Comparison of SARS-cov-2 RdRp protein with SARS-cov RdRp protein

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SUMMARY
The World Health Organization (WHO) declared, on January 30, 2020, a public health emergency of international scope because of the emergence of a new virus called SARS-cov-2. This new virus belongs to the coronavirus family and has a protein called RNA-dependent RNA polymerase (RdRp) which is responsible for the replication of viral RNA. RdRp protein is one of the most primary targets for antiviral drug discoveries. The aim of this paper was to compare the amino acid sequence of the RdRp of SARS-cov-2 with that of SARS-cov. Thus, we found that there is a 96% sequence similarity between them. Indeed, there is only a difference at the level of 32 amino acids. Interestingly, only one residue at C Motif and two residues at D Motif are different. However, all the residues of the motifs A, B, E, F and G are 100% identical with those of SARS-cov-RdRp.

Since the end of 2019, a new virus called SARS-cov-2 has emerged from Wuhan province, Hubei region in China, and was spread to approximately 213 countries. The virus affected more than eighteen million people and caused the death of more than seven hundred thousand people (WHO 2020). Morocco state declared a state of health emergency and containment as of Friday March 20, 2020, in order to contain the spread of this virus. To date, more than four thousand Moroccan patients have been confirmed to have covid-19, the disease caused by the SARS-cov-2 virus, and over one hundred infected people have died.

Like SARS-cov and MERS-cov, SARS-cov-2 can cause respiratory and enteric disease in animal and human hosts. Indeed, in 2002, the zoonotic SARS-cov emerged
into human populations and spread to 26 countries with a ~10% case fatality rate (Cheng et al. 2007; Peiris et al. 2003; Ye et al. 2020). Also, MERS-CoV that began in Saudi Arabia infected approximately 2,500 cases with a ~36% case fatality rate (Báez-Santos et al. 2014; Elfiky 2017; Hemida et Alnaeem 2019).

SARS-cov-2 is enveloped virus and has a linear single-stranded positive RNA genome, with an extension near 29903 bp (NCBI Reference Sequence: NC_045512.2). It is formed by the structural proteins like Spike protein, Nucleocapsid (N), Matrix (M) and Envelope (E); and non-structural proteins, such as RNA-dependent RNA polymerase (RdRp) and proteases (Ceraolo et Giorgi 2020; Ren et al. 2020; Wu et al. 2020; Muralidharan et al. 2020; S. A. Khan et al. 2020; Sarma et al. 2020; Gupta et al. 2020). The aim of this paper is to present the characteristics of the RNA-dependent RNA polymerase protein by comparing its structure with that of SARS-cov.

RNA-dependent RNA polymerase contains 932 amino acids. It plays a very important role in the replication of viral RNA and it is one of the most primary targets for the antiviral drug. Alignment of the SARS-cov-2 RdRp with SARS-cov RdRp revealed a sequence identity of 96.35% (Figure 1). Indeed, there is a difference of 32 amino acids between the two RdRps.

In 2019, Kirchdoerfer et al. determined the 3D-structure of SARS-cov RdRp bound to its essential co-factors, nsp7 and nsp8, using single particle cryo-electron microscopy (pdb: 6NUR) (Figure 2) (Kirchdoerfer et Ward 2019).

Like all viral polymerases, the authors determined seven regions of conserved motifs (A - G) involved in the fixation and catalysis of matrices and nucleotides. Indeed, the single-stranded RNA model passes along the G motif before entering the active site, which is composed of the A and C motifs and supported by the B and D motifs. The NTPs access the active site via a tunnel and interacts with the F motif. The E motif interacts with the nucleotide 3’ of the primer strand and the synthesized product leaves the active site via the RNA exit tunnel (Figure 2) (Bressanelli et al. 2002; Bruenn 2003; Gong et Peersen 2010; Kirchdoerfer et Ward 2019; Poch et al. 1989; Zamyatkin et al. 2009).

In March 2020, Gao et al determined the three-dimensional structure of RdRp of SARS-cov-2 using cryo-electron microscopy (Figure 2). The structural alignment between Sars-cov-RdRp (pdb id: 6nur) and Sars-cov-2-RdRp (pdb id: 6m71) has an RMSD of 0.519 Å over 791 aligned residues with 96.97% sequence identity (Figure 2) (Gao et al. 2020).

SARS-cov-2 RdRp does not present a large structural difference with SARS-cov RdRp apart from the 32 mutations presented in the figure 1. Interestingly, only one residue at C Motif and two residues at D Motif are different. However, all the residues of the motifs A, B, E, F and G are 100% identical with those of SARS-cov-RdRp.
Figure 1: Sequence alignment of SARS-cov-2-RdRp and SARS-cov-RdRp using ClustalW. Red rectangles show the difference in amino acids between the two RNA-dependent RNA polymerases.
Figure 2: Three-dimensional structures of SARS-cov-2-RdRp and SARS-cov-RdRp viewed using YASARA software

Conflicts of Interest

The authors declare that they have no competing interest.

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