Immunoinformatics Prediction of an Epitope Based Peptide Vaccine for Neisseria Gonorrhea Dihydrolipoamide Acetyltransferase Protein

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Abstract: Sexually transmitted infections (STIs) such as *Gonorrhea* is associated with serious morbidity and mortality rates in the world considering the multiple virulence factors possessed. The disease is manifested as salpingitis, pelvic inflammatory disease (PID), and bacteremia and is controlled by macrophages, dendritic cells, neutrophils, T cells, epithelial cells and cytokines. Dihydroliponamide acetyltransferase, a component of the mitochondrial pyruvate complex can be used as immunogenic target. Recent changes in the strain allowed the bacteria to acquire resistance against antibiotics.Vaccination remains an alternative to prevention against the disease. This study predicts an effective epitope-based vaccine against dihydrolipoamide acetyltransferase of *Neisseria Gonorrhea* using immunoinformatics approaches. Sequences retrieved from NCBI were passed on several prediction tests to analyze for possible B-cell, T-cell MHC class I epitopes and class II. Two epitopes showed high binding affinity for B-cells, while thirteen epitopes showed high binding affinity for MHCI and forty-five for MHCII. A population coverage of 100% for combined MHC I and II dictates the huge number of individuals who will benefit from formulating the vaccine. We recommend invivo and invitro studies to prove our prediction results.

Keywords:*Immunoinformatics, Neisseria Gonorrhea, Dihydroliponamide Acetyltransferase, Peptide vaccine, Epitope.*

INTRODUCTION

Sexually transmitted infections(STIs) such as *Gonorrhea* is considered one of the major threat to the public health. It is also associated with serious morbidity and mortality[1-3]. Almost one million persons suffered from a curable STI daily[4]. *Neisseria Gonorrhea* which is the causative agent of Gonorrhea, is a gram-negative diplococcus. It poses a growing threat to the public health concern, as evident by the estimated 78 million infections per year[5].*N. Gonorrhea* infections usually start at the urogenital, rectal, and nasopharyngeal mucosa. The infection can ascend, causing salpingitis, pelvic inflammatory disease (PID), bacteremia, and it can cross the endothelial barrier even disseminated gonococcal infection (DGI) [6]. The pathogenesis of gonorrhea is regulated by macrophages, dendritic cells, neutrophils, T cells, epithelial cells and cytokines[7].N. gonorrhoeae has multiple virulence factors like lipooligosaccharide (LOS), type IV pili, opacity associated (Opa) proteins, and an outer membrane porin PorB, that among other roles will help the bacteria to survive in the presence of serum.[5]Nucleic acid amplification tests (NAAT) are the preferred method used for diagnosis of *N. Gonorrhea* infection.[8]

Furthermore, *Neisseria Gonorrhea* is able to accumulate different mutations leading to the emergence of clinical isolates with clinically significant levels of resistance to currently or previously used antibiotics such as sulfa-drugs, penicillins and tetracyclines which has led the WHO to consider adding *N. Gonorrhea* infections to the category of untreatable infections[9-12]. With the absence of effective vaccines, and the lack of prolonged immunity after infection due to multiple evading mechanisms, society relies on antibiotics to reduce the spread of the gonococcus in the community [6, 13, 14].

The aim of this study is to predict an effective epitope-based vaccine against *dihydrolipoamide acetyltransferase* enzyme of *N. gonorrhea* using immunoinformatics approaches. No previous reports were found for *N. gonorrhea* epitope-based vaccine so this is considered the first study to our knowledge to use insilico approach to design an epitope-based vaccine.

Literature showed that there are twenty one potentially immunogenic proteins in the *N. Gonorrhea* genome that could be used as immunogenic targets for vaccine design. Dihydrolipoamide acetyltransferase (DLAT) is one of those targets[15]. It is a component of the mitochondrial pyruvate complex (PDC), and is considered as a novel metabolic longevity factors for many species[16].

Vaccination is generally considered to be the most cost effective method of preventing infectious diseases[17]. Understanding the relation between epitope and antibody interaction is the key to design potent and safe vaccines, and effective new model of diagnostics[18, 19]. These epitopes are capable of inducing B cell and T cell-mediated immunity[17]. Immunoinformatics research focuses on the design and study of algorithms for mapping possible B- and T-cell epitopes. This type of peptide- based vaccine is easier to construct and have a more chemical stability than traditional vaccines. Using such techniques(reverse vaccinology) to analyze the sequence areas with potential binding sites can lead to the development of new vaccines[20].

MATERIALS AND METHODS

Protein Sequence Retrieval

Neisseria Gonorrhea owns a total of 11 strains were retrieved from National Center for Biotechnology Information (NCBI) database on July 2019 in FASTA format. The retrieved protein strains had length of 529 with name dihydrolipoamide acetyltransferase.

