

Host Change -Tropism Pattern of Human Coronaviruses Suggesting the Engineered Nature of Severe Acute Respiratory Syndrome Coronavirus 2

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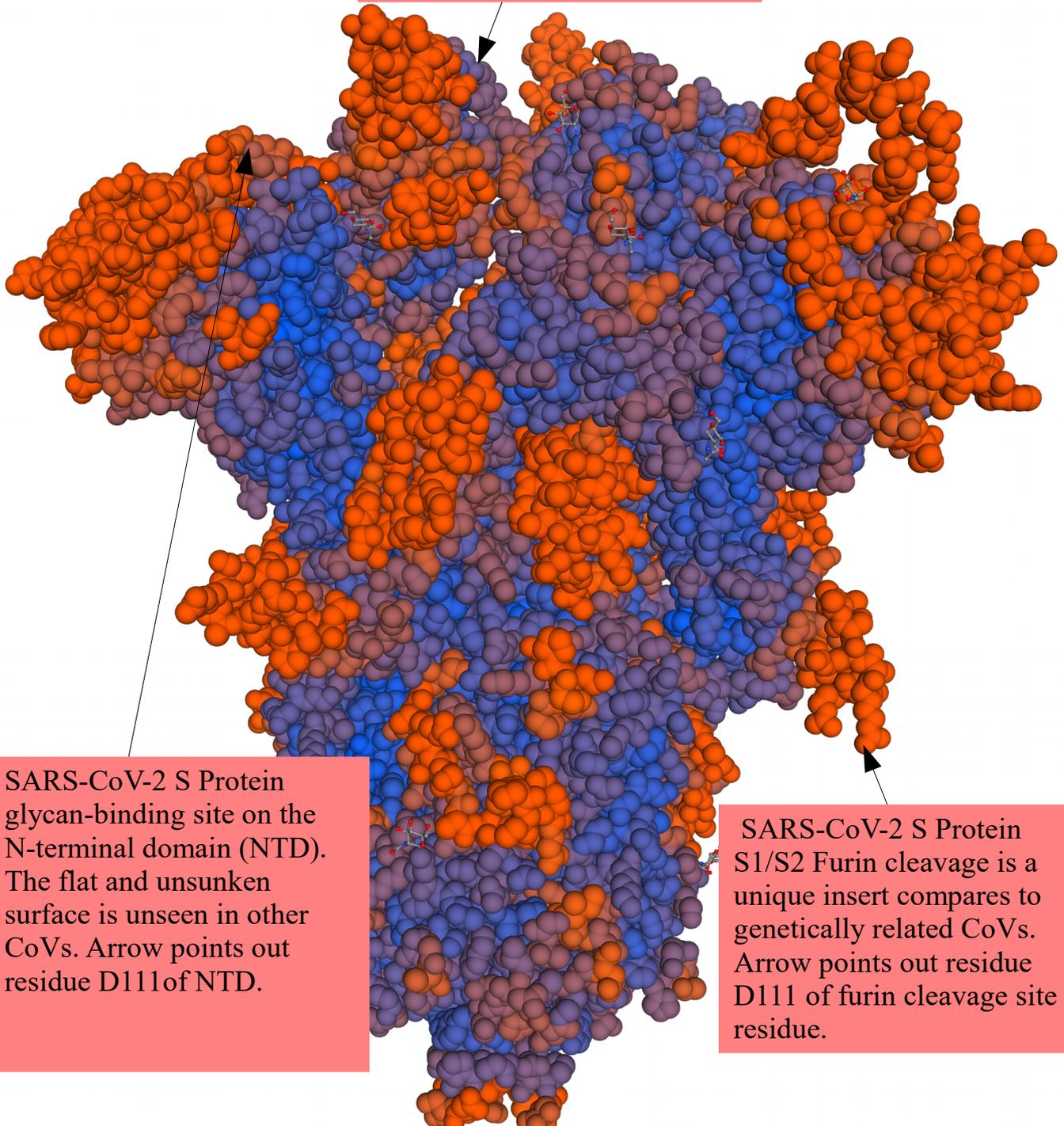
Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the seventh and the unique human CoV with pandemic potential. The host tropism and infection pattern of SARS-CoV-2 have 3 fundamental differences compared to the previous six human pathogenic CoVs, i.e. HCoV-229E, HCoV-OC43, SARS-CoV, HCoV-HKU1, HCoV-NL63, and MERS-CoV. N-terminal domain (NTD) of CoVs Spike (S) Protein contains a specific glycan-binding region as the first contact area with the new host. Specific glycan-binding immune receptors e.g. C-type lectins recognize NTD of S Protein of CoV and exterminate the virus before its adaptation. According to Canyon Hypothesis CoVs sunk this glycan-binding domain beneath the surface of S Protein to evade host immune system e.g. MERS-CoV glycan-binding domain 280 Å² under its S Protein surface or HCoV-229E deleted its glycan-binding NTD during its host tropism. Strikingly, SARS-CoV-2 does not have a single amino acid (aa.) alteration or deletion on its glycan-binding region NTD of its S Protein compares to its parent virus BatCoV RaTG13. The flat and unsunken surface of SARS-CoV-2 NTD S Protein conflicting with the general adaptation and survival pattern of all CoVs. Secondly, based on the template-switching model, CoVs pause their replication on certain domains and have recombinations on these specific sites. SARS-CoV-2 and BatCoV RaTG13 are both betacoronavirus lineage B and their genomes are almost identical except 4 aa. inserts between the S1/S2 enables the virus to cleavage by host cell furin protease. However, other betacoronavirus lineage B members and the clinical strains of SARS-CoV-2 do not have any alterations on S Protein S1/S2 suggesting SARS-CoV-2 obtained this trait with a one-time unique event. Thirdly, after host adaptation CoVs improve their host cell interaction with certain aa. substitutions on their receptor binding domain (RBD) that considered as positive selection site. SARS-CoV-2 had 22 aa. substitutions on S Protein RBD compare to BatCoV RaTG13. However, despite millions of SARS-CoV-2 infections, RBD has not indicated a single high-frequency aa. substitution suggesting the too-perfect angiotensin-converting enzyme 2 (ACE2) binding that was gained with a one-time alteration. Unlike the RBDs of other CoVs, SARS-CoV-2 RBD is not a positive selection site. In summary, i) flat and unaltered

NTD, ii) conserved RBD, and iii) unique S1/S2 insert of S Protein of SARS-CoV-2 suggesting its engineered nature. Engineering of CoVs is not a speculation since 18 research projects to develop genetically modify CoVs as pandemic potential pathogens paused by United States Government Moratorium in 2014.

Keywords: Severe Acute Respiratory Syndrome Coronavirus 2 , Genetically Engineered, novel pathogens with pandemic potential PPP, Canyon Hypothesis, Template-switching model

SARS-CoV-2, S Protein receptor-binding domain (RBD) is not a high-frequency positive selection site unlike other CoVs. Arrow points out residue Q498 of RBD.



SARS-CoV-2 S Protein glycan-binding site on the N-terminal domain (NTD). The flat and unsunken surface is unseen in other CoVs. Arrow points out residue D111 of NTD.

SARS-CoV-2 S Protein S1/S2 Furin cleavage is a unique insert compares to genetically related CoVs. Arrow points out residue D111 of furin cleavage site residue.

Structural model of SARS-CoV-2 S Protein

1. Introduction to Human Pathogenic CoVs

The global pandemic of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is ongoing with the confirmed cases inclined from 6,065 on 29 January 2020 to 1,391,890 on 8 April 2020 (Steffens 2020). Coronaviruses (CoVs) first described in 1969 based on their pleomorphic, circular, 80-160 nanometer in diameter shape with 15-nanometer club-shaped projections (so-called spike proteins) that resembles a crown (corona in Latin) (Bradburne 1969). SARS-CoV-2 is the seventh but the first and only CoV with pandemic potential (Forni 2017)(Steffens 2020). Several projects aimed to genetically engineer Middle East respiratory syndrome (MERS-CoV) and Severe acute respiratory syndrome coronavirus (SARS-CoV) mutant strains to develop vaccines on as a preemptive measure for the possible future pandemics (Lipsitch 2014)(Inglesby 2016). In 2014, 18 of these pathogens with pandemic potential (PPP) CoV projects paused by U.S. Government Moratorium (Inglesby 2016). The reason was the potential risk of PPP viruses escape from laboratories due to a 0.2% chance of a laboratory-acquired infection per BSL3 laboratory in one year. (Inglesby 2016). Therefore, genetic engineering of CoVs with pandemic potential is not a speculation, and SARS-CoV-2 could be a PPP virus with laboratory origin. To investigate the PPP origin of SARS-CoV-2 we must understand how the previous six CoVs naturally adapted to humans. The first human pathogenic coronavirus HCoV-229E detected in 1962 at the Chicago that was possibly originated from African Sundevall's roundleaf bat CoVs, around 200 years ago via zootonic transmission from the alpaca (Hamre 1966)(Corman 2015)(Forni 2017)(De Sabato 2019). The second human pathogenic CoV HCoV-OC43 detected in 1964 at Maryland that was possibly originated from Norway Rats CoVs, around 120 years ago via zootonic transmission from the cow (McIntosh 1967)(Forni 2017)(Lau 2015). The third human pathogenic CoV SARS-CoV detected in 2002 in Foshan, China that was possibly originated from Chinese horseshoe bat CoV, 35 to 20 years ago via zootonic transmission from the civet (de Wit 2016)(Forni 2017)(Hu 2015)(Ge 2013). The fourth human pathogenic CoV HCoV-HKU1 detected in 2002 in Hong Kong that was possibly originated from Norway Rat CoV, 70 years ago via zootonic transmission from the rodent (Forni 2017)(Woo 2005)(Lau 2015). The fifth human pathogenic CoV HCoV-NL63 was first isolated in 1988 and identified in 2004 at the Rotterdam Netherlands that was possibly originated from African trident bat CoV, 563 to 822 years ago via unknown zootonic transmission agent (Fouchier 2004) (Forni 2017)(De Sabato 2019). The sixth human pathogenic CoV MERS-CoV detected in 2012 in the Kingdom of Saudi Arabia (KSA) that was possibly originated from South African Bat CoV, around 14 years ago via zootonic transmission from the camel (Forni 2017)(Hu 2015)(Ithete 2013).

The seventh human pathogenic CoVs SARS-CoV-2 detected in 2019 in Wuhan, China that was possibly originated from Intermediate horseshoe bat CoV around 11 years ago via zoonotic transmission from the pangolins (Patiño-Galindo 2020)(Zhou 2020)(Ren 2020).

2. Pathogenicity of CoVs

The low-pathogenic and endemic HCoV-229E, HCoV-NL63, and HCoV-OC43, and HCoV-HKU1 could be detected in 42% of the patients with acute cough or acute lower respiratory tract infection (Zlateva 2015). The high-pathogenic and epidemic SARS-CoV and MERS-CoV cause severe symptoms such as pneumonia, and renal failure (de Wit 2016). SARS-CoV spread to 27 countries in 2002-2003 with 8,096 cases and 774 deaths up to 10% fatality rate but disappeared in 2004 (de Wit 2016). The MERS-CoV found to be less human-to-human transmissible compare to the SARS-CoV cases were detected in KSA, Jordan, United Kingdom, and South Korea since 2012 (de Wit 2016). MERS-CoV epidemics is ongoing with 2494 cases, and 858 deaths (fatality rate 34.4%) as in November 2019 (Tai 2019). SARS-CoV-2 has a lower fatality rate (2–3%) compare to MERS-CoV (34.4%) and SARS-CoV (10%) despite its pandemic potential (de Wit 2016)(Tai 2019) (Steffens 2020).

3. Function of the Human CoV S Protein

The most important section of CoVs during its host tropism or introduction to a new host is its S Protein. CoVs have trimeric S protein with S1 and S2 subunits, that S1 subunit divide into N-terminal domain (NTD) and C-terminal domain (CTD) (Ou 2020). The first interaction of CoVs with their new host cells is through S Protein NTD that contains carbohydrate-binding ("lectin") region (Chen 2013)(Bakkers 2017). CoVs S protein NTD conducts weak and reversible interaction low-affinity hydrogen bonds with surface glycans e.g. sialic acid, heparan sulfate proteoglycans (HSPGs), and C-type lectin receptors (CLRs) to scan their cell entry receptors (Hulswit 2016) (Ruben 2020). However, CLRs could detect this glycan based surface motion and trigger an immune response (Bermejo-Jambrina 2018). Strikingly, some of the viruses could utilize CLRs endocytosis for cell entry and infection (Bermejo-Jambrina 2018). After roaming the cell surface CoVs detect and bind to entry receptors e.g. angiotensin-converting enzyme 2 (ACE2), dipeptidyl peptidase 4 (DPP4), aminopeptidase N (ANPEP) with S Protein RBD located on S1 subunit CTD (Forni 2017)(Ou 2020). After entry receptor binding, CoVs utilize host cell surface trypsin- or subtilisin-like furin proteases cleave the S Protein S1/S1 domain (Yuan 2020)(Ou 2020).

3.1 Composition and Function of HCoV-229E S Protein

HCoV-229E S protein i) NTD does not bind to sialic acid and HSPGs, ii) RBD binds to ANPEP iii) cleaved by type II transmembrane serine proteases (TMPRSS2) and trypsin-like protease (HAT) (Bertram 2013)(Furin 2017). HCoV-229E S Protein compares to its parent virus Bat CoV has 187 amino acid (aa.) deletion on NTD that aims to evade host immune receptors CLR's detecting glycan-binding viruses (Table 1)(Li 2019). Since HCoV-229E S protein NTD does not have the glycan-binding capacity in the expense of evading host immune system. During host tropism HCoV-229E had aa. 8 substitutions compare to its parent virus Bat CoV on its RBD which was predicted on the aa. residues 308–408 (Table 1)(Li 2019). Based on the Clustal W analysis based on 29 HCoV-229E strains, S Protein RBD indicated 36 aa. substitutions suggesting the positive selection site of RBD and attempts of low-pathogenicity virus for adaptation (Chibo 2006)(Table 1)(Supplementary material 1).

