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COMPUTATIONAL PREDICTION OF B-CELL AND T-CELL SPECIFIC PEPTIDE VACCINE AGAINST *ELIZABETHKINGIA MENINGOSEPTICA*

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Abstract

Elizabethkingia meningoseptica is an opportunistic pathogen associated with nosocomial infections, particularly in immunocompromised individuals. Despite its clinical significance, there is a lack of targeted vaccines against this bacterium. The development of effective vaccines requires a comprehensive understanding of the specific immune responses, particularly those mediated by B-cells and T-cells.The identified B-cell and T-cell epitopes demonstrated strong antigenicity and immunogenicity. The multi-epitope subunit vaccine induced a robust humoral and cellular immune response.This study presents a comprehensive strategy for the identification of B-cell and T-cell-specific vaccine candidates for *E. meningoseptica*. Using a combination of bioinformatics and immunoinformatics approaches, potential antigens were identified for their ability to elicit robust B-cell and T-cell responses. Epitope prediction algorithms were employed to identify B-cell epitopes with high antigenicity, surface exposure, and conservation. T-cell epitopes were predicted based on major histocompatibility complex (MHC) binding affinity, ensuring immunogenicity.The selected antigens and epitopes hold promise for the development of a targeted vaccine against this pathogen. Future studies will focus on the in vivo efficacy of the vaccine candidates, potentially paving the way for clinical trials and the development of a much-needed preventive tool against *E. meningoseptica* infections. This study aimed to identify B-cell and T-cell specific vaccine candidates for *E. meningoseptica*, focusing on antigens that elicit robust immune responses and confer protection against infection.

Keywords-Universal health, diseases,well being,international health policy,Elizabethkingia meningoseptica, peptide vaccine.

Introduction

A vaccine against E. meningoseptica is crucial for preventing antibiotic-resistant infections, particularly in healthcare settings. As a resistant pathogen causing opportunistic infections, its prevalence poses a serious threat, especially to immunocompromised individuals. A vaccine would provide a targeted and effective means of preventing E. meningoseptica infections, reducing healthcare-associated morbidity and mortality.(1) By offering a proactive defense strategy, the vaccine contributes to global public health efforts, minimizing the economic burden of treating antibiotic-resistant infections and addressing the challenges posed by emerging pathogens.(2) Overall, a vaccine is pivotal for long-term protection, reducing healthcare costs, and preserving the efficacy of existing antibiotic treatments.

Elizabethkingia meningoseptica, a Gram-negative bacterium, poses a serious health threat due to its multidrug resistance and association with healthcare-acquired infections. Found in hospital environments, it primarily affects immunocompromised individuals, leading to severe morbidity and mortality. (3).*Elizabethkingia meningoseptica* is known for its intrinsic resistance to a broad spectrum of antibiotics, making the management of infections caused by this bacterium challenging.(4)The development of a vaccine against E. meningoseptica is crucial for preventing antibiotic-resistant infections, reducing healthcare-associated risks, and safeguarding vulnerable populations. Such a vaccine would address a pressing global health concern by offering a targeted defense strategy against this resilient and opportunistic pathogen.

B-cell and T-cell specific vaccine is vital for generating a comprehensive and coordinated immune response. B-cells produce antibodies, essential for neutralizing pathogens, while T-cells orchestrate cellular immunity, eliminating infected cells. Such a vaccine ensures a dual defense, enhancing the body's ability to combat diverse infections effectively.(2,5) By stimulating both arms of the immune system, it fosters immunological memory, providing sustained protection. This targeted approach is particularly crucial for pathogens evading traditional vaccine strategies. B-cell and T-cell specificity maximizes the vaccine's efficacy, offering a versatile solution against infectious diseases and contributing significantly to global health by preventing outbreaks, reducing morbidity, and saving lives.