Determination of conserved regions

The retrieved sequences of *Neisseria gonorrhea* were showed by multiple sequence alignment (MSA) using ClustalW tool of BioEdit Sequence Alignment Editor Software version 7.2.5 to define the conserved regions.

Sequenced-Based Method

The reference sequence of *Neisseria gonorrhea* was (YP_207709.1). The reference sequence is submitted to different prediction tools at the Immune Epitope Database (IEDB) analysis resource (http://www.iedb.org/) to predict various B and T cell epitopes. The epitope for B and T cell would be filtered form the conserved epitope

B Cell Epitope Prediction

B cell epitopes is the portion of the vaccine that interacts with B lymphocytes. Candidate epitopes were analysed bya number of B cell prediction methods from IEDB (http://tools.iedb.org/bcell/), to identify the surface accessibility, antigenicity and hydrophilicity with the aid of random forest algorithm, a form of unsupervised learning. The Bepipred Linear Epitope Prediction 2 was used to predict linear B- cell epitope with default threshold value of 0.500 (http://tools.iedb.org/bcell/result/). The Emini Surface Accessibility Prediction tool was used to discover the surface accessibility with default threshold value of 1.000 (http://tools.iedb.org/bcell/result/). The Kolaskar and Tongaonker Antigenicity method was used to find the antigenic places of candidate epitope with default threshold value 1.037 (http://tools.iedb.org/bcell/result/). The Parker Hydrophilicity Prediction tool was used to find the hydrophilic, accessible, or movable regions with default threshold value of 1.621.

T- Cell Epitope Prediction MHC Class I Binding

The portion of the vaccine is T cell that cooperates with T lymphocytes. Analysis of peptide binding to the MHC (Major Histocompatibility complex) class I molecule was assessed by the IEDB MHC I prediction tool (http://tools.iedb.org/mhci/) to predict cytotoxic T cell epitopes. The presentation of peptide complex to T lymphocyte undergoes a number of steps. Artificial Neural Network (ANN) 4.0 prediction method was used to predict the binding affinity. Before the prediction, all human allele lengths were selected and set to 9 amino acids. The half-maximal inhibitory concentration (IC50) value required for all conserved epitopes to bind at score less than 100 were selected. [21-27]

T- Cell Epitope Prediction MHC Class II Binding

T- cell epitopes interacting with MHC Class II were assessed by the IEDB MHC II prediction tool (http://tools.iedb.org/mhcii/) for helper T cells. Human allele reference set was used to regulate the interaction potentials of T cell epitopes and MHC Class II allele (HLA DR, DP and DQ). NN-align method was used to predict the binding affinity. IC50 values at score less than 500 were selected. [28-31]

Population Coverage

In IEDB, the population coverage link was selected to analyse the epitopes. This tool gives an illustration about the fraction of individuals predicted to respond to a given set of epitopes with known MHC restrictions (http://tools.iedb.org/population/iedbinput). The appropriate checkbox for calculation was checked based on MHC I, MHC II separately and combination of both.

Homology Modelling

The 3D structure was modelled using raptorX (http://raptorx.uchicago.edu) i.e. a protein structure prediction server developed by Xu group, outstanding at predicting 3D structures for protein sequences without close homologs in the Protein Data Bank (PDB). USCF chimera (version 1.13.1rc) was the program used for visualizing and editingthe molecular structure of the promising epitopes (http://www.cgl.uscf.edu/chimera).

