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The Effect of RBD-Based Vaccines on Covid-19 XBB 1.5 Subvariant

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Abstract

COVID-19 (Coronavirus disease 2019 or severe acute respiratory syndrome coronavirus 2) is a transmissible illness affected by a virus of the Coronaviridae family. Omicron is one of the COVID-19 variants of SARS-CoV-2 that firstly informed from Botswana B.1.1.529 was the original subvariant of omicron and then numerous sub-variants of Omicron have appeared comprising: BA.1, BA.2, BA.3, BA.4, and BA.5, BQ.1 and BQ.1.1, XBB.1, and XBB 1.5. The aim of this *in silico* research is to investigate the effect of monovalent (monovalent) vaccines on the XBB.1.5 variant. In this *in silico* study the sequence of spike protein obtained from NCBI and then the mutations of XBB 1.5 were add to obtained sequence. Since most of the currently used vaccines belong to the RBD region, in this study the RBD mutations were analyzed. All B cell and T cell epitopes of original strain (Wuhan) recorded and the epitopes that changed via mutation (XBB 1.5) were removed. The original virus has 10 B-cell epitopes in the RBD region. 5 of these epitopes were not mutated (unchanged. Besides the B cells epitopes, 45 alleles of T cell epitopes were also unchanged. The result of this study informed that the monovalent vaccine can produce humoral and especially cellular immunity and the vaccines help protect against severe illness, hospitalization, and death. The mutations will certainly reduce the effectiveness of monovalent vaccine, so the use of bivalent vaccines is recommended. Some countries do not have bivalent vaccines; these countries can still use monovalent vaccines.

Keywords: Covid-19; Vaccine; XBB 1.5; Monovalent; Bivalent

Abbreviations: RBD: Receptor Binding Domain; FDA: USA Food and Drug Administration; IEDS: Immune Epitope Database Server; NCBI: National Center for Biotechnology Information.

Introduction

COVID-19 (Coronavirus disease 2019 or severe acute respiratory syndrome coronavirus 2) is a transmissible illness affected by a virus of the Coronaviridae family. The virus was first reported from Wuhan, China, in December 2019 [1], and then spread to other countries. The Coronavirus disease 2019 symptoms comprise headache, loss of smell, fever, fatigue, cough, and loss of taste and breathing [2,3].

Omicron is one of the COVID-19 variants of SARS-CoV-2 that firstly informed from Botswana B.1.1.529 was the original subvariant of omicron and then numerous sub-variants of Omicron have appeared comprising: BA.1, BA.2, BA.3, BA.4, and BA.5 [4]. In October 2022, two sub-variants

of BA.5 called BQ.1 and BQ.1.1 have reported [5]. Towards the end of 2022 XBB.1.5, which is grown from the XBB sub-variant has emerged. By the end of 2022, 40.5% of new cases of US have been infected by XBB [6].

The spike protein of the Omicron is characterized by at least 34 mutations (30 amino acid substitutions, three deletions, and one amino acid insertion). Remarkably, 15 aa substitutions are in the RBD (Receptor Binding Domain). The RBD amino acid substitutions are following as: G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y and Y505H. XBB.1 is a subvariant of omicron, through two other Spike protein mutations (N460K, F490S) and XBB.1.5 is a subvariant of XBB, with an extra Receptor Binding Domain mutation S486P. The XBB.1.5 subvariant was detected in the US on October 2022. The variant has also been detected in the EU and Asia [7]. As of 11 January 2023, more than 669 million people have been infected, with about 6.7 million deaths. Different vaccines have been used throughout the pandemic and several research studies are proceeding to recognize potential antivirals or different drugs to treat COVID-19 patients [8].

COVID-19 vaccination supports protecting people by producing antibody responses without you having to experience potentially severe disease or post-COVID conditions. Getting sick with COVID-19 can cause severe illness or death [9]. There are a small number of updated vaccines in the world. For example a booster dose of Omicron BA- 4 / BA- 5 the bivalent vaccine has been approved for emergency use via USA Food and Drug Administration (FDA) (pfizer.com, 2023). Zou, et al. reported that the bivalent BA.4/5 vaccine is more immunogenic than the original BNT162b2 monovalent vaccine against circulating Omicron subvariants (BA.4/5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1) [10]. Whereas xbb 1.5 is the most transmissible variant, but there is no published research on the effect of monovalent (non-updated) vaccines on XBB. 1.5 Variant. The aim of this in silico research is to investigate the effect of monovalent (non-updated) vaccines on the XBB.1.5 variant.

