Journal of Advanced Zoology

ISSN**: **0253-7214
*Volume **44** Issue **S-4 Year 2023** Page **146**:**157***

Identification of B cell and T cell specific peptide vaccine for *Moraxella catarrahalis.*

V.R.S.Harshitha and Sathish Sankar*
Department of Microbiology, Centre for Infectious Diseases, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai 600077
Vantipalli Raga Sai Harshitha
Graduate Saveetha Dental College, Saveetha Institute of Medical and Technical Science, Saveetha University, Chennai 77, Tamil Nadu, India.
Email.152101002.sdc@saveetha.com
*Corresponding author
Dr. Sathish Sankar
Department of Microbiology Saveetha Dental College and Hospitals Saveetha Institute of Medical and Technical Science Saveetha University Chennai 600077 Tamil Nadu, India
Email: sathishsankar.sdc@saveetha.com

https://doi.org/10.17762/jaz.v44iS4.2410

Article History

Received: 12 Sept 2023
Revised: 10 Oct 2023
Accepted:12 Nov 2023

Abstract :

Introduction:

Moraxella catarrhalis is a gram-negative bacterium that commonly causes respiratory tract infections, particularly in individuals with compromised immune systems or underlying respiratory conditions. In recent years, there has been growing interest in developing peptide-based vaccines to target specific antigens of M. catarrhalis for B cell and T cell immune responses.

Materials and methods:

Moraxella catarrhalis, a heat shock protein (hsp65) gene,complete cds. Amino acid sequence for the above entry was retrieved from the NCBI database. Fasta sequences were used for B cell and T cell epitope prediction. Bepipred Linear epitope Prediction 2.0 online server program was used to predict the B cells immunogenic epitopes MHC-1 binding promiscuous T cell epitopes were identified using IEDB analysis resource with HLA allele reference set. The resulting epitopes

were analyzed.

Results:

Peptide LGEQKESPFDALSER was selected as it was homologous (100%)to the Moraxella Catarrhalis and the length was 15 mers appropriate as a candidate vaccine. .MHC 1 bindingT cell epitope prediction was carried out by using IEDB analysis resource online server program.

Discussion:

Peptide LGEQKESPFDALSER was selected as it was homologous (100%)to the Moraxella Catarrhalis and the length was 15 mers appropriate as a candidate vaccine.MHC 1 bindingT cell epitope prediction was carried out by using IEDB analysis resource online server program.

Conclusion:

The identification of B cell and T cell specific peptide vaccines for Moraxella catarrhalis is a multi-step process aimed at understanding the immune response against the pathogen and designing a targeted vaccine. By characterizing the immune response, researchers can identify the specific antigens and epitopes that trigger an immune response in infected individuals.

Keywords:

Moraxella catarrhalis,peptide vaccine,B cell epitopes,T cell epitopes,Universal heath, Diseases, Well being, Health, International Health policy.

Introduction:

Moraxella catarrhalis is a gram-negative bacterium that commonly causes respiratory tract infections, particularly in individuals with compromised immune systems or underlying respiratory conditions(1) .In recent years, there has been growing interest in developing peptide-based vaccines to target specific antigens of M. catarrhalis for Bcell and T cell immune responses.B cells and T cells play crucial roles in the adaptive immune response. B cells produce antibodies that can recognize and bind to specific antigens, while T cells recognize and destroy cells infected with pathogens or provide help to other immune cells(2).By identifying B cell and T cell specific peptides derived from M. catarrhalis antigens, it is possible to design peptide vaccines that can induce a targeted immune response against the bacterium.

In addition, up to 2.5–10% of adults with stable COPD have lower respiratory tract colonizations by M. catarrhalis . Due to highly inflammatory bacterial cell wall antigens sloughing into the airway, lower airway colonization increases airway inflammation in COPD patients(3).A vaccine that targets exacerbations in adults with COPD as well as otitis media in children is necessary due to the major clinical implications of M. catarrhalis. Since it is a non encapsulated bacterium, M. catarrhalis doesn't release exotoxins. Many outer membrane proteins (OMPs) have been the main focus of recent vaccine studies as potential vaccines(4).Thus far, only a small number of OMPs have been investigated and are presently undergoing various stages of assessment as part of an endeavor to create a multicomponent vaccine against M.catarrhalis.