RESULTS

Multiple Sequence Alignment

Eleven *N. Gonorrhea* species *dihydrolipoamide acetyltransferase* (DLAT) protein were selected for Multiple Sequence Alignment to show areas of conservation. (Figure 1)

```
EFE03  1    --------MSIVEIKVPDIGGHESVDIIAVEVKAGDTIAVDDTLITLETDKATMDVPADAAGVVKEVKVKVGDKISEGGVILTVE
EEZ43  1    MKKIKGTQ.............................................................................
YP_20  1    --------...............N.............................................................
KMY24  1    MKKIKGTQ...............N.............................................................
AAW89  1    --------...............N.............................................................
KLS77  1    --------...............N.............................................................
SUA12  1    --------...............N.............................................................
SBM92  1    --------.............................................................................
WP_01  1    --------...............N.............................................................
WP_00  1    --------.............................................................................
OOD38  1    --------...............N.............................................................

EFE03  93   AQPAPAAAGGATVQVAVPDIGGHTDVDVIAVEIKVGDTVAEDDTLITLETDKATMDVPCTAAGVVKAVFLKVGDKVSEGSAIIEV
EEZ43  101  .....................................................................................
YP_20  93   .....................................................................................
KMY24  101  ....................................................................S................
AAW89  93   .....................................................................................
KLS77  93   .....................................................................................
SUA12  93   .....................................................................................
SBM92  93   .....................................................................................
WP_01  93   .....................................................................................
WP_00  93   .....................................................................................
OOD38  93   .....................................................................................

EFE03  193  AAAPAAVPTSAAPAAVPTSASPAAAKIDEAAFAKAHAGPSARKLARELGVDLGQVKGSGLKGRIMGDDIKAFVKSVMQGGAAKPA
EEZ43  201  ........---------....................................................................
YP_20  193  .....................................................................................
KMY24  201  ........---------....................................................................
AAW89  193  .....................................................................................
KLS77  193  .....................................................................................
SUA12  193  .....................................................................................
SBM92  193  .....................................................................................
