# Preliminary identification of potential vaccine targets for 2019-nCoV based on SARS-CoV immunological studies

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## Abstract

The beginning of 2020 has seen the emergence of the 2019 novel coronavirus (2019-nCoV) outbreak. Since the first reported case in the Wuhan city of China, 2019-nCoV has spread to other cities in China as well as to multiple countries across four continents. There is an imminent need to better understand this novel virus and to develop ways to control its spread. In this study, we sought to gain insights for vaccine design against 2019-nCoV by considering the high genetic similarity between 2019-nCoV and the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), and leveraging existing immunological studies of SARS-CoV. By screening the experimentally-determined SARS-CoV-derived B cell and T cell epitopes in the immunogenic structural proteins of SARS-CoV, we identified a set of B cell and T cell epitopes derived from the spike (S) and nucleocapsid (N) proteins that map identically to 2019-nCoV proteins. As no mutation has been observed in these identified epitopes among the available 2019-nCoV sequences (as of 29 January 2020), immune targeting of these epitopes may potentially offer protection against 2019-nCoV. For the T cell epitopes, we performed a population coverage analysis of the associated MHC alleles and proposed a set of epitopes that is estimated to provide broad coverage globally, as well as in China. Our findings provide a screened set of epitopes that can help guide experimental efforts towards the development of vaccines against 2019-nCoV.

## Introduction

The ongoing outbreak of 2019 novel Coronavirus (2019-nCoV) in the Wuhan city (Hubei province) of China (C. Wang, Horby, Hayden, & Gao, 2020) and its alarmingly quick transmission to 25 other countries across the world (Centers-of-Disease-Control-and-Prevention, 2020) has resulted in World Health Organization (WHO) declaring a global health emergency on 30 January 2020 (World-Health-Organization, 2020b). This came just one month after the first reported case on 31 December 2019 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). WHO, in its first emergency meeting (World-Health-Organization, 2020a), estimated the fatality rate of 2019-nCov to be around 4%. Worldwide collaborative efforts from scientists are underway to understand this novel and rapidly spreading virus, and to develop effective interventions for controlling and preventing it (Heymann, 2020; Huang et al., 2020; Xin Liu & Wang, 2020; Zhou et al., 2020).

Coronaviruses are positive-sense single-stranded RNA viruses belonging to the family Coronaviridae. These viruses mostly infect animals, including birds and mammals. In humans, they generally cause mild respiratory infections, such as those observed in the common cold. However, some recent human coronavirus infections have resulted in lethal endemics, which include the SARS-CoV (Severe Acute Respiratory Syndrome coronavirus) and MERS-CoV (Middle East Respiratory Syndrome coronavirus). Both of these zoonotic coronaviruses belong to the genus Betacoronavirus within Coronaviridae. SARS-CoV originated from Southern China and caused an endemic in 2003. A total of 8,098 cases of SARS-CoV infection were reported globally including 774 associated deaths, and an estimated case-fatality rate of 14-15% (https://www.who.int/csr/sars/archive/2003_05_07a/en/). The first case of MERS-CoV occurred in Saudi Arabia in 2012. Since then, a total of 2,494 cases of MERS-CoV infection have been reported including 858 associated deaths, and an estimated high case-fatality rate of 34.4% (https://www.who.int/emergencies/mers-cov/en/). While no case of SARS-CoV has been reported since 2004, MERS-CoV has been around since 2012 and caused multiple sporadic outbreaks in different countries.

Like SARS-CoV and MERS-CoV, the recent 2019-nCoV belongs to the Betacoronavirus genus (Lu et al., 2020). It has a genome size of ~30 kilobases which, like other coronaviruses, encodes for multiple structural and non-structural proteins. The structural proteins include the spike (S) protein, the envelope (E) protein, the membrane (M) protein, and the nucleocapsid (N) protein. With 2019-nCoV being discovered very recently, there is currently a lack of immunological information available about the virus (e.g., information about immunogenic proteins and immunogenic epitopes eliciting antibody or T cell responses). Preliminary studies suggest that the 2019-nCoV is quite similar to SARS-CoV based on the full-length genome phylogenetic analysis (Lu et al., 2020; Zhou et al., 2020), and the putatively similar cell entry mechanism and human cell receptor usage (Hoffmann et al., 2020; Letko & Munster, 2020; Zhou et al., 2020). Due to this apparent similarity between the two viruses, previous research

that has provided an understanding of protective immune responses against SARS-CoV may potentially be leveraged to aid vaccine development for 2019-nCoV.

Various reports related to SARS-CoV suggest a protective role of both humoral and cell-mediated immune responses. For the former case, antibody response generated against the S protein, the most exposed protein of SARS-CoV, has been shown to protect from infection in mouse models (Deming et al., 2006; Graham et al., 2012; Yang et al., 2004). In addition, multiple studies have shown that antibodies generated against the N protein of SARS-CoV, a highly immunogenic and abundantly expressed protein during infection (Lin et al., 2003), were particularly prevalent in SARS-CoV-infected patients (X Liu et al., 2004; J. Wang et al., 2003). While being effective, the antibody response was found to be short-lived in convalescent SARS-CoV patients (Tang et al., 2011). In contrast, T cell responses have been shown to provide long-term protection (Fan et al., 2009; Peng et al., 2006; Tang et al., 2011), even up to 11 years post-infection (Ng et al., 2016), and thus has attracted more interest for a prospective vaccine against SARS-CoV [reviewed in (W. J. Liu et al., 2017)]. Among all SARS-CoV proteins, T cell responses against the structural proteins have been found to be the most immunogenic in peripheral blood mononuclear cells of convalescent SARS-CoV patients as compared to the non-structural proteins (C. K.-F. Li et al., 2008). Further, of the structural proteins, T cell responses against the S and N proteins have been reported to be the most dominant and long-lasting (Channappanavar, Fett, Zhao, Meyerholz, & Perlman, 2014).

Here, by analysing available experimentally-determined SARS-CoV-derived B cell epitopes (both linear and discontinuous) and T cell epitopes, we identify and report those that are completely identical and comprise no mutation in the available 2019-nCoV sequences (as of 29 January 2020). These epitopes have the potential, therefore, to elicit a cross-reactive/effective response against 2019-nCoV. We focused particularly on the epitopes in the S and N structural proteins due to their dominant and long-lasting immune response previously reported against SARS-CoV. For the identified T cell epitopes, we additionally incorporated the information about the associated MHC alleles to provide a list of epitopes that seek to maximize population coverage globally, as well as in China. Our presented results can potentially narrow down the search for potent targets for an effective vaccine against the 2019-nCoV.

