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WORD COUNT	1712	TIME SUBMITTED	17-MAR-2022 05:46PM
		PAPER ID	83761268

Name of Journal: *World Journal of Virology*
Manuscript NO: 74200
Manuscript Type: ORIGINAL ARTICLE

Basic Study

Omicron variant and change of electrostatic Interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor

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Abstract

BACKGROUND

SARS CoV2 variants are currently a new hazard. Since the first appearance of classical SARS CoV2 in late 2019, pathogen genetic alterations have continued to occur, and some new hazardous forms have already emerged. The underlying pathophysiological process leading to clinical issue is molecular change caused by genetic mutation.

AIM

The impact of a molecular alteration is interesting. A change in the interaction between receptor binding domain of SARS-CoV-2 and the ACE2 is an interesting issue.

METHODS

The authors conducted a study to see how mutations are associated with electrostatic Interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor. In this report, three important COVID-19 variants: beta, delta, and omicron are investigated.

RESULTS

According to this study, there is a change of electrostatic interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor due to each studied variant. The most change is detected in omicron variant following by delta variant and beta variant.

CONCLUSION

This can support the clinical observation that the omicron variant has an increased transmissibility comparable to the wild type and other variants.

Key Words: omicron; COVID-19; SARS CoV2; ACE2; electrostatic

mungmunpuntipantip R, Wiwanitkit V. Omicron variant and change of electrostatic Interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor. *World J Virol* 2022; In press

Core Tip: Change of electrostatic Interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor can support the clinical observation that the omicron variant has an increased transmissibility comparing to the wild type and other variants.

INTRODUCTION

In late 2019, a novel coronavirus epidemic emerged in Asia and quickly spread throughout the world [1]. A pandemic occurs, resulting in millions of cases of COVID-19 all across the world. The disease has already infected over 200 million individuals worldwide, resulting in millions of deaths. Since the initial appearance of classical severe acute respiratory syndrome coronavirus 2 (SARS CoV2) in late 2019, scientists have been keeping a tight eye on the pathogen's genetic mutations all across the world [2]. Several pathogenic genetic mutations have been identified, and several variants have already proven to be troublesome novel variants [2 - 3].

The delta variant is one of the dangerous mutations that has spread globally [4 - 5]. Because transmission of the delta variation is higher than that of COVID-19, it can provide a concern in disease control. A newer form, the delta plus variant, has also been discovered and it is now being considered in clinical practice [6 - 7]. The impact of novel variations on disease epidemiology and clinical characteristics is interesting. The newest troublesome variant of concern, the omicron variant was discovered in Africa in November 2021 [8]. There are various structural alterations in this new variant molecule. Omicron is spreading in a raid manner, and many nations have already reported cases [9].

Clinically, the underlying pathophysiological mechanism that can result in a clinical disease is molecular change caused by genetic mutation. The impact of molecular changes is interesting, but it has received little research. The clinical impact of the omicron mutation is unknown. Pathogenesis may change as a result of molecular changes. A change in the interaction between receptor binding domain of SARS-CoV-2 with the ACE2 is an interesting issue. The authors conducted a study to see how mutations are associated with electrostatic Interactions between the receptor binding domain of SARS-CoV-2 with the ACE2 receptor. In this report, three important COVID-19 variants: beta, delta, and omicron are investigated.

MATERIALS AND METHODS

The current research is in the field of medical molecular bioinformatics. It's part of a series of experiments aimed at determining the effects of molecular changes in mutants of SARS CoV2. The goal of this research is to see how electrostatic interactions between SARS CoV2 and ACE2 receptor changes according to the emerging variants. For the investigation of change of electrostatic interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor, the authors apply a conventional informatics technique as described in a recent publication [10].

Various protein-protein interactions are known to be dominated by electrostatic interactions. [11]. Analysis was performed according to the published protocol

[10]. Briefly, we look into the impact of electrostatic interactions on binding energetics. At the molecular level, both Molecular mechanics MM and Monte Carlo MC simulations were used to assess the interaction between receptor binding domain of spike viral protein and ACE2. The protein structure was obtained from the protein data bank and used in all computations (PDB ID: 6m17). to begin, the crystal structure was optimized using the python-based openMM [12] technique. Then, using MCCE [13], rotamers were created, with each rotatable bond rotated by 60 degrees to precisely sample the sidechain conformations. Finally, the Poisson Boltzmann equation was utilized to calculate electrostatic interactions using optimized protein structures with the most occupied conformers [10]. When DELPHI is used to calculate pairwise electrostatic interactions between conformers, it is referred to as DELPHI [10]. The Boltzmann distribution for all conformers was then estimated using MC sampling for the WT and altered structures at pH 7 using MCCE. For single and double mutant structures, as well as the wild type, the electrostatic and van der Waals contributions to the interaction energies of SARS-CoV-2/ACE2 were estimated [10].