WP_01  193  .....................................................................................
WP_00  193  .....................................................................................
OOD38  193  .....................................................................................

EFE03  293  PKVDFSKFGNVEVKELSRIKKISGQNLSRNWVVIPHVTVHEEADMTELEEFRKQLNKEWEREGVKLSPLAFIIKASVSALKAFPE
EEZ43  292  .....................................................................................
YP_20  293  .....................................................................................
KMY24  292  .....................................................................................
AAW89  293  .....................................................................................
KLS77  293  .....................................................................................
SUA12  293  .....................................................................................
SBM92  293  .....................................................................................
WP_01  293  .....................................................................................
WP_00  293  .....................................................................................
OOD38  293  .....................................................................................

EFE03  393  FNIGFAADTPNGLVVPVIKDVDQKGLKQISQELTELSKKAREGKLKPQEMQGACFTISSLGGIGGTGFTPIVNAPEVAILGVCKS
EEZ43  392  .....................................................................................
YP_20  393  .....................................................................................
KMY24  392  .....................................................................................
AAW89  393  .....................................................................................
KLS77  393  .....................................................................................
SUA12  393  .....................................................................................
SBM92  393  .....................................................................................
WP_01  393  .....................................................................................
WP_00  393  .....................................................................................
OOD38  393  .....................................................................................

EFE03  493  MCPLSLSFDHRVIDGAAGMRFTVFLANLLKDFRRITL
EEZ43  492  .....................................
YP_20  493  .....................................
KMY24  492  .....................................
AAW89  493  .....................................
KLS77  493  .....................................
SUA12  493  .....................................
SBM92  493  .....................................
WP_01  493  .....................................
WP_00  493  .....................................
OOD38  493  .....................................
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Figure 1: Multiple sequence alignment of N. Gonorrhea, DLAT protein showing the highly conservative protein

