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Short communication

SARS-CoV-2 variant Omicron (B.1.1.529) is in a rising trend of mutations increasing the positive electric charge in crucial regions of the spike protein S

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An increase in the positive electric charge of SARS-CoV-2 variant Omicron (B.1.1.529) was reported and the electrostatic interaction between the spike protein S and ACE2 receptor was estimated. The results presented here suggest that electrogenic mutations in specific regions of the S protein and the electrostatic force may facilitate viral infection of the host cell.

Keywords: coronavirus; COVID-19; SARS-CoV-2; Omicron; spike protein S; amino acids; electric charge; potential energy, electrostatic interaction

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Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ACE2, Angiotensin converting enzyme 2; S, spike protein; RBD, receptor-binding domain; RBM, receptor-binding motif; S1/S2, cleavage area; aa, amino acid; D, Aspartic Acid; E, Glutamic Acid; K, Lysine; R, Arginine

INTRODUCTION

The new SARS-CoV-2 B.1.1.529 variant of concern, Omicron (pdf1), detected at the beginning of November 2021, is characterized by 37 point mutations in the structural elements, four small deletions, and one small insertion. Of these, 30 missense substitutions are in the spike protein (S), with half of them in the receptor-binding domain (RBD), where 10 of them are concentrated in the receptor-binding motif (RBM). Two mutations had been found in the cleavage area (S1/S2). Eight mutations in RBD and S1/S2 refer to charged amino acids (D, E, K, R).

MATERIALS

Data were obtained from the UK Health Security Agency technical briefings 15 (pdf2) and 29 (pdf1).

RESULTS AND DISCUSSION

Arithmetic calculations show that charged amino acid mutations in the RBD and S1/S2 regions give a net increase in the positive charge (ΔQ= +4 [e]). Such an outcome is in line (Fig. 1) with a previously demonstrated trend of SARS-CoV-2 variants' charge evolution (Pawłowski, 2021a).

The recently described B.1.1.529 variant causes a lot of anxiety. The consequences of detected 42 changes in the sequence of structural elements are still intensely investigated. Whether they would cause a change in the virulence of the virus still remains an open question. The resulting conformational changes may modify the lock-key interaction of RBD with the ACE2 cell surface receptor or with the host's antibodies. Regardless of this, an increase in the positive charge at the RBD end of the S protein will increase a long-range electrostatic attraction between the spike and the negatively charged ACE2 contact zone (Fig. 2). At a distance of about 3 nm, the energy of this interaction is higher than the energy of thermal motion. Furthermore, additional charges may change multipolar interactions of the approaching molecules (Pawłowski, 2021b). They may also modify virus's interaction with charged antibodies, e.g. in the S1/S2 cleavage area.

CONCLUSIONS

The above results indicate that electrogenic mutations in specific regions of the S protein and the electrostatic force may be an important weapon used by the virus when attacking cells. As a result, the Coulomb attraction between the S protein and ACE2 is greater and stronger for Omicron than the "wild-type" virus. At a distance of 1 nm, the energy difference equals 14 k_BT. As an origi-

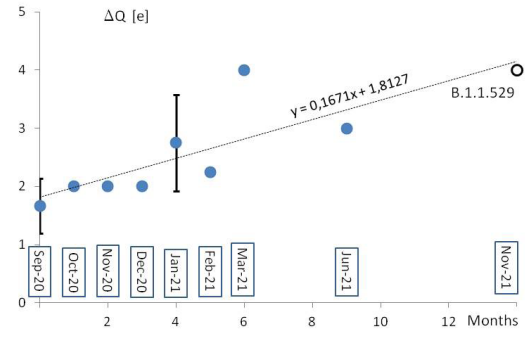

Figure 1. A mean increase of the net electric charge in RBD and S1/S2 cleavage regions in the virus lineages reported monthly by ECDC from September 2020 to June 2021, as shown in a previous report (Pawłowski, 2021a), but with the new B.1.1.529 variant (pdf1) added (open circle).
The estimated charge means the charge of the amino acids at neutral pH, expressed in elementary charge units. For reference, virus B.1 was taken as "wild-type" (with no D614G mutation or other spike protein changes). Standard deviation of the population (vertical bar) is shown. The calculations take into account the D, E, K, and R amino acids which are charged under physiological conditions. For simplicity, the values of aa charge +/-1 [e] were assumed, and the charge of histidine was neglected. The parameters of trend line slightly differ from the previous estimate.

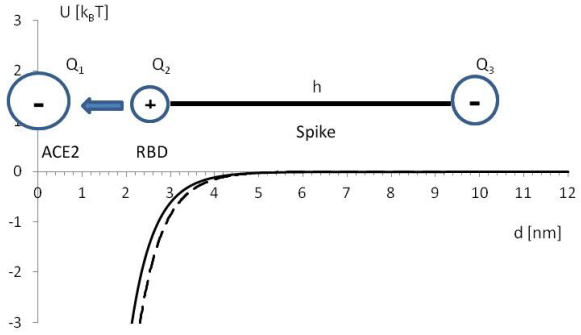

Figure 2. Although the overall net charge of spike protein S in the Omicron variant is negative (–8 [e]), the spike is finally attracted to the negatively charged receptor ACE2 (–28 [e]).
This is due to the electrostatic interaction with the positively charged RBD (+10 [e]), overwhelming the repulsion of negatively charged (–18 [e]), more distant regions of S. The presented potential electrostatic screened energy, U, is estimated for charged S protein and ACE2 as a function of distance, d, between the protein and the receptor surface. Three-point model (RBD, S interior, ACE2) and screened Coulomb energy $U=Q_1Q_2Exp(-d/L_D)/(4\pi\varepsilon_0\varepsilon d)+Q_1Q_3Exp(-(d+h)/L_D)/(4\pi\varepsilon_0\varepsilon d)$ was assumed, with the charge values Q_1= –28 [e], Q_2= +7 [e], and Q_3= –19 [e], for the "wild-type" variant, or Q_2= +10 [e], and Q_3= –18 [e], for the Omicron variant. The dielectric permittivity of a vacuum ε_0= 80 [F/m], the Debye screening length L_D= 0.7 nm, and the spike half-length h=7.5 nm were assumed. The lines represent estimation for "wild-type" (continuous), and the Omicron (broken), variants of SARS-CoV-2. The arrow indicates the resultant direction of attraction of the spike.

nally positive electric charge of the nucleocapsid protein has been also increased (Hodcroft, 2021) in the Omicron variant, SARS-CoV-2 deserves to be called the "electric" virus.

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