Although M. catarrhalis is generally thought to be a commensal limited to humans, research conducted in the last few years has shown that it is now a significant infectious agent in the upper and lower respiratory tract and the cause of roughly 17% of pediatric acute otitis media infections(5).Moreover, M. catarrhalis has been linked to various infections, including meningitis, endocarditis, and bacteremia, particularly in patients with compromised immune systems(6).The creation of a potent vaccine is a top health priority because M. catarrhalis has shown signs of rising antibiotic resistance in recent years. Here, we present a newly developed multitope vaccine that is based on the mapped epitopes of vaccine candidates that have been culled from the entire M. catarrhalis proteome(7).

While there isn't currently an FDA-approved M. catarrhalis, there are several stages of development for them.M. catarrhalis adhesive proteins have been extensively studied as possible vaccine candidates (8).These are proteins found on the outside of the membrane that enable the microbe to attach to its target receptor in the respiratory system of humans, marking the beginning of bacterial pathogenesis (9).When administered to animal models, this vaccine improved the removal of bacteria from the lungs(10).

Materials and methods :

Moraxella catarrhalis, a heat shock protein (hsp65) gene,complete cds. Amino acid sequence for the above entry was retrieved from the NCBI database. Fasta sequences were used for B cell and T cell epitope prediction. Bepipred Linear epitope Prediction 2.0 online server program was used to predict the B cells immunogenic epitopes MHC-1 binding promiscuous T cell epitopes were identified using IEDB analysis resource with HLA allele reference set. The resulting epitopes were analyzed.

Prior to epitope prediction, the SignalP-5.0 Server was used to predict the presence and location of signal peptides based on the amino acid sequence of filtered proteins. The mature polypeptides that were thus obtained were then examined using the Immune Epitope Database's prediction tools (IEBD). While IEBD recommended a 2.22 prediction method and a full HLA reference set that covers >99% in terms of population coverage for analysis of MHC-II binding, MHC-I binding was detected by applying NetMHCpan EL 4.0 as a prediction method and an

HLA allele reference set that provides >97% in terms of population coverage. Using IEBD, antibody epitope prediction was also carried out.

M. catarrhalis BBH18's entire proteome was obtained This strain was chosen because it is the NCBI reference M. catarrhalis strain. The entire proteome of M. catarrhalis was subjected to protein prioritization using the reverse vaccinology technique. First, the Geptop 2.0 web server was used to identify essential proteins, which are necessary for M. catarrhalis to survive and have an essentiality cutoff of 0.24. By comparing the orthology and phylogeny of query proteins with the datasets defined experimentally in the database of essential genes (DEG) ,this server finds essential proteins. Subsequently, the subcellular localization of the essential proteins was examined using the online server . The identification of the exoproteome was the ultimate result of this filtration process. These proteins were used to calculate the potential for virulence. After being filtered out in the previous step, the proteins were searched against the human proteome using BLASTp from the NCBI. Proteins with ≥35% identity were removed because they were thought to identified transmembrane helices in the proteins from the previous step, predicted the molecular weight of the proteins.

Results:

Peptide LGEQKESPFDALSER was selected as it was homologous (100%)to the Moraxella catarrhalis and exhibits antigenic diversity, making the development of traditional vaccines challenging. Peptide vaccines offer a targeted strategy by focusing on specific epitopes that are conserved and immunogenic. This approach is particularly relevant for a bacterium with variable surface antigens.

The table 1 shows the peptides identified by the program considering many factors including amino acid composition, their length,sequence number, score, percentile mark, etc. Table 2 shows B cell response. Peptide (9mer or 10mer) induces a good T cell immune response. Among these, peptides around 15-25 mer induce ideal B cell response.