B-cell epitope prediction

The reference sequence of *N. Gonorrhea* DLAT was subjected to Bepipred linear epitope 2, EMINI surface accessibility, Kolaskar&Tongaonkar antigenicity and Parker hydrophilicity prediction methods to test for various immunogenicity parameters (Table 1). Two epitopes have successfully passed the three tests. (Table 1)

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Table 1: List of conserved epitopes that had successfully passed the three tests.

Peptide	Start	End	Length	Kolaskar&Tongaonkar antigenicity score (TH: 1.03)	Emini surface accessibility score (TH: 1)	Parker Hydrophilicity prediction score (TH: 1.43)
HVTVHEEAD	328	336	9	1.057	1.202	3.3
VTVHEEAD	329	336	8	1.051	1.098	3.45

T- Cell epitope predictions

MHC class- I binding peptides

The reference sequence was analyzed using (IEDB) MHC-1 binding prediction tool to predict T cell epitopes interacting with different types of MHC Class I alleles. Seventy peptides were predicted to interact with different MHC-I alleles. The most promising epitopes with their corresponding MHC-1 alleles and IC50 scores as shown in (Table 2)

Table 2: T-cell peptides binding MC class I alleles with lowest IC50 and highest number of HLA- hits

Peptides	MHC Class I alleles	No. of MHC-I hits	IC50
FAADTPNGL	HLA-C*03:03, HLA-C*12:03, HLA-A*68:02, HLA-B*35:01, HLA-B*39:01, HLA-C*05:01	6	3.32
FAPRLMCPL	HLA-C*03:03, HLA-A*02:06, HLA-C*12:03, HLA-C*14:02	4	8.48
TVFLANLLK	HLA-A*68:01, HLA-A*11:01, HLA-A*03:01, HLA-A*30:01	4	10.56
FTISSLGGI	HLA-A*68:02, HLA-A*02:06, HLA-A*26:01	3	5.19
KLSPLAFII	HLA-A*02:01, HLA-A*02:06, HLA-A*32:01	3	25.74
TSASPAAAK	HLA-A*68:01, HLA-A*11:01, HLA-A*03:01	3	21.28
AQAAAPAAV	HLA-A*02:06, HLA-B*39:01	2	14.87
FTVFLANLL	HLA-A*68:02, HLA-A*02:06	2	10.04
HEEADMTEL	HLA-B*40:01, HLA-B*40:02	2	8.72
LMCPLSLSF	HLA-B*15:01, HLA-A*32:01	2	4.3
REGVKLSPL	HLA-B*40:02, HLA-B*40:01	2	21.67
SVMQGGAAK	HLA-A*11:01, HLA-A*03:01	2	17.51
TAAGVVKAV	HLA-A*68:02, HLA-C*12:03	2	13.34

MHC class- II binding peptides

The reference sequence was analyzed using (IEDB) MHC-II binding prediction tool there were 438 predicted epitopes found to interact with MHC-II alleles. The most promising epitopes with their corresponding alleles and IC50 scores are shown in (Table 3).

Table 3. T-cell peptides binding MC class II alleles with lowest IC50 and highest number of HLA- hits

Peptide	hits	ic50
GMRFTVFLANLLKDF	27	7.5
MRFTVFLANLLKDFR	24	7.8
RFTVFLANLLKDFRR	24	7.1
AGMRFTVFLANLLKD	23	17.9
FTVFLANLLKDFRRI	23	8.2
IIKASVSALKAFPEF	23	8.4
AAGMRFTVFLANLLK	22	18.8
AFIIKASVSALKAFP	21	4.5
FIIKASVSALKAFPE	21	6.1
LAFIIKASVSALKAF	21	4.5
PLAFIIKASVSALKA	21	5.7
SPLAFIIKASVSALK	21	6.8
EGVKLSPLAFIIKAS	19	139.4
GAAGMRFTVFLANLL	19	22.5
LSPLAFIIKASVSAL	19	8.7
LVLKNYFNIGFAADT	19	24

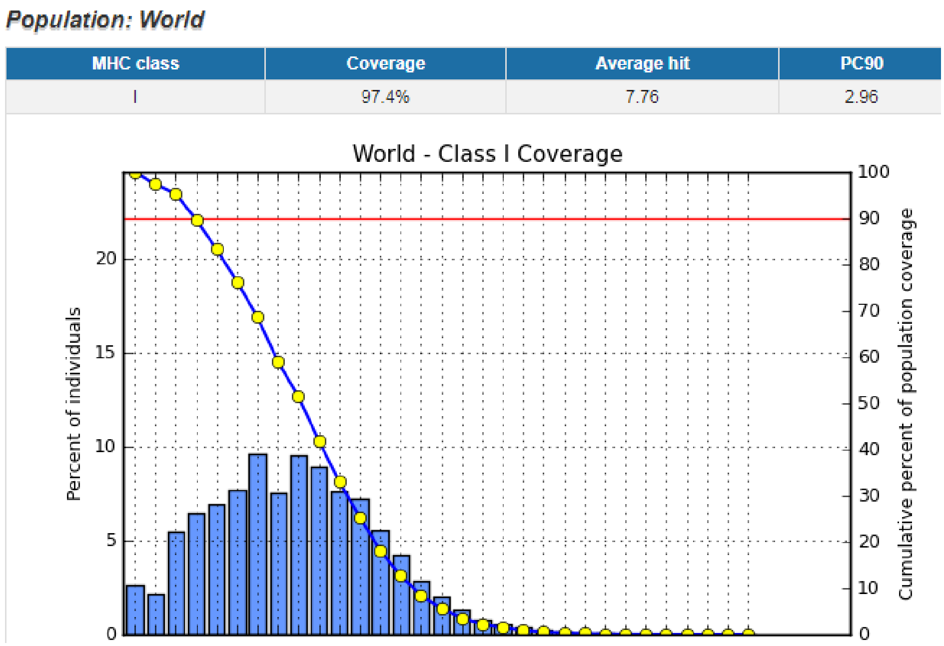
VFLANLLKDFRRITL	19	7.6
VLKNYFNIGFAADTP	19	27.4
NLVLKNYFNIGFAAD	18	82.7
VKLSPLAFIIKASVS	18	42.5
DNLVLKNYFNIGFAA	17	57.8
GDNLVLKNYFNIGFA	17	53
IDGAAGMRFTVFLAN	17	48.2
REGVKLSPLAFIIKA	17	74.4
TVFLANLLKDFRRIT	17	12.1
GVKLSPLAFIIKASV	16	80.6
IKASVSALKAFPEFN	16	12.6
LKNYFNIGFAADTPN	16	20.3
SVSALKAFPEFNASL	16	66.4
APEVAILGVCKSQIK	15	87.2
ASVSALKAFPEFNAS	15	41.8
DIKAFVKSVMQGGAA	15	54.7