B-cell and T-cell specific vaccines are designed to stimulate the immune system's specific branches, enhancing the body's ability to recognize and eliminate the pathogen. B-cells are responsible for producing antibodies, while T-cells play a critical role in coordinating and regulating the immune response.Developing a vaccine that targets both B-cells and T-cells is

essential for achieving a comprehensive and long-lasting immune response against E. meningoseptica. This can be accomplished by identifying antigens that are specifically recognized by B-cells for antibody production and T-cells for cell-mediated immunity.

Materials and Methods

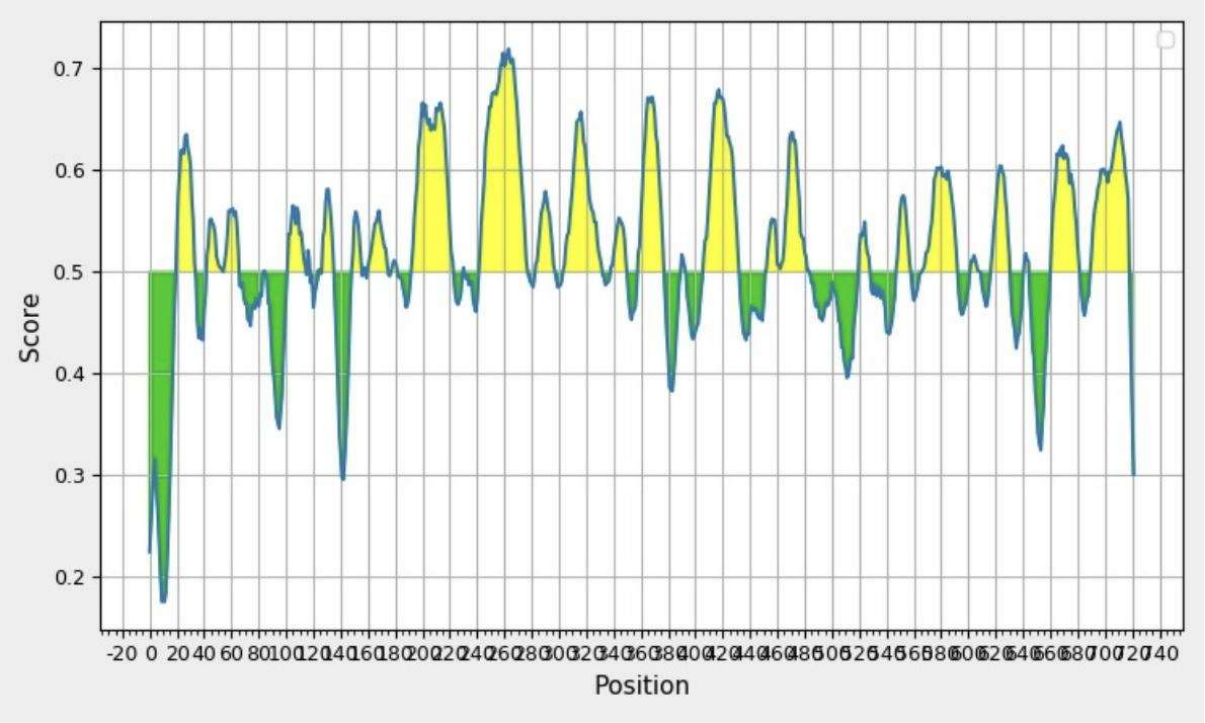
Identifying B-cell and T-cell specific antigens for a vaccine against Elizabethkingia meningoseptica involves a combination of immunoinformatics, bioinformatics, and experimental validation.Bioinformatic tools are employed to predict potential B-cell and T-cell epitopes within the proteome. This involves identifying regions likely to be recognized by antibodies (B-cell epitopes) and those that bind to major histocompatibility complexes (MHC) for T-cell recognition.The overall antigenicity of predicted epitopes are assessed using bioinformatics tools.Utilize bioinformatics tools are utilized to analyze the genomic data of *E. meningoseptica*. Identify potential B-cell epitopes within the extracted antigens by predicting antigenic regions, surface exposure, and conservation across strains.Major histocompatibility complex (MHC) binding affinity analysis to identify regions that are likely to be presented to T cells.Both class I and class II MHC molecules for comprehensive T-cell epitope prediction.