## Materials and Methods

**Acquisition and processing of sequence data.** A total of 39 whole genome sequences of 2019-nCoV were downloaded on 29 January 2020 from the GISAID database (https://www.gisaid.org/CoV2020/) (Table 1) excluding five sequences (EPI_ISL_ 402120, EPI_ISL_402121, EPI_ISL_402126, EPI_ISL_403928 and EPI_ISL_403931) that likely have spurious mutations resulting from sequencing errors (http://virological.org/t/novel-2019-coronavirus-genome/319/18, http://virological.org/t/clock-and-tmrca-based-on-27-genomes/347, and http://virological.org/t/novel-2019-coronavirus-genome/319/11). These nucleotide sequences were aligned to the GenBank reference sequence (accession ID:

NC_045512.2) and then translated into amino acid residues according to the coding sequence positions provided along the reference sequence for the 2019-nCoV proteins (orf1a, orf1b, S, ORF3a, E, M, ORF6, ORF7a, ORF8, N, and ORF10). These sequences were aligned separately for each protein using the MAFFT multiple sequence alignment program (Katoh & Standley, 2013). Reference protein sequences for SARS-CoV and MERS-CoV were obtained following the same procedure from GenBank using the accession IDs NC_004718.3 and NC_019843.3, respectively.

**Acquisition and filtering of epitope data.** SARS-CoV-derived B cell and T cell epitopes were searched on the NIAID Virus Pathogen Database and Analysis Resource (ViPR) (https://www.viprbrc.org/; accessed January 29, 2020) (Pickett et al., 2012) by querying for the virus species name: "Severe acute respiratory syndrome-related coronavirus" from human hosts. We limited our search to include only the experimentally-determined epitopes that were associated with at least one positive assay: (i) B cell positive assays (e.g., enzyme-linked immunosorbent assay (ELISA)-based qualitative binding) for B cell epitopes and (ii) either T cell positive assays (such as enzyme-linked immune absorbent spot (ELISPOT) or intracellular cytokine staining (ICS) IFN-$\gamma$ release) or major histocompatibility complex (MHC) positive binding assays for T cell epitopes. The number of B cell and T cell epitopes obtained from the database following the above procedure is listed in Table 2.

**Population-coverage-based T cell epitope selection.** Population coverages for sets of T cell epitopes were computed using the tool provided by the Immune Epitope Database (IEDB) (http://tools.iedb.org/population/; accessed January 29, 2020) (Vita et al., 2019). This tool uses the distribution of MHC alleles (with at least 4-digit resolution, e.g., A*02:01) within a defined population (obtained from http://www.allelefrequencies.net/) to estimate the population coverage for a set of T cell epitopes. The estimated population coverage represents the percentage of individuals within the population that are likely to elicit an immune response to at least one T cell epitope from the set. To identify the set of epitopes associated with MHC alleles that would maximize the population coverage, we adopted a greedy approach: (i) we first identified the MHC allele with the highest individual population coverage and initialized the set with their associated epitopes, (ii) we progressively added epitopes associated with other MHC alleles that resulted in the largest increase of the accumulated population coverage. We stopped when no increase in the accumulated population coverage was observed by adding epitopes associated with any of the remaining MHC alleles.

**Constructing the phylogenetic tree.** We used the publicly available software PASTA v1.6.4 (Mirarab et al., 2015) to construct a maximum-likelihood phylogenetic tree of each structural protein using the available sequence data of SARS-CoV, MERS-CoV, and 2019-nCoV. We additionally included the Zaria Bat coronavirus strain (accession ID: HQ166910.1) to serve as an outgroup. The appropriate parameters for tree estimation are automatically selected in the software based on the provided sequence data. For visualizing the constructed phylogenetic trees, we used the publicly available

software Dendroscope v3.6.3 (Huson & Scornavacca, 2012). Each constructed tree was rooted with the outgroup Zaria Bat coronavirus strain, and circular phylogram layout was used.

## Results and Discussion

**Structural proteins of 2019-nCoV are genetically similar to SARS-CoV, but not to MERS-CoV.** The 2019-nCoV has been observed to be close to SARS-CoV—much more so than MERS-CoV—based on full-length genome phylogenetic analysis (Lu et al., 2020; Zhou et al., 2020). We checked whether this is also true at the level of the individual structural proteins (S, E, M, and N). A straightforward reference-sequence-based comparison indeed confirmed this, showing that the M, N, and E proteins of 2019-nCoV and SARS-CoV have over 90% genetic similarity, while that of the S protein was notably reduced (but still high) (Fig. 1a). The similarity between 2019-nCov and MERS-CoV, on the other hand, was substantially lower for all proteins (Fig. 1a); a feature that was also evident from the corresponding phylogenetic trees (Fig. 1b). We note that while the former analysis (Fig. 1a) was based on the reference sequence of each coronavirus, it is indeed a good representative of the virus population, since very few amino acid mutations have been observed in the corresponding sequence data (Supplementary Fig. 1). It is noteworthy that while MERS-CoV is the more recent coronavirus to have infected humans, and is comparatively more recurrent (causing outbreaks in 2012, 2015, and 2018) (https://www.who.int/emergencies/mers-cov/en/), 2019-nCoV is closer to the SARS-CoV which has not been observed since 2004.

Given the close genetic similarity between the structural proteins of SARS-CoV and 2019-nCoV proteins, we attempted to leverage immunological studies of the structural proteins of SARS-CoV to potentially aid vaccine development for 2019-nCoV. We focused specifically on the S and N proteins as these are known to induce potent and long-lived immune responses in SARS-CoV (Channappanavar et al., 2014; Deming et al., 2006; Graham et al., 2012; W. J. Liu et al., 2017; X Liu et al., 2004; J. Wang et al., 2003; Yang et al., 2004). We used the available SARS-CoV-derived experimentally-determined epitope data (see Materials and Methods) and searched to identify T cell and B cell epitopes that were identical—and hence potentially cross-reactive—across SARS-CoV and 2019-nCoV. We first report the analysis for T cell epitopes, which have been shown to provide a long-lasting immune response against SARS-CoV (Channappanavar et al., 2014), followed by a discussion of B cell epitopes.