3.2. Composition and Function of HCoV-OC43 S Protein

HCoV-OC43 S protein i) NTD binds to sialic acids especially 9-O-acetylated sialic acid ii) CTD does not have a RBD function (Bertram 2013)(Furin 2017)(Ruben 2020). However, HCoV-OC43 S Protein utilizes virus surface protein hemagglutinin-esterase receptor-destroying enzyme for virus entry (Huang 2015). HCoV-OC43 S Protein NTD was predicted on the aa. residues 15-302 (Ruben 2019). HCoV-OC43 S Protein compares to its parent virus Rat CoV has 122 aa. substitutions and 10 aa. inserts on NTD that aim to evade host immune receptors CLR's detect glycan-binding viruses (Table 2). Since HCoV-OC43 sialic acid-binding NTD is a positive selection site and aa. substitutions on the residues of 33, 90, 93, 120, 184, and 195 associated with higher pathogenic genotypes B and C (Lau 2011)(Ren 2015). Based on the Clustal W analysis of 46 HCoV-OC43 strains indicated 63 aa. substitutions on the NTD for the ongoing adaptation (Table 2) (Supplementary material 2).

3.3. Composition and Function of Human SARS-CoV S Protein

SARS-CoV S protein i) NTD does not bind to sialic acids but binds HSPGs, CLR's and immune system cell surface receptor Mannose-binding lectin ii) RBD binds to ACE2 and CLR's CD209L as cell entry receptors (Steffens 2004)(Gramberg 2005)(Han 2007)(Zhou 2010)(Lang 2011)(Furin 2017).

SARS-CoV S Protein NTD and RBD were predicted on the aa. residues 18-292 and 318-513, respectively (Yuan 2020). During host tropism, SARS-CoV S Protein compares to its parent virus Bat CoV had 61 aa. substitutions on its NTD suggesting the effort of the virus to evade glycan-

binding host immune receptors (Table 3). However, SARS-CoV S Protein compares to its parent virus Bat CoV had only 8 aa. substitutions on its RBD that suggesting its weak and limited adaptation to its ACE2 receptor (Table 3). This is important to note that betacoronavirus lineage B member SARS-CoV host tropism pattern mechanism is compatible with other CoVs and opposite with the betacoronavirus lineage B member SARS-CoV-2 that perfectly adapted to ACE2 receptor with a one-time event. Another important aspect that the SARS-CoV does not have deletions and inserts on its S Protein during host tropism (Table 3).

During its limited infection period between 2002-2004, SARS-CoV, S protein RBD mutations K479N and S487T mediated host change from the civet to human and human-to-human transmission, respectively(Li 2015). These two mutations contributed significantly to the SARS-CoV epidemic in 2002 to 2003 (Li 2015). SARS-CoV is genetically the most related CoVs to the SARS-CoV-2 had a completely different pattern of mutations through its infection. During the epidemics, SARS-CoV initially, had low-pathogenicity strains with aa. substitutions on residues of S Protein NTD 147, 228, 240 and RBD 479 and S2 821, and 1080 (Kan 2005). However, SARS-CoV further had high-pathogenicity strains with aa. substitutions on residues of S Protein RBD 360, 462, 472, 480, 487, S1 Subunit 609, 613, 665, and S2 subunit 743, 765, and 1163 (Kan 2005). The SARS-CoV global epidemic strains emerged with the aa. substitutions on residues of S Protein NTD 227, 244 RBD 344, and S2 subunit 778 (Kan 2005). Therefore, SARS-CoV had many adaptation mutations on its S Protein NTD and RBD during its limited number of infections. Based on the Clustal W analysis of 17 SARS-CoV isolates indicated 12 aa. substitutions on the RBD providing the positive selection site nature of the RBD and failed adaptation attempts of the extinct virus (Table 3)(Supplementary material 3).

3.4. Composition and Function of HCoV-HKU1 S Protein

HCoV-HKU1 S protein i) NTD binds to sialic acids ii) CTD does not have an RBD function (Bertram 2013)(Furin 2017)(Ruben 2020). However, HCoV-HKU1 could bind to host cell surface protein sialate-9-O-acetylerase and S Protein utilizes virus surface protein hemagglutinin-esterase receptor-destroying enzyme for virus entry (Huang 2015). HCoV-HKU1 S protein could interact and mediate infection using the HLA-C class I receptor (Chan 2009). HCoV-HKU1 S Protein NTD was predicted on the aa. residues 14-288 (Ruben 2019). HCoV-HKU1 S Protein compares to its parent virus Rat CoV has 116 aa. substitutions, 8 aa. deletions, and 6 aa insert on NTD that aim to evade host immune receptors CLRs detect glycan-binding viruses (Table 4). In 22 strains HCoV-HKU1 collected March 2003 to February 2005 had numerous recombinations and

substitutions on RNA-dependent RNA polymerase (RdRp), S Protein, and nucleocapsid (N) genes e.g. S protein gene of the isolate N18 (GenBank DQ415914) had 2 recombination insert and numerous substitutions compare to genotype B strain (GenBank AY884001.1) (Woo 2006). HCoV-HKU1 14 isolates from HCoV-HKU1 indicated S1 NTD aa. substitutions (W197F), S1 CTD (F613Y), and S1 domain (S752F), which is close to putative serine protease S1/S2 cleavage site (RRKRR at residues 756–760) suggested influencing antigenic, cell binding capacity and membrane fusion capacities, respectively (Dominguez 2014). Based on the Clustal W analysis of 39 HCoV-HKU1 strains indicated 51 aa. substitutions on the NTD for the ongoing adaptation addition to numerous substitutions on the rest of the S Protein (Table 4)(Supplementary material 4).

3.5. Composition and Function of HCoV-NL63 S Protein

HCoV-NL63 S protein i) NTD does not bind to sialic acids ii) CTD RBD binds ACE2 for cell entry (Furin 2017). HCoV-NL63 suggested not to have functional sialic acid-binding NTD that aims to evade host immune receptors CLRs detect glycan-binding viruses and its RBD was predicted on the aa. residues 481 - 616 (Table 5)(Mou 2013). During host tropism, HCoV-NL63 S Protein compares to its parent virus Rat CoV had a massive amount of aa. substitutions on its RBD only 34 of 135 aa. residues remained the same (Table 5). However, more pathogenic strains of HCoV-NL63 has an aa. substitution I507 L on the RBD (Wang 2020). Based on the Clustal W analysis of 39 HCoV-NL63 indicated 4 aa. substitutions on the RBD, however, the virus had more variation on non-functional NTD compare to the rest of the genome (Table 5)(Supplementary material 5).

3.6. Composition and Function of MERS-CoV S Protein

MERS-CoV S protein i) NTD binds to sialic acids ii) RBD binds DPP4 and iii) cleaved by furin and TMPRSS2 for cell entry (Park 2019)(Kleine-Weber 2019) (Zmora 2018)(Zhang 2020).

Additionally, MERS-CoV found to be interacting with the membrane-associated 78-kDa glucose-regulated protein (GRP78) and carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) without cell entry activity (Hin Chu 2018)(Chan 2016).

MERS-CoV S Protein NTD and RBD were predicted on the aa. residues 18-350 and 381-588, respectively (Yuan 2020). During host tropism, MERS-CoV S Protein NTD and RBD compares to its parent virus Bat CoV had a massive amount of aa. substitutions and several inserts (Table 6).

MERS-CoV S protein NTD binding burry sialic acid molecules (e.g. α 2,6-linked sialic acid and 5-N-acetyl neuraminic acid) 280 Å² inside the protein via hydrogen bonds (Park 2019). The sunken nature of the MERS-CoV S protein glycan-binding NTD is possibly due to its heavy modifications during the host change (Figure 6). Additionally, MERS-CoV S Protein mutations on S1(R652),

linker (K854, M939), S2 Heptad Repeat 1 (Q1020R/H) S2 domains (V1060, T1202I, Q1208H), linker (S1114, S1148, I1180) Heptad Repeat 2 (A1275) suggested for effective for host tropism (Forni 2015). In MERS-CoV S Protein S2 region Heptad Repeat domain alterations increased pathogenicity since the S2 domain is responsible for virus entry into the host cells (Cotten 2014). MERS-CoV strains S Protein NTD had several aa substitutions (Cotten 2014)(Park 2019). However, aa. substitutions H91Y, S133N/R, and Q304K were detected only in South Korean, England-KSA, and United Arab Emirates isolates, respectively (Park 2019). MERS-CoV strains in South Korea gained resistance to antibodies and blood serum infusion with aa substitutions at the S protein RBD residues D510G and I529T (Kleine-Weber 2019). Based on the Clustal W analysis of 34 MERS-CoV strains indicated 11 aa. substitutions on the RBD and 10 aa substitutions on NTD for the ongoing adaptation (Table 6)(Supplementary material 6).

3.7. Composition and Function of Human SARS-CoV-2 S Protein

SARS-CoV-2 S protein i) NTD binds sialic acids and possibly HSPGs ii) RBD binds ACE2 and iii) cleaved by furin TMPRSS2 for cell entry (Hoffmann 2020)(Bestle 2020)(Fantini 2020)(Mycroft-West 2020). SARS-CoV-2 host tropism pattern is significantly different compare to genetically related CoV betacoronavirus lineage B member SARS-CoV. The SARS-CoV-2 S Protein NTD aa. composition rich with aromatic, basic, and Gly, Pro and/or Ser residues has a high chemical affinity to sialic acids (Fantini 2020). Additionally, SARS-CoV-2 S Protein flat surface NTD improves the sialic acid-binding capacity which is sunken inside the NTD of S Protein or even sacrificed in many viruses to evade host cell immunity (Rossmann 1989)(Hulswit 2016)(Fantini 2020).

SARS-CoV-2 S Protein NTD binds to sialic acids localized on ganglioside GM1 rich lipid rafts while RBD binds adjacent ACE2 receptor which improves cell surface interaction with dual-binding (Fantini 2020). Based on the studies on MERS-CoV addition to the cell surface attachment the sialic acid-binding capacity was more important due to its capacity to facilitate cell-cell membrane fusion and virus spread within the infected tissues to the adjacent cells (Qing 2020). Therefore the smooth surface of the SARS-CoV-2 NTD sialic acid-binding domain not only assisting the surface attachment but also intercellular transmission to adjacent uninfected cells after the cell entry (Qing 2020).

Another critical feature of SARS-CoV-2 S protein is the putative furin cleavage site (PRRARSV) between the S1/S2 subunits similar to MERS-CoV putative furin cleavage site (PRSVRSV) since they are the only Human pathogenic CoVs with furin cleavage sites (Zhang 2020). However, SARS-CoV-2 S Protein can be cleaved by trypsin and TMPRSS2(Ou 2020)(Hoffmann 2020). Since

both TMPRSS2 and furin are essential for SARS-CoV-2 S Protein cleavage (Bestle 2020). ACE-2 receptor present on cell surfaces of the several organs e.g. oral, nasal, and intestinal mucosa, alveolar epithelial cells in lung, stomach, skin, lymph nodes, thymus, bone marrow, spleen liver, kidney, brain, arterial, venous endothelial cells, and arterial smooth muscle however furin is highly expressed in lungs, therefore, SARS-CoV-2 utilize respiratory tract cells more effectively compare to other CoVs (Coutarda 2020) (Steffens 2004).

SARS-CoV-2 S Protein NTD and RBD were predicted on the aa. residues 111–158 and 319-541, respectively (Fantini 2020)(Shang 2020). During host tropism, SARS-CoV S Protein NTD had 61 aa. substitutions compare to its parent virus Bat CoV S Protein NTD, conversely, SARS-CoV-2 S Protein NTD had no alterations on its sialic-acid binding NTD compares to its parent virus Bat CoV S Protein NTD(Tables 3 and 7). The most critical NTD residues in sialic acid binding are D111, Q134, F135, N137, R158 and S161 (Fantini 2020). Since SARS-CoV-2 NTD sialic acid-binding domain found to be conserved with RaTG13 and has not shown any aa. substitutions in 11 isolated with different geographical origins (Fantini 2020). Additionally, SARS-CoV S Protein RBD had 8 aa. substitutions compares to its parent virus Bat CoV S Protein RBD, conversely SARS-CoV-2 S Protein RBD had 22 aa. substitutions compare to its parent virus Bat CoV S Protein RBD (Tables 3 and 7). Another important aspect that the SARS-CoV did not have any deletions and inserts on its S Protein during the host tropism, conversely the SARS-CoV-2 had a precise 12 nucleic acid insert that enables the virus to be cleaved by host cell surface protease furin. Based on the database of China National Center for Bioinformation, 2019 Novel Coronavirus Resource (2019nCoV) at the Mutation Analysis of the S protein in SARS-COV-2 subsection is listing 329 aa. substitutions on S protein, which 39 of them on RBD. However, these mutations have very low frequency and none of the RBD mutations are on the direct ACE2 interaction residues on critical residues K417, G446, Y449 L455 F486 N487 Y489 Q493 Q498 T500 N501 G502 Y505 (Shang 2020). The only S Protein mutation with high frequency is D614G which is also only seen in Europe and North America (Pachetti 2020). Based on the Clustal W analysis of 92 SARS-COV-2 strains indicated 3 low-frequency aa. substitutions (Supplementary material 7). The first strain of the SARS-COV-2 sequence is almost unaltered after millions of infections. This is clear that SARS-COV-2 S Protein does not have any positive selection site on its NTD and RBD. This is conflicting with the ongoing adaptation pattern of other human CoVs. Additionally, none of these clinical isolates have recombination on its S1/S2 cleavage site (Supplementary material 7).