Epitope mapping is done to identify specific regions within the synthetic peptides that elicit strong B-cell and T-cell responses.Epitope mapping is a process that identifies specific regions within a protein or peptide—known as epitopes—that elicit an immune response. Epitope mapping plays a crucial role in vaccine development, guiding the identification of precise regions that trigger robust immune responses.This helps usdesign targeted vaccines that effectively stimulate B-cell and T-cell immunity against specific pathogens or diseases.

Using the server https://www.uniprot.org/proteomes, the protein databases were analyzed for suitable target for the identification of vaccine candidate.Outer membrane receptor proteins involved in mostly iron transport was selected for the study.Elizabethkingia meningoseptica ATCC 13253 = NBRC 12535 strain ATCC 13253 contig00001, whole genome shotgun sequence (GenBank: ASAN01000001.1) was used for the study.Amino acid sequence for the above entry was retrieved from NCBI database.Bepipred Linear Epitope Prediction 2.0 online server program was used to predict the B cell immunogenic epitopes and the resulted epitopes were analyzed.Peptide RMSFRTTNQTPGVVLNNRYDS was selected as it was homologous (100%) to the M. abscessus strain and the length was 20 mers appropriate as a candidate vaccine. MHC I – binding T cell epitope prediction was carried out using http://tools.iedb.org/mhci/ online server program.This tool will take in an amino acid sequence, or set of sequences and determine each subsequence's ability to bind to a specific MHC class I molecule.HLA allele reference set were used for the prediction and the peptides were sorted by the prediction score as well.

Results

Figure 1:graphical representation of the immunogenic regions.



The peptide chain of E.miningoseptica is obtained and examined to identify immunogenic and non immunogenic parts of the peptide chain.The graph also the position and score of each peptide. The yellow region represents the immunogenic peptides and the green region represents non immunogenic sites of the peptide.The peptides belonging to the yellow region are valid candidates for vaccine preparation due to their immunogenic property.

Table 1: The list of immunogenic B-cell peptides

No	Start	End	Peptide	Length
1	21	34	ETNTKEKSKEKEIQ	14
2	43	54	KAVEQKPDRTIF	12
3	56	66	FSEQPNLNSGS	11
4	85	85	M	1
5	102	115	NISSNDLTAFLEGM	14
6	117	118	AN	2
7	125	125	V	1

8	128	136	QPGAEFPAT	9
9	149	156	SAKSYLTA	8
10	158	159	YS	2
11	161	175	GYRFSNYDKFRSKVN	15
12	179	182	VLNS	4
13	193	223	AGNTYRESFNSTQTDDIFSNFADRYQRSNF A	31
14	231	231	L	1
15	243	277	NQYNNDSYIDASGKQVVNNITQTYQNTGK SKNETY	35
16	284	297	TYQKKFSDKDKKLD	14
17	304	332	NYRTNFNQFSNFITPNTGIVYYPENKSDQ	29
18	339	350	VDYAQPLKIMDG	12
19	359	377	YEKLNFETQSASVTNLDYQ	19
20	390	393	KYKK	4
21	407	432	ISGTTLTRDDNNNLVNTDLTPFKKFK	26
22	453	484	YNKKISLPSISFLNPNNTNYQGPNVDFKGNP F	32
23	521	528	ERDGDRIS	8
24	548	558	VPFMLFTKPLS	11
25	567	593	PDKINLLYFYVGYQFQDIKDIKEQKGM	27
26	603	608	ILPKDI	6
27	618	631	TKGNYYYFMPLHPI	14
28	642	645	KFNK	4
29	662	682	RMSFRTTNQTPGVVLNNRYDS	21

30	691	718	YKIPTRNKLAKVDQNMLNQDVSKEDNGS	28

It shows the list of B cell peptides found in the immunogenic region of the sample of E.meningoseptica.It also shows the position of the peptide along with its length.The optimum length of B cell peptide required for vaccine preparation should be 15-25 units.Therefore the the sequence of peptide chosen for the vaccine will be RMSFRTTNQTPGVVLNNRYDS. This sequence has a length of 21 units which is in range for ideal length required.