**Mapping the SARS-CoV-derived T cell epitopes that are identical in 2019-nCoV, and determining those with greatest estimated population coverage.** The SARS-CoV-derived T cell epitopes used in this study were experimentally-determined from two different types of assays (Pickett et al., 2012): (i) T cell-positive assays, which tested for a T cell response against epitopes, and (ii) MHC-positive assays, which tested for epitope-MHC binding. We aligned these T cell epitopes across the 2019-nCoV protein sequences. Among the 115 T cell epitopes that were reported in T cell-positive assays (Table 2), we found that 27 epitope-sequences were identical within 2019-nCoV proteins and comprised no

mutation in the available 2019-nCoV sequences (as of 29 January 2020) (Table 3). Interestingly, all of these were present in either the N (16) or S (11) protein. However, these 27 epitopes were associated with only five distinct MHC alleles (at 4-digit resolution): HLA-A*02:01, HLA-B*40:01, HLA-DRA*01:01, HLA-DRB1*07:01, and HLA-DRB1*04:01. Consequently, the accumulated population coverage of these epitopes (see Materials and Methods for details) is estimated to be low for the global population (59.76%) as well as for China (32.36%). Note that for 6 of these 27 epitopes, the associated MHC alleles were not reported, and hence they could not be used in the population coverage computation.

To expand the search and identify potentially effective T cell targets covering a higher percentage of the population, we next considered the set of T cell epitopes that were experimentally-determined using MHC-positive assays (Table 2), derived from either the S or N protein. Epitopes determined using MHC-positive assays may also generate a positive T cell response. This has been reported for some of the identified epitopes (Table 3); however, establishing this more broadly requires further experimental investigation. Of the 959 epitopes reported in MHC-positive assays, we found that 253 epitope-sequences have an identical match in 2019-nCoV proteins (listed in Supplementary Table 1), with 80% being MHC class I restricted epitopes (Supplementary Table 2). Importantly, 109 of the 253 epitopes were derived from either the S (71) or N (38) protein. Interestingly, mapping the 71 S-derived epitopes onto the resolved crystal structure of the SARS-CoV S protein (Fig. 2) revealed that 3 of these (GYQPYRVVVL, QPYRVVVLSF, and PYRVVVLSF) were located entirely in the SARS-CoV receptor-binding motif, known to be important for virus cell entry (F. Li, 2005).

Similar to previous studies on HIV and HCV (Ahmed, Quadeer, Morales-Jimenez, & McKay, 2019; Dahirel et al., 2011; Quadeer et al., 2014), we estimated population coverages for various combinations of these 107 epitopes. Our aim was to determine sets of epitopes with maximum population coverage, potentially aiding the development of subunit vaccines against 2019-nCoV. For selection, we adopted a greedy computational approach (see Materials and Methods), which identified a set of T cell epitopes estimated to maximize population coverage in China, the country most affected by the 2019-nCoV outbreak. This set comprised of multiple T cell epitopes associated with 15 distinct MHC class I alleles and was estimated to provide an accumulated population coverage of 85.89% (Table 4). We also identified another set of T cell epitopes, associated with 14 distinct MHC class I alleles, that was estimated to maximize global population coverage (94.4%) (Table 5). We note that the estimated population coverage of this specific set of epitopes was lower for China (83.65%) as certain MHC alleles (e.g., HLA-A*02:01) associated with some of these epitopes are less frequent in the Chinese population (Table 5).

A recent study predicted T cell epitopes for 2019-nCoV that may be presented by a population from the Asia-Pacific region (Ramaiah & Arumugaswami, 2020). This study has multiple differences to our work. First, the authors focused on MHC Class II epitopes, while here we considered both MHC Class I and II epitopes. Interestingly, while we found a few MHC Class II epitopes using our approach

(Supplementary Table 2), none of these appeared in our identified epitope set (Tables 4 and 5), due to their comparatively low estimated population coverage. Second, computational tools were used to predict MHC Class II epitopes in (Ramaiah & Arumugaswami, 2020), while here we analysed the SARS-CoV-derived epitopes that have been determined experimentally using MHC-positive assays, and which match identically with the available 2019-nCoV sequences (as of 29 January 2020).

Since the identified T cell epitopes (Tables 4 and 5) were determined experimentally using MHC-positive assays, we believe this provides motivation to conduct further experimental studies to determine their specificity to natural T cell responses against 2019-nCoV. Furthermore, as the epitopes are estimated to provide a broad population coverage (globally as well as in China), they present potentially useful candidates for guiding experimental efforts towards developing universal subunit vaccines against 2019-nCoV.

**Mapping the SARS-CoV-derived B cell epitopes that are identical in 2019-nCoV.** Similar to T cell epitopes, we used in our study the SARS-CoV-derived B cell epitopes that have been experimentally-determined from B cell-positive assays (Pickett et al., 2012). These epitopes were classified as: (i) linear B cell epitopes (antigenic peptides), and (ii) discontinuous B cell epitopes (conformational epitopes with resolved structural determinants).

We aligned the 298 linear B cell epitopes (Table 2) across the 2019-nCoV proteins and found that 61 epitope-sequences, all derived from structural proteins, have an identical match and comprised no mutation in the available 2019-nCoV protein sequences (as of 29 January 2020). Interestingly, a large number (56) of these were derived from either the S (32) or N (24) protein (Table 6), while the remaining (5) were from the M and E proteins (Supplementary Table 3).

On the other hand, all 6 SARS-CoV-derived discontinuous B cell epitopes obtained from the ViPR database (Table 7) were derived from the S protein. Based on the pairwise alignment between the SARS-CoV and 2019-nCoV reference sequences (Supplementary Fig. 2), we found that none of these mapped identically to the 2019-nCoV S protein, in contrast to the linear epitopes. For 3 of these discontinuous B cell epitopes there was a partial mapping, with at least one site having an identical residue at the corresponding site in the 2019-nCoV S protein (Table 7).