EVAILGVCKSQIKPV	15	58.9
RVIDGAAGMRFTVFL	15	27.3
WEREGVKLSPLAFII	15	49.8
DGAAGMRFTVFLANL	14	34.3
DTIAVDDTLITLETD	14	21.1
EMQGACFTISSLGGI	14	68.9
EREGVKLSPLAFIIK	14	65.7
IKAFVKSVMQGGAAK	14	32.6
KASVSALKAFPEFNA	14	19.4
KLSPLAFIIKASVSA	14	14.2
KNYFNIGFAADTPNG	14	16.3
NYFNIGFAADTPNGL	14	8.5
VSALKAFPEFNASLD	14	47

Population coverage:

All MHC II epitopes and I were assessed for population coverage against the whole world using IEDB population coverage tool. For MHC 1, epitopes with highest population coverage were KLSPLAFII (44.14%) and FAADTPNGL (35.02%)(Table 4, Figure 2). For MHC class II, the epitopes that showed highest population coverage were GMRFTVFLANLLKDF (99.93%), AGMRFTVFLANLLKD (99.86%), AAGMRFTVFLANLLK (99.84%), RFTVFLANLLKDFRR (99.81%), and MRFTVFLANLLKDFR (99.81%)(Table 5, Figure 3). As for combined MHC II and I peptides, the global population coverage percentage was approximately 100% (figure 4).

Table 4: Showing peptides binding to MHC class I with the highest global population coverage percentages

Epitope	**Global Population coverage**
FAADTPNGL	35.02%
FAPRLMCPL	22.29%
KLSPLAFII	44.14%
TSASPAAAK	35.75%
TVFLANLLK	38.86%
Total global coverage	**97.4%**



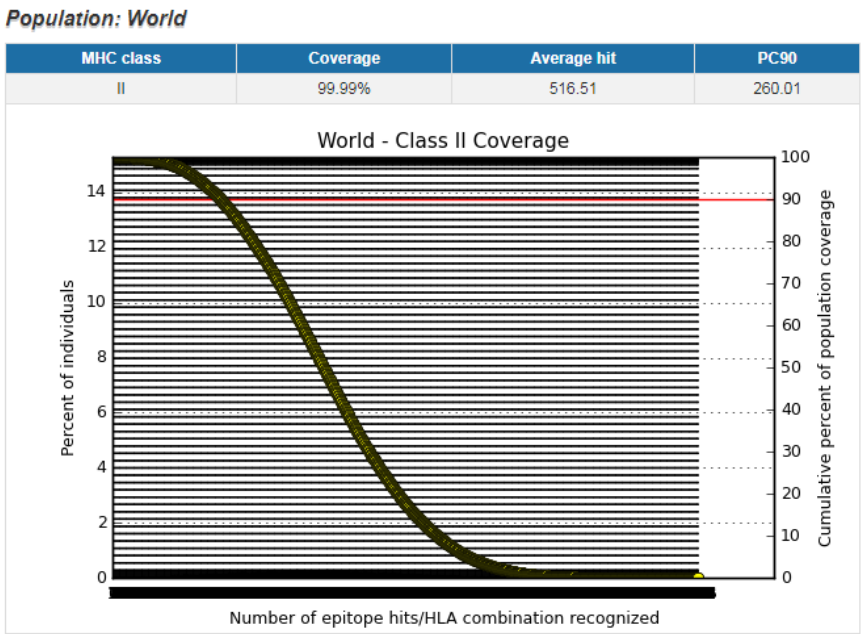
Population: World

MHC class	Coverage	Average hit	PC90
I	97.4%	7.76	2.96

Figure 2: Graph showing the global population coverage of peptides binding to MHC-I alleles

Table 5: Peptides binding to MHC-II alleles with the highest global population coverage percentages

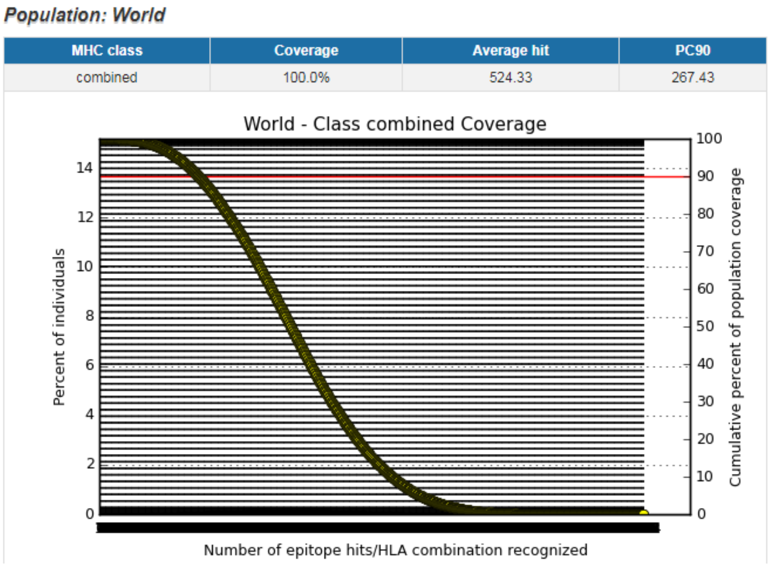
Epitope	Global population Coverage
GMRFTVFLANLLKDF	99.93%
AGMRFTVFLANLLKD	99.86%
AAGMRFTVFLANLLK	99.84%
RFTVFLANLLKDFRR	99.81%
MRFTVFLANLLKDFR	99.81%
Total global coverage	**99.99%**



Population: World

MHC class	Coverage	Average hit	PC90
II	99.99%	516.51	260.01

Figure 3: Graph showing global population coverage of peptides binding MHC-II alleles



Population: World

MHC class	Coverage	Average hit	PC90
combined	100.0%	524.33	267.43

Figure 4: Graph showing the global coverage percentage of combined MHC II and I alleles

Homology modelling:

PDB ID 4n72A was predicted using raptor X software, and visualized using Chimera (version 1.13.1rc) for the most promising peptides that showed low IC50 values, high Global population coverage percentages and high numbers of HLA- allele hits. (Figures 5, 6and 7)

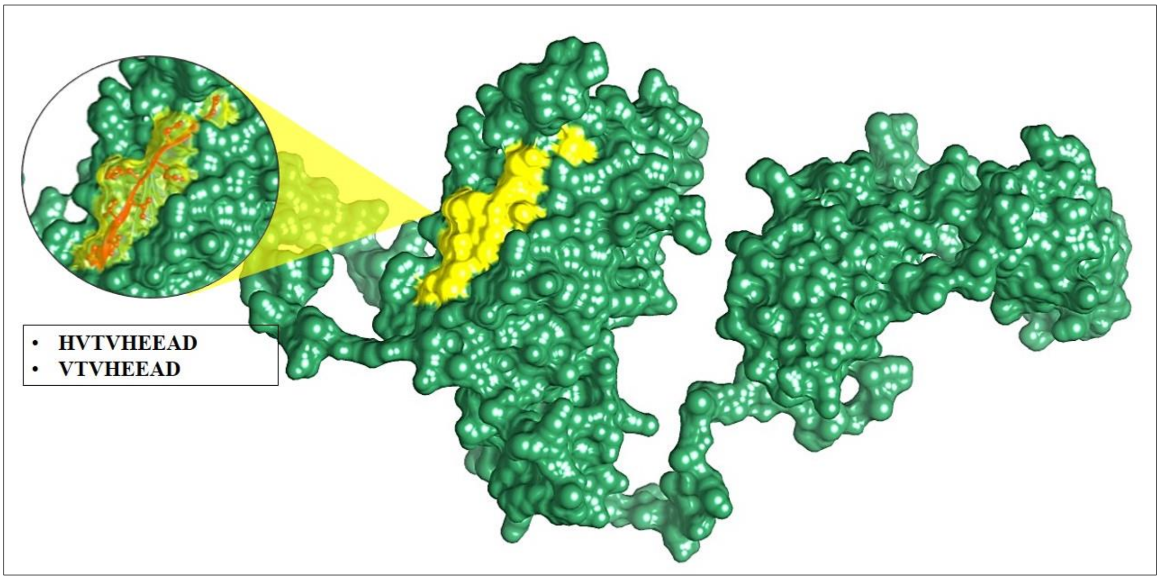


Figure 5: Three-dimensional structure of DLAT protein of N. Gonorrhea showing most promising B- cell peptides, which are both located in the same position from 328 to 336.using chimera (version 1.13.1rc)

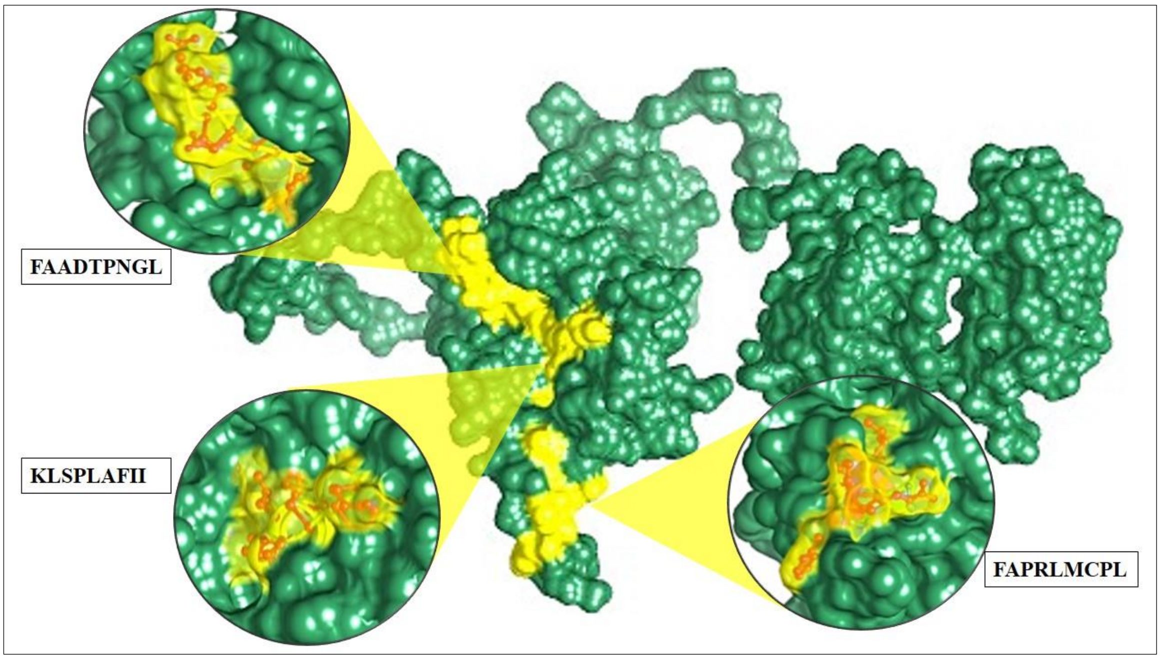


Figure 6: Three-dimensional structure of DLAT protein of N. gonorrhea visualizing most promising T-cell peptides binding to MHC-I alleles.Using chimera (version 1.13.1rc)

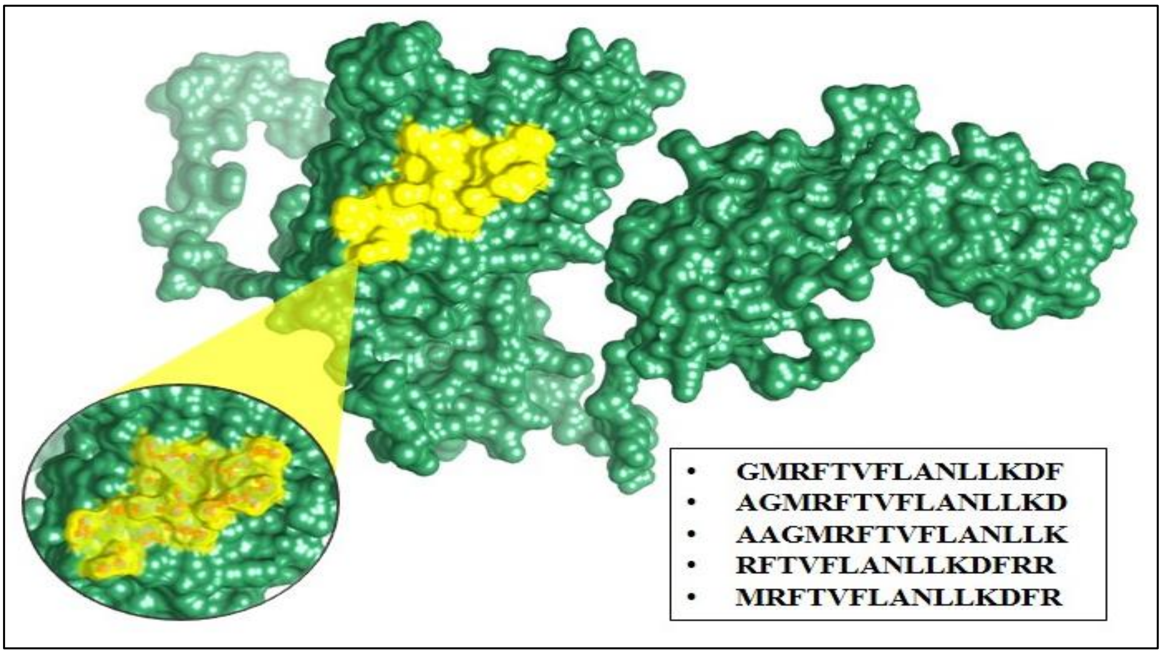


Figure 7: Three-dimensional structure of DLAT protein of N. gonorrhea visualizing most promising T-cell peptides binding to MHC-II alleles, located at the same positions from 508 to 526, using chimera (version 1.13.1rc)

Discussion

