

In-silico structural modelling and prediction of conformational B- cell epitopes of potential vaccine candidate PRE- binding protein

Sanasam Bijara Devi¹ and Sanjeev Kumar²

Email ID: jarasanasam@gmail.com

Abstract

Malaria is a life threatening infectious disease causes by *Plasmodium* species, wherein *Plasmodium falciparum* being the most lethal causes severe malaria [1,2]. *Plasmodium* parasites have a complex life cycle and employed several immunity evading mechanism that enable the parasite to multiply and survive avoiding the host immunity [3]. Alternative pathway and multiple proteins are available to achieve similar function if any pathway got blocked which makes vaccine development a difficult task [4]. The rise in drug-resistant *Plasmodium* parasites and the unavailability of an effective vaccine lead to major challenges in controlling the parasite. Drug resistance has been also reported towards Artemisinin combination therapies (ACTs), which is the most accepted and recommended therapy, giving a major impact to the human health [5]. And RTS,S/AS01, which is the only accepted vaccine, has low efficacy and doesn't provide full protection [6]. Therefore, it is of utmost important to identify novel potential targets that can be directed for therapeutic intervention [7]. The present study hypothesized highly conserved protein, PRE-binding protein (PREBP), as a potential vaccine candidate for malaria vaccine development. PREBP is an exposed surface protein with high antigenic property and conservancy among other species of the parasite. In the present study, conservancy, localisation and the antigenicity of PREBP was determined by using different bioinformatics tools. And the 3D structure of PREBP (Figure1) was modelled using Robetta tool [8] and the quality of the generated model was further validated by generating Ramachandran plot . Conformational B cell epitopes of the protein were predicted using Ellipro [9]. The generated 3-D structure of the protein can be further used for other structural analysis and docking studies. And the resulted epitopes might be of great importance as a vaccine subunit in the development of an effective malaria vaccine.

Keywords: PREBP, vaccine, epitopes, *Plasmodium falciparum*, malaria

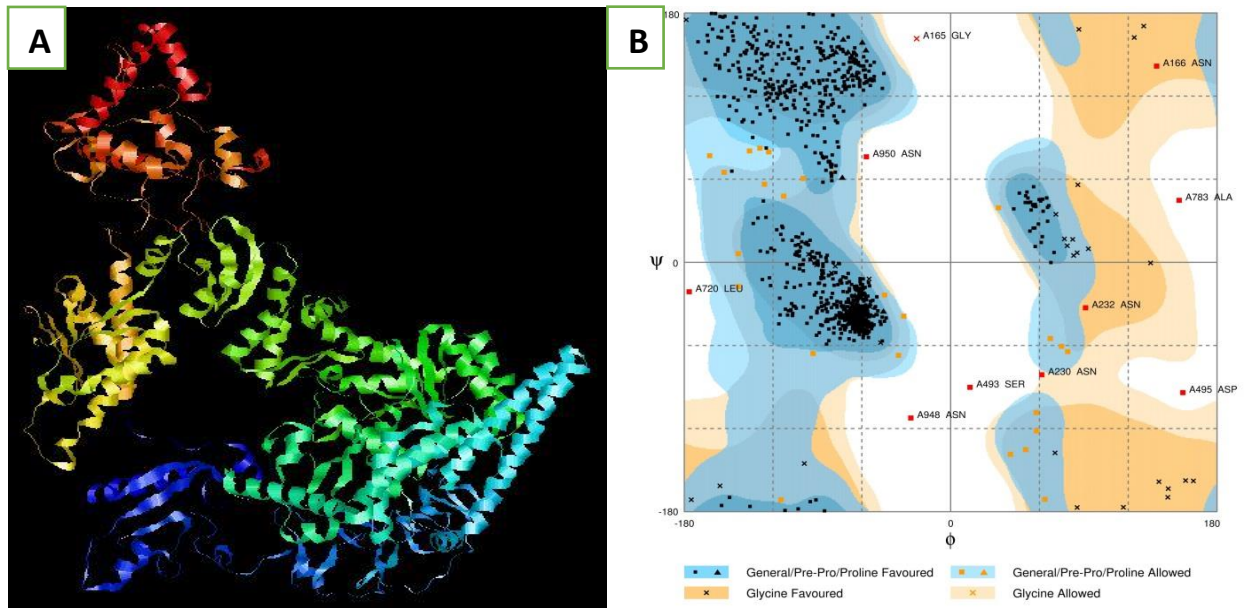


Figure 1 A) Modeled 3D structure of PREBP B) Ramachandran plot of the modeled 3D structure showing 96.9% residues in the favored region.