Table 2: The list of immunogenic T cell peptides

allele	seq_num	start	end	length	peptide	score	percentile_rank
HLA-B*35:01	2	44	52	9	VPVGDVVQY	0.995464	0.01
HLA-B*58:01	1	40	48	9	HSQPGKTIW	0.991228	0.01
HLA-B*57:01	1	40	48	9	HSQPGKTIW	0.988158	0.01
HLA-B*35:01	2	43	52	10	FVPVGDVVQY	0.980638	0.01
HLA-B*57:01	1	39	48	10	RHSQPGKTIW	0.975665	0.04
HLA-B*58:01	1	39	48	10	RHSQPGKTIW	0.956581	0.03
HLA-A*02:06	1	55	63	9	KIVDAVELV	0.915895	0.03
HLA-B*58:01	2	5	13	9	VTLDTNEKF	0.888592	0.07
HLA-B*53:01	2	44	52	9	VPVGDVVQY	0.868537	0.03
HLA-B*57:01	2	5	13	9	VTLDTNEKF	0.859151	0.16

HLA-A*68:02	2	16	24	9	TTSFIPETI	0.847485	0.04
HLA-B*57:01	1	45	53	9	KTIWVEHKL	0.835433	0.17
HLA-A*26:01	2	43	52	10	FVPVGDVVQY	0.814344	0.04
HLA-A*33:01	1	5	13	9	DFALSLLRR	0.783705	0.03
HLA-A*02:01	1	52	60	9	KLVKIVDAV	0.783215	0.09
HLA-A*02:03	1	52	60	9	KLVKIVDAV	0.779358	0.06
HLA-A*02:01	1	55	63	9	KIVDAVELV	0.776064	0.09
HLA-B*15:01	1	16	25	10	RQVQTDQGHF	0.746983	0.1
HLA-A*02:06	1	52	60	9	KLVKIVDAV	0.742976	0.09
HLA-B*58:01	1	45	53	9	KTIWVEHKL	0.732894	0.16
HLA-A*02:03	1	55	63	9	KIVDAVELV	0.729066	0.09
HLA-A*01:01	1	19	27	9	QTDQGHFTM	0.721844	0.09
HLA-B*53:01	2	43	52	10	FVPVGDVVQY	0.702291	0.06

The table contains a list of T cell peptides found in the immunogenic region of the the sample of E.meningoseptica.It also contains the position,length,allele,score and percentile rank of each peptide.The T cell peptide chosen for vaccine should have a high score and a lower percentile.The length can be 10 units long.Therefore there are multiple

Discussion

Developing a B-cell and T-cell specific vaccine for E. meningoseptica would require a comprehensive understanding of the bacterium's antigens. B-cell-specific vaccines typically target surface structures, while T-cell-specific vaccines focus on internal proteins. (6)Collaboration between immunologists and microbiologists is crucial for identifying suitable antigens and optimizing vaccine efficacy. Continuous research is essential for refining vaccine candidates and ensuring a balanced immune response.