4. S Protein Host Change Patterns In CoVs

The general host tropism pattern of the Coronaviruses has two major essential patterns i) S protein RBD alterations to surface recognition and ii) deletion on glycan-binding NTD (Hulswit 2016). This is important to stress that the Bat or Rodent CoVs subject to most of these changes during the initial zoonotic transmit to the animal. Therefore, hypothetically engineered BatCoV RaTG13 strain possibly infected animals during its laboratory escape that lead to infection of the pangolin (Zhang 2020)(Andersen 2020). Thus, the detection of the SARS-CoV-2 initially in the pangolin (Andersen 2020) or any other animal does not change its unusual and possibly engineered host tropism pattern.

4.1. SARS-CoV-2 NTD Composition Conflicting with the “Canyon Hypothesis”

The formation of canyons, depression zones, or cavities on the surfaces of the influenza virus, human rhinovirus, Mengo virus explained with "Canyon Hypothesis" by the Distinguished Professor Michael G. Rossmann (Rossmann 1989). CoVs S Protein glycan-binding domains originated from host human galectins (host lectins) to act as coreceptors were suggested to increase CoVs host range (Chen 2013)(Hulswit 2016). The CoVs S Protein NTD and human galectins have the same structural folds but different sugar-binding patterns (Chen 2013). Additionally, human galectins have open and easy reachable glycan-binding domain is sunken in CoVs (except SARS-CoV-2) to hide glycan-binding sites from the host immune system (Chen 2013). In CoVs (except SARS-CoV-2) S Protein NTD glycan-binding domain also called viral lectins has diverse sugar-binding modes with a common feature to hide their domains in cavities to limit the access of antibodies and immune cells (Peng 2011). This pattern of CoVs was considered as an evolutionary measure to limit host immune system recognition (Hulswit 2016). Besides the S Protein NTD glycan-binding region could be sacrificed to evade host immunity since its presence was considered less essential compared to RBD in some of the viruses (Hulswit 2016).

Based on the genomic analysis of six human CoVs with their parent bat or rodent CoVs indicate several deletions inserts and recombinations on their S Protein NTD to evade from host glycan-binding immune receptors, are compatible with the "Canyon Hypothesis". For example, MERS-CoV S Protein NTD protein sinking sialic acid molecule 280 Å² inside the protein cavity (Park 2019). However, the unnatural flat pattern of SARS-CoV-2 S protein NTD is conflicting with the evolutionary host tropism strategy of not only the Human CoVs but also many different human pathogenic viruses (Rossmann 1989)(Peng 2011)(Chen 2013)(Hulswit 2016)(Fantini 2020).

4.2. SARS-CoV-2 Recombination Pattern is not Compatible with Template Switching (Copy-Choice) Mechanism

The high rate of RNA recombinations in Coronaviruses was explained with the template-switching (copy-choice) mechanism (Makino 1986). Coronavirus RNA has discontinuous and nonprogressive replication in its host cells, and the replication pause at specific RNA sites to creates blocks of free RNA that could fuse into another set of Coronavirus replication leading the formation of different Recombinant Coronavirus Strains (Makino 1986). The pauses of the RNA replication of Coronaviruses could be the case of mixed infection with other Coronaviruses, other Viruses, and even the host RNA blocks (gene stealing from the host).

As mentioned above CoVs S Protein glycan-binding domain with the human galectin origin suggesting the active recombination site or RNA replication stops on NTD (Chen 2013)(Hulswit 2016). For example in Human CoV-HKU1 compare to genetically related HCoV-OC43 high rate of recombination in specific ORFs e.g. p65 to nsp10 suggesting the presence of several RNA replications stops in these domains (Woo 2005).

However, not only inserts but recombinations could occur with deletions in the CoVs. Both HCoV229E and genetically related Alpaca CoV has a major 185 to 404 deletion in the spike S1 region compare to genetically related BatCoV (Corman 2015). Strikingly, orf8 was deleted in HCoV-229E compare to related alpaca and parent bat virus suggesting the alpaca is the first interhost of the bat virus (Corman 2015).

In CoVs, without any selection pressure, random RNA-RNA recombination within the population amongst the different strains could happen at the certain regions named as hot spots (Banner 1991). SARS-CoV-2 S Protein S1/S2 site furin recognition motif does not exist in other 'lineage B' betacoronaviruses e.g. Pangolin-CoV or RaTG13 suggesting that S Protein S1/S2 is not a recombination hot spot or RNA stop based on template switching (copy-choice) model (Makino 1986)(Andersen 2020). However "future discoveries" of polybasic cleavage sites in related CoVs could weaken the engineered origin of the SARS-CoV-2 S Protein S1/S2 site furin recognition motif (Andersen 2020).

4.3. SARS-CoV-2 RBD is not High Frequency Positive Selection Site

The CoVs genomes have hot spots with a high frequency of a.a. substitutions also called positive selection sites that favor host tropism, antibody resistance, or immune evasion (Forni 2017).

However, clinical SARS-CoV-2 isolates have only one single frequent mutation D614G on S Protein (Pachetti 2020). Thus based on the mutation rate and patterns in clinical isolates of SARS-

CoV-2 S Protein is not a hot spot unlike other human CoVs, SARS-CoV-2 and BatCoV RaTG13 RNA-dependent RNA polymerase (RdRp), S Protein and whole-genome homologies are 100 %, 97%, 96.2%, respectively (Zhang 2020). SARS-CoV-2 preserved its genome during the adaptation against the mutagenic immune system of Pangolin and/or Human cells and cellular alkylating agents (Barr 2010). Since the RBD of the SARS-CoV-2 had very intense modifications compare to SARS-CoV RBD but not having such modifications throughout the genome under the same mutagenic stress. This RBD site-specific targeted substitutions could be accomplished using several methods, e.g., Modified Microbial Nucleic Acid (Sequence from the method GenBank: FV537210.1), Artificial chromosome constructs containing nucleic acid sequences capable of directing the formation of a recombinant RNA-virus (Sequence 1 from Patent WO0139797 GenBank: AX154950.1), Recombinant feline coronavirus S proteins (Sequence 1 from patent US 6280974 GenBank: AR166169.1). Additionally, the method of PCR-generated insertions on SARS-CoV was documented several times (Becker 2008). The confirmation of this argument is that the clinical isolates with RBD mutations cannot compete with the engineered SARS-CoV-2 that was configured with the too-perfect ACE2 receptor binding interaction which is the reason of low-frequency.

Results and Discussion

SARS-CoV-2 is the seventh but the first CoVs with the pandemic potential. SARS-CoV-2 is genetically related to BatCoV RaTG13 (Zhang 2020). CoVs like as RaTG13 are infecting the gastrointestinal system of the bats since they have detected in feces and intestines of the bats (Drexler 2014). Bats cope against CoVs with a high amount of antibody accumulation (Drexler 2014). Approximately 83 Bat species are consumed at 33 different countries e.g. 13 species in New Guinea and 14 species in the Philippines (Mickleburgh 2009). Additionally, the higher risk of CoVs transmission to other animals and humans is not due to meat consumption but contamination of water sources since CoVs exist in bat excrements (Corman 2015). The number of bat species consumed in China is only 5 and it is likely an exotic food consumption unlike underdeveloped countries that bat bushmeat is a protein source (Mickleburgh 2009). Additionally, the risk of drinking water contamination in China is extremely low compare to underdeveloped countries where bats contaminate wells and pond humans rely on water such as KSA that MERS-CoV infected camels limited desert water sources contaminated by African Bats (Corman 2015). Therefore, the risk of novel CoVs infections in China is lower compare to underdeveloped countries or countries with scarce water sources.

The host tropism pattern of the previous six CoVs was profoundly evaluated to understand the genomic mechanism of naturally occurring CoVs. Additionally, the mutation patterns of the CoVs during their infections on human hosts were examined using genomic alignment. SARS-CoV-2 host tropism pattern has discrepancies compare to other CoVs. The SARS-CoV-2 S Protein NTD contains flat surface glycan-binding conflicts with the Canyon Hypothesis. Since most of the viruses either sacrifice or sink this critical domain to evade host immune responses. SARS-CoV-2 recombination pattern of the insert of furin cleavage site during host tropism is a unique and one-time event conflict with the genomic composition of genetically related CoVs and template switching (copy-choice) mechanism. SARS-CoV-2 genome is almost identical to the origin Bat CoV but it is only mutated on RBD another one-time event as well. The "too perfect" RBD does not have any high-frequency mutations in the clinical strains. The RBD of SARS-CoV-2, unlike other human pathogenic CoVs, is not a positive selection site.

The engineered origin of the SARS-CoV-2 was mainly rejected (Andersen 2020) the question is how SARS-CoV-2 survived the immunity of pangolins or humans during the very first interaction with its flat easy-target sialic acid-binding domain? SARS-CoV-2 indicate the low frequency of mutations on its RBD and how the virus obtained such effective RBD compositions without destroyed by pangolin or human immunity due to its easy target sialic acid-binding domain? Why only the RBD had mutations meanwhile the rest of the genome was almost unaltered?

Betacoronavirus lineage B CoVs including SARS-CoV S Protein does not have a pattern of recombination on S1/S2 region how SARS-CoV-2 obtained that ability and how we do not see any further recombinations in the clinic SARS-CoV-2 strains? SARS-CoV-2 clinic strains do not have any high-frequency mutations on NTD and RBD how the virus obtained such perfect and precise host cell membrane interaction capacity, unlike SARS-CoV, perished due to its failed adaptation? Why we have not seen any pandemic caused by CoVs before? Why these pandemics did not emerge in places where people rely on water sources shared with bats or bats consumed as bushmeat? In summary, if SARS-CoV-2 is not an engineered Bat CoVs RaTG13, its unnatural host tropism pattern and pandemic potential compare to other human pathogenic CoVs raising those questions.

Genomic Sources and Online Tools

The CoV S protein amino acid sequences used in this study was obtained form The Nucleotide database of National Center for Biotechnology Information, U.S. National Library of Medicine 8600 Rockville Pike, Bethesda MD, 20894 USA <https://www.ncbi.nlm.nih.gov/nucleotide/>. The sequences were aligned using the online tool Multiple Sequence Alignment by CLUSTALW of

Bioinformatics Center, Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan, <https://www.genome.jp/tools-bin/clustalw>. SARS-CoV-2 Wuhan December 2019 isolate (GenBank MT019529.1) S protein was modelled using online tool SWISS-MODEL of Protein Structure Bioinformatics Group c/o Prof. Torsten Schwede Swiss Institute of Bioinformatics Biozentrum, University of Basel Klingelbergstrasse 50/70 CH-4056 Basel / Switzerland, <https://swissmodel.expasy.org/interactive/KqpmAW/models/>.

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BatCoV KT253269.1	MFLLIVACVLIHIAAGQINNNCLDGNRVGIQTMQLGLPPNVTALVTGYLPDKWHCTSNHNN
HuCoV229E NC_002645	MFVLLIVAYALHIAAG-----
Residues 1-15	**:*:*:* * **

BatCoV KT253269.1	NNVSYSGKGFVFLDITDGEASFALVDTGAFSTDRKYLLYLNHILYGGGYVKLKICKWSQY
HuCoV229E NC_002645	-----
Residues	

BatCoV KT253269.1	VDFNAPSASIFSSSCIIDFKTADKKGRVLGFSASGDTVRIHWSDAVHTVYVPGASAWSRV
HuCoV229E NC_002645	-----
Residues	

BatCoV KT253269.1	NVRCPKIAACYFSITEDPIAVNVTITNGLITSYSVCNGCVGYAENIFAVESGGYIPSDFA
HuCoV229E NC_002645	-----CCITNGLNTSYSVCNGCVGYAENIFAVESGGYIPSDFA
Residues 16-53	*****:*****

BatCoV KT253269.1	FNNWFLLTNTSSVVDGVVRSVQPLLLNCLWVVEGLQSTTGFVYFNGTGRGCGNGFSSGGL
HuCoV229E NC_002645	FNNWFLLTNTSSVVDGVVRSVQPLLLNCLWVVEGLRFTTGFVYFNGTGRGDCNGFSSDVL
Residues 54-113	*****:*****

BatCoV KT253269.1	SDVLRYNLNFSSNSEDLRRGTILFKTSYGVVVFYCTNNTLVSGDAHIFPGTVLGNFYCF
HuCoV229E NC_002645	SDVLRYNLNFEN---LRGTILFKTSYGVVVFYCTNNTLVSGDAHIFPGTVLGNFYCF
Residues 114-169	***:*****:*****:*****:*****

BatCoV KT253269.1	VNTTIGNETTSAFVFGALPKTVREFVISRTGHFYINGRYFTLGNVAVNFNVTTAETDF
HuCoV229E NC_002645	VNTTIGNETTSAFVFGALPKTVREFVISRTGHFYINGRYFTLGNVAVNFNVTTAETDF
Residues 170-229	*****:*****

BatCoV KT253269.1	WTVAFASYADVLINVSHTSIANIICYNSVINRLRCDQLSFDVDPDFYSTSPIQSVELPES
HuCoV229E NC_002645	WTVAFASYADVLINVSHTSIANIICYNSVINRLRCDQLSFDVDPDFYSTSPIQSVELPVS
Residues 230-289	***:*****:*****:*****:*****

BatCoV KT253269.1	IVSLPVYKHTSILLYVDFKQSGSGTFCNCPYGVNITLANFNETKGPLCVDTSHFHTK
HuCoV229E NC_002645	IVSLPVYKHTSILLYVDFKQSGGGKFCNCPYGVNITLANFNETKGPLCVDTSHFHTK
Residues 290-349	*****:*** * *****:*****:*****:*****

BatCoV KT253269.1	YVAVYANVGSWSASVDITGNCPFSFGKVNNFVKFGSVCFLKDI PGGCAMPIVANWAYIKY
HuCoV229E NC_002645	YVAVYANVGSWSASVDITGNCPFSFGKVNNFVKFGSVCFLKDI PGGCAMPIVANWAYSKEY
Residues 350-409	***** * *:*****:*****