This study proposes candidate peptides to design a peptide-based vaccine against *Neisseria gonorrheae* targeting its immunogenic dihydrolipoamide acetyltransferase protein. Two epitopes (HVTVHEEAD, and VTVHEEAD) are suggested to be promising B- cell epitopes for passing antigenicity, hydrophlicity and surface accessibility tests. Eight epitopes were predicted to elicit T-cell response. (FAADTPNGL, FAPRLMCPL, and KLSPLAFII) interacts with MHC-I allele while, (GMRFTVFLANLLKDF, AGMRFTVFLANLLKD, AAGMRFTVFLANLLK, RFTVFLANLLKDFRR, and MRFTVFLANLLKDFR) interacted with MHC-II alleles.

Two B-cell peptides passed Bepipred linear epitope 2, Emini surface accessibility (threshold of 1), Kolaskar & Tongaonkar antigenicity (threshold of 1.03) and Parker hydrophilicity (threshold of 1.43) prediction tests. These peptides also share the same amino acid positions starting from 328, 329, respectively and ending at position 336. However, HVTVHEEAD having the ideal peptide length of nine amino acids makes it a stronger peptide candidate.

Seventy T-cell epitopes with half-maximum inhibitory concentration (IC50) <100 were predicted to interact with MHC I alleles. The coverage of worldwide population for all of the MHC I epitopes was 97.4%.Threeepitopes were the most promising according to their affinity to bind the highest number of MHC1 alleles, global population coverage, and low IC50 scores. FAADTPNGL is the strongest candidate due to its binding capacity to six HLA-alleles enriched with a low IC50 score of 3.32 and coverage of 35.02% of the global population. KLSPLAFII and FAPRLMCPL are also strong candidates with high global population coverage percentages (44.14% and 22.29%, respectively), and low IC50 scores of (25.74 and 8.48, respectively)

Four hundred thirty-eight T-cell Epitopes were predicted to interact with MHC II alleles with IC50 < 500.Forty-five of them had the highest efficacy and affinity to bind to the highest number of MHC II alleles, excluding certain alleles for MHC II. The best epitope was GMRFTVFLANLLKDF (99.93%), with 27 HLA hits and an IC50 of 7.5.The five strongest peptide candidates are sharing similar positions starting from 508 and ending at position 526, indicating high conservancy and antigenicity of that area. The total population coverage was massive with a percentage of 99.99% for all conserved MHC II epitopes.

As for combined MHC II and I peptides, the total global population coverage percentage was a 100%.These epitopes have the ability to induce a T-cell immune response by strongly interacting with MHC I & MHC II alleles. Thus, effectively generating a cellular and humoral immune response to the invading pathogen.

DLAT protein had been reported by previous studies to be able to induce an immune response. A study by Christen et al., 1994, suggests that the E2 subunit of pyruvate dehydrogenase complex is an autoantigen in halothane hepatitis and reports reactivity of the protein with anti-CF_3CO antibodies. [32] Another study by Fussey et al., 1990, reported that dihydrolipoamide acetyltransferase was also recognized as one of the auto-antigens that causes primary biliary cirrhosis (PBC), which is a chronic cholestatic liver disease characterized by the