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Original Article

Predicted epitopes of malarial merozoite surface protein 1 by bioinformatics method: a clue for further vaccine development

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Background and purpose: Malarial merozoite surface protein 1 (MSP-1) may have value as a protective immunogen in novel vaccines against malaria. This study was performed to find potential T-cell epitopes for MSP-1 of *Plasmodium vivax*.

Methods: Computation analysis of available MSP-1 of the *P. vivax* malaria sequence was performed to find potential T-cell epitopes using MHCPred version 2.0. Alleles for binding affinity prediction were selected and the peptides with the best binding affinities for each allele were investigated.

Results: The peptides with the best predicted binding affinities were human leukocyte antigen (HLA)-DRB0101, HLA-A0203, and HLA-DRB0701, which showed significantly lower 50% inhibitory concentration values than the other alleles.

Conclusion: These data are useful for further vaccine development because the promiscuous peptide binders enable reduction of the number of predicted epitopes without compromising the population coverage required for vaccine design.

Key words: Alleles; Epitopes; Malaria; Merozoite surface protein 1

Introduction

Malaria is an important potentially fatal mosquito-borne parasitic infection in tropical regions [1]. Despite decades of control success and networks of country-wide health infrastructure, malarial infection is still a threat to health in tropical and non-tropical countries [2]. Development and approval of new vaccines are required to control the emerging pandemic of this infection. Based on advances in bioinformatics, application of immunomics could be an alternative approach to vaccine development [3,4].

Advanced technologies for vaccine development, such as genome sequence analysis, microarrays, proteomics, high-throughput cloning, bioinformatics database tools, and computational vaccinology, can be used to further the process of vaccine development for several diseases, including currently emerging diseases.

Prediction of peptide binding to major histocompatibility complex (MHC) molecules is a fundamental step for epitope discovery–driven vaccine development. Current developments in computational vaccinology help to analyze antigen processing and presentation, and the characterization of determined targets of immune response. Databases and data mining are the 2 basic tools for the disposal of present in silico vaccinologists around the world. As vaccinologists have to manage an expanding volume of information available from genome databases, they are currently focusing on epitope mapping tools to screen vaccine candidates [3,4]. New databases have been produced that facilitate epitope prediction.

It is important for vaccine development to detect the antigenic specific targets for protective antibodies and to realize the consequences of sequence variation [5]. There is an urgent requirement for a vaccine against malaria, and proteins on the surface of the

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malarial merozoite are good targets for development as vaccine candidates because they are overt to antibody. However, it is possible that the parasite has evolved mechanisms to escape and to create a protective immune response to these proteins [6]. Malarial merozoite surface protein 1 (MSP-1) is a suitable candidate for malarial vaccine development, as its C-terminal sequence is the target of protective antibody. MSP-1 is cleaved by proteases in 2 processing steps, the second of which releases the bulk of the protein from the surface and completes during final red blood cell invasion [6]. MSP-1 is a target for vaccine development, [5-7] and MSP-1 of *Plasmodium falciparum* has been well studied. However, knowledge of *Plasmodium vivax*, another problematic malarial species, is limited. Therefore, this study was performed to find potential T-cell epitopes for MSP-1 of *P. vivax*. The preliminary data from the computational analysis of MSP-1 using a new bioinformatics tool are reported.

Methods

Computation analysis of available MSP-1 of the *P. vivax* malaria sequence (accession number = AAO62014, 173 residues) was performed to find potential T-cell epitopes using MHCPred version 2.0 (a bioinformatics tool; available from: www.jenner.ac.uk/MHCPred) [8]. The selected alleles for binding affinity prediction were human leukocyte antigen (HLA)–A0101, HLA-A0201, HLA-A0202, HLA-A0203, HLA-A0206, HLA-A0301, HLA-A1101, HLA-A3101, HLA-A6801, HLA-A6802, HLA-B3501, HLA-DRB0101, HLA-DRB0401, and HLA-DRB0701. The peptides with the best binding affinities for each allele were investigated.

Results

The results of the computational analysis included peptides and their corresponding 50% inhibitory concentration (IC_{50}) value. The peptides with the best-predicted binding affinities are shown in Table 1. HLA-DRB 0101, HLA-A 0203, and HLA-DRB 0701 showed significantly lower IC_{50} values than the other alleles.

Table 1. Peptides with the best-predicted binding affinities for each allele.

Allele	Peptide	IC_{50}
HLA-A0101	50 ETGTTGNTV58	126.47
HLA-A0201	12 KLKDFIPKI20	4.17
HLA-A0202	158 YLQKLLDFL166	9.38
HLA-A0203	148 APAPTMSKL156	2.29
HLA-A0206	25 ATEKNKPTV33	16.11
HLA-A0301	11 DKLKDFIPK19	51.76
HLA-A1101	37 AVVQPPQHQ71	11.40
HLA-A3101	38 IVAKGQSLR46	131.83
HLA-A6801	163 LDFLKSAYA171	16.63
HLA-A6802	98 SVQAAQVQQ106	10.94
HLA-B3501	148 APAPTMSKL156	215.77
HLA-DRB0101	140 PSTPAAAVA148	0.80
HLA-DRB0401	98 SVQAAQVQQ106	28.97
HLA-DRB0701	70 HQVVNAVTV78	3.16

Abbreviations: IC_{50} = 50% inhibitory concentration value; HLA = human leukocyte antigen

Discussion

Identification of epitopes capable of binding multiple HLA types will significantly rationalize the development of new vaccines [9]. In this study, a new bioinformatics tool, MHCPred version 2.0, was used to predict potential T-cell epitopes. MHCPred was designed as a partial least squares–based multivariate robust statistical tool for the quantitative prediction of peptide binding to MHC, an important checkpoint on the antigen presentation pathway within adaptive cellular immunity [8]. MHCPred uses robust statistical models for both class I alleles (HLA-A0101, HLA-A0201, HLA-A0202, HLA-A0203, HLA-A0206, HLA-A0301, HLA-A1101, HLA-A3101, HLA-A6801, HLA-A6802, and HLA-B3501) and class II alleles (HLA-DRB0101, HLA-DRB0401, and HLA-DRB0701) [8]. The computational analysis included peptides and their corresponding IC_{50} values, which further shows the binding affinity. Usually, peptides with predicted binding affinities of <500 nM are classified as good binders, whereas those with binding affinities >5000 nM are determined as non-binders [10]. The technique used for this study was similar to that used in other recent reports [11-13], and is accepted for its efficacy and validity in epitope prediction [10,14,15]. With 90% correct predictions, MHCPred is currently the most reliable predictive tool [15].

The peptides with the best binding affinities for each allele were investigated. These peptides are useful markers for further vaccine development, and can save time by minimizing the number of tests needed to find possible epitopes, which are new targets for vaccine development. A previous study has successfully used the immunomics technique to determine other malarial epitopes [16] and found that the immunomics-based approach is valid and acceptable.

There were some limitations to this study. The results are predicted, hence further confirmation is required. In vitro synthesis of the determined peptide and in vivo experimental study to test the efficacy are required for further vaccine development.

In this study, computational analysis was used to determine the potential T-cell epitopes of MSP-1. The results showed that 140 PSTPAAAVA148 corresponding to the HLA-DRB0101 allele is the best binding affinity peptide.

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