MULTI EPITOPE PEPTIDE VACCINE PREDICTION AGAINST SUDAN EBOLA VIRUS USING IMMUNO-INFORMATICS APPROACHES

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Abstract

Sudan Ebola virus is single stranded negative sense RNA genome belonging to Filovirus Filoviridae family that causes hemorrhagic fever. There is no treatment or vaccine for it, thus the aim of this study is to design a peptide vaccine using immuoinformatics approaches to analyze the glycoprotein of the all strain of SUDV, to determine the conserved region which is further studied to predict all possible epitopes that can be used as a peptide vaccine. A total of 21 Sudan Ebola virus glycoprotein retrieved from NCBI database were aligned to determine the conservancy and to predict the epitopes using IEDB analysis resource. Three epitopes predicted as a peptide vaccine for B cell (PPPPDGVR, ETFLQSPP, LQSPPIRE). For T cell four epitopes showed high affinity to MHC class I (FLYDRLAST, IIIAIIALL, MHNQNALVC and RTYTILNRK) and high coverage against Sudan and the whole world population alleles. Also in MHC class II, Four epitopes that interact with most frequent MHC class II alleles (FAEGVIAFL, FLRATTELR, FLYDRLAST and FVWVIILFQ) with high coverage against Sudan and the whole world population. We recommend in vivo and in vitro study to prove the effectiveness of these predicted epitopes as a peptide vaccine.

Introduction

Ebola virus is belonging to Filoviruses Filoviridae family which is zoonotic pathogen that causes hemorrhagic fever for both human and nonhuman primate with high rate of death that exceeded 80% (1-8). The first appearance of Ebola virus in Sudan, Yambuku, Nzara and Democratic Republic of Congo was in 1976 then it spread into a village near the Ebola River (2,4). The main Ebola virus glycoprotein (GP) is the only viral protein responsible for the attachment and immune response in the host cells which is found on the surface of the virus thus it's the main target for designing a vaccine, GP post-translationally yield GP1 and GP2 subunits (9-16). The first successful vaccine for Ebola virus developed in guinea pig using plasmid DNA, GP and sGP enhance cytotoxic and humoral responses but the efficacy of this DNA vaccine has been less effective in humans (17).

Our aim is to design a vaccine for Ebola virus using peptide of its glycoprotein as an immunogen to stimulate protective immune response.

Methodology

A total of 21 Sudan Ebola virus strains' glycoprotein were retrieved from NCBI (http://www.ncbi.nlm.nih.gov/protein/?term=sudan+ebola+virus+glycoprotein) database in June 2016. These 21 strains sequences retrieved are from different parts of the world (include 11 collected from Uganda and 4 from Sudan).

Then the candidate epitopes were analyzed by different prediction tools from Immune Epitope Database IEDB analysis resource (http://www.iedb.org/) (18,19), to predict the epitopes that may binds to B and T cells and to determine the population coverage after determination of conservancy using Bioedit software.

Homology modeling conducted using Phyre2 online server (http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index) and the showing of predicted epitopes in the structure of the glycoprotein done using Chimera software (Chimera-1.8).

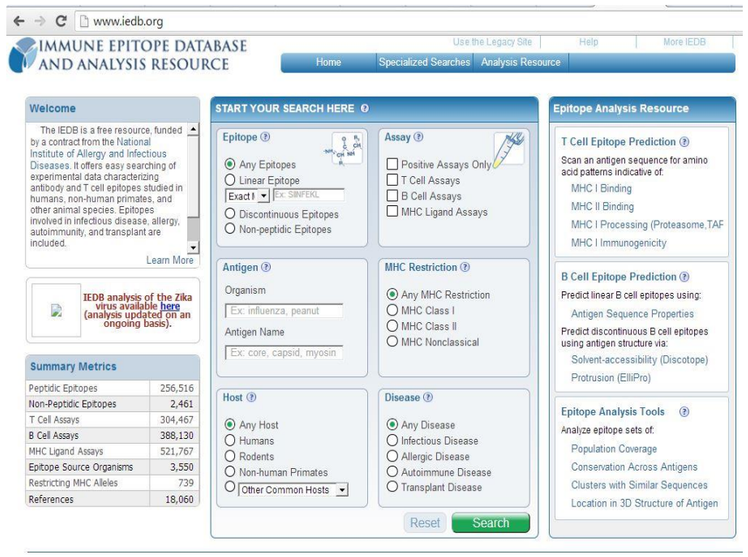

Figure 1: IEDB website

Results

Many epitopes predicted to stimulate the immune system (B and T cells) depending on specific criteria.