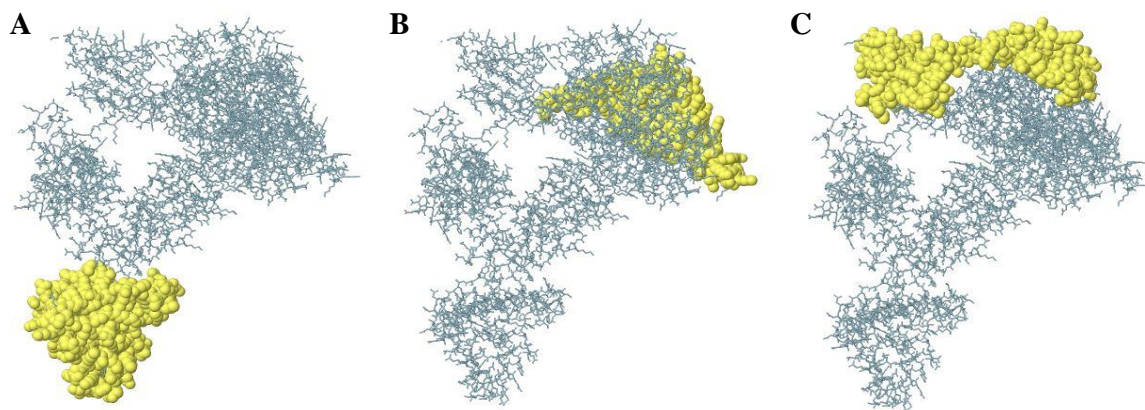


Figure 2 Structures of the conformational B-cell epitopes of PREBP

Table 1 Discontinuous B-cell epitopes of PREBP predicted by Ellipro

S/N	Residues	No. of residues	Scores	3D Structure
1.	A:N953, A:N954, A:S955, A:S956, A:S957, A:N958, A:G959, A:G960, A:A961, A:F962, A:N963, A:N964, A:S965, A:Y966, A:H967, A:E968, A:S969, A:R970, A:Y971, A:N972, A:N973, A:R974, A:H975, A:S976, A:N977, A:N978, A:S979, A:S980, A:S981, A:A982, A:H983, A:H984, A:R985, A:K986, A:S987, A:H988, A:K989, A:S990, A:T991, A:S992, A:R993, A:S994, A:A995, A:P996, A:G1008, A:I1011, A:N1012, A:T1013, A:D1015, A:E1016, A:K1017, A:A1018, A:F1019, A:P1020, A:S1021, A:L1022, A:H1023, A:D1024, A:V1025, A:T1026, A:N1027, A:M1028, A:Q1029, A:S1030, A:K1031, A:K1032, A:N1033, A:K1034, A:K1035, A:L1036, A:S1037, A:Q1038, A:S1039, A:N1040, A:Q1041, A:T1042, A:T1043, A:N1044, A:T1045, A:K1046, A:K1047, A:H1048, A:E1049, A:Q1050, A:A1051, A:P1052, A:Q1053, A:I1054, A:D1055, A:K1056, A:Q1057, A:T1058, A:N1059, A:K1060, A:N1061, A:E1062, A:E1063, A:D1064, A:K1065, A:E1066, A:N1067, A:Q1068, A:P1069, A:K1070, A:N1071, A:E1072, A:V1073, A:H1074, A:A1075, A:E1076, A:T1077, A:D1078, A:V1079, A:T1080, A:K1081, A:N1082, A:E1083, A:T1084, A:Q1085, A:E1086, A:K1087, A:E1088, A:E1089, A:Q1090, A:Q1091, A:Q1092, A:E1093, A:K1095, A:K1096, A:D1097, A:K1098, A:Q1099, A:E1100, A:N1102, A:Q1103, A:E1104, A:L1105, A:N1106, A:Q1107, A:T1108, A:E1109, A:K1110, A:E1111, A:Q1112, A:E1113, A:K1114, A:E1115, A:Q1116, A:E1117, A:K1118, A:E1119, A:E1121, A:K1122, A:E1123, A:Q1124, A:E1125, A:K1126, A:E1127, A:Q1128, A:E1129, A:K1130, A:E1131, A:Q1132, A:E1133, A:K1134, A:Q1135, A:S1136, A:N1137, A:E1138, A:N1139	170	0.794	Fig.2 (A)
2.	A:S238, A:D239, A:K242, A:D243, A:W244, A:K245, A:K246, A:E247, A:I248, A:K249, A:L250, A:K251, A:E252, A:D253, A:E254, A:R255, A:K256, A:K257, A:S258, A:E259, A:N260, A:D261, A:L262, A:K263, A:K264, A:K265, A:F266, A:V267, A:K268, A:L269, A:N270, A:K271, A:A272, A:D273, A:N274, A:Y275, A:K276, A:N277, A:I278, A:N279, A:D280, A:K281, A:E283, A:A284, A:E285, A:I286, A:K287, A:K288, A:K289, A:I290, A:E291, A:I292, A:E293, A:N294, A:F295, A:I296, A:S297, A:T298, A:I299, A:N300, A:S301, A:T302, A:I303, A:S304, A:R305, A:F306, A:N307, A:G308, A:Q309, A:T310, A:T311, A:R312, A:P313, A:I314, A:N315, A:M316, A:K317, A:L318, A:S319, A:S320, A:A321, A:D322, A:M323, A:E324, A:C327, A:A330, A:K331, A:K333, A:I337, A:N338, A:P339, A:K340, A:N341, A:L342, A:E343, A:E344, A:I345, A:E346, A:E347, A:A348, A:N349, A:T350, A:Y351, A:I352, A:N353, A:Y354, A:L355, A:E356, A:E357, A:Q358, A:L359, A:S360, A:I361, A:T362, A:K363, A:N364, A:Y365, A:E366, A:N367, A:F368, A:K369, A:N370, A:F371, A:Q372, A:N373, A:R374, A:L375, A:I376, A:S377, A:L378, A:R379, A:K380, A:I381, A:C382, A:E383, A:L386, A:K387, A:E388, A:N389, A:L390, A:K391, A:S392, A:M393, A:N394, A:E395, A:T396, A:K397, A:I398, A:Q399, A:E400, A:K402, A:L403, A:R404, A:V406, A:D407, A:I410, A:K411	157	0.777	Fig.2 (B)

