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RESEARCH ARTICLE

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A bioinformatics approach to design a novel epitope-based vaccine against simian immunodeficiency virus (*Retroviridae*: *Lentivirus*)

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Abstract

Simian Immunodeficiency Viruses (SIV) have been found to naturally infect African nonhuman primates (NHP). This causative agents are important and one of the special interest as the root cause of the HIV/AIDS pandemic, one of the most threatening infectious diseases worldwide. The aim of this study was to design an epitope-based vaccine using bioinformatics approaches of the circulating SIV in Kenya, Africa. In this study, we used 17 partial SIV envelope glycoprotein genes retrieved from GenBank® (National Center for Biotechnology Information, USA). We analysed the candidate epitopes using the Immune Epitope Database and Analysis Resource. Then, we performed the protective antigens prediction usingVaxiJen. Interestingly, this study revealed the data of B cell epitope prediction, protective antigens prediction, and molecular phylogenetic of circulating SIV in Kenya, Africa. In sum, this study can be used to design a novel epitope-based vaccine against SIV. We suggest further studies to conduct confirmatory experiments (*in vitro* and *in vivo*).

Keywords: B cell epitope prediction, Bioinformatics, Simian immunodeficiency virus, Molecular phylogenetics

Introduction

Retroviruses are a virus family of major medical and veterinary importance. It is recognized that HIV-1 and HIV-2 are the result of cross-species transmissions of the SIV[1]. However, HIV-1 originates from SIVcpz. Bailes *et al*. reported that SIVcpz is a recombinant virus between SIVgsn from *Cercopithecus nictitans* and SIVrcm from *Cercocebus torquatus*[2]. Greenwood *et al.* stated that SIV naturally infects wild African NHP; more than 40 different species have been infected with SIV[3].

Moreover, on the basis of SIV genomic sequences, there are currently six major phylogenetic lineage of SIVs: (i) SIVmnd-1 in *Mandrillus sphinx*; (ii) SIVsm in *Cercocebus atys*; (iii) SIVcpz in *Pan troglodytes*; (iv) SIVagm in four species of *Chlorocebus aethiops*; (v) SIVcol in *Colobus guereza*; and (vi) SIVsyk in *Cercopithecus albogularis*[4]. Furthermore, *Retrovirus* envelope glyproteins interact with cell receptors and are the targets for antiviral immune response in infected hosts. The envelope glycoproteins of SIV are important for virus infection; they mediate the binding and fusion to the target cells. The envelope glycoprotein is synthesized as a gp160 which is claved into two subunits, gp120 and gp41, by a cellular protease[5].

In addition, vaccines have been proven to decrease morbidity and mortality levels of infectious diseases. Today, epitope-based vaccines are indicating its progress in the clinical trial phases. Progress made on methods in molecular biology and biotechnology is driving the construction of the novel concepts in vaccinology. Synthetic recombinant proteins containing epitopes can be produced efficiently via bioprocessing and modern biotechnology methods[6]. Thus, epitope-based vaccine is proposed to be a new potential candidate for obtaining a novel and effective SIV vaccine. In the present study, we applied bioinformatics analysis to reveal the data of B cell epitope prediction, protective antigens prediction, and molecular phylogenetic of circulating SIV strain from African green monkey originally isolated in Kenya, Africa via GenBank®.

Materials and methods

SIV Isolates

All isolates were retrieved from GenBank® (National Center of Biotechnology Information, USA) (Table 1). All samples are isolated from African green monkey in Kenya, Africa.

Nucleotide Sequence Preparation

SIV nucleotide sequences (envelope glycoprotein gene; partial gene) from all isolates were retrieved from GenBank® (National Center of Biotechnology Information, USA). Multiple sequence alignment of nucleotide sequences were carried out using MEGA X software.

Prediction of B-Cell Epitope and Protective Antigens

B cell epitope, also known as B cell antigenic determinant, is a specific antigen region that has high affinity with B cell lymphocytes. Its interaction induces B cell to produce the antigen-specific antibody and memory cell[7]. To predict the B cell epitope, we used the methods provided by the IEDB online webserver (www.iedb.org) with default thresholds and VaxiJen v2.0 (www.ddg-pharmfac.net/vaxijen/).

Molecular Phylogenetic Analysis

We analysed the molecular phylogenetic analysis using MEGA X. The data was carried out using the maximum likelihood to obtain a phylogenetic tree. Then, the phylogenetic tree was tested using a bootstrap test on 1000 replications, and the Tamura-Nei substitution model, referring to Tamura *et al*.[8].