The research type of SARS CoV2 included both wild type and mutation-free SARS CoV2. In silico mutation assignment is by PyMol (PyMol, version 2.4). The variants studied are: a) beta (K417N, E484K, and N501Y assigned mutations), b) delta (T478K, P681R, and L452R assigned mutations), and c) omicron (K417N, E484K, and N501Y assigned mutations) (A67V, T95I, G142D, L212I, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K and L981F assigned mutations).

The overall electrostatic interactions value for wild type is derived from the previously mentioned bioinformatic procedure. The already described molecular changes are used for simulation to get the overall electrostatic interactions value for each specific variant. Then we calculated the effects of the aforementioned mutations and compared our findings to those of the wild type (native) protein. In brief, the effect of variant on electrostatic interactions is calculated based on a direct comparison to the baseline

electrostatic interactions value in wild type. For calculation, the derived overall electrostatic interactions for wild type and each SARS CoV2 variant are used as basic parameters. For each type, the change of electrostatic interactions comparing to wild type is calculated by the formula "change of electrostatic interactions comparing to wild type = 100 x (electrostatic interactions in that type/ electrostatic interactions of wild type)" and presented in per centage.

RESULTS

According to this study, the electrostatic interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor for wild type, beta variant, delta variant and omicron variant SARS-CoV-2 is presented in Figure 1. The values are equal to -39.38, -41.26, - 163.82 and -643.71 kCal/mol, respectively.

There is a change of electrostatic interactions between receptor binding domain of SARS-CoV-2 with the ACE2 receptor due to each studied variant. The most change is detected in omicron variant following by delta variant and beta variant (Table 1).

DISCUSSION

In clinical genetics, a genetic change may occur, which may result in a new clinical condition. The clinical problem caused by the pathogen's genetic variation has already been noticed in COVID-19 [4 - 5]. In clinical virology, a mutation in the SARS CoV2 virus could occur, and the new variety could be clinically significant. SARS CoV2 variations have been reported in a number of places. The changes occur at the receptor-binding region of the spike glycoprotein, which is critical for binding to the ACE2 receptor. The interaction between receptor and SARS CoV2 is a significant factor of sickness, according to pathophysiology.

Basically, several alterations have been discovered in the omicron variant's molecular structure. The mutations could lead to a shift in molecular pathogenesis. A key feature, electrostatic interaction with receptor, is evaluated in this study. The ability of SARS CoV2 to bind to a receptor is a critical factor in its transmission. There is no doubt that

the new variant spreads quickly [7], which is explained by the change in electrostatic interactions between receptor and SARS CoV2.

As a result, measuring changes in virus-receptor electrostatic interactions can help researchers better understand disease pathogenesis. According to this study, there has been a significant change in electrostatic interactions. The change of electrostatic interaction is well described in delta variant [10] and the change is also observed in omicron variant. In delta variant, a replacement due to mutation result in electrostatic interaction change and the increased magnitude of electrostatic interactions is corresponding to the increased transmissibility of the virus [14].

According to this study, there is a different change of electrostatic interactions between receptor binding domain of SARS-CoV-2 and the ACE2 receptor due to different SARS-CoV-2 variant. The most change is detected in omicron variant following by delta variant and beta variant. According to Table 1, the greatest per centage of change comparing to wild type is detected in omicron variant. The greatest degree of change indicates the most changes in electrostatic interactions, which can also indicate major changes in clinical features. When compared to wild type, the omicron variant poses around 16 times more electrostatic interactions, implying a significantly stronger connection between the virus and its receptor.

This can support the clinical observation that the omicron variant has an increased transmissibility comparable to the wild type and other variants. The data from this preliminary is useful for explaining the pathogenesis of the omicron variant. Further studies on the detailed flexibility of molecular binding, molecular mass change and immunological epitoipic change will give more data for final conclusion on the virological properties of the variant.

CONCLUSION

According to this study, each investigated variant alters the electrostatic interactions between the SARS-CoV-2 receptor binding domain and the ACE2 receptor. The omicron variant shows the biggest alteration, followed by the delta and beta variants.

This could back up the clinical observation that the omicron variant is more transmissible than the wild type and other SARS-CoV-2variants.

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