Material and Methods

This study aimed to investigate the XBB 1.5 mutations by Bioinformatic analysis. In this in silico study the sequence of spike protein obtained from NCBI (NCBI Reference Sequence: YP_009724390.1) and then the mutations of XBB 1.5 were add to obtained sequence (Figure 1).

```
RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFT
NVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDI
STEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNF
```

Figure 1: The RBD sequence of original strain (COVID-19).

Most vaccines (Pfizer, Moderna, Sputnik V, Novavax, Astrazeneca, Soberana, Spikogen, Cov Pars, Noora and etc) are designed by targeting the RBD region. For this reason the B and T cell epitopes of original virus (Wuhan) which are obtained and mutated epitopes are evaluated (Figure 2).

```
RVQPTESIVRFPNITNLCPFHEVFNATTFASVYAWNRKRISNCVADYSVIYNFAPFFAFKCYGVSPTKLNDLCFT
NVYADSFVIRGNEVSQIAPGQTGKIADYNYNLPDDFTGCVIAWNSNKLDSKPSGNYKYLYRLFRKSKLKPFERDI
STEIYQAGNTPCNGVAGPNCYSPLQSYGFRPTYGVGHQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNF
```

Figure 2: The RBD sequence of COVID-19 XBB 1.5 subvariant.

B-cell epitopes were acquired by Immune Epitope Database server (IEDB) [11,12]. We used PropredI for prediction of MHC class I epitopes. In this research the epitopes were evaluated for their binding affinity with all HLA alleles (p values <0.05 were considered significant) [13,14]. After that the epitopes changed as a result of the mutation and the epitopes that were not affected by the mutation were recorded and then compared.

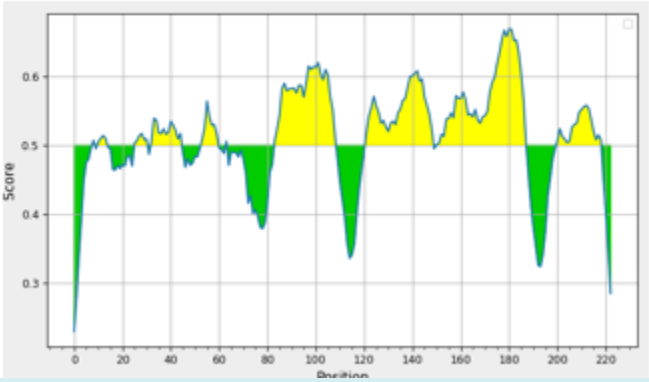
Result and Discussion

Since most of the currently used vaccines belong to the RBD region, in this study the RBD mutations were analyzed. The spike protein sequence of severe acute respiratory syndrome coronavirus-2 was obtained from National Center for Biotechnology Information (NCBI). The B cell epitopes (predicted by IEDB) having a score higher than

0.35 were selected and PropredI was used for prediction of MHCI epitopes. All B cell and T cell epitopes of original strain (Wuhan) recorded and the epitopes that changed via mutation (XBB 1.5) were removed.

The original virus has 10 B-cell epitopes in the RBD region. 5 of these epitopes were not mutated (unchanged). The unchanged epitopes are shown in Figure 3.

a



b

No.	Sequence
1.	RVQPTE
2.	VSPT
3.	LKP
4.	RD
5.	TVCGPKKSTN

Figure 3: The unchanged B cell epitopes. A: The location of epitopes and scores. B: .The amino acid sequence of unchanged B cell epitopes.

Besides the b cells epitopes, 45 alleles of T cell epitopes were also unchanged (Table 1).