BatCoV KT253269.1	YTIGSLYVSWSDGDGITGVPVPEGVSSFMNVTLDCTKYNIYDVSGVGVIRVSNDFLN
HuCoV229E NC_002645	YTIGSLYVSWSDGDGITGVPVPEGVSSFMNVTLDCTKYNIYDVSGVGVIRVSNDFLN
Residues 410-469	***** *****:*****:*****:*****

BatCoV KT253269.1	GIVYTSISGNLLGFKDVSNGTIYSITPCNPPDLVVYQQA VVGAMLSENSTSYGFSNVVE
HuCoV229E NC_002645	GIVYTSISGNLLGFKDVTNGTIYSITPCNPPDLVVYQQA VVGAMLSENSTSYGFSNVVE
Residues 470-529	** ** * *****:***** *****

BatCoV KT253269.1	LENFFYASNGTYNCTDAVLTYSSFGVCADGSI IAVQPRNVSYDGVSAIVTANLSIPSNWT
HuCoV229E NC_002645	LPKFFYASNGTYNCTDAVLTYSSFGVCADGSI IAVQPRNVSYDGVSAIVTANLSIPSNWT
Residues 530-589	** :***** .*****
BatCoV KT253269.1	TSVQVEYLQITSTPIVVDCSTYVCNGNVRVVELLKQYTSACKTIEDALRISARLESADVS
HuCoV229E NC_002645	TSVQVEYLQITSTPIVVDCSTYVCNGNVRVVELLKQYTSACKTIEDALRISARLESADVS
Residues 590-649	*****
BatCoV KT253269.1	EMLTFDKKAFTLANVSSFGENLSSVIPSLPTGSRVAGRSAIEDILFNKVVTSGLGTVD
HuCoV229E NC_002645	EMLTFDKKAFTLANVSSFGENLSSVIPSLPTGSRVAGRSAIEDILFNKLVTSGLGTVD
Residues 650-709	***** :***** .***** :*****
BatCoV KT253269.1	ADYKKCTKGLSIADLACAQYYNGIMVLPGVADAERMAMYTGSLIGGMALGGLTSAVAIPF
HuCoV229E NC_002645	ADYKKCTKGLSIADLACAQYYNGIMVLPGVADAERMAMYTGSLIGGMALGGLTSAVAIPF
Residues 710-769	***** :***** :***
BatCoV KT253269.1	SLAQARLNLYVALQTDVLQENQKILAASFNKAITNIVDAFTGVNDAITQTSQAQTVATA
HuCoV229E NC_002645	SLAQARLNLYVALQTDVLQENQKILAASFNKAITNIVDAFTGVNDAITQTSQAQTVATA
Residues 770-829	** :***** :***** :*****
BatCoV KT253269.1	LNKIQDVVNQQGNLNHLTSQLRQNFQAISSSIQAIYDRLDTIQADQQVDRLITGRLAAL
HuCoV229E NC_002645	LNKIQDVVNQQGNLNHLTSQLRQNFQAISSSIQAIYDRLDTIQADQQVDRLITGRLAAL
Residues 830-889	***** :*****
BatCoV KT253269.1	NFVFAQTLTKYTEVRASRQLAQQKVNCEVKVKSQSNRYGFCGNGTHIFSVNAAPEGLVFLH
HuCoV229E NC_002645	NFVFSHTLTKYTEVRASRQLAQQKVNCEVKVKSQSNRYGFCGNGTHIFSVNAAPEGLVFLH
Residues 890-949	*. **:***** :*****
BatCoV KT253269.1	TVLLPTDYKDVEAWSGMCVDGD-GYVTRQPNLALYKEDDKFRITSRIMFEPRIPTMADFV
HuCoV229E NC_002645	TVLLPTDYKDVEAWSGLCVDGTYGYVTRQPNLALYKEDGNYFRITSRIMFEPRIPTMADFV
Residues 950-1009	***** :***** :*** ** :***** . :***** :*****
BatCoV KT253269.1	QIENCNVTFVNISSRAELQTVPEYIDVNKTLOLLEKLPNYTVPDLGVQYNTILNLTN
HuCoV229E NC_002645	QIENCNVTFVNISSRAELQTVPEYIDVNKTLOLSYKLPNYTVPDLGVQYNTILNLTN
Residues 1010-1069	***** :**** :***** :* ***** * :***** .
BatCoV KT253269.1	EISTLENKSAELNYTVQKLQTLIDNINSTLVDLKWLNRVETYKWPWWVWLCISVVLIFV
HuCoV229E NC_002645	EISTLENKSAELNYTVQKLQTLIDNINSTLVDLKWLNRVETYKWPWWVWLCISVVLIFV
Residues 1070-1129	***** :*****
BatCoV KT253269.1	VSMLLLCCCSTGCCGFFSCVASSTKGCCESTKLPYYDVEKIHQ
HuCoV229E NC_002645	VSMLLLCCCSTGCCGFFSCVASSRGGCCESTKLPYYDVEKIHQ
Residues 1130-1173	***** :*** :*****

Table 1. S Protein sequence alignment of the first sequenced isolate of HCoV-229E (GenBank ID NC_002645) Alphacoronavirus (Corman 2015) and genetically related CoV from Bat species,

Hipposideros spp. CoV strain BtCoV/KW2E/Hip_cf._rub/GHA/2011 (GenBank ID KT253269.1) (De Sabato 2019). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

RatCoV KM349744.1	MVIFLLLFAEPVFGIIGDFKCT--QSWINSAASPPPISTEVVDVINGVGTYYVLRVY
HuCoVOC43 NC_005147	-MFLILLISLFTFAVIGDKTSDTSYINDKDTGPFPISTEDVDVINGIGTYYVLRVY
Residues 1-59	:::***: ..*::***:*** **::** : *****:***:***:*****:***
RatCoV KM349744.1	LNTSLLLTGYYFVSGSYLRNLLKGTQWLSNWFPPFLSEFNSGIFVKARNKPKVPLNGI
HuCoVOC43 NC_005147	LNTLFLNGYYFVSGSYLRNMLKGSVLLSRNWFPPFLSDFINGIFAKVKNKLIKDRV
Residues 60-119	***:*.:.****.*** **:: **:: ** ** *****:* .***.:.:* : : :
RatCoV KM349744.1	THSEFGTIVFGTSFVNTTYTIVLEP---STQIVNGKLIIGTLASVCQYTMCEYPTICN
HuCoVOC43 NC_005147	MSEFPATIGTSFVNTSYSVVQFRTINSTQDGYNKLQGLLEVSVQYNMCEYPTICN
Residues 120-179	:*** :*.:.:*::***:***:***:*** ** ** ** ** .** * * .****.*****:* * :
RatCoV KM349744.1	PLNGRPSLWHSASIGIVPCLYRNFTYNVADNYFHFYQGGTFYAYVGDKSPITLL
HuCoVOC43 NC_005147	PLNGNRKELWHLDTGVVSCLYRNFTYDYNADNYFHFYQGGTFYAYFTDTGVVTKFL
Residues 180-239	* ** * .*** . *::***:*****:* ** :*****:*****. *.. :*.:*
RatCoV KM349744.1	FVYVLGTVVTHYYVPLVCN---ARQTYEYWVTPLIKREYLLVFDNGVITNAVDCA
HuCoVOC43 NC_005147	FVYVLGMALSHYYVPLTCNSKVKNGFTLEYWVTPLSROYLLAFNODGIIFNAVDCA
Residues 240-299	*:**** .*:***:***.*** ** ***** .*:***.*: :*: * **** *
RatCoV KM349744.1	FMSEIQCMQNKIPVTVGYELGYTVQPIADVYRRLNLPDCEIEQWLNDQVPSPI
HuCoVOC43 NC_005147	FMSEIKCKTQSIAPPTGVYELGYTVQPIADVYRRLNLPDCEIEQWLNDKSVPSPI
Residues 300-359	.****:* ** * * *****.***** ***** **::** * ** .****:..**
RatCoV KM349744.1	RKTFSNCFNFMSSLSKVRATSFSCNNIDASKIYMCFGSITIDKFAIPNSRKVDLQ
HuCoVOC43 NC_005147	RKTFSNCFNFMSSLSFIQADSFICNNIDAKIYMCFSITIDKFAIPNGRQVDLQ
Residues 360-419	*****:*** :*: **::***:***.*** *****.*****:***.***
RatCoV KM349744.1	SGYLQNYNYRIDSATSCQLYGI PANNVTVTKHNPSGWNNGFVDFKPLNIGQ
HuCoVOC43 NC_005147	SGYLQSFNYRIDSATSCQLYNLPAANVSVSRENPSTWNKRFVDFKPLNIGQ
Residues 420-479	**:.*:***:* :*****.*** **::** : ** **::**:* . : :
RatCoV KM349744.1	KYSALYSTMCFNVPNDYCPCKLG---CPTGTVERPQIGTSTSGQPIYDCP
HuCoVOC43 NC_005147	NHDVYVAQCFKAPKNCPCKLNKSGVSGPGKNNIGTCTPAGTNYLTCDNLCTP
Residues 480-539	:::***: **:.*:***:*****. **:: ** *****:*** *
RatCoV KM349744.1	PWLTSSACKQTPATVGVGOYCYGVGVMAQCAPSPMPGNSILTCSCSNTQYSAGNSQ
HuCoVOC43 NC_005147	KATGTYKCFQTKSLVGTGEHCGLAVKSDYCG-----GNSCTGRPC
Residues 540-580	: * ** : ***:***:***:*** ** *
RatCoV KM349744.1	AWTSFGADTCLSGENCQVFANVLLNNSGTTCTDLQKANTDIIIVGVCVNYDLYG
HuCoVOC43 NC_005147	AFLGWSADSCLEKCNIFANVLLNNSGTTCTDLQKANTDIIIVGVCVNYDLYG
Residues 581-640	*: ..***:***.***:***:***:*** **::*** **::*****:***:***:***** **
RatCoV KM349744.1	GIFTEVNATYYNSWQNLLYDSNGLYGFKDFITNRTYMIRSCYSGRVSAAYHSDTE
HuCoVOC43 NC_005147	GIFTEVNATYYNSWQNLLYDSNGLYGFRDYITNRTYMIRSCYSGRVSAAFHANSSE
Residues 641-700	***.*****.*****.***:***:***:*****.***:***:***** **

RatCoV KM349744.1	LYRNLIKCSYVFNNNISISRSVITVFDSYLGCVVNA DD DDIAEAVGSCNLTVGSGYCVDYS
HuCoVOC43 NC_005147	LFERNIKCNYVFNN SI TRQLQPI N VFDSYLGCVVNA YN NSTAISVQ TC DLTVGSGYCV DYSK
Residues 701-760	*:***:*.*****.:. . . *.***** .: . * : * :*:*****.

RatCoV KM349744.1	TWRAKRD LN TGYR I TNFEPFVPTLVNDSVESVGGLYEIQIPTEFTIGNLEEFVQ T SPKV
HuCoVOC43 NC_005147	N R SRGAI T TGYR F TNFEPF T VNSVNDSE F VGGLYEIQIPSEFTIGNMEEFVQ T SPKV
Residues 761-820	. * : : . : ***** : ***** . . ***** : ***** : ***** : ***** : *****

RatCoV KM349744.1	TIDCAAFVCGDYAACREQLVEYGSFCDNIN T IILNEVNSMI DT SQL AS TLMNGVTLS SR
HuCoVOC43 NC_005147	TIDCAAFVCGDYAAC K SQ L VEYGSFCDNIN A IILNEVNELI DT IQ Q VANS LM NGVTLS TK
Residues 821-880	*****:*****.:*****:*****:*.***.:**:* :*:*****:*

RatCoV KM349744.1	LKDGISFNQDDINFSVMGCVGSNCISHR--SAIEDILFNKVKLSDVGFVDAYNNCTCGS
HuCoVOC43 NC_005147	LKDG V FN V DDINFS P VLGC L GS C SKASSAIEDIL F DKVKLSDVGFVEAYNNCTCGA
Residues 881-940	***:.* * *****.:**:*:* * . *****:***:*****:***** *

RatCoV KM349744.1	EIRD L V C VQS F N G IKVLPPV L SE S QMSGYATGVGLSM L F P FSAAAGV P F T MSVQYRING
HuCoVOC43 NC_005147	EIRD L I C V QS Y K G IKVLPPV L SE N QISGY T LAATSAS L F P L W TAAAGV P F Y LN V QYRING
Residues 941-1000	*****:*****.:*****:***.*:***: . . : *** :*:***** :.*****

RatCoV KM349744.1	LGV T M D V L NQ N Q K IANAFN N ALAIQNGFDATNSALAKIQSVVNANAEALNNLLQQLSN
HuCoVOC43 NC_005147	LGV T M D V L SQ N Q K IANAFN N ALYAIQEGFDATNSALVKIQAVVNANAEALNNLLQQLSN
Residues 1001-1060	*****.****:***** ***:*****.****:*****:*****

RatCoV KM349744.1	RFGAISSSLQEILSRLDALEA V QIDRLINGRLTALNAYVSQQLSDITLVKFSASQATEK
HuCoVOC43 NC_005147	RFGAIS S SLQEILSRLDALEA E AQIDRLINGRLTALNAYVSQQLSDITLVKFSASQAMEK
Residues 1061-1120	*****:*****:*****.:*****:***** *****:***:**

RatCoV KM349744.1	VNECVKSQS T R N F C GNGNHI S LVQNAPYGLYFIHFSY C PTKY T AV V SPGLC I AGD V G
HuCoVOC43 NC_005147	VNECVKSQS S R N F C GNGNHI S LVQNAPYGLYFIHFSY V PTKY V TAR V SPGLC I AGD R G
Residues 1121-1180	*****:*.*****:*****:***** *****.* *****:*** *