Table 1:Predicted B cell peptide

No	Start	End	Peptide	Length
1	71	74	KQFN	4
2	88	89	QP	2

3	104	104	T	1
4	106	110	GTPLD	5
5	121	121	A	1
6	124	129	RYFSHD	6
7	132	132	E	1
8	139	153	LGEQKESPFDALSER	15
9	166	169	STQQ	4
10	176	183	VSKTVNT	8
11	186	195	YRIFDKLGID	10
12	209	209	L	1

Figure 1:B cell response recording immunogenicity and non immunogenic response

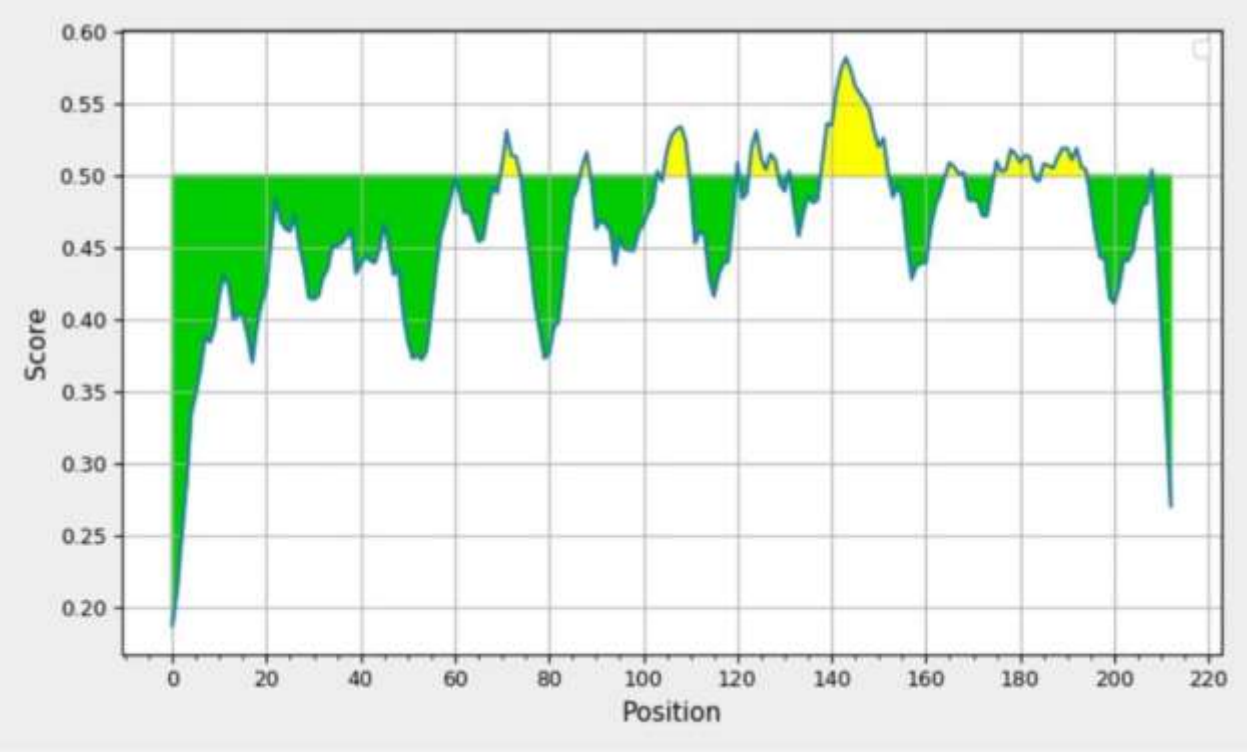

TABLE 2: T cell response to identify ideal T cell peptide

allele	seq_num	start	end	length	peptide	score	percentile_rank	
HLA-B*40:01	3	29	37	9	AEQLAETVL	0.982634	0.01	
HLA-A*68:01	3	42	51	10	ESPFDALSER	0.967207	0.02	
HLA-A*02:06	2	27	35	9	KQFNPNIKV	0.942316	0.02	
HLA-A*31:01	4	19	27	9	KTVNTYRYR	0.941137	0.01	