Mapping the residues of the B cell epitopes onto the available structure of the SARS-CoV S protein revealed that the linear epitopes (Table 6) map to seemingly less-exposed regions, away from the most exposed region, the “spike head” (Fig. 3a). In contrast, all discontinuous B cell epitopes (Table 7) map onto the spike head region (Fig. 3b, *top panel*), which contains the receptor-binding motif of the SARS-CoV S protein (F. Li, 2005). We observe that few residues of the discontinuous epitopes that lie within the receptor-binding motif are identical within SARS-CoV and 2019-nCoV (Fig. 3b). It has been reported recently that 2019-nCoV is able to bind to the same receptor as SARS-CoV (ACE2) for cell entry,

despite having multiple amino acid differences with SARS-CoV's receptor-binding motif (Hoffmann et al., 2020; Letko & Munster, 2020; Lu et al., 2020; Zhou et al., 2020). Whether the antibodies specific to this motif maintain their binding and elicit an immune response against 2019-nCoV warrants further experimental investigation.

A related preliminary analysis of linear B cell epitopes has been reported online on the ViPR database website (https://www.viprbrc.org/brcDocs/documents/announcements/Corona/2019-nCov-ViPR-report_24JAN2020.pdf). Different from our analysis, which is focused on linear and discontinuous SARS-CoV-derived epitopes, they considered linear B cell epitope data for all Betacoronaviruses from human hosts. While only a summary of their results has been provided so far, preventing direct comparison of the individual epitopes, the number of linear B cell epitopes reported to map identically to 2019-nCoV is comparable to our findings.

## Conclusion

To summarize, motivated by the high genetic similarity between the structural proteins of SARS-CoV and 2019-nCoV, we analysed the available experimentally-determined SARS-CoV-derived T cell and B cell epitopes and identified sets of epitopes that map identically to 2019-nCoV proteins. The absence of any mutation in these identified epitopes among the available 2019-nCoV sequences (as of 29 January 2020) suggests their potential for eliciting an effective T cell and antibody response in 2019-nCoV. We also screened the identified T cell epitopes using a population coverage criterion and reported a set of epitopes that can provide an estimated population coverage of 94.4% globally and 83.65% in China.

We acknowledge that this is a preliminary analysis based on the limited sequence data available for 2019-nCoV (as of 29 January 2020). As the virus continues to evolve and as more data is collected, it is expected that additional mutations will be observed. Such mutations will not affect our analysis, provided that they occur outside of the identified epitope regions. If mutations do occur within epitope regions, then these epitopes may be further screened (in line with the conservative filtering principle that we have employed), thereby producing a more refined epitope set.

## Data and code availability

All sequence and immunological data, and all scripts for reproducing the results are available at https://github.com/faraz107/2019-nCoV-T-Cell-Vaccine-Candidates.

## Acknowledgements

We thank all the authors, the originating and submitting laboratories (listed in Supplementary Table 4) for their sequence and metadata shared through GISAID, on which this research is based.

M.R.M. and A.A.Q. were supported by the General Research Fund of the Hong Kong Research Grants Council (RGC) [Grant No. 16204519]. S.F.A. was supported by the Hong Kong Ph.D. Fellowship Scheme (HKPFS).

## Conflict of interest

The authors declare that they have no conflict of interest.

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## Figures

a

Percentage sequence identity with 2019-nCoV

| | S protein | N protein | M protein | E protein |
|---|---|---|---|---|
| SARS-CoV | 76.0% | 90.6% | 90.1% | 94.7% |
| MERS-CoV | 4.6% | 7.6% | 6.3% | 30.5% |

b

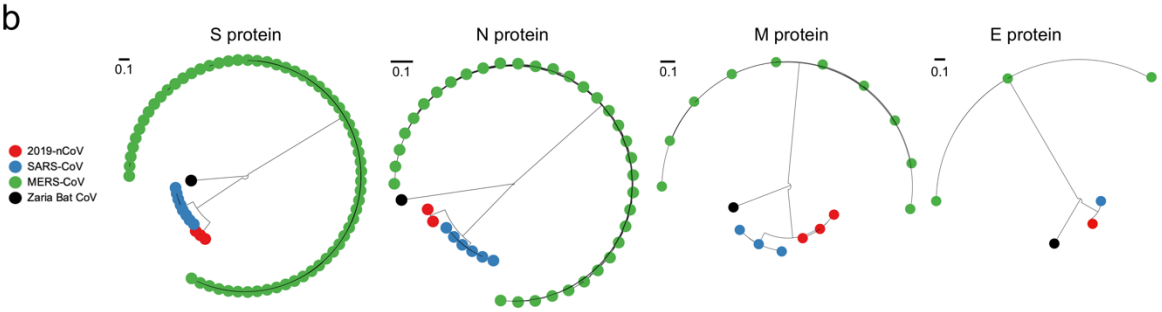



**Figure 1. Comparison of the similarity of structural proteins of 2019-nCoV with the corresponding proteins of SARS-CoV and MERS-CoV.** (a) Percentage genetic similarity of the individual structural proteins of 2019-nCoV with those of SARS-CoV and MERS-CoV. The reference sequence of each coronavirus (Materials and Methods) was used to calculate the percentage genetic similarity. (b) Circular phylogram of the phylogenetic trees of the four structural proteins. All trees were constructed using PASTA (Mirarab et al., 2015) and rooted with the outgroup Zaria Bat CoV strain (accession ID: HQ166910.1).

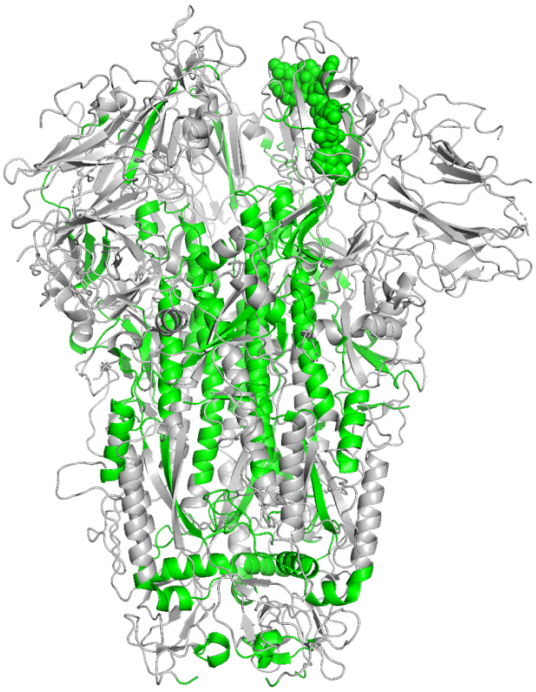


**Figure 2. Location of identified T cell epitopes on the SARS-CoV S protein structure (PDB ID: 5XLR).** Residues of the SARS-CoV-derived T cell epitopes (determined using MHC-positive assays that were identical in 2019-nCoV) are shown in green color. The 3 overlapping epitopes (GYQPYRVVVL, QPYRVVVLSF, PYRVVVLSF) that lie within the SARS-CoV receptor-binding motif are shown as spheres.