RatCoV KM349744.1	VAPKSGYF I K V N D K W M F TGSAYY H PEPIT N D N V I M N NCAV N E T KAP V V L N T S I P N L P D
HuCoVOC43 NC_005147	E APKSGYF V N V N T W M Y T G S Y Y PEPIT E N N V V M S TCAV N E T KAP V V L N T S I P N L P D
Residues 1181-1240	:*****.:**.*:***.*:*****:***:*.*****:*** *:*****

RatCoV KM349744.1	FKEELD K W F KN Q SVAPDLS L L E RINVTFLDLQ E EM D R I Q D AIK K LN D SYINL K IGTY
HuCoVOC43 NC_005147	FKEELD Q W F KN Q SVAPDLS-- L D V INVTFLDLQ E EM N R L Q E AIK V LN Q SYINL K IGTY
Residues 1241-1298	*****:*****:***** * : ***** * *:***:*** * *:*****:****

RatCoV KM349744.1	E V YV K W P W V YV L L L I G LAGVA V L V L L F F VCCCTGCG S SCF K KCG S CCDDY G G H Q D I V V K T S
HuCoVOC43 NC_005147	E V YV K W P W V YV L L L I C LAGVA V L V L L F F IC C CTGCG S SCF K KCG S CCDDY T G V Q E L V V K T S
Residues 1299-1358	* ***** *****:*****:*****:*****.* ***** * : : * :***

RatCoV KM349744.1	HDD
HuCoVOC43 NC_005147	HDD

Table 2. S Protein sequence alignment of the first sequenced isolate of HCoV-OC43 (GenBank ID NC_005147) betacoronavirus lineage A (Ben Hu 2015) and genetically related CoV from Rat species, *Rattus norvegicus* CoV strain HKU24 (GenBank ID KM349744.1) (lau 2015). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

BatCoV KC881006	VKLLVLFVATLSSSYTIEKCLDFDRTPANTQFLSSHRGVYYPDIIFRSNVLHLVQDHF
HuSars-CoV NC_004718	-MFTLLFLTLSSGSDLDRCTFDVQVAFNYTCHTSSMRGVYYPDIIFRSNTLLVLDLFL
Residues 1-59	::.*:* *.*. :.:* *** .* *. ** *****:*****:.*:.* ** *

BatCoV KC881006	LPFVSNVTFRTFGLNFDNPLIPFKDGIYFAATEKSNVIRGWVFGSTMNKSQSVIIMNN
HuSars-CoV NC_004718	LPFVSNVTFRTINHTFGNPLIPFKDGIYFAATEKSNVIRGWVFGSTMNKSQSVIIMNN
Residues 60-119	*** **** * *:. .*.**:*****:*****:*****:***

BatCoV KC881006	STNLVIRACNFELCDNPFVVLKSNNTQIPSYIFNAFNCTFEYSKDFNLDLGERKGNF
HuSars-CoV NC_004718	STNLVIRACNFELCDNPFVAVKPMCTQHTMIFNAFNCTFEYSDAFSLDVSEKSGNF
Residues 120-179	***:*****.* *. .** : **:*****:.* .**:.**.* **

BatCoV KC881006	KLLREFVFNKDGFLVYVSGYQPTSAASGLPTGFNALKPIFKLPLGINITNFRLLTAFV
HuSars-CoV NC_004718	KLLREFVFNKDGFLVYVSGYQPTDVVRDLFSGFNALKPIFKLPLGINITNFRLLTAFV
Residues 180-239	*.*****:*****:*.*****... .**:*:*****:*****:***.

BatCoV KC881006	FRFLYWGTSAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEDKGI
HuSars-CoV NC_004718	FAQLYWGTSAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEDKGI
Residues 240-299	* * *****

BatCoV KC881006	YQTSNFRVAPSKEVVRFPNITNLCPFGEVFNATFSPSVYAWERKISNCVADYSVLYNST
HuSars-CoV NC_004718	YQTSNFRVAPSGLVVRFPNITNLCPFGEVFNATFSPSVYAWERKISNCVADYSVLYNST
Residues 300-359	*****.* * :*****:*****:*****:*****:*****

BatCoV KC881006	SFSTFKCYGVSATKLNLDLCSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDEFSGC
HuSars-CoV NC_004718	SFSTFKCYGVSATKLNLDLCSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDEFSGC
Residues 360-419	***** ***** **

BatCoV KC881006	VLAWNTRNIDATGTGNYNYKYRSLRHGKLRPFERDISNVPFSPDGKPCPPALNCYWPLN
HuSars-CoV NC_004718	VLAWNTRNIDATGTGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCPPALNCYWPLN
Residues 420-479	*****.* ***** *****:*****

BatCoV KC881006	DYGFYITNGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLT
HuSars-CoV NC_004718	DYGFYITNGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLT
Residues 480-539	*****.* *****

BatCoV KC881006	PSSKRFQPFQQFGRDVSDFDTSVRDPKTSEILDSPCSFGGVSVITPGTNSSEVAVLYQ
HuSars-CoV NC_004718	PSSKRFQPFQQFGRDVSDFDTSVRDPKTSEILDSPCAFSGGVSVITPGTNSSEVAVLYQ
Residues 540-599	*****:*****:*****

BatCoV KC881006	DVNCTDVPVAIHADQLTPSWRYSTGNNVFQQTQAGCLIGAEHVDTSEYCDIPIGAGICAS
HuSars-CoV NC_004718	DVNCTDVPSTAIHADQLTPAWRYSTGNNVFQQTQAGCLIGAEHVDTSEYCDIPIGAGICAS
Residues 600-659	*****.* *****:*** *****

BatCoV KC881006	YHTVSLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMKTSVD
HuSars-CoV NC_004718	YHTVSLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMKTSVD
Residues 660-719	***** *****

BatCoV KC881006	CNMYICGDSTECANLLLQYGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKPTPLKDF
HuSars-CoV NC_004718	CNMYICGDSTECANLLLQYGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKPTPLKYF
Residues 720-779	*****.*****
BatCoV KC881006	GGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNG
HuSars-CoV NC_004718	GGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNG
Residues 780-839	*****
BatCoV KC881006	LTVLPPLLTDMMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLY
HuSars-CoV NC_004718	LTVLPPLLTDMMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLY
Residues 840-899	*****
BatCoV KC881006	ENQKQIANQFNKAISQIQESLTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVL
HuSars-CoV NC_004718	ENQKQIANQFNKAISQIQESLTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVL
Residues 900-959	*****
BatCoV KC881006	NDILSRLDKVEAEVQIDRLITGRQLSQTYYVTQQLIRAAEIRASANLAATKMSECVLGQS
HuSars-CoV NC_004718	NDILSRLDKVEAEVQIDRLITGRQLSQTYYVTQQLIRAAEIRASANLAATKMSECVLGQS
Residues 960-1019	*****
BatCoV KC881006	KRVDFCGKGYHLSMFPQAAPHGVVFLHVTVYVPSQERNFTTAPAICHEGKAYFPREGVFVF
HuSars-CoV NC_004718	KRVDFCGKGYHLSMFPQAAPHGVVFLHVTVYVPSQERNFTTAPAICHEGKAYFPREGVFVF
Residues 1020-1079	*****
BatCoV KC881006	NGTSWFITQRNFFSPQIITTDNTFVSGSCDVVIGIINNTVYDPLQPELDSFKEELDKYFK
HuSars-CoV NC_004718	NGTSWFITQRNFFSPQIITTDNTFVSGSCDVVIGIINNTVYDPLQPELDSFKEELDKYFK
Residues 1080-1139	*****.*****
BatCoV KC881006	NHTSPDVDLGDISGINASVVNIQKEINRLNEVAKNLNESLIDLQELGKYEQYIKWPYVW
HuSars-CoV NC_004718	NHTSPDVDLGDISGINASVVNIQKEINRLNEVAKNLNESLIDLQELGKYEQYIKWPYVW
Residues 1140-1199	*****.*****
BatCoV KC881006	LGFIAGLIAIVMVTILLCCMTSCCCLKGACSCGSCCKFDEDDSEPVKGVKLVHT
HuSars-CoV NC_004718	LGFIAGLIAIVMVTILLCCMTSCCCLKGACSCGSCCKFDEDDSEPVKGVKLVHT
Residues 1200-1255	*****

Table 3. S Protein sequence alignment of the first sequenced isolate of Human Sars-CoV/Tor2 (GenBank ID NC_004718) betacoronavirus lineage B (Ben Hu 2015) and genetically related CoV from Bat species, *Rhinolophus sinicus* CoV strain Rs3367 (GenBank ID KC881006) (Ge 2013). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

RatCoV KM349744.1	ALLYRNLKCSYVNNNISISRSVIRYFDSYLGCVFNADDDIAEAVGSCNLTVGSGLCVD
HuCoVHKU1 NC_006577	ALLYRNLKCSYVNN--ISLTTQPYFDSYLGCVFNADNLTIDYSVSCALRMGSGFCVD
Residues 690-746	*****:* ** :. *****.***: :*. ** * :*:***

RatCoV KM349744.1	YS-----TWRAKRDNTGYRLTNFEPFVPTLVNDSVESVGGLYEIQIPTEFTIGNLEEF
HuCoVHKU1 NC_006577	YNSPSSSSSRKRKRSISASRYRFTFEPFNVSEVNDSESVGGLYEIKIPTNFTIVQEEF
Residues 747-806	*.* : * :*.:.:*.:.**** :*:***:*****:***:*** . ***

RatCoV KM349744.1	VQTI SPKVTIDCAA FVC GDYAACREQLVEYGS FCDNIN TILNEVNSMIDTSQYQIAS TLM
HuCoVHKU1 NC_006577	QTN SPKVTIDCSL FVC SNYAACHDLISEYGFCDNIN SILDEVNGLLDTTQLH VADTLM
Residues 807-866	:*.*****: ***:***: : * ***:*****:***:***: :*:*** :*:***

RatCoV KM349744.1	NGVTLSSRLKDGISFNQDINFSSVMGCVGNCIS-HRSATIEDLFNKVKLSDVGFVLDAY
HuCoVHKU1 NC_006577	QVTLSSNLNLTNLHFQVDNINFSLVGCIGPHCSRSRFFEDLFDKVKLSDVGFVLDAY
Residues 867-926	:*****.*: .: * : *:*:*:*:*:*:* * * ** :*:***:*****:***:***

RatCoV KM349744.1	NNCTQGSEIRDLV CVQSFNGIKVLPPLSESGYATGVGLSMIFPFSAAAGVPTMS
HuCoVHKU1 NC_006577	NNCTGGSEIRDLV CVQSFNGIKVLPPLSESGYTAATVAAMFPPMSAAAGVPTSLN
Residues 927-986	*** *****:*****:*****:***:***:*. . : :*:***:*****:***:..

RatCoV KM349744.1	VQYRINGLGVMTDVLNQNKVIANAFNNALTAIQNGF DATNSALAKIQSVVNAHALNN
HuCoVHKU1 NC_006577	VQYRINGLGVMTDVLNKNQKLIATAFNNALLSIQNGFSATNSALAKIQSVVNSNAHALNS
Residues 987-1046	*****:***:*. ***** :*****.*****:***:***.

RatCoV KM349744.1	LLQQLSNRFGAIISSSLQEILSRLEALEAQVQIDRLINGRLTALNAYVSQQLSDIILVKFS
HuCoVHKU1 NC_006577	LLQQLFNKFGAIISSSLQEILSRLEALEAQVQIDRLINGRLTALNAYVSQQLSDIILVKFG
Residues 1047-1106	**** * :*****:*****:*****:*****:*****:*****:*****:*****.

RatCoV KM349744.1	ASQATEKVNCEKVSQS TRVNF CGNGNHILSLVQNAPYGLYFHFYSYQPTKYTTAVSPGL
HuCoVHKU1 NC_006577	AALAMEKVNCEKVSQSPRINFCGNGNHILSLVQNAPYGLLFMHFSYKPIISFKTVVSPGL
Residues 1107-1166	*: * :*****.*:*****:***** * :***:* .:. * . *****

RatCoV KM349744.1	CLAGDVG VAPKSGYFIKVNDRWMTGSAYYHPEPI TNDNVTMMNCAVNFTKAPLVVLT
HuCoVHKU1 NC_006577	CTSGDVG IAPKSGYFIKHNDHWMFTGSAYYHPEPISDRKNVVMNVCVNFTKAPLVVLT
Residues 1167-1226	*:*****:***.***** ** :*****:***:***:..*:*:*:* * **

RatCoV KM349744.1	STPNLPDFKEELDKWFKNQSSVAPLISLDERINVTFLDLQEMDRIQDAIKLNSYIN
HuCoVHKU1 NC_006577	SVPKLSDFESELSHWFKNQISTAPNLTLNLHTINATFLDLYEMNLIQESIKSLNNSYIN
Residues 1227-1286	*:*. * :*. :*. :*****:*. * :*. :*. * . * . ***** ** : * :*. * :*. * :***

RatCoV KM349744.1	LKIGTYEMYVKWPWYVWLLI GLAGVAVLVLLFFVCCCTGCGSCFKKCGSCCDYGGHC
HuCoVHKU1 NC_006577	LKIGTYEMYVKWPWYVWLLISFSFLIFLVLLFFVCCCTGCGSCFKKHNCCDYGGHH
Residues 1287-1346	** :*****:*****:..: . *****:*****:***. ** .***:****:

RatCoV KM349744.1	DIVVKTSHDD
HuCoVHKU1 NC_006577	DIVVKTSHDD
Residues 1347-1356	*: * :*****

Table 4. S Protein sequence alignment of the first sequenced isolate of HCoV-HKU1 (GenBank ID NC_006577) betacoronavirus lineage A (Ben Hu 2015) and genetically related CoV from Rat species, *Rattus norvegicus* Rat CoV strain HKU24 (GenBank ID KM349744.1) (lau 2015). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

BatCoV KY073744.1	MKLF TFM CIL SLGLA QKTCFS- GDYRE LK LG L PPSV NATVTG YLP FN W SCDS NS AGGR Y Y
HuCoVNL63 AY567487.2	MKLF LILL V FLAS CF FTCN S NANL S MLQL GP DNS STIVT GLLP HW FCAN Q TS----
Residues 1-56	**** : : : * . * . . * * * . : * : * : * . . : * * * * : * * . : * . :

BatCoV KY073744.1	AN ITNAHG V F VG Y FTG DRAS AF GL SS K F DEN Y Q MY FG HR NQ NS FR VR R ICK W ES VQ VP
HuCoVNL63 AY567487.2	--- V YS ANG F F Y ID V GN HR S AF L H T GY D AN Q Y I Y V T N E I G N AS V TL K ICK S R N IT
Residues 57-113	. : . * . . * : : * * * . * : . : * * * * : * . : . * : . * : . .