HLA-A*68:01	2	16	24	9	NINGVEATR	0.909744	0.07	
HLA-A*03:01	2	43	52	10	AQPYPSMLLK	0.908978	0.03	
HLA-B*08:01	2	30	38	9	NPNIKVLAV	0.889342	0.02	
HLA-B*58:01	4	16	24	9	VSAKTVNTY	0.887623	0.07	
HLA-B*57:01	4	16	24	9	VSAKTVNTY	0.884592	0.13	
HLA-A*68:01	4	17	25	9	SAKTVNTYR	0.882423	0.1	
HLA-B*15:01	2	50	58	9	LLKAGVNGY	0.881509	0.03	
HLA-A*31:01	4	17	25	9	SAKTVNTYR	0.873936	0.04	
HLA-A*02:03	3	47	55	9	ALSEREKQV	0.853015	0.04	
HLA-A*11:01	2	43	52	10	AQPYPSMLLK	0.837635	0.06	
HLA-A*30:02	4	16	24	9	VSAKTVNTY	0.830678	0.02	
HLA-B*40:01	3	49	57	9	SEREKQVAM	0.827877	0.1	

HLA-B*15:01	4	16	24	9	VSAKTVNTY	0.825778	0.05	
HLA-A*02:01	1	21	30	10	MLDDDPNIEV	0.800869	0.08	
HLA-A*02:01	1	20	28	9	RMLDDDPNI	0.792584	0.08	

In the B cell response graph, the part highlighted in yellow shows immunogenic response and the part highlighted in green shows non-immunogenic response. Then we have represented the peptides for immunogenic response in the form of a table. The ideal peptide should be of length 20 mer to induce B cell response. From the peptides obtained we can say that, the peptide LEQKESPFDALSER was selected as it was homologous (100%)to the Moraxella catarrhalis and exhibits antigenic diversity, making the development of traditional vaccines challenging. Peptide vaccines offer a targeted strategy by focusing on specific epitopes that are conserved and immunogenic. This approach is particularly relevant for a bacterium with variable surface antigens.

Discussion:

Traditional methods of developing vaccines, like attenuated or killed vaccines, take a long time because it can take decades to create a vaccine that works(11). Furthermore, the fact that many microorganisms are hard to grow or weaken and cause unfavorable immune reactions supports the need for a radical change in the methodology used to develop vaccines(12). In recent times, there has been a shift in the vaccine development process towards a more efficient and time-efficient genome pre-screening approach.The antigenic diversity of Moraxella catarrhalis makes the creation of conventional vaccines difficult(13).By concentrating on particular, conserved, and immunogenic epitopes, peptide vaccines provide a targeted approach. This strategy is especially pertinent for bacteria that have changing surface antigens(14).

The pathogenic bacteria Moraxella catarrhalis is linked to otitis media, respiratory infections, and flare-ups of chronic obstructive pulmonary disease (COPD). Creating a peptide vaccine may be a useful tactic in the fight against M. catarrhalis infections.The search for peptides specific to B cells centers on epitopes that stimulate the production of antibodies. These antibodies have the ability to increase phagocytosis, prevent adhesion, and neutralize bacterial toxins.Peptides unique to T cells stimulate cellular immunity. While CD8+ T cells have the ability to directly destroy infected cells, CD4+ T cells support B cells and other immune cells. Both arms of the

immune system should be stimulated by a comprehensive vaccine.It is essential to choose important antigenic proteins for M. catarrhalis(3).Epitope mapping is a technique that uses experimental assays and bioinformatics tools to find regions that interact with B cell receptors (BCRs) or are presented in major histocompatibility complexes to T cells.