Results

Epitopes from all samples of SIV isolates are predicted on the tools.iedb.org/bcell to determine the potential for B cell recognition with an accuracy of around 75%, this prediction works based on a specific algorithm with a combination of Hidden Markov Model (HMM) statistical methods and trend scale[7]. After being tested using B cell epitope prediction, predicted peptides are tested using the VaxiJen v2.0 to determine the characteristics of immunogenicity or protective antigens including non-antigens or antigens so that they can be distinguished. The performance of this server uses the alignment principle 'alignment-independent prediction', but now it is developed based on the physicochemical properties of the target protein without alignment. So that, the prediction has an accuracy of around 70% to 89%[9,10].

Prediction of B-Cell Epitope and Protective Antigens

Table 1. The results of B cell epitope prediction analysis and the protective antigens prediction of SIV isolates using the platform from the IEDB and VaxiJen.

	NCBI Accession Number	Predicted Peptides	Position	Lenght	Protective Antigens
1	MG590109.1	GFAPTNVRRYTGGHERQK	252-269	18	Yes
2	MG590110.1	NNKNRTNVTLSPPIE	183-197	15	Yes
3	MG590111.1	GFAPTEVRRYTGGHERQK	253-270	18	Yes
4	MG590112.1	TVDADHNSCNGSRTSPRAPGPCV	133-155	23	Yes
5	MG590113.1	GFAPTEVRRYTGGHERQK	250-267	18	Yes
6	MG590114.1	GFAPTEVRRYTGGHERQK	242-259	18	Yes
7	MG590115.1	GFAPTEVRRYTGGHERQK	245-262	18	Yes
8	MG590116.1	TVDADHNQCNGTNQRKGRAPGPCV	146-169	24	Yes
9	MG590117.1	GFAPTDVRRYTGGHERQK	243-260	18	Yes
10	MG590118.1	VDADHNKCNSTKSKSKSPGPCV	140-161	22	Yes
11	MG590119.1	GFAPTEVRRYTGGHERQKR	250-268	19	Yes
12	MG590120.1	DADHNRCGNTTGRKGNAPGPCV	149-170	22	Yes
13	MG590121.1	GFAPTNVRRYTGGHERQ	90-107	18	Yes
14	MG590122.1	VDADHNPCNNTRKRGNAPGPCV	247-263	17	Yes
15	MG590123.1	GFAPTEVRRYTGGHERQK	251-268	18	Yes
16	MG590124.1	GFAPTEVRRYDGRSRQK	149-170	22	Yes
17	MG590125.1	DYNKCNGSSRGRAPGPCV	252-268	17	Yes

Molecular phylogenetic analysis from SIV isolates.