BatCoV KY073744.1	TL PR D PP V AP K DC I V DK Q F Y Q FA H K G H K I Y G T H S GR V R I H S T V G V H N F Y V P G AS N WD
HuCoVNL63 AY567487.2	F DF L SN A SS S FD C I V N L L F TE Q LG A F---- L GT T SG E T V R L H L Y N V T R T F Y V P A Y K LT
Residues 114-169	. . : . * : * : * * : . * : * : * : * : * : * : * : * : * : * : * : * : * : * : * :

BatCoV KY073744.1	T V A I A C D N P T S C Y H S V V T Q L A T V V Q T DD K L I S S F E P C Q N C E G F A E N V F A V E A S G K I P S
HuCoVNL63 AY567487.2	K L S V K C Y F N Y S C V E S V V N A T V T V N V T H N - G V V N Y T V C DD C N G T E N I F S V Q Q D G I P N
Residues 170-228	. : : : * * * * . * * * . * * * * : * : : * : : * : : * : : * : : * : : * : * : * : * : * : * :

BatCoV KY073744.1	D F S F N N W F L L T N S S V V D G K V R S I Q P L K V L C L R A V S L L S T K E V I S L S G V N A D K - C N G H S
HuCoVNL63 AY567487.2	C F F F N N W F L L T N S S T L V D G V S R L Q P L R L T C L W V E P G L K S S T G F V Y F N A T G S D V N C N G Y Q
Residues 229-288	. * . * * * * * * * . * : * * * * * * * * : * * * * * * * * : * * * * * * * * : * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	I N E T A G A L R F N L N F T S N P I N A L S G K I F I S S S F G N V T I F C S N S S D P G S S A D A F I A M G S T S
HuCoVNL63 AY567487.2	I N S V D V M R Y N L N F S A N S L D N L K S G V I V F K T L O Y D V L F Y C S N S S S -- G V I D T T I P E G S S
Residues 289-346	* : * : * * * : * : * * * : * * * * : * * * * : * * * * : * * * * : * * * * : * * * * : * * * * :

BatCoV KY073744.1	AA V Y C F A N S T E G N V T S L D F I G L P V T V R E F V A A T G Q L Y I N G F N Y F S L P D I L S V D F V K S
HuCoVNL63 AY567487.2	Q P Y C F I N S T I N T H V S T F V G L P E T V R E I V A A T G Q F Y I N G F N Y F S L G F I E A V N F N V I T
Residues 347-406	. * * * * * * : . . . * : * : * * * * * * * * : * * * * * * * * : * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	D N V T D F W T V A Y T Q F V D T L V A V N N T I Q E V L Y C D D V I H K L K C S Q L S F L E D G F Y S A S L V R D
HuCoVNL63 AY567487.2	A S A T D F W T V A F A T F V D V L V N V S A T I Q N L L Y C D S P F E K L O C E H L E F G L D G F Y S A N F L D
Residues 407-466	. * * * * * * : : * * * * * * * * . * * * : * * * * * * . : * * * * * * * * . * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	E R L D K T E V T L P T H S D H S N V T L Y S F N T Y S S T C T T K P D H V T S C Q Y N V T I V G E N D G P V C V K
HuCoVNL63 AY567487.2	N V L E E T Y V A L P T Y Q H T D I N F T A S F G G - S C Y V K K P H Q V N I S L N G N T S V C V R T S H F S I R
Residues 467-525	: * : * * * * * : : * * * * * : . . . * . * * * * * . . . * * : * * :

BatCoV KY073744.1	S K Q F T P L L Q T S I P T G Y V S V E S G S C P F N F L K L K N Y L T F D S L C F S T K Q L P G G S M L I K R S N
HuCoVNL63 AY567487.2	Y I Y N R V K S G S P D S S W H I Y L K S G S C P F S F S K L N F Q R F K T I C F S T V E V P G S C N F P L E A T W
Residues 526-585	. . : . . : : * * * * * * * * * * : * * * * * * * * : * * * * * * * * : * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	V N Y N S D I G - V I Y S H S P G N I L G V P O A S T G V K D L S Y I V T D V C T Y I Y G K S G K G I R K T N
HuCoVNL63 AY567487.2	H Y T S Y T I V G A L Y V T W S E G N S I L G V P Y P V S G I R E F S N I V L N N C T K Y N I Y D Y V G I G I R S S N
Residues 586-645	. * . : * * : * * * * * * * . : * * * * * * * * : * * * * * * * * . * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	S S L P A G I M Y T S S G S L L G F K N V T D S T V Y T V T P C A T A T Q L A V Y K Q R V L G A I T A V K N D S E G F
HuCoVNL63 AY567487.2	Q S L A G G I T Y V S S G N L L G F K N V S T G N I F I V T P C N O P D Q V A V Y Q S I L G A M T A V N E S R Y G L
Residues 646-705	. * * . * * * * * * * * * * * * : . : : * * * * . * * * * * * * * : * * * * * * * * : * * * * * * * * :

BatCoV KY073744.1	NSTLLPLFYYSNGKVNCTEPIILVYSIGICPDGTMIQIKPVETPQVVAPIVTANLSI
HuCoVNL63 AY567487.2	QNLQLPNFYYSNGGNCTAVMTYSNFGICADGSIIFVPRPNSSDNGISAITTANLSI
Residues 706-765	:. * ** *** ** * ** * ..:.*.:**.*:.* :.* :.: :.:*:*:**.*
BatCoV KY073744.1	PLNFTTSVQVEYLQLSRPVSVDCATYVCGNPRCLTLLTQYSACKTAEEALQLAALE
HuCoVNL63 AY567487.2	PLNFTTSVQVEYLQLTSTPTIVVDCATYVCGNPRCKNLLKQYTSACKTLEDALRLAALE
Residues 766-825	* *:******:.* * : ***** ***** .**.*:*:** *:*:*:*:**
BatCoV KY073744.1	ASEVNSMIKLSPTAIDNANKLGVSTYQGGFNLSVVPQTPASTSGSFRGSFIEDLLFNKV
HuCoVNL63 AY567487.2	TNEVSSMLTFDSNAFSLANVTSEGEYN---LSVVPQENIRSSIVAGRSALIEDLLFSKV
Residues 826-881	:.*:*:*:*:*:*:*:*:* * .. * : *:*:* * : * * :*****.**
BatCoV KY073744.1	VTSGGLTVDADYKCTKGLSIADLACAQYYNGIMVLPGVDAEEMAMYTASLIGSMVGG
HuCoVNL63 AY567487.2	VTSGGLTVDADYKCTKGLSIADLACAQYYNGIMVLPGVDAEEMAMYTASLIGSMVGG
Residues 882-941	:*****.*.*.******.******.***:*:**.* *:*:**
BatCoV KY073744.1	LSAASIPFSLAVQSRNLNYVALQTDVLQENQKILAASFNKAISSITQAFTEVNDATQTS
HuCoVNL63 AY567487.2	LSAASIPFSLAVQSRNLNYVALQTDVLQENQKILAASFNKAINNIVASFSSVNDATQTA
Residues 942-1001	*:*:**:*:**:*:******.******.*.* :.*:*:**:*:**
BatCoV KY073744.1	QAITVAGALNKIQVNVNQGSALSHLTQQLQNNFQAISSSIEDIYNRLDSLAAQAQVDR
HuCoVNL63 AY567487.2	QAITVVTIALNKIQVNVNQGSALSHLTQQLQNNFQAISNSIQAIYNRLDSLAAQAQVDR
Residues 1002-1061	:** ** : *****.***:*:**.***.***.***.***.***.***.***.***.***
BatCoV KY073744.1	LITGRLAALNSFVQQLTRQTVRARSRELAMQKINECVKSQSDRYGFCGNGTHLFSIANA
HuCoVNL63 AY567487.2	LITGRLAALNSFVQQLNKYTVRGRSRLAACQKINECVKSQSNRYGFCGNGTHLFSIVNS
Residues 1062-1121	*****.***:*:**.***.***.***.***.***.***.***.***.***.***.***.***
BatCoV KY073744.1	APFGLLFLHTVLPFDYVTVEAWSGICFGGDKGFLRDFQLTLIKYDNKYKVTSRMFQP
HuCoVNL63 AY567487.2	APFGLLFLHTVLPFDYKNVKAWSGICVDGIYGVLRQPNLVLVSDNGVFRVTSRVMFQP
Residues 1122-1181	**:******:* ** .:******.* * ::*:** :.* * . :. :.*** **
BatCoV KY073744.1	RNAEISDFIQISNCVQFINLTQDQVDVIPEYVDVNKTLQEEALSKLFPNYTKPDLSDLVF
HuCoVNL63 AY567487.2	RLPVLSDFVQISNCVQFINISRVELHTVIPDYVDVNKTLQEEAQLFPKYVKNPDLTPF
Residues 1182-1241	* . :***:* *:* * *:*:* :.: *:*:******.* :.***:***.***.*
BatCoV KY073744.1	NQTYLNLSSSIDQLECKAESLNTTIKQLQSLIDQINSTLVLDLEWLNRFENYIKWPWWVWL
HuCoVNL63 AY567487.2	NQTYLNLSSLEQLEAKTASLFTTVELOGLIDQINSTLVLDLKLNRFFENYIKWPWWVWL
Residues 1242-1301	* *****:.* * * : * : *:*:***.****** *:* : * . *****
BatCoV KY073744.1	IIAVVLIFFVSLIMFCCIATGCGCCSCMTSSLRGCCDCGSTKLPYYEFKVVHVQ
HuCoVNL63 AY567487.2	IIAVVLIFFVSLIMFCCLSGCGCCNCLTSSLRGCCDCGSTKLPYYEFKVVHVQ
Residues 1302-1356	**:***:*:*:*:*:*:*:* * ** .:***:******.******

Table 5. S Protein sequence alignment of the first sequenced isolate of HCoV-NL63 (GenBank ID AY567487.2) Alphacoronavirus (Ben Hu 2015) and genetically related CoV from Bat species,

Triaenops afer CoV strain BtKYNL63-9a (GenBank ID KY073744.1) (De Sabato 2019). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

BatCoV KC869678.4	MTYSVFPLMCLLFIIGANAKIVTLFGNDATGYCPSVDMQPSYFIQHNWEEPIDMKADGV
MERS-CoV JX869059	----MIHSVFLMFLLLPTESYVDVGHDSVKSACIEVDIQQTFDKTWERPIDVSKADGI
Residues 1-56	:: : ** *: : :: . * *:. . * : : : ** . ** : . ** :
BatCoV KC869678.4	IYFNGRTYSNITLQTTNLFPGKGLGTOYVYASNHK-STANDAFISNYSYYGNPFGIGI
MERS-CoV JX869059	IYFGRTYSNITITYOGLFFYQGLHGDYVYSA GHATGTTPOKLFVANYSQDVKQFANGF
Residues 57-116	***:*****: .*** :** * *****: . :*:. * : ** : * : ** :
BatCoV KC869678.4	VIRIGONANKTGVIVG-QAQTMLFKIYPALMLGSSFGNFSAMKSGAYFNHTLLILPSK
MERS-CoV JX869059	VIRIGAAANSTGVIVISFSTSATIRKIYPALMLGSSVGNFSDG-KMGRFFNHTLLVLFDG
Residues 117-175	*.*** ** .** : ** : . . : * : ** : ** : ** : ** : ** : ** : ** :
BatCoV KC869678.4	CGTVFQVAYCLLQPRTESKCPGNSNYVSYFLADSPSDCSSTSEIRNGLRDIRKIFNLV
MERS-CoV JX869059	CGTLLRAFYCLLQPRSCNHCFAGNSYTSFATYHTPATDCSDGNYNRNASLNSFKEYFNLR
Residues 176-235	***: : . ** : * : ** : . ** : . . . * : . : * : . * : . . . : **
BatCoV KC869678.4	NCTYFEEFNVTADERAEWFGIQVLAQGVHLVTSRKNGFNSNMLFATVFIYDKLNYITV
MERS-CoV JX869059	NCTFMYTYNITLDELEWFGIQVLAQGVHLFSRQVVDLYGGMVGFATLFPVYDTIKYYSI
Residues 236-294	***: : : * : * * ***** * ***** : * * . : . : * * * * : * * : : * * :
BatCoV KC869678.4	IERSVITPSNQRDAWAAFYIYPLHQLSYLLNFVNGYITQAADCGINDYTQLICSYGDFN
MERS-CoV JX869059	IERSISICSDRDAWAAFYVYKQLQELTFLDFSVNGYIRRAIDCGINDLSQLFCSYSESF
Residues 295-354	** : * : . . : * . ***** : * * : * : * * : * * : * * : * * : * * : * * :
BatCoV KC869678.4	MKSGVYSISYYSAKPVGAYYEAHVYFDCNFTLFRERAPTIMOYKREVFTRCNYNLSILL
MERS-CoV JX869059	VEKSGVYSVSEFAKPSGSVVEQAEVVECDFSELSGTEPPQVYNERKRVFTNCNYNLEKLL
Residues 355-414	::*****.* :.*** *: * : * : * : * : * : * : * : * : * : * : * : * :
BatCoV KC869678.4	SLVQVDEFVCDKIPALATGCYSSLTVDWFATPYAWKSYLAIGSADRIVRFNYNODYSN
MERS-CoV JX869059	SLEFSVNDFTCSQISPAATASNCYSSLIIDYFSYPLSMKSDLSVSSAGHISCFNYKQSESN
Residues 415-474	**..* : * : * : * * : * : * * * : * : * * : * : * * : * : * * : * : * :
BatCoV KC869678.4	PSCRHISKVNSSIG-ISYAGAYSITNCNYGATNKDDVVKPGRASQOCITGALNSFTTG
MERS-CoV JX869059	PTCILATVPHNLTITIKPLKYSYINKSRLLSDDRTEVPQLVNANQYSPCVSIVPSTVW
Residues 475-534	* : * * : . * : . : * : . ***** : * . : . . * : . * : . : . * . : . . * .
BatCoV KC869678.4	QLWAYNFGGVPYR----VSRLTYTDHLSDELDMVYVITVKYEPGAETVCPKQIRPDYST
MERS-CoV JX869059	EDGDYIRKQLSPLEGGGWLVASGSTVAMTEQLMGFGITVQYGTDTNSVCPKLEFAN-DT
Residues 535-594	: * : . : * : : * : * : * : * : * : * : * : * : * : * : * : * :
BatCoV KC869678.4	NITHLIGSCISYDIYGITGTGVFLCNATGIRQQRFVYDKFDNIIGFHSDDGNYYCVAPC
MERS-CoV JX869059	KIASQLGNCEVYSIYGVSGRQVFNQNTAVGVRQQRFVYDAYQNVGYYSDDGNYCLRAC
Residues 595-654	: * : * * : * : * : * : * :
BatCoV KC869678.4	VSVFVSVIYDRTNQYATLFGSVACCHIS TMAAQFSRETRASLVS RNQN-LLQT VGCV
MERS-CoV JX869059	VSVFVSVIYDKETKTHATLFGSVACCHIS STMSQFSRSTRSMLKRDSTYGLQTVGCV
Residues 655-714	*****. * : : ***** : * * : * : * * : * * : * * : * * : * * :