The pathogenic bacteria Moraxella catarrhalis is linked to otitis media, respiratory infections, and flare-ups of chronic obstructive pulmonary disease (COPD). Creating a peptide vaccine may be a useful tactic in the fight against M. catarrhalis infections.The search for peptides specific to B cells centers on epitopes that stimulate the production of antibodies. These antibodies have the ability to increase phagocytosis, prevent adhesion, and neutralize bacterial toxins.Methods such as peptide microarrays, phage display, or epitope prediction algorithms are used to identify linear and conformational B cell epitopes within particular proteins. B cell epitopes with high affinity are essential for strong antibody responses.Potential T cell epitopes can be identified with the help of peptides' binding to MHC molecules. This includes MHC binding affinity prediction algorithms or MHC tetramer staining assays. Functional assays are necessary for T cell epitope validation.

B cell and T cell epitopes are combined into a single construct in the development of a peptide vaccine. This guarantees a strong and well-coordinated immune response. For long-term protection, it is essential to ensure the induction of immunological memory. After a subsequent exposure, memory B cells and memory T cells can quickly and effectively respond by remembering details about the pathogen.Antigenic variation in M. catarrhalis could pose a challenge to the long-term stability of vaccine efficacy.Differences in the host immune response between individuals can affect how effective the vaccine is. Animal models are used in preclinical research to evaluate the safety, immunogenicity, and protective effectiveness of vaccines.Clinical Examinations: In order to proceed to clinical trials, the vaccine must first be tested in humans for efficacy, safety, and immunogenicity (15).Various stages evaluate increasing

To trigger a humoral immune response, B cell-specific peptide antigens must be identified. These peptides ought to have the ability to stimulate the synthesis of antibodies that are opsonized or neutralized against Moraxella catarrhalis, thereby blocking the pathogen's colonization and spread(16).Cellular immunity requires the activation of T cell responses. Strong cellular reactions, such as the activation of cytotoxic T cells and the development of immunological memory, can be elicited by T cell-specific peptides. This improves the host's capacity to identify and eradicate Moraxella catarrhalis in the event of another exposure(17).The genomic and proteomic analysis of Moraxella catarrhalis strains serves as the foundation for identifying potential antigenic targets. Examining the bacterial surface proteins and secreted proteins aids in pinpointing candidates that interact with the host immune system.Utilizing bioinformatics tools to predict B cell and T cell epitopes is a critical step(18).The prediction

algorithms help identify regions of proteins that are likely to induce strong immune responses. This step ensures a rational and targeted approach to peptides (19).

Designing synthetic peptides based on predicted B and T cell epitopes is a practical application of the study's findings. These synthetic peptides can be manufactured for further in vitro and in vivo evaluations, serving as potential components of a peptide.The identification of B and T cell-specific peptides is expected to contribute to the development of a highly effective Moraxella catarrhalis vaccine(20) .Targeting both arms of the immune system increases the likelihood of a robust and comprehensive immune response, providing protection against vaccines.Focusing on conserved and immunogenic epitopes has the potential to provide broad protection against diverse Moraxella catarrhalis strains(21).This is a significant advantage, especially considering the variability in surface antigens observed in this bacterium.The study's findings may contribute to broader knowledge on vaccine design strategies, especially for pathogens with antigenic variability. Lessons learned from this research could potentially be applied to the development of peptide vaccines against other infectious agents(22).

The identified peptides must undergo rigorous validation and testing, including in vitro assays and animal models, to confirm their immunogenicity and protective efficacy.Transitioning from preclinical studies to clinical trials is a critical step in assessing the safety and effectiveness of the peptide.The potential variability in Moraxella catarrhalis strains should be considered. Continued surveillance and adaptation of the vaccine to cover prevalent strains will be essential.

Conclusion:

The identification of B cell and T cell specific peptide vaccines for Moraxella catarrhalis is a multi-step process aimed at understanding the immune response against the pathogen and designing a targeted vaccine. By characterizing the immune response, researchers can identify the specific antigens and epitopes that trigger an immune response in infected individuals. This knowledge is then used to map B cell and T cell epitopes, which are essential for designing vaccines that stimulate the production of antibodies and activate cellular immune responses. The ultimate goal is to develop a peptide vaccine that incorporates the identified B and T cell epitopes, which can elicit a robust immune response against Moraxella catarrhalis.