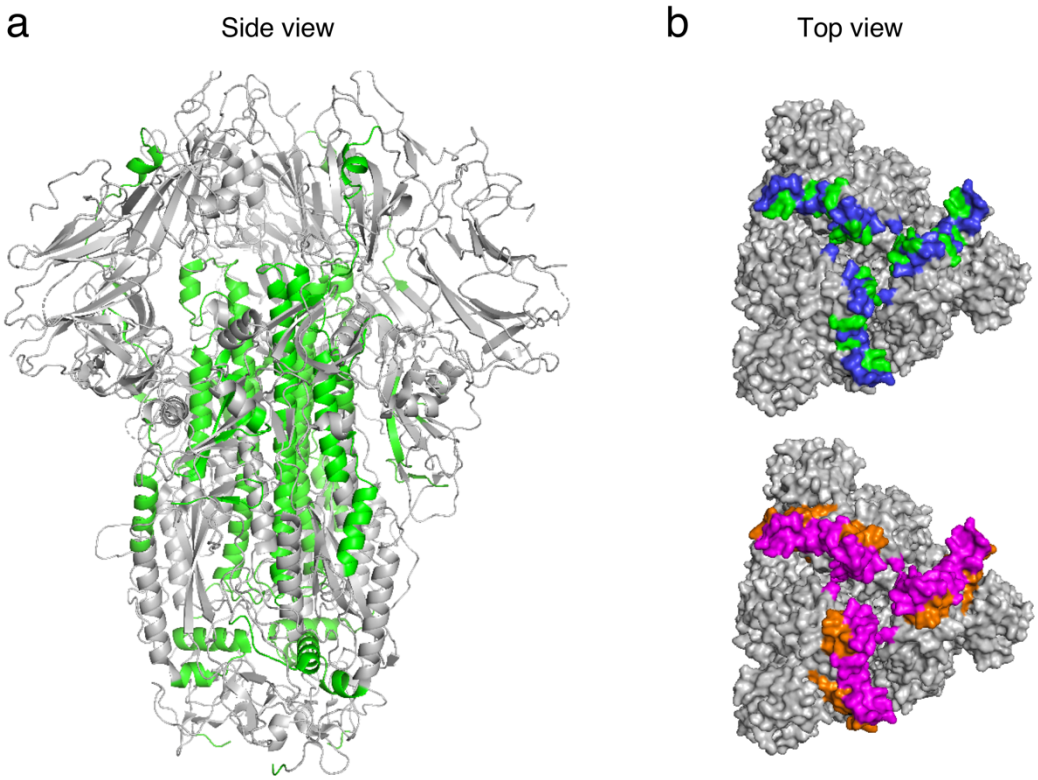



**Figure 3. Location of SARS-CoV-derived B cell epitopes on the SARS-CoV S protein structure (PDB ID: 5XLR).** (a) Residues of the linear B cell epitopes, that were identical in 2019-nCoV (Table 6), are shown in green color. (b) (*Top panel*) Location of discontinuous B cell epitopes that share at least one identical residue with corresponding 2019-nCoV sites (Table 7). Identical epitope residues are shown in green color, while the remaining residues are shown in blue color. (*Bottom panel*) Location of the receptor-binding motif of SARS-CoV. Residues in discontinuous B cell epitopes within the motif are indicated in magenta color, while the remaining motif residues are shown in orange color.

## Tables

**Table 1. GISAID accession IDs of the 39 whole genome sequences of 2019-nCoV used in this analysis.**

| | | | | |
|---|---|---|---|---|
| EPI_ISL_402119 | EPI_ISL_402132 | EPI_ISL_403937 | EPI_ISL_406034 | EPI_ISL_406538 |
| EPI_ISL_402123 | EPI_ISL_403929 | EPI_ISL_403962 | EPI_ISL_406036 | EPI_ISL_406592 |
| EPI_ISL_402124 | EPI_ISL_403930 | EPI_ISL_403963 | EPI_ISL_406223 | EPI_ISL_406593 |
| EPI_ISL_402125 | EPI_ISL_403932 | EPI_ISL_404227 | EPI_ISL_406531 | EPI_ISL_406594 |
| EPI_ISL_402127 | EPI_ISL_403933 | EPI_ISL_404228 | EPI_ISL_406533 | EPI_ISL_406595 |
| EPI_ISL_402128 | EPI_ISL_403934 | EPI_ISL_404253 | EPI_ISL_406534 | EPI_ISL_406596 |
| EPI_ISL_402129 | EPI_ISL_403935 | EPI_ISL_404895 | EPI_ISL_406535 | EPI_ISL_406597 |
| EPI_ISL_402130 | EPI_ISL_403936 | EPI_ISL_406031 | EPI_ISL_406536 | |

**Table 2. Filtering criteria and corresponding number of SARS-CoV-derived epitopes obtained from the ViPR database.**

| Filtering criteria | | Number of epitopes |
|---|---|---|
| B cell positive assays | Linear B cell epitopes | 298 |
| | Discontinuous B cell epitopes | 6 |
| MHC positive assays | T cell epitopes | 959 |
| T cell positive assays | T cell epitopes | 115 |