BatCoV KC869678.4	MGFHETNDTVEECHLSLGQSLCAFPNTNLRSGRSTFGLG-----SLAYNSPLRVDALN
MERS-CoV JX869059	GLVNSSLFEVCKLFLGQSLCAFPDTPSTLTFRSVRSVPGEMRLASLAFNHPIQVDQLN
Residues 715-774	:*: ::. **:*.*.*****:* ... : ** . : : *:*:* *:* **
BatCoV KC869678.4	SSFVKVSLPLNFFGVQTQEYIETSIQKIIVDCKQYVCNGFAKCELLEQYGFCSKINQA
MERS-CoV JX869059	SSFVKLSLPLNFFGVQTQEYIETSIQKIIVDCKQYVCNGFAKCEQLLREYGFCSKINQA
Residues 775-834	** *:*: **:*****:*:***:***** ***:**.:*****
BatCoV KC869678.4	LHGANLRQDDSVRNLFESVKTPQTVPLTTGFGGFNLTLLLEPLSVSTGSSNARSAEELL
MERS-CoV JX869059	LHGANLRQDDSVRNLFESVKSSQSSPLIFGFGGFNLTLLLEPLSVSTGSSARSAEELL
Residues 835-894	***** ***: * : .****:*****:*:*** .****:***
BatCoV KC869678.4	FDSVTIADPGYMQGYDDCMQQGPASARDLICAQYVAGYKVLPLMDVNMEAAYTSSLGSS
MERS-CoV JX869059	FDSVTIADPGYMQGYDDCMQQGPASARDLICAQYVAGYKVLPLMDVNMEAAYTSSLGSS
Residues 895-954	** .*****
BatCoV KC869678.4	IAGVGTAGLSSFAAIPFAQSI FYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT
MERS-CoV JX869059	IAGVGTAGLSSFAAIPFAQSI FYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT
Residues 955-1014	** .*****:*****
BatCoV KC869678.4	TNEAFQKVQDAVNNNAQALAKLASELSNTFGAISSSIGDIIQRLDVLEQEVQIDRLINGR
MERS-CoV JX869059	TNEAFQKVQDAVNNNAQALAKLASELSNTFGAISSSIGDIIQRLDVLEQDAQIDRLINGR
Residues 1015-1074	***** .*****:*****:*****:*****:*****
BatCoV KC869678.4	LTTLNAFVAQQLVRSESAARSAQLAKDKVNECVKQSRSGFCGQGTHIVSFVINAPNGL
MERS-CoV JX869059	LTTLNAFVAQQLVRSESAARSAQLAKDKVNECVKQSRSGFCGQGTHIVSFVINAPNGL
Residues 1075-1134	***** *****:*. *****:*****
BatCoV KC869678.4	YFMHVGYPSPCHIEVVAAYGLCDANPTNCIAPVNGYFIKNTNTRSADEWSYTGSSFYAP
MERS-CoV JX869059	YFMHVGYPSPCHIEVVAAYGLCDANPTNCIAPVNGYFIKNTNTRTVDEWSYTGSSFYAP
Residues 1135-1194	*****:*.*****:*****:*****:*****:*****:*. *****
BatCoV KC869678.4	EPITLNTRYVAPQVTYQNISNLPPPLLSNSTGIDFKDELDEFKKNVSTNIPNFGSLTQ
MERS-CoV JX869059	EPITLNTKYVAPQVTYQNISNLPPPLLSNSTGIDFKDELDEFKKNVSTNIPNFGSLTQ
Residues 1195-1254	***:***:*****:*** ***** .**** ***:*****.*****:***
BatCoV KC869678.4	INTTLLDLSCGEMLAQEVVKALNESYIDLKELGNITYYNKWPWYIWLGFIAGLVALALCV
MERS-CoV JX869059	INTTLLDLTYEMLSLQEVVKALNESYIDLKELGNITYYNKWPWYIWLGFIAGLVALALCV
Residues 1255-1314	*****: ***:**:*****:*****:*****:*****:*****
BatCoV KC869678.4	FFILCCTGCGTSCMGKLCNRCCDYEEYDLEPHKIHVH
MERS-CoV JX869059	FFILCCTGCGTSCMGKLCNRCCDYEEYDLEPHKIHVH
Residues 1315-1353	***** .*:*****:*****:***

Table 6. S Protein sequence alignment of the first sequenced isolate of MERS-CoV (GenBank ID JX869059) betacoronavirus lineage C (Ben Hu 2015) and genetically related CoV from the Bat

species, *Neoromicia capensis* CoV strain Neoromicia/PML-PHE1/RSA/2011 (GenBank ID KC869678.4) (Ithete 2013). Green-red amino acid substitution during the host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

BatCoV RaTG13 MN996532.1	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSSTRGVYYPDKVFRSSVLHITQDLFLPFFS
SarsCov2 MT019529.1	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSSTRGVYYPDKVFRSSVLHSTQDLFLPFFS
Residues 1-60	*****

BatCoV RaTG13 MN996532.1	NVTWFHAIHVSQTNGIKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLV
SarsCov2 MT019529.1	NVTWFHAIHVSQTNGIKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLV
Residues 61-120	*****

BatCoV RaTG13 MN996532.1	NNATNVVIKVCFFQFCNDPFLGVYHKNKNSWMESEFRVYSSANNCTFEYVSQPFLMDLE
SarsCov2 MT019529.1	NNATNVVIKVCFFQFCNDPFLGVYHKNKNSWMESEFRVYSSANNCTFEYVSQPFLMDLE
Residues 121-180	*****

BatCoV RaTG13 MN996532.1	GKQGNFKNLREFVFNIDGYFKIYSKHTPINLVRDLPFGFSALEPLVDLPIGINITRFQT
SarsCov2 MT019529.1	GKQGNFKNLREFVFNIDGYFKIYSKHTPINLVRDLPFGFSALEPLVDLPIGINITRFQT
Residues 181-240	*****

BatCoV RaTG13 MN996532.1	LLALHRSYLTPGDSSSGWTAGAAAYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK
SarsCov2 MT019529.1	LLALHRSYLTPGDSSSGWTAGAAAYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK
Residues 241-300	*****

BatCoV RaTG13 MN996532.1	CTLKSFTVEKGIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATIFASVYAWNRRKRISN
SarsCov2 MT019529.1	CTLKSFTVEKGIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATIFASVYAWNRRKRISN
Residues 301-360	*****

BatCoV RaTG13 MN996532.1	CVADYSVLVNSISFSTFKCYGVSPTKLNLDLCTNVYADSFVIGDEVRQIAPGQTGKIAD
SarsCov2 MT019529.1	CVADYSVLVNSISFSTFKCYGVSPTKLNLDLCTNVYADSFVIGDEVRQIAPGQTGKIAD
Residues 361-420	*****

BatCoV RaTG13 MN996532.1	YNYKLPDDFTGCVIAWNSKHIDAKKGGNENLYRLFRKANLKPFERDISTEIQAGSKPC
SarsCov2 MT019529.1	YNYKLPDDFTGCVIAWNSNNLDSKVGGNENLYRLFRKANLKPFERDISTEIQAGSKPC
Residues 421-480	*****

BatCoV RaTG13 MN996532.1	NGQTGLNICYPLRYGYFPTDGVGHQPYRVVLSFELLNAPATVCGPKKSTNLVKNKCVN
SarsCov2 MT019529.1	NGVEGFNICYPLRQSYGYFOPTDGVGHQPYRVVLSFELLNAPATVCGPKKSTNLVKNKCVN
Residues 481-540	** *:***:** *** **:*:**:*****:*****

BatCoV RaTG13 MN996532.1	FNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLIILDITPCSFGGVSVITP
SarsCov2 MT019529.1	FNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLIILDITPCSFGGVSVITP
Residues 541-600	*****

BatCoV RaTG13 MN996532.1	GTNLSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNSY
SarsCov2 MT019529.1	GTNLSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNSY
Residues 601-660	***:*****

BatCoV RaTG13 MN996532.1	ECDIPIGAGICASYQTQNTS-----RSVASQSI IAYTMSLGAENSVAYSNNIAIPTNFTI
SarsCov2 MT019529.1	ECDIPIGAGICASYQTQNTSPRRARRSVASQSI IAYTMSLGAENSVAYSNNIAIPTNFTI
Residues 661-720	*****

BatCoV RaTG13 MN996532.1	SVTTEILPVSMTKTSVDCTMYICGDSTECSNLLQYGSFCTQLNRALTGIAVEQDKNTQE
SarsCov2 MT019529.1	SVTTEILPVSMTKTSVDCTMYICGDSTECSNLLQYGSFCTQLNRALTGIAVEQDKNTQE
Residues 721-780	*****
BatCoV RaTG13 MN996532.1	VFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDC
SarsCov2 MT019529.1	VFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDC
Residues 781-840	*****
BatCoV RaTG13 MN996532.1	LGDI AARDL ICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAM
SarsCov2 MT019529.1	LGDI AARDL ICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAM
Residues 841-900	*****
BatCoV RaTG13 MN996532.1	QMAYRFNGIGVTVQNVLYENQKLIANQFN SAIGKIQDSLSTASALGKLQDVVNQNAQALN
SarsCov2 MT019529.1	QMAYRFNGIGVTVQNVLYENQKLIANQFN SAIGKIQDSLSTASALGKLQDVVNQNAQALN
Residues 901-960	*****
BatCoV RaTG13 MN996532.1	TLVKQLSSNFGAISSVLNDILSRDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRA
SarsCov2 MT019529.1	TLVKQLSSNFGAISSVLNDILSRDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRA
Residues 961-1020	*****
BatCoV RaTG13 MN996532.1	SANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPA
SarsCov2 MT019529.1	SANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPA
Residues 1021-1080	*****
BatCoV RaTG13 MN996532.1	ICHDKAHFPREGV FVSNGTHWFVTQRNFYEPQIITDNTFVSGCDVVIGIVNNTVYDP
SarsCov2 MT019529.1	ICHDKAHFPREGV FVSNGTHWFVTQRNFYEPQIITDNTFVSGCDVVIGIVNNTVYDP
Residues 1081-1140	*****
BatCoV RaTG13 MN996532.1	LQPELDSFKEELD KYFKNHTSPD VDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDL
SarsCov2 MT019529.1	LQPELDSFKEELD KYFKNHTSPD VDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDL
Residues 1141-1200	*****
BatCoV RaTG13 MN996532.1	QELGKYEQYIKWPWYIWLGFIAGLIAIMVTIMLCMTSCC SCLKGCCSCGSCCKFDEDD
SarsCov2 MT019529.1	QELGKYEQYIKWPWYIWLGFIAGLIAIMVTIMLCMTSCC SCLKGCCSCGSCCKFDEDD
Residues 1201-1260	*****
BatCoV RaTG13 MN996532.1	SEPVLKGVKLHYT
SarsCov2 MT019529.1	SEPVLKGVKLHYT
Residues 1261-1273	*****

Table 7. S Protein sequence alignment of the first sequenced isolate of SARS-CoV-2 BetaCoV/Wuhan/IPBCAMS-WH-01/2019 (GenBank ID MT019529.1) betacoronavirus lineage B (Ren LL 2020) and genetically related CoV from the Bat species, *Rhinolophus affinis* CoV strain RaTG13, (GenBank ID MN996532.1) (Zhou P 2020). Green-red amino acid substitution during the

host tropism, green-blue ongoing mutations at the residue after the host tropism. Blue amino acid substitution at the clinical isolate. Purple recombination in the form of deletion or insert.