Conflict of interest:
The author declares that there were no conflicts of interests in the present study.

Refrences:

1. How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-attributable Disease : a Report of the Surgeon General. 2010. 728 p.

2. Stern PL, Beverley PCL, Carroll M. Cancer Vaccines and Immunotherapy.

3. Smith FG. Core Topics in Critical Care Medicine. Cambridge University Press; 2010.

4. Kaparakis-Liaskos M, Kufer TA. Bacterial Membrane Vesicles: Biogenesis, Functions and Applications. Springer Nature; 2020. 258 p.

5. Venkova T, Yeo CC, Espinosa M. The Good, The Bad and The Ugly: Multiple Roles of Bacteria in Human Life. Frontiers Media SA; 2018. 518 p.

6. Mandell GL, Bennett JE. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 1995. 1489 p.

7. Cheesbrough M. District Laboratory Practice in Tropical Countries. Cambridge University Press; 2006.

8. von Gabain A, Klade C. Development of Novel Vaccines: Skills, Knowledge and Translational Technologies. Springer Science & Business Media; 2012. 306 p.

9. Roos KL, Tunkel AR. Bacterial Infections of the Central Nervous System. Elsevier Health Sciences; 2010. 293 p.

10. National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Board on Health Sciences Policy, Committee on Equitable Allocation of Vaccine for the Novel Coronavirus. Framework for Equitable Allocation of COVID-19 Vaccine. National Academies Press; 2020. 273 p.

11. National Research Council, Institute of Medicine, Division of Health Promotion and Disease Prevention. Vaccine Supply and Innovation. National Academies Press; 1985. 223 p.

12. Mak TW, Saunders ME. The Immune Response: Basic and Clinical Principles. Academic Press; 2005. 1216 p.

13. Tettelin H, Medini D. The Pangenome: Diversity, Dynamics and Evolution of Genomes. Springer Nature; 2020. 311 p.

14. Institute of Medicine, Board on Health Promotion and Disease Prevention, Immunization Safety Review Committee. Immunization Safety Review: Multiple Immunizations and Immune Dysfunction. National Academies Press; 2002. 152 p.

15. Switalski L, Höök M, Beachey E. Molecular Mechanisms of Microbial Adhesion: Proceedings of the Second Gulf Shores Symposium, held at Gulf Shores State Park Resort, May 6–8 1988, sponsored by the Department of Biochemistry, Schools of Medicine and Dentistry, University of Alabama at Birmingham, Birmingham, Alabama. Springer Science & Business Media; 2012. 226 p.

16. National Research Council, Institute of Medicine, Committee on the Health Effects of Indoor Allergens. Indoor Allergens: Assessing and Controlling Adverse Health Effects. National Academies Press; 1993. 321 p.

17. National Research Council, Division on Earth and Life Studies, Board on Life Sciences, Committee on Scientific Milestones for the Development of a Gene Sequence-Based Classification System for the Oversight of Select Agents. Sequence-Based Classification of Select Agents: A Brighter Line. National Academies Press; 2010. 237 p.

18. Institute of Medicine, Board on Global Health, Forum on Microbial Threats. The Science and Applications of Synthetic and Systems Biology: Workshop Summary. National Academies Press; 2011. 570 p.

19. Willott JF. Handbook of Mouse Auditory Research: From Behavior to Molecular Biology. CRC Press; 2001. 736 p.

20 Tuomanen EI. The Pneumococcus. 2004. 480 p.

21. Institute of Medicine, Division of Health Promotion and Disease Prevention, Committee to Study Priorities for Vaccine Development. Vaccines for the 21st Century: A Tool for Decisionmaking. National Academies Press; 2001. 476 p.

22. National Research Council, Division on Earth and Life Studies, Board on Life Sciences, Institute of Medicine, Board on Health Sciences Policy, Committee on the Use of Chimpanzees in Biomedical and Behavioral Research. Chimpanzees in Biomedical and Behavioral Research: Assessing the Necessity. National Academies Press; 2012. 200 p.