Article

Structurally Observed Electrostatic Features of the COVID-19 Coronavirus-Related Experimental Structures inside Protein Data Bank: A Brief Update

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Abstract: Since the Coronavirus disease (COVID-19) outbreak at the end of 2019, the past two months has seen an acceleration both in and outside China in the R&D of the diagnostics, vaccines and therapeutics for this novel coronavirus. As one of the molecular forces that determine protein structure, electrostatic effects dominate many aspects of protein behaviour and biological function. Thus, incorporating currently available experimental structures related to COVID-19, this article reports a simple python-based analysis tool and a LaTeX-based editing tool to extract and summarize the electrostatic features from experimentally determined structures, to strengthen our understanding of COVID-19’s structure and function and to facilitate machine-learning and structure-based computational design of its neutralizing antibodies and/or small molecule(s) as potential therapeutic candidates. Finally, this article puts forward a brief update of the structurally observed electrostatic features of the COVID-19 coronavirus.

Keywords: COVID-19; Electrostatic feature; Salt bridging network; Structural update

1. Introduction

On 31 December 2019, WHO was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province of China. The coronavirus disease (COVID-2019) was identified as the causative virus by Chinese authorities on January 7, 2020. The recent emergence of the COVID-2019 coronavirus disease is putting the whole world, instead of China alone, on alert [1–4]. Since the COVID-19 coronavirus disease outbreak, the past two months has seen a series of studies in the R&D of the diagnostics, vaccines and therapeutics for COVID-19 [5–8]. From a structural point of view, this article aims to investigate the electrostatic features embedded in experimentally determined COVID-19 coronavirus-related structures.

2. Materials and Methods

As of March 4, 2020, the Protein Data Bank (PDB) [9] hosts only four COVID-19 coronavirus-related experimental structures, as listed in Table 1 below:

| No. | PDB ID | Structure Title |
|-----|--------|-----------------|
| 1   | 6LU7   | The crystal structure of covid-19 main protease in complex with an inhibitor n3 |
| 2   | 6LVN   | Structure of the 2019-ncov hr2 domain |
| 3   | 6LXT   | Structure of post fusion core of 2019-ncov s2 subunit |
| 4   | 6VSB   | Prefusion 2019-ncov spike glycoprotein with a single receptor-binding domain up |

Table 1. Experimentally determined COVID-19 Coronavirus-related structures inside Protein Data Bank (PDB [9]) as of March 4, 2020. All the structures were retrieved from the PDB [9] website with a text search covid-19.
Among the four COVID-19 Coronavirus-related structures, three were determined using X-ray crystallography and one using electron microscopy (PDB ID:6VSB), as listed in Table 2.

| PDB ID | Molecular IDs | Chain IDs | Experiments            |
|--------|---------------|-----------|------------------------|
| 6LU7   | 1,2           | A, C      | X-ray crystallography  |
| 6LVN   | 1             | A, B, C, D| X-ray crystallography  |
| 6LXT   | 1             | A, B, C, D, E, F | X-ray crystallography |
| 6VSB   | 1             | A, B, C   | Electron microscopy    |

Table 2. Molecular and chain IDs of the four COVID-19 Coronavirus-related structures inside PDB as of March 4, 2020.

After the four structures were accessed and downloaded directly from the PDB website [9], a comprehensive set of salt bridging analysis was carried out as described in [10] previously. Nonetheless, no hydrogen bonding network analysis was carried out here because usually hydrogen atoms are missing from experimentally determined biomolecular structures solved using X-ray crystallography.

3. Results

With the electrostatic analysis as described previously in [10], this article puts forward a comprehensive set of electrostatic interaction features for the four COVID-19 coronavirus-related structures as of March 4, 2020, all included as a large set of separate tables in the supplementary file supplementary.pdf, including specifically:

1. all salt bridges formed within all four COVID-19 coronavirus-related structures as of March 4, 2020.
2. all interfacial salt bridges formed within all four COVID-19 coronavirus-related structures as of March 4, 2020.
3. all salt bridges formed within all four COVID-19 coronavirus-related structures as of March 4, 2020, PDB ID-specifically for all four COVID-19 coronavirus-related structures.
4. all interfacial salt bridges formed within all four COVID-19 coronavirus-related structures as of March 4, 2020, PDB ID-specifically for all four COVID-19 coronavirus-related structures.

No side chain or main chain hydrogen bond was structurally identified for the four COVID-19 coronavirus-related structures (Tables 2 and 1), as shown in supplementary file supplementary.pdf.

4. Conclusion and Discussion

For the first time, this article reports a comprehensive set of electrostatic features sucked out of the currently (as of March 4, 2020) available COVID-19 coronavirus-related structures inside PDB [9] in both PDF format (supplementary file supplementary.pdf) and also LaTeX format, i.e., a series of machine-readable -importable and -analyzable .tex files zipped in the supplementary file scan.zip. In supplementary file scan.zip, a simple python-based analysis tool and a LaTeX-based editing tool [11] were included to extract and summarize the electrostatic features from experimentally determined structures, where a set of PDB files (representing experimentally determined protein structures) are to be plugged into a set of python scripts included in cmd.py. Afterwards, cmd.py is to be executed with a simple command (python cmd.py) on a Linux machine terminal to produce the final supplementary file supplementary.pdf, summarizing the structurally observed electrostatic features of the four COVID-19 coronavirus-related experimental structures as of March 4, 2020.

Finally, along with the python-based analysis tool and a LaTeX-based editing tool [11], the structurally observed electrostatic features of the four COVID-19 coronavirus-related experimental structures constitute a preliminary starting point pointing towards a clear, coherent and comprehensive map of COVID-19’s structure and function and also machine-learning and structure-based computational design of neutralizing antibodies [11] and/or small molecule(s) as potential therapeutic candidates against future outbreaks of the COVID-19 coronavirus diseases.
Author Contributions: Conceptualization, W.L.; methodology, W.L.; software, W.L.; validation, W.L.; formal analysis, W.L.; investigation, W.L.; resources, W.L.; data duration, W.L.; writing—original draft preparation, W.L.; writing—review and editing, W.L.; visualization, W.L.; supervision, W.L.; project administration, W.L.; funding acquisition, not applicable.

Funding: This research received no external funding.

Conflicts of Interest: The author declares no conflict of interest.

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