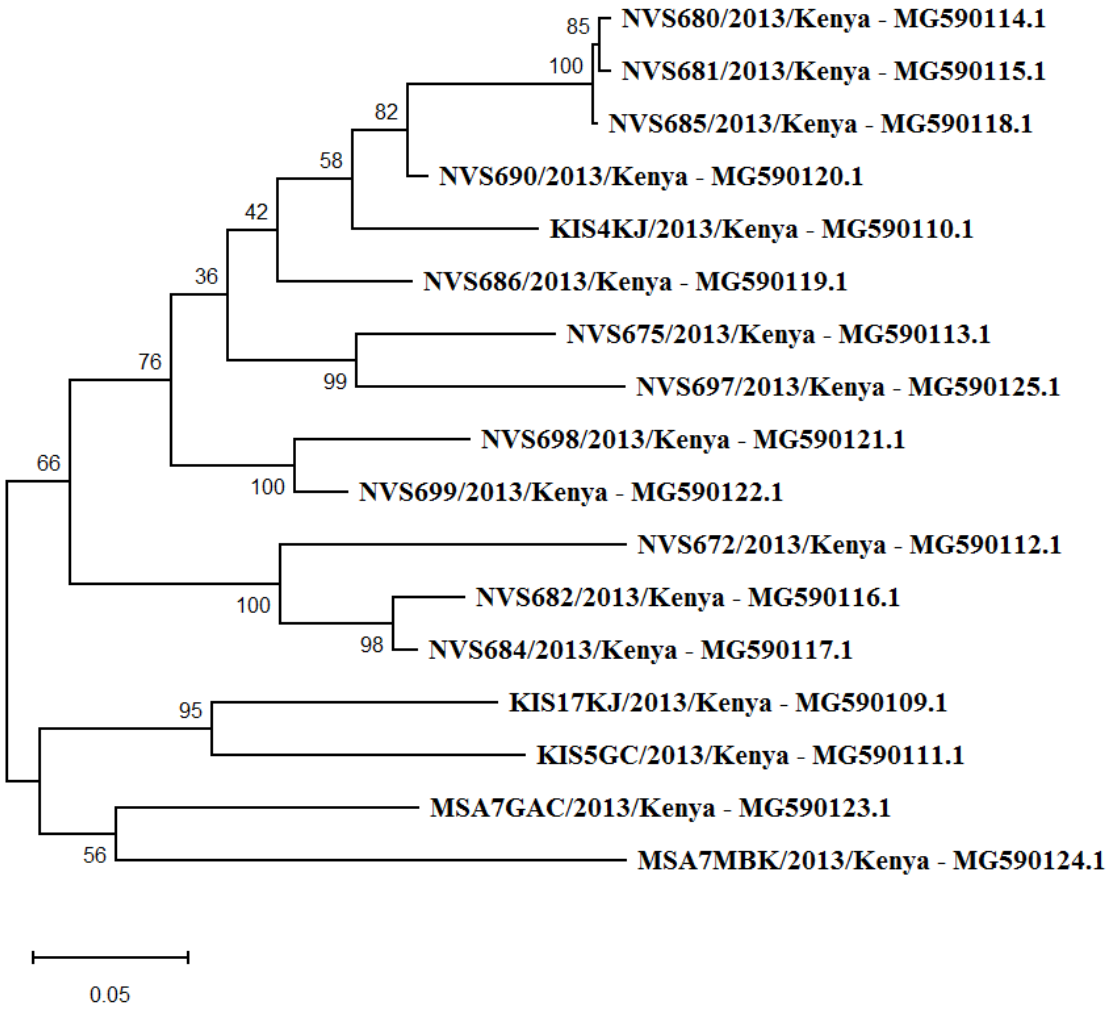

Figure 1. The results of molecular phylogenetic analysis from SIV isolates.

Discussion

Epitope-based vaccines have not yet reached the market. In contrast, more than 60 therapeutic peptides are commercially available[11]. However, research and development of epitope-based vaccines have received significant attention in the pharmaceutical industry over the past decade, due to the progress made in methods such as immunoinformatics, recombinant DNA technology, advanced cell-culture techniques, and design of immunogens[6]. Epitope-based vaccines play a vital role in present volume research and show certain advantages over conventional vaccines, including good safety, high specificity, stability, ease of production and storage. As a result, epitope-based vaccines have become an increasingly popular field of vaccinology[12]. Many studies have identified the potency of epitope-based antigens that can efficiently generate high immunity and its protection against various pathogens. The approach has been applied to develop and evaluate vaccines against various infectious agents, such as HIV, Zika virus, and etc. Future studies should consider appropriate adjuvants exploration of that can be used in conjunction with epitope-based vaccination strategies in optimalizing immunization protocols together with evaluation criteria[13].

The results of the B cell epitope prediction and VaxiJen prediction analysis conducted on all SIV isolates obtained from NCBI can be found in Table 1. In addition, B cell epitope prediction is a method used to predict protein regions that can be recognized as an epitope response to B cell. The epitope is part of an antigen molecule that binds to antibodies[14]. This area is very important and can be used as a

basis for designing certain types of vaccines or specific antibodies. To design a seed vaccine, the epitope must be considered to determine the active side of the antigen which will later be used to bind to the antibodies. A good epitope usually has a length of more than nine predicted peptides[15]. In this study, all isolates have more than nine predicted peptides.

Molecular phylogenetic analysis is used in a wide range of studies to address both applied and fundamental issues of virus research, including phylogeography, diagnostics, evolution, origin, epidemiology, forensic studies, and taxonomy of viruses. It can provide an evolutionary perspective on variation of any trait that can be measured for a group of viruses[16]. Molecular phylogenetic analysis in this study revealed the genetic relationship between SIV isolates from African green monkey in Kenya, Africa (see Figure 1).

So far, vaccination is an effective approach to control disease in animal health. Vaccines are agents that enhance the adaptive immune response. Vaccination can reduce the effects of infection and disease. Thus, the immune system recognizes the vaccine agent as a foreign object, then destroys and remembers it. In addition, a new concept of reverse vaccinology has revolutionized the study of vaccine development. The ability to sequence the whole genome from virulent organism has led some to screen *in silico* for the most protective antigens before conducting confirmatory experiments (*in vitro* and *in vivo*). Apart from advantages, such as low cost and speed, the success of bioinformatics approach depends on the accuracy of predictions, and many tools are available to facilitate this process[9].

Conclusions

In this study, we have revealed the data of B cell epitope prediction, protective antigens prediction, and molecular phylogenetic of circulating SIV in Kenya, Africa. In sum, the results of this study can be used to design a novel epitope-based vaccine against SIV. We suggested further study to conduct confirmatory experiments (*in vitro* and *in vivo*).

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Conflicts of Interest

The authors declare no conflict of interest in any capacity, including competing or financial.

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