presence of antimitochondrial autoantibodies in the serum [33].A study by Corona et al., 2013, reported that the metabolic enzyme DLAT protein was one of the immunodominant proteins identified from *Mycoplasma Mycoides* subspecies *Capri* isolates using immunoproteomic approach. [34] In addition, a study by Zhao et al., 2012, identified DLAT protein along with other proteins as immunogenic stimulants in *Mycoplasma Capricolum* subspecies *Capripneumoniae* strain *M1601* using immunoblotting techniques. [35]

Different attempts to design a vaccine to prevent infections of *N. Gonorrhoeae* had been reported. Only four candidates (whole cell, partially autolyzed, pilus-based, or protein I-based) vaccines have made it to clinical trials and none of them was approved by the FDA. [36] Petousis-Harris et al., 2017, reported a retrospective case-control study in New Zeland in which they assessed the effectiveness of the outer membrane vesicle (OMV) meningococcal B vaccine (MeNZB) against gonorrhoea in young adults aged 15-30 years. The results reported reduced rates of Gonorrhoea diagnosis. However, the correlation remains unknown and the MeNZB vaccine is no longer available. [36] [37] [38] Earlier in 1983, a large gonococcal pillus vaccine trial was undertaken. Around 3250 volunteers were involved. However, no overall protection was detected. [39] Another vaccine target was the protein I, a major outer membrane protein without intrastrain variations capable of eliciting an immune response. Later on, it was reported that not all gonococci populations carry Protein I on their surfaces. [39] [40] These examples raise hopes in the possibility of designing an effective and efficient epitope- based vaccine against *N. Gonnorhoeae*. Especially that the global population coverage percentage predicted was of 100%, indicating massive beneficiaries of the vaccine.

This study was limited by being strictly computational. In addition, MHC-II alleles (HLA-DRB5*01:01, HLA-DRB3*01:01, HLA- DRB4*01:01, and HLA-DPA1*01) had not given results when analyzed by population coverage tool. Future in-vivo and in-vitro studies are highly recommended for the promising peptides.

Conclusion

There is a growing need of a vaccination for N. Gonnorhoeae with the increasing drug resistant gonococcal infections. Using *insilico* prediction methods to design vaccines is highly appreciated due to the marked reduction in cost, time and effort. In addition, peptide-based vaccines had proved their efficiency as many candidates made it to clinical trials. Although the development of a gonococcal vaccine has been unsuccessful to date, we have presented ten candidate B- and T-cell peptides (HVTVHEEAD, VTVHEEAD, FAADTPNGL, FAPRLMCPL, KLSPLAFII, GMRFTVFLANLLKDF, AGMRFTVFLANLLKD, AAGMRFTVFLANLLK, RFTVFLANLLKDFRR, and MRFTVFLANLLKDFR) capable of inducing physiologic immune response against dihydrolipoamide acetyltransferase of *N. gonnorhoeae.*

Data availability

The data supporting our findings in this study are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare that they have no competing interests.

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