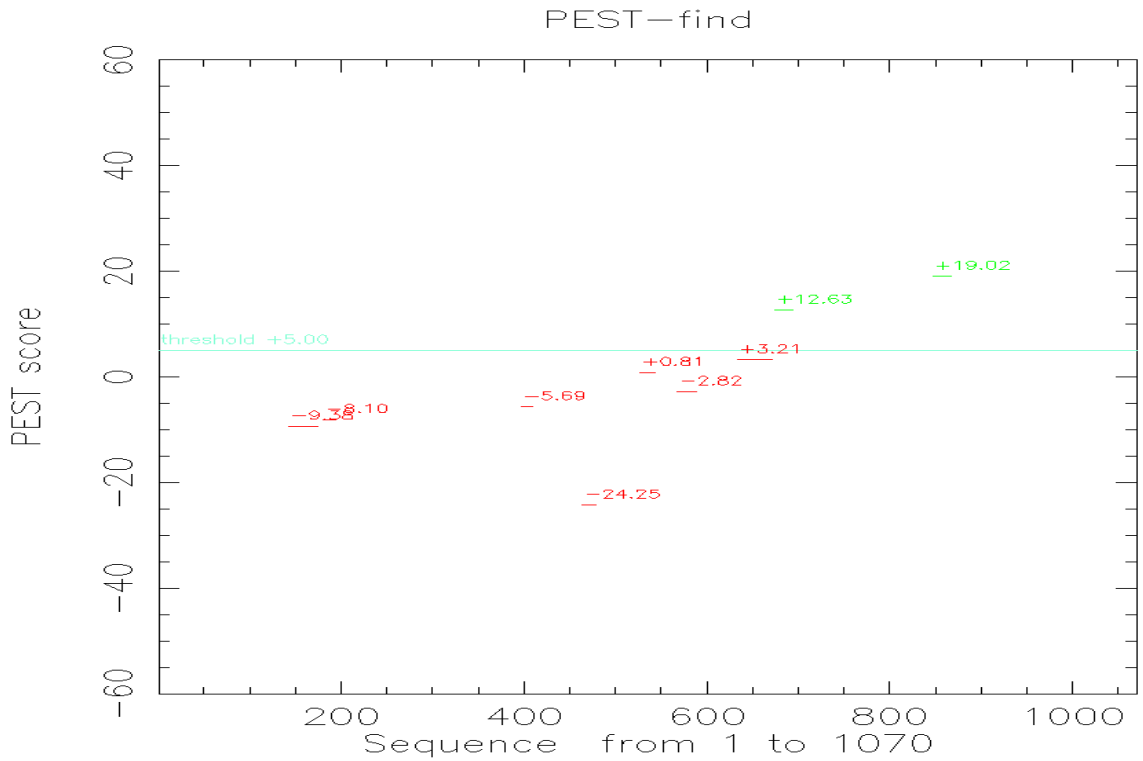

FIGURE 1

Conclusions;-

The output from PEST FIND shows the highest potential. The reports show us poor and potential PEST motifs together with their PEST score, mass percent of DEPST and their hydrophobicity index present in P22290.

The PEST score shows

Motifs below the threshold PESTscore (5.0) are considered as poor, while PEST scores above the (5.0) score are of real biological interest.

Results;-

A bioinformatics methodology PEST FIND for identifying potentially secreted *P. vivax* P22290 proteins was used . This methodology shows the result of identifying poor and potential PEST motifs area together with their PEST score, mass percent of DEPST and their hydrophobicity index present in P22290. The Motifs below the threshold PESTscore (5.0) are considered as poor, while PEST scores above the (5.0) score are of real biological interest. The higher the PEST score, the more likely is degradation of proteins mediated via 'potential' PEST motifs in *P.vivax*.

This kind of bioinformatics approach for *P.vivax* protein P22290 with specific functions plays very important role for supporting the protein large-scale analyses of sites for inserting protein P22290 in erythrocytes surface that could be found in the identification of special sites or areas of particular gene which help in encoding and has efficiency of being highly suitable for new target antigens for vaccine development against *P.vivax*and also for drug design against malaria.