3. A:V16, A:N17, A:K18, A:N19, A:S20, A:V22, A:M26, A:A29, A:L30, 137 0.66 Fig.2 (C)
A:N32, A:D33, A:K34, A:K35, A:Q36, A:G37, A:G38, A:S39, A:K40,
A:S54, A:N55, A:A56, A:H57, A:M58, A:N59, A:G60, A:S61, A:I62,
A:Q63, A:K65, A:K66, A:E67, A:E68, A:N69, A:E70, A:L71, A:E72,
A:N73, A:N74, A:K75, A:K76, A:L77, A:N78, A:H79, A:K80, A:N81,
A:N82, A:L83, A:N86, A:C87, A:V88, A:I89, A:K90, A:S91, A:K92,
A:E93, A:V94, A:V95, A:K96, A:G97, A:G98, A:D99, A:Q100,
A:K101, A:N102, A:E103, A:G104, A:Q105, A:A106, A:K107,
A:K108, A:K109, A:N110, A:N111, A:N112, A:N113, A:N114,
A:N115, A:K118, A:K119, A:K120, A:G121, A:T122, A:E124,
A:D126, A:D138, A:D139, A:K140, A:K154, A:N155, A:K156,
A:G157, A:S158, A:N159, A:N160, A:K161, A:K162, A:Y163,
A:V164, A:G165, A:M171, A:K172, A:V173, A:E174, A:L175,
A:M176, A:D177, A:N181, A:N182, A:N183, A:S184, A:T185,
A:N186, A:T187, A:S193, A:N194, A:N195, A:N208, A:N209,
A:N210, A:N211, A:N212, A:N213, A:N214, A:N215, A:K216,
A:N217, A:K218, A:N219, A:N220, A:N221, A:N222, A:N223,
A:N224, A:N225, A:I226, A:I227, A:S228
-

References

- [1] Kantele A, Jokiranta TS. Review of Cases With the Emerging Fifth Human Malaria Parasite , Plasmodium knowlesi. *Clin Infect Dis* 2011;52:1356–62. doi:10.1093/cid/cir180.
- [2] Artavanis-Tsakonas K, Tongren JE, Riley EM. The war between the malaria parasite and the immune system: Immunity, immunoregulation and immunopathology. *Clin Exp Immunol* 2003;133:145–52. doi:10.1046/j.1365-2249.2003.02174.x.
- [3] Hafalla JC, Silvie O, Matuschewski K. Cell biology and immunology of malaria. *Immunol Rev* 2011;240:297–316. doi:10.1111/j.1600-065X.2010.00988.x.
- [4] Kinyanjui SM. The immunology of Malaria. *Malar. Parasites*, 2012, p. 175–200.
- [5] Mokgethi-Morule T, N'Da DD. Cell based assays for anti-Plasmodium activity evaluation. *Eur J Pharm Sci* 2016;84:26–36. doi:10.1016/j.ejps.2016.01.001.
- [6] Mahmoudi S, Keshavarz H. Efficacy of phase 3 trial of RTS,S/AS01 malaria vaccine : The need for an alternative development plan. *Hum Vaccine Immunother* 2017;13:2098–101.
- [7] Kaur K, Jain M, Kaur T, Jain R. Antimalarials from nature. *Bioorganic Med Chem* 2009;17:3229–56. doi:10.1016/j.bmc.2009.02.050.
- [8] Kim DE, Chivian D, Baker D. Protein structure prediction and analysis using the Robetta server. *Nucleic Acids Res* 2004;32:W526–31. doi:10.1093/nar/gkh468.
- [9] Ponomarenko J, Bui H-H, Li W, Fusseder N, Bourne PE, Sette A, et al. ElliPro: a new structure-based tool for the prediction of antibody epitopes. *BMC Bioinformatics* 2008;9:514. doi:10.1186/1471-2105-9-514.