**Table 3. SARS-CoV-derived T cell epitopes obtained using T cell-positive assays that are identical in 2019-nCoV.**

| Protein | IEDB ID | Epitope | MHC Allele[1] | MHC Allele Class[1] |
|---|---|---|---|---|
| N | 125100 | ILLNKHID | HLA-A*02:01 | I |
| N | 1295 | AFFGMSRIGMEVTPSGTW | NA | NA |
| N | 190494 | MEVTPSGTWL | HLA-B*40:01 | I |
| N | 21347 | GMSRIGMEV | HLA-A*02:01 | I |
| N | 27182 | ILLNKHIDA | HLA-A*02:01 | I |
| N | 2802 | ALNTPKDHI | HLA-A*02:01 | I |
| N | 28371 | IRQGTDYKHWPQIAQFA | NA | NA |
| N | 31166 | KHWPQIAQFAPSASAFF | NA | NA |
| N | 34851 | LALLLLDRL | HLA-A*02:01 | I |
| N | 37473 | LLLDRLNQL | HLA-A*02:01 | I |
| N | 37611 | LLNKHIDAYKTFPPTEPK | NA | NA |
| N | 38881 | LQLPQGTTL | HLA-A*02:01 | I |
| N | 3957 | AQFAPSASAFFGMSR | NA | II |
| N | 3958 | AQFAPSASAFFGMSRIGM | NA | NA |
| N | 55683 | RRPQGLPNNTASWFT | NA | I |
| N | 74517 | YKTFPPTEPKKDKKKK | NA | NA |
| S | 100048 | GAALQIPFAMQMAYRF | HLA-DRA*01:01 DRB1*07:01 | II |
| S | 100300 | MAYRFNGIGVTQNVLY | HLA-DRB1*04:01 | II |
| S | 100428 | QLIRAAEIRASANLAATK | HLA-DRB1*04:01 | II |
| S | 16156 | FIAGLIAIV | HLA-A*02:01 | I |
| S | 2801 | ALNTLVKQL | HLA-A*02:01 | I |
| S | 36724 | LITGRLQSL | HLA-A2 | I |
| S | 44814 | NLNESLIDL | HLA-A*02:01 | I |
| S | 50311 | QALNTLVKQLSSNFGAI | HLA-DRB1*04:01 | II |
| S | 54680 | RLNEVAKNL | HLA-A*02:01 | I |
| S | 69657 | VLNDILSRL | HLA-A*02:01 | I |
| S | 71663 | VVFLHVTYV | HLA-A*02:01 | I |

[1]NA: Not available

**Table 4. Set of SARS-CoV-derived S and N protein T cell epitopes that maximize estimated population coverage for China.**

| Epitopes[1] | MHC Allele Class | MHC Allele | Accumulated Population Coverage in China (%) |
|---|---|---|---|
| AQALNTLVK, ASANLAATK, GSFCTQLNR, GVVFLHVTY, MTSCCSCLK, SFIEDLLFNK, SVLNDILSR, TQNVLYENQK, ATEGALNTPK, KTFPPTEPK, QQQGQTVTK, QQQGQTVTKK, QQQQGQTVTK, SASAFFGMSR | I | HLA-A*11:01 | 43.48 |
| VYDPLQPEL | I | HLA-A*24:02 | 60.68 |
| ALNTLVKQL, FIAGLIAIV, IITTDNTFV, LLFNKVTLA, LLLQYGSFC, LLQYGSFCT, NLNESLIDL, RLDKVEAEV, RLNEVAKNL, RLQSLQTYV, VLNDILSRL, VVFLHVTYV, ALNTPKDHI, GMSRIGMEV, ILLNKHIDA, LALLLLDRL, LLLDRLNQL, LLLLDRLNQL, LQLPQGTTL, TTLPKGFYA, VLQLPQGTTL, ILLNKHID, LLLLDRLNQ | I | HLA-A*02:01 | 69.63 |
| LQIPFAMQM | I | HLA-B*15:01 | 73.9 |
| DEDDSEPVL, SEPVLKGVKL, GMEVTPSGTWL, MEVTPSGTWL | I | HLA-B*40:01 | 77.23 |
| DSFKEELDKY | I | HLA-A*26:01 | 78.98 |
| VQIDRLITGR, ASAFFGMSR, SQASSRSSSR | I | HLA-A*31:01 | 80.62 |
| LSPRWYFYY | I | HLA-A*01:01 | 82.03 |
| VRFPNITNL | I | HLA-C*14:02 | 83.27 |
| SLIDLQELGK, ALALLLLDR, KTFPPTEPKK, QLPQGTTLPK | I | HLA-A*03:01 | 84.4 |
| FPNITNLCPF | I | HLA-B*35:01 | 85.07 |
| GYQPYRVVVL, PYRVVVLSF | I | HLA-A*23:01 | 85.45 |
| QELGKYEQYI, YEQYIKWPWY | I | HLA-B*44:02 | 85.64 |
| LIDLQELGKY, RVDFCGKGY, GTTLPKGFY, VTPSGTWLTY | I | HLA-A*30:02 | 85.78 |
| IGAGICASY, TPSGTWLTY | I | HLA-A*29:02 | 85.89 |

[1] Multiple SARS-CoV-derived epitopes that were reported in positive-MHC assays are shown for each allele.

**Table 5. Set of SARS-CoV-derived S and N protein T cell epitopes that maximize estimated population coverage globally.**

| Epitopes[1] | MHC Allele Class | MHC Allele | Global Accumulated Population Coverage (%) | Accumulated Population Coverage in China (%) |
|---|---|---|---|---|
| ALNTLVKQL, FIAGLIAIV, IITTDNTFV, LLFNKVTLA, LLLQYGSFC, LLQYGSFCT, NLNESLIDL, RLDKVEAEV, RLNEVAKNL, VLNDILSRL, VLYQDVNCT, VVFLHVTYV, ALNTPKDHI, GMSRIGMEV, ILLNKHIDA, LALLLLDRL, LLLDRLNQL, LQLPQGTTL, TTLPKGFYA, VLQLPQGTTL, ILLNKHID, LLLLDRLNQ | I | HLA-A*02:01 | 39.08 | 14.62 |
| VYDPLQPEL | I | HLA-A*24:02 | 55.48 | 36.11 |
| CVADYSVLY, LSPRWYFYY | I | HLA-A*01:01 | 66.78 | 39.09 |
| SLIDLQELGK, ALALLLLDR, KTFPPTEPKK, QLPQGTTLPK | I | HLA-A*03:01 | 76.14 | 41.68 |
| AQALNTLVK, ASANLAATK, GSFCTQLNR, GVVFLHVTY, MTSCCSCLK, SFIEDLLFNK, SVLNDILSR, TQNVLYENQK, ATEGALNTPK, KTFPPTEPK, QQQGQTVTK, QQQGQTVTKK, QQQQGQTVTK, SASAFFGMSR | I | HLA-A*11:01 | 83.39 | 73.43 |
| CMTSCCSCLK | I | HLA-A*68:01 | 85.71 | 74.25 |
| DSFKEELDKY | I | HLA-A*26:01 | 87.86 | 76.39 |
| GYQPYRVVVL, PYRVVVLSF | I | HLA-A*23:01 | 89.7 | 76.99 |
| VQIDRLITGR, ASAFFGMSR, SQASSRSSSR | I | HLA-A*31:01 | 91.37 | 78.96 |
| IGAGICASY, TPSGTWLTY | I | HLA-A*29:02 | 92.49 | 79.12 |
| LIDLQELGKY, RVDFCGKGY, GTTLPKGFY, VTPSGTWLTY | I | HLA-A*30:02 | 93.14 | 79.33 |
| LQIPFAMQM | I | HLA-B*15:01 | 93.72 | 82.23 |
| QELGKYEQYI, YEQYIKWPWY | I | HLA-B*44:02 | 94.22 | 82.44 |
| VRFPNITNL | I | HLA-C*14:02 | 94.4 | 83.65 |

[1] Multiple SARS-CoV-derived epitopes that were reported in positive-MHC assays are shown for each allele.