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REFERENCES

1. S.P. Wertheimer and J.W. Barnwell ,"*Plasmodium vivax* interaction with the human Duffy blood group glycoprotein: identification of a parasite receptor-like protein", Exp Parasitol.,vol. 69,no. 3,**(1989)**,pp.340–50.
2. Miller, L. H, S. J. Mason, D. F. Clyde and M. H. McGinniss,"The resistance factor to *Plasmodium vivax* in blacks: the Duffy-blood-group genotype", New England Journal of Medicine., vol. 295, no. 6**, (1976)**, pp. 302-304.
3. J. L. Cole-Tobian, A. Cortés, M. Baisor, W. Kastens, J. Xainli, M. Bockarie and C. L. King, "Age-acquired immunity to a *Plasmodium vivax* invasion ligand, the Duffy binding protein", The Journal of infectious diseases.,vol.186, no.4, **(2002)**,pp. 531-539.
4. J. H. Adams, D. E. Hudson, M. Torii, G. E. Ward, T. E. Wellems, M. Aikawa and L. H. Miller,"The Duffy receptor family of *Plasmodium knowlesi* is located within the micronemes of invasive malaria merozoites", Cell., vol. 63,no.1,**(1990)**,pp.141-153.
5. C. A. Guerra, R. W. Snow and S. I. Hay, "Mapping the global extent of malaria in 2005",Trends in Parasitology., vol. 22,no.8,**(2006)**,pp. 353-358.
6. E. Chen, N. D. Salinas, F. B. Ntumngia, J. H. Adams and N. H. Tolia,"Structural analysis of the synthetic Duffy Binding Protein (DBP) antigen DEKnull relevant for Plasmodium vivax malaria vaccine design", PLoS neglected tropical diseases.,vol. 9,no.3, **(2015)**, pp. e0003644.
7. J. D. Batchelor, B. M. Malpede, N. S. Omattage, G. T. DeKoster, K. A. Henzler-Wildman and N. H. Tolia, "Red blood cell invasion by *Plasmodium vivax*: structural basis for DBP engagement of DARC", PLoS pathogens., vol. 10,no.1,**(2014)**, pp. e1003869.
8. J. G. Beeson and B. S. Crabb,"Towards a vaccine against Plasmodium vivax malaria", *PLoS medicine.*,vol. *4*,no. 12, **(2007)**,pp. e350.
9. L. Babaeekho, S. Zakeri and N. D. Djadid, "Genetic mapping of the duffy binding protein (DBP) ligand domain of *Plasmodium vivax* from unstable malaria region in the Middle East", The American journal of tropical medicine and hygiene., vol. 80,no.1**, (2009)**,pp. 112-118.
10. S. P. Wertheimer and J. W. Barnwell, "*Plasmodium vivax* interaction with the human Duffy blood group glycoprotein: identification of a parasite receptor-like protein", Experimental Parasitology., vol. 69, no.3, **(1989)**, pp.340-350.
11. R. Horuk, C. E. Chitnis, W. C. Darbonne, T. J. Colby, A. Rybicki, T. J. Hadley and L. H. Miller ,"A receptor for the malaria parasite Plasmodium vivax: the erythrocyte chemokine receptor", Science.,*vol. 261*,no. 5125, **(1993)**,pp. 1182-1184.
12. M. C. Szabo, K. S. Soo, A. Zlotnik and T. J. Schall, "Chemokine class differences in binding to the Duffy antigen-erythrocyte chemokine receptor", Journal of Biological Chemistry., vol.270, no. 43,**(1995)**,pp. 25348-25351.
13. R. L. D. Machado, Á. A. R. D. A. Couto, C. E. Cavasini and V. S. P. Calvosa, "Malaria outside the Brazilian Amazonian region: the situation in Santa Catarina State", Revista da Sociedade Brasileira de Medicina Tropical.,vol. 36,no.5, **(2003)**, pp. 581-586.
14. H. G. Klein and D. J. Anstee," *Mollison's blood transfusion in clinical medicine*", John Wiley & Sons, **(2014)**.
15. J. Xainli, J. H. Adams and C. L. King,"The erythrocyte binding motif of Plasmodium vivax Duffy binding protein is highly polymorphic and functionally conserved in isolates from Papua New Guinea", *Molecular and biochemical Parasitology.*, vol. *111*,no. 2, **(2000)**,pp.253-260.

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