Identifying the immunogenicity region of a peptide is an important step in understanding its potential to induce an immune response. Immunogenicity is the ability of a substance, such as a peptide, to provoke an immune response in an organism(7).The immunogenicity region of the peptide sample of E.meningoseptica is carefully examined using computational tools and algorithms to predict potential epitopes within a peptide sequence (8)These tools often consider factors such as peptide binding to major histocompatibility complex (MHC) molecules, which is crucial for T cell recognition.The immunogenicity of a peptide is often associated with specific regions called epitopes or antigenic determinants.Epitopes are recognized by the immune system, particularly by antibodies or T cells.To determine which regions of the E.miningoseptica peptide chain are immunogenic and which are not, the peptide chain is extracted and analysed.Each peptide's position and score are also displayed on the graph. The immunogenic peptides are shown by the yellow region, and the non-immunogenic peptide sites are shown by the green region.Because of their immunogenic qualities, the peptides in the yellow area are suitable candidates for vaccine production.

Bioinformatics tool,BepiPred are used to predict B cell epitopes within selected antigens.These tools analyze the protein sequence to identify regions likely to induce a strong antibody response.Peptides of optimal length for B cell responses typically range from 10 to 30 amino acids. Shorter peptides may be less immunogenic, while longer peptides may have reduced accessibility to B cell receptors(9).Longer peptides may have reduced accessibility to B cell receptors due to steric hindrance. Optimal peptides should allow for effective binding to B cell receptors.There fore the B cell peptide used for vaccine should be RMSFRTTNQTPGVVLNNRYDS. This sequence has a length of 21 units which is in range for ideal length required.

Selecting T-cell peptides for a vaccine involves a careful consideration of several factors to ensure that the vaccine induces a robust and targeted immune response.T-cell peptides are presented by either Class I or Class II major histocompatibility complex (MHC) molecules. Class I MHC presents peptides to CD8+ cytotoxic T cells, while Class II MHC presents peptides to CD4+ helper T cells. Ensure that the selected peptides have high binding affinity to the relevant MHC molecules to enhance their presentation(10).Epitope prediction algorithms are used to identify potential T-cell epitopes within the selected antigens.These algorithms analyze protein sequences to predict regions that are likely to be recognized by T cells. T cell epitope prediction was carried out using http://tools.iedb.org/mhci/ online server.The T cell peptide chosen for vaccine should have a high

score and a lower percentile.The length can be 10 units long and there are multiple allele suitable for the vaccine.(11)

Nosocomial infections, commonly acquired within healthcare facilities, pose a significant threat to vulnerable patient populations. (12)Over recent years, *Elizabethkingia meningoseptica* has emerged as a notable nosocomial pathogen, challenging traditional views of its environmental presence. This gram-negative bacterium is particularly concerning due to its intrinsic resistance to multiple antibiotics and its ability to survive in diverse hospital environments.Initially recognized as an environmental organism, *E. meningoseptica* has transitioned to a clinically relevant pathogen. It is associated with a spectrum of infections, including pneumonia, bloodstream infections, meningitis, and surgical site infections, primarily affecting immunocompromised patients, neonates, and those with underlying health conditions.(13)*E. meningoseptica* is renowned for its resistance to a broad range of antibiotics, including beta-lactams, aminoglycosides, and fluoroquinolones.Therefore it is important to study potential vaccine against. E.meningoseptica

(14)

Conclusion

The identification of B-cell and T-cell specific vaccine candidates for E. meningoseptica involves a thorough understanding of the pathogen's antigens, immune responses, and host-pathogen interactions.Through a combination of bioinformatics, proteomic, and genomic analyses, potential antigens of E. meningoseptica have been identified.The selected B-cell and T-cell epitopes have been assessed for their immunogenicity. This involves evaluating their ability to stimulate a strong and specific immune response in vitro.In conclusion, the identification of B-cell and T-cell specific vaccine candidates for E. meningoseptica represents a significant step toward developing an effective immunization strategy against this pathogen. The comprehensive approach, from antigen identification to preclinical validation, underscores the potential of the vaccine in preventing or mitigating E. meningoseptica infections. Continued research and collaboration are essential for translating these findings into practical and clinically relevant vaccine options.

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