**Table 6. SARS-CoV-derived linear B cell epitopes (total 56 epitopes) from S and N proteins that are identical in 2019-nCoV.**

| Protein | IEDB ID | Epitope |
|---|---|---|
| N | 15814 | FFGMSRIGMEVTPSGTW |
| N | 21065 | GLPNNTASWFTALTQHGK |
| N | 22855 | GTTLPK |
| N | 28371 | IRQGTDYKHWPQIAQFA |
| N | 31116 | KHIDAYKTFPPTEPKKDKKK |
| N | 31166 | KHWPQIAQFAPSASAFF |
| N | 31692 | KKSAAEASKKPRQKRTA |
| N | 33669 | KTFPPTEPKKDKKKK |
| N | 37640 | LLPAAD |
| N | 38249 | LNKHIDAYKTFPPTEPK |
| N | 38648 | LPQGTTLPKG |
| N | 38657 | LPQRQKKQ |
| N | 48067 | PKGFYAEGSRGGSQASSR |
| N | 50741 | QFAPSASAFFGMSRIGM |
| N | 50965 | QGTDYKHW |
| N | 51483 | QLPQGTTLPKGFYAE |
| N | 51484 | QLPQGTTLPKGFYAEGSR |
| N | 51485 | QLPQGTTLPKGFYAEGSRGGSQ |
| N | 52117 | QQQGQTVTKKSAAEASKK |
| N | 55683 | RRPQGLPNNTASWFT |
| N | 60379 | SQASSRSS |
| N | 60669 | SRGGSQASSRSSSRSR |
| N | 63729 | TFPPTEPK |
| N | 75235 | YNVTQAFGRRGPEQTQGNF |
| S | 10778 | DVVNQNAQALNTLVKQL |
| S | 11038 | EAEVQIDRLITGRLQSL |
| S | 12426 | EIDRLNEVAKNLNESLIDLQELGKYEQY |
| S | 14626 | EVAKNLNESLIDLQELG |
| S | 15972 | FGEVFNAT |
| S | 16183 | FIEDLLFNKVTLADAGF |
| S | 18515 | GAALQIPFAMQMAYRFN |
| S | 18594 | GAGICASY |
| S | 2092 | AISSVLNDILSRLDKVE |
| S | 22321 | GSFCTQLN |
| S | 27357 | ILSRLDKVEAEVQIDRL |
| S | 30987 | KGIYQTSN |
| S | 3176 | AMQMAYRF |
| S | 32508 | KNHTSPDVDLGDISGIN |
| S | 41177 | MAYRFNGIGVTQNVLYE |
| S | 462 | AATKMSECVLGQSKRVD |
| S | 47479 | PFAMQMAYRFNGIGVTQ |
| S | 50311 | QALNTLVKQLSSNFGAI |
| S | 51379 | QLIRAAEIRASANLAAT |
| S | 52020 | QQFGRD |
| S | 53202 | RASANLAATKMSECVLG |
| S | 54599 | RLITGRLQSLQTYVTQQ |
| S | 558417 | EIDRLNEVAKNLNESLIDLQELGKYEQY |
| S | 558455 | LYQDVN |
| S | 558456 | LYQDVNC |
| S | 558457 | LYQDVNCT |
| S | 59425 | SLQTYVTQQLIRAAEIR |
| S | 6476 | CKFDEDDSEPVLKGVKLHYT |
| S | 67220 | TVYDPLQPELDSFKEEL |
| S | 70719 | VRFPNITNLCPFGEVFN |
| S | 7868 | DDSEPVLKGVKLHYT |
| S | 9094 | DLGDISGINASVVNIQK |