Epitope	Allele
VLSFELLHA	HLA-A*0201
VVVLSFELL	HLA-A*0205
KCYGVSPTK	HLA-A*1101
CYGVSPTKL	HLA-A24
VYAWNRKRI	
RVVVLSFEL	
KCYGVSPTK	HLA-A3
QIAPGQTGK	
VQPTESIVR	HLA-A*3101
VYADSFVIR	
SVYAWNRKR	HLA-A*3302
VYADSFVIR	
SVYAWNRKR	HLA-A68.1
ASVYAWNRK	
RKRISNCVA	HLA-A20
FKCYGVSPT	
ELLHAPATV	HLA-A2.1
VRFPNITNL	HLA-B14
ESIVRFPNI	
VRFPNITNL	HLA-B*2702

VRFPNITNL	HLA-B*2705
NRKRISNCV	
QPTESIVRF	HLA-B*3501
GPKKSTNLV	
FERDISTEI	HLA-B*3701
NDLCFTNVY	
QPTESIVRF	HLA-B*3801
CYGVSPTKL	
VRFPNITNL	HLA-B*3901
RVVVLSFEL	HLA-B*3902
DDFTGCVIA	HLA-B40
FELLHAPAT	
NDLCFTNVY	HLA-B*4403
IAPGQTGKI	HLA-B*4403
LPDDFTGCV	
GPKKSTNLV	
IAPGQTGKI	HLA-B*5101
LPDDFTGCV	
GPKKSTNLV	
IAPGQTGKI	HLA-B*5102
GPKKSTNLV	
IAPGQTGKI	HLA-B*5103
LPDDFTGCV	
NVYADSFVI	HLA-B*5201
LPDDFTGCV	HLA-B*5301
FPNITNLCP	
FPNITNLCP	HLA-B*5401
LPDDFTGCV	HLA-B*51
FPNITNLCP	
FTNVYADSF	HLA-B*5801
QPTESIVRF	
FERDISTEI	HLA-B60
FERDISTEI	HLA-B61
FELLHAPAT	
DDFTGCVIA	
GQTGKIADY	HLA-B62
RISNCVADY	
RVVVLSFEL	HLA-B7
VVVLSFELL	
APGQTGKIA	

RKRISNCVA	HLA-B*0702
GPKKSTNLV	
KPFERDIST	
WNRKRISNC	HLA-B8
VSPTKLNDL	
GPKKSTNLV	
ESIVRFPNI	
VVVLSFELL	HLA-Cw*0301
VRFPNITNL	
CYGVSPTKL	HLA-Cw*0401
QPTESIVRF	
VSPTKLNDL	HLA-Cw*0602
RVVVLSFEL	
VRFPNITNL	
NDLCFTNVY	HLA-Cw*0702
VRFPNITNL	MHC-Db
VYAWNRKRI	
VVVLSFELL	MHC-Db
CGPKKSTNL	MHC-Dd
VSPTKLNDL	
CYGVSPTKL	MHC-Kd
VYAWNRKRI	
FERDISTEI	MHC-Kk
TESIVRFPN	
FELLHAPAT	
ESIVRFPNI	
QPTESIVRF	MHC-Ld
VSPTKLNDL	

Table 1: The amino acid sequence of T cell (MHC I) epitopes.

Since most monovalent vaccines target the Receptor Binding Domain (RBD) of the spike protein of COVID-19, in this *in silico* study, the RBD mutations of XBB 1.5 has been investigated. The results acquired from the IEDB indicated that there are a minimum of five highest score B cell epitopes that remained unchanged. The PropredI analysis indicated that there are still 45 unchanged and common epitopes (for different MHCI) between the original variant (Wuhan) and XBB 1.5.

XBB.1.5 is a subvariant of the XBB, and is currently expected to have a large growth advantage over previously circulating variant in the world, even though these estimates are related with important uncertainty. There is a risk that this variant may have an increasing effect on the number of COVID-19 cases in the world. The result of this study informed that the monovalent vaccine can produce humoral and especially cellular immunity and the vaccines help protect against severe illness, hospitalization, and death. The mutations will certainly reduce the effectiveness of monovalent vaccine, so the use of bivalent vaccines is recommended. Some countries do not have bivalent vaccines; these countries can still use monovalent vaccines.

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