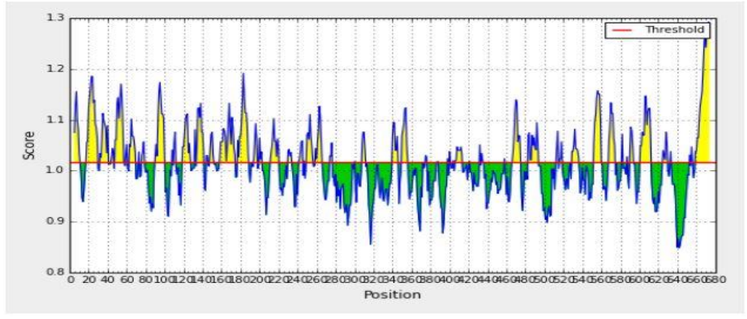

Figure 2: Kolaskar and Tongaonkar antigenicity prediction

Yellow areas above threshold (red line) are proposed to be a part of B cell epitope. While green areas are not.

Table 1: B-cell epitpoes prediction depending on surface accessibility and antigenicity

Epitope	Start	End	Length	Surface accessibility [a]	Antigenicity score [b]
1*GSGVSTDIPSATKRWGFRSGVPP	72	94	23	0.291	1.003
1*VSTDIPSATKR	75	85	11	1.091	1.016
VSYEAGEWAE	97	106	10	0.614	1
2*KKPDGSECLPPPPDGVRG	114	131	18	1.369	1.018
2*PPPPDGVR	123	130	8	1.669	1.031
KAQGTGPCPGD	140	150	11	0.574	0.995
3*ETFLQSPPIREA	191	202	12	1.009	1.016
3*ETFLQSPP	191	198	8	1.204	1.032
3*LQSPPIRE	194	201	8	1.323	1.035

1* peptide from 72 to 94 gives higher score if it is shorten (75 to 85) in all tools.
2* peptide from 114 to 131 gives higher score if it is shorten (123 to 130) in all tools.
3* peptide from 191 to 202 gives higher score if it is shorten (191 to 198) or (194 to 201) in all tools.
a: default threshold value 1.000. b: default threshold value 1.016.
Position of peptides is according to position of amino acids in the glycoprotein(GP).

In stimulation of T cell the prediction depends on the binding of epitopes to the MHC class I and II alleles.

Table 2: population coverage of proposed epitopes that binds to Sudan and World alleles

Epitope	Coverage World Class I	Coverage Sudan Class I	Total HLA hits	Epitope(core sequence)	Coverage World Class II	Coverage Sudan Class II	Total HLA hits
FLYDRLAST	46.73%	39.93%	3	FAEGVIAFL	99.67%	97.24%	21
IIIAIIALL	42.53%	34.71%	3	FLRATTELR	99.69%	97.36%	21
MHNQNALVC	35.14%	67.96%	3	FLYDRLAST	99.38%	95.87%	19
RTYTILNRK	43.03%	32.96%	5	FVWVIILFQ	99.72%	95.94%	18
Epitope set	**85.08%**	**91.30%**		**Epitope set**	**99.97%**	**99.22%**	

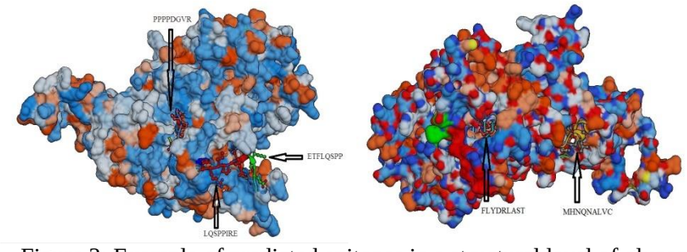

Figure 3: Example of predicted epitopes in a structural level of glycoprotein

Conclusion

As the increase of incidence of viral infections by new lethal viruses and infection of human by viruses that earlier recognized as a zoonotic, the need of new available technology increases. Bioinformatics techniques cover this need, and reduce the time and effort consumed in designing of new vaccines and therapies. Sudan Ebola virus is life threatening infection which enforces the need of developing a protective vaccine. The fact that all Ebola species accompanied with high mortality rates increases the need of developing a vaccine against all filoviruses. Several epitopes proposed in this study especially FLYDRLAST which is suggested before by Pratik Narain Srivastava et al, to be a peptide vaccine against Ebola virus, could be a powerful multi epitope vaccine against SUDV after in vivo and in vitro verifications.