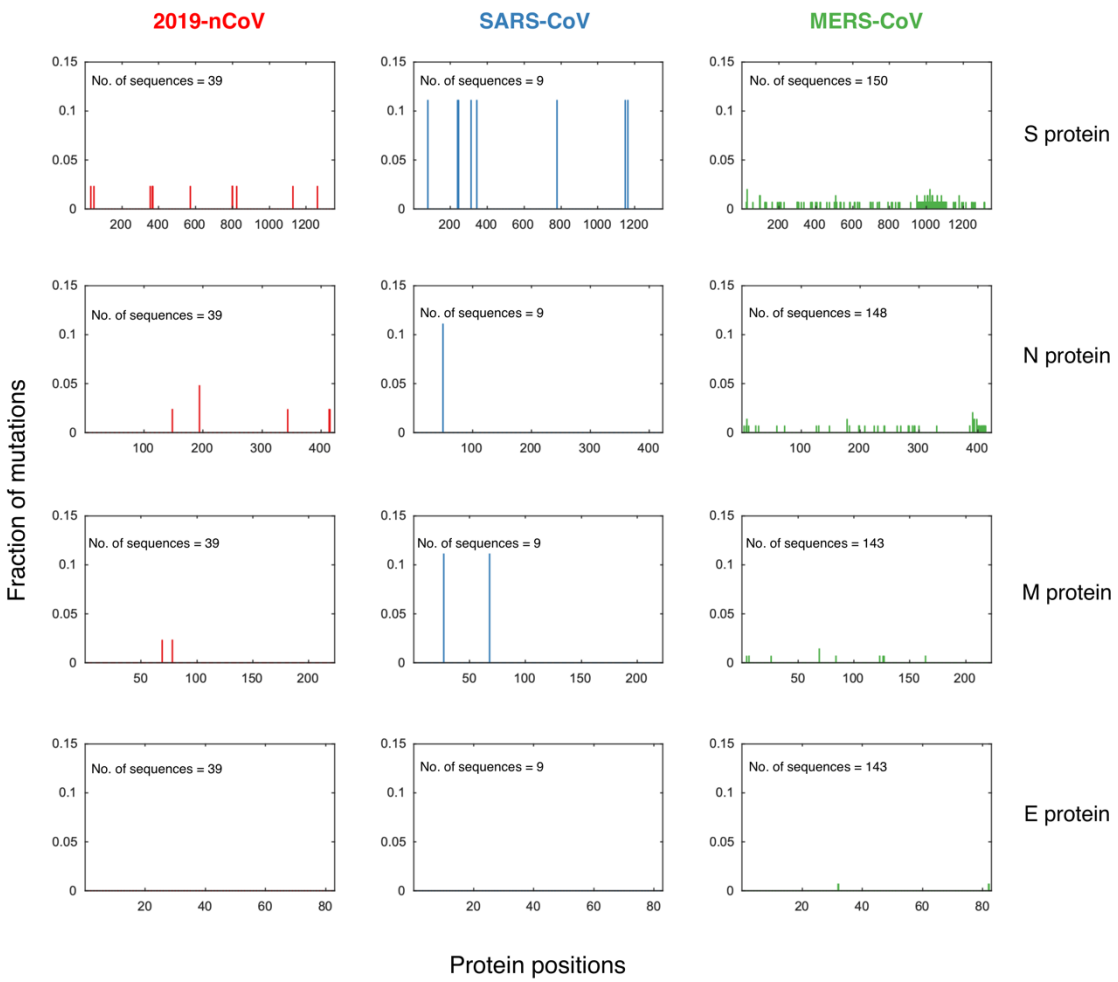
**Table 7. SARS-CoV-derived discontinuous B cell epitopes that have at least one site with an identical amino acid to the corresponding site in 2019-nCoV.**

| IEDB ID | SARS-CoV S protein residues[1,2] |
|---|---|
| 910052 | G446, P462, D463, Y475 |
| 77444 | T359, T363, K365, K390, G391, D392, R395, R426, Y436, G482, Y484, T485, T486, T487, G488, I489, G490, Y491, Q492, Y494 |
| 77442 | R426, S432, T433, Y436, N437, K439, Y440, Y442, P469, P470, A471, L472, N473, C474, Y475, W476, L478, N479, D480, Y481, G482, Y484, T485, T486, T487, G488, I489, Y491, Q492 |

[1] Residues are numbered according to the SARS-CoV S protein reference sequence, accession ID: NP_828851.1.

[2] Residues in the epitopes identical in the 2019-nCoV sequences are underlined.

## Supplementary Figures




**Supplementary Figure 1. Fraction of mutations in the observed sequences of the structural proteins of the three coronaviruses.** Mutation is defined here as an amino acid difference from the reference sequence of the respective coronavirus; accession IDs: NC_045512.2 (2019-nCoV), NC_004718.3 (SARS-CoV), and NC_019843.3 (MERS-CoV).

```
MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLPFYSNVTGFH 70
MFVFLVLLPLVSSQCVNLTTRTQ--LPPAYTN--SFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFH 70
** **  * * *       *       * **   *  *******  ***  *  ******** **** **

TINHT-------FGNPVIPFKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVIRACNFELC 140
AIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIVNNATNVVIKVCEFQFC 140
 *          * *** ** ** *** *****  *** ** *   * **  * ** *****  * *  *

DNPFFAV----SKPMGTQTHTMIFDNAFNCTFEYISDAFSLDVSEKSGNFKHLREFVFKNKDGFLYVYKG 210
NDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVFKNIDGYFKIYSK 210
  **  *                   * ****** *  *  *   * **** ******** **    *

YQPIDVVRDLPSGFNTLKPIFKLPLGINITNFRAIL----TAFSPAQDI--WGTSAAAYFVGYLKPTTFM 280
HTPINLVRDLPQGFSALEPLVDLPIGINITRFQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFL 280
  **  ***** **  * *   ** ***** *   *        *      *   **** **** * **

LKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPSGDVVRFPNITNLCPFGEVFNATK 350
LKYNENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATR 350
*** ***********   ** * **  ***   *********** *    ******************

FPSVYAWERKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTG 420
FASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTG 420
* ***** ** **************  ********** ******** ********  ** **********

VIADYNYKLPDDFMGCVLAWNTRNIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTP-PAL 490
KIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGF 490
 ************ *** ***  * *    ***** **  *   * *******         **

NCYWPLNDYGFYTTTGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSS 560
NCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESN 560
*** **  ***  * * *************** ********* ** * ** **************** *

KRFQPFQQFGRDVSDFTDSVRDPKTSEILDISPCAFGGVSVITPGTNASSEVAVLYQDVNCTDVSTAIHA 630
KKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHA 630
* * ********  * ** **** * ***** ** ************ *  *********** *  ****

DQLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVS----LLRSTSQKSIVAYT 700
DQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYQTQTNSPRRARSVASQSIIAYT 700
***** ** **** ***** **********  **************** *        **    ** ***

MSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQYGSFCTQLNRA 770
MSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRA 770
*****  * ***** ******* ** ***  **** ****** ********** ****************

LSGIAAEQDRNTREVFAQVKQMYKTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAGFMKQ 840
LTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQ 840
* *** *** ** ******** ****  * ************* ** ******************** **

YGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRF 910
YGDCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRF 910
** ***** ********************** *** ** **  ** * **********************

NGIGVTQNVLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSV 980
NGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSV 980
*************** ****** **  ** **  *  *********************************

LNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKG 1050
LNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKG 1050
**********************************************************************

YHLMSFPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIIT 1120
YHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIIT 1120
******** ************** ** ********** *** ******** *** ** *****  *****

TDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRL 1190
TDNTFVSGNCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRL 1190
**************** ******************************************************

NEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCGSCCKF 1260
NEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKF 1260
****************************** **************** ************* *********

DEDDSEPVLKGVKLHYT 1277
DEDDSEPVLKGVKLHYT 1277
*****************
```

**Supplementary Figure 2. Pairwise sequence alignment of the reference sequences of the S proteins of SARS-CoV and 2019-nCoV (accession ID: NP_828851.1 and YP_009724390.1, respectively)**. Identical residues are indicated by *.