CLUSTALW Result

Supplementary Material 1 Sequence Alignment of HuCoV229E Isolates

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Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

Sequence format is Pearson

Sequence 1: NC_002645.1 1173 aa
Sequence 2: MN369046.1 1171 aa
Sequence 3: MN306046.1 1171 aa
Sequence 4: KM055531.1 1171 aa
Sequence 5: KM055537.1 1171 aa
Sequence 6: KM055538.1 1171 aa
Sequence 7: KM055551.1 1170 aa
Sequence 8: KM055554.1 1170 aa
Sequence 9: KM055557.1 1170 aa
Sequence 10: KY996417.1 1171 aa
Sequence 11: KY983587.1 1171 aa
Sequence 12: KY674919.1 1170 aa
Sequence 13: KY684760.1 1171 aa
Sequence 14: KF514430.1 1170 aa
Sequence 15: KF514429.1 1170 aa
Sequence 16: KF514431.1 1170 aa
Sequence 17: KF514433.1 1170 aa
Sequence 18: JX503060.1 1171 aa
Sequence 19: JX503061.1 1170 aa
Sequence 20: AB691763.1 1173 aa
Sequence 21: AB691764.1 1170 aa
Sequence 22: AB691767.1 1170 aa
Sequence 23: DQ243966.1 1170 aa
Sequence 24: DQ243971.1 1170 aa
Sequence 25: DQ243973.1 1170 aa
Sequence 26: DQ243974.1 1170 aa
Sequence 27: DQ243977.1 1170 aa
Sequence 28: DQ243979.1 1170 aa
Sequence 29: DQ243980.1 1170 aa

Start of Pairwise alignments

Aligning...

Sequences (1:2) Aligned. Score: 93.766
Sequences (1:3) Aligned. Score: 93.766
Sequences (1:4) Aligned. Score: 94.1076
Sequences (1:5) Aligned. Score: 94.2784
Sequences (1:6) Aligned. Score: 94.3638
Sequences (1:7) Aligned. Score: 94.4444

Sequences (1:8) Aligned. Score: 94.5299
Sequences (1:9) Aligned. Score: 94.7863
Sequences (1:10) Aligned. Score: 94.4492
Sequences (1:11) Aligned. Score: 93.8514
Sequences (1:12) Aligned. Score: 94.5299
Sequences (1:13) Aligned. Score: 93.8514
Sequences (1:14) Aligned. Score: 95.1282
Sequences (1:15) Aligned. Score: 95.812
Sequences (1:16) Aligned. Score: 94.7009
Sequences (1:17) Aligned. Score: 95.1282
Sequences (1:18) Aligned. Score: 94.4492
Sequences (1:19) Aligned. Score: 94.5299
Sequences (1:20) Aligned. Score: 99.5737
Sequences (1:21) Aligned. Score: 94.5299
Sequences (1:22) Aligned. Score: 94.5299
Sequences (1:23) Aligned. Score: 97.0085
Sequences (1:24) Aligned. Score: 96.2393
Sequences (1:25) Aligned. Score: 95.2991
Sequences (1:26) Aligned. Score: 95.2991
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Sequences (1:28) Aligned. Score: 94.5299
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Guide tree file created: [clustalw.dnd]

There are 28 groups
Start of Multiple Alignment

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Group 3: Sequences: 4 Score:19229
Group 4: Sequences: 2 Score:19232
Group 5: Sequences: 6 Score:19226
Group 6: Sequences: 2 Score:19263
Group 7: Sequences: 2 Score:19217
Group 8: Sequences: 3 Score:19202
Group 9: Sequences: 5 Score:19144
Group 10: Sequences: 6 Score:19165
Group 11: Sequences: 2 Score:19255
Group 12: Sequences: 3 Score:19263
Group 13: Sequences: 9 Score:19129
Group 14: Sequences: 2 Score:19276
Group 15: Sequences: 11 Score:19119
Group 16: Sequences: 12 Score:19066
Group 17: Sequences: 13 Score:19107
Group 18: Sequences: 19 Score:19028
Group 19: Sequences: 20 Score:19036
Group 20: Sequences: 21 Score:19060
Group 21: Sequences: 22 Score:19061
Group 22: Sequences: 2 Score:19264
Group 23: Sequences: 24 Score:19061
Group 24: Sequences: 25 Score:19023
Group 25: Sequences: 26 Score:18954
Group 26: Sequences: 2 Score:19283
Group 27: Sequences: 3 Score:18776
Group 28: Sequences: 29 Score:18486
Alignment Score 2857391

CLUSTAL-Alignment file created [clustalw.aln]

clustalw.aln

CLUSTAL 2.1 multiple sequence alignment

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JX503061.1 MFVLLVAYALLHIAGCQTTNGMNTSHSVCNGCVGHSENVFAVESGGYIPSNFAFNNWFL
DQ243980.1 MFVLLVAYALLHIAGCQTTNGMNTSHSVCNGCVGHSENVFAVESGGYIPSNFAFNNWFL

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DQ243971.1
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Select tree menu ▼

Exec

[\[clustalw.aln\]](#)[\[clustalw.dnd\]](#)[\[readme\]](#)

Select tree menu ▾

Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

Sequence format is Pearson

Sequence 1:	NC_005147.1	1361	aa
Sequence 2:	MN306036.1	1358	aa
Sequence 3:	MN306042.1	1358	aa
Sequence 4:	MN306053.1	1358	aa
Sequence 5:	MK303619.1	1358	aa
Sequence 6:	KU745533.1	1358	aa
Sequence 7:	NC_006213.1	1353	aa
Sequence 8:	MH121121.1	1358	aa
Sequence 9:	MG197709.1	1362	aa
Sequence 10:	MG977444.1	1359	aa
Sequence 11:	MF314143.1	1362	aa
Sequence 12:	KY014282.1	1362	aa
Sequence 13:	MF374983.2	1358	aa
Sequence 14:	KY983583.1	1358	aa
Sequence 15:	KY554972.1	1358	aa
Sequence 16:	KY674917.1	1358	aa
Sequence 17:	KX538964.1	1358	aa
Sequence 18:	KX344031.1	1358	aa
Sequence 19:	KU131570.1	1359	aa
Sequence 20:	KF572840.1	1361	aa
Sequence 21:	KF923886.1	1362	aa
Sequence 22:	KF923889.1	1362	aa
Sequence 23:	KF923890.1	1358	aa
Sequence 24:	KF923897.1	1358	aa
Sequence 25:	KF923914.1	1358	aa
Sequence 26:	KF923923.1	1358	aa
Sequence 27:	KF963229.1	1353	aa
Sequence 28:	KF963231.1	1361	aa
Sequence 29:	KF963232.1	1361	aa
Sequence 30:	KF963234.1	1363	aa
Sequence 31:	KF963240.1	1358	aa
Sequence 32:	KF572808.1	1362	aa
Sequence 33:	KF572818.1	1361	aa
Sequence 34:	KF572833.1	1358	aa
Sequence 35:	KF572872.1	1358	aa
Sequence 36:	KF923891.1	1358	aa
Sequence 37:	KF923900.1	1361	aa
Sequence 38:	KJ958218.1	1358	aa
Sequence 39:	KF530062.1	1356	aa
Sequence 40:	KF530065.1	1356	aa

Sequence 41: KF530068.1 1361 aa
Sequence 42: KF530073.1 1356 aa
Sequence 43: KF530083.1 1356 aa
Sequence 44: JN129834.1 1361 aa
Sequence 45: AY903458.1 1361 aa
Sequence 46: AY903460.1 1361 aa

Start of Pairwise alignments

Aligning...

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Sequences (22:28) Aligned. Score: 95.8119
Sequences (22:29) Aligned. Score: 95.8119
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Sequences (22:37) Aligned. Score: 95.2976
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Sequences (36:45) Aligned. Score: 99.3373
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Sequences (45:46) Aligned. Score: 99.9265
Guide tree file created: [clustalw.dnd]

There are 45 groups
Start of Multiple Alignment

Aligning...
Group 1: Sequences: 2 Score:22616
Group 2: Sequences: 3 Score:22621
Group 3: Sequences: 2 Score:22625
Group 4: Sequences: 5 Score:22601
Group 5: Sequences: 6 Score:22590
Group 6: Sequences: 7 Score:22585
Group 7: Sequences: 2 Score:22604
Group 8: Sequences: 3 Score:22603
Group 9: Sequences: 2 Score:22624
Group 10: Sequences: 5 Score:22516
Group 11: Sequences: 6 Score:22521
Group 12: Sequences: 7 Score:22508

Group 13:	Sequences:	2	Score:22597
Group 14:	Sequences:	9	Score:22523
Group 15:	Sequences:	2	Score:22431
Group 16:	Sequences:	3	Score:22437
Group 17:	Sequences:	2	Score:22594
Group 18:	Sequences:	5	Score:22472
Group 19:	Sequences:	14	Score:22385
Group 20:	Sequences:	15	Score:22442
Group 21:	Sequences:	22	Score:22444
Group 22:	Sequences:	23	Score:22359
Group 23:	Sequences:	2	Score:22656
Group 24:	Sequences:	3	Score:22622
Group 25:	Sequences:	2	Score:22653
Group 26:	Sequences:	5	Score:22611
Group 27:	Sequences:	28	Score:22421
Group 28:	Sequences:	2	Score:22619
Group 29:	Sequences:	3	Score:22518
Group 30:	Sequences:	31	Score:22285
Group 31:	Sequences:	2	Score:22494
Group 32:	Sequences:	3	Score:22175
Group 33:	Sequences:	2	Score:22560
Group 34:	Sequences:	3	Score:22540
Group 35:	Sequences:	4	Score:22536
Group 36:	Sequences:	7	Score:21911
Group 37:	Sequences:	2	Score:22435
Group 38:	Sequences:	3	Score:22515
Group 39:	Sequences:	4	Score:22419
Group 40:	Sequences:	5	Score:22403
Group 41:	Sequences:	6	Score:22451
Group 42:	Sequences:	7	Score:22388
Group 43:	Sequences:	8	Score:22308
Group 44:	Sequences:	15	Score:21814
Group 45:	Sequences:	46	Score:21571

Alignment Score 8581234

CLUSTAL-Alignment file created [[clustalw.aln](#)]

[clustalw.aln](#)

CLUSTAL 2.1 multiple sequence alignment

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KF923890.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISDSTDVDVTNGLGTYVYVLR
KY554972.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISDSTDVDVTNGLGTYVYVLR
KY674917.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISDSTDVDVTNGLGTYVYVLR
KF923923.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISDSTDVDVTNGLGTYVYVLR
KF572872.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISDSTDVDVTNGLGTYVYVLR
MN306036.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISIDSTDVDVTNGLGTYVYVLR
MN306053.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISIDSTDVDVTNGLGTYVYVLR
MN306042.1      MFLILLISLPTAFAVIGDLNCLDPRLRGSFNNRDTGPPSISIDSTDVDVTNGLGTYVYVLR
MH121121.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISIDSTDVDVTNGLGTYVYVLR
KY983583.1      MFLILLISLPTAFAVIGDLNCLDPRCLKGSFNNRDTGPPSISIDSTDVDVTNGLGTYVYVLR
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KF572872.1 TNFEPFTVNSVNDSELPVGGGLYEIQIPSEFTIGNMEEFIQTSSPKVTIDCAAFVCGDYAA
MN306036.1 TNFEPFTVNSVNDSELPVGGGLYEIQIPSEFTIGNMEEFIQTSSPKVTIDCAAFVCGDYAA
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MN306042.1 TNFEPFTVNSVNDSELPVGGGLYEIQIPSEFTIGNMEEFIQTSSPKVTIDCAAFVCGDYAA
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KU745533.1 TNFEPFTVNSVNDSELPVGGGLYEIQIPSEFTIGNMEEFIQTSSPKVTIDCAAFVCGDYAA
MF374983.2 TNFEPFTVNSVNDSELPVGGGLYEIQIPSEFTIGNMEEFIQTSSPKVTIDCAAFVCGDYAA
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KF923890.1 CKLQLVEYGSFCDNINAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVDINIF
KY554972.1 CKLQLVEYGSFCDNINAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVDINIF
KY674917.1 CKLQLVEYGSFCDNINAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVDINIF
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KF572872.1 CKLQLVEYGSFCDNINAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVDINIF
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KF572808.1
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KF923890.1
KY554972.1

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KF572818.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
KF923900.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
JN129834.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
AY903458.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
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MF314143.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
KU131570.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
KY014282.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
KF923886.1 AGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTGYPELVIKTSHDD
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Select tree menu ▾

Exec

[\[clustalw.aln\]](#)[\[clustalw.dnd\]](#)[\[readme\]](#)

Select tree menu ▾

Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

Sequence format is Pearson

Sequence 1: AY274119.3 1255 aa
Sequence 2: AY278554.2 1255 aa
Sequence 3: AY282752.2 1255 aa
Sequence 4: AY291315.1 1255 aa
Sequence 5: AH012999.2 1255 aa
Sequence 6: AY338174.1 1255 aa
Sequence 7: AP006561.1 1255 aa
Sequence 8: AY310120.1 1255 aa
Sequence 9: AY427439.1 1255 aa
Sequence 10: AY345988.1 1255 aa
Sequence 11: AY463060.1 1255 aa
Sequence 12: AY502924.1 1255 aa
Sequence 13: AY508724.1 1255 aa
Sequence 14: AY648300.1 1255 aa
Sequence 15: AY654624.1 1255 aa
Sequence 16: AY714217.1 1255 aa
Sequence 17: AY613952.1 1255 aa

Start of Pairwise alignments

Aligning...

Sequences (1:2) Aligned. Score: 99.761
Sequences (1:3) Aligned. Score: 99.9203
Sequences (1:4) Aligned. Score: 99.8406
Sequences (1:5) Aligned. Score: 99.4422
Sequences (1:6) Aligned. Score: 99.9203
Sequences (1:7) Aligned. Score: 99.9203
Sequences (1:8) Aligned. Score: 99.8406
Sequences (1:9) Aligned. Score: 99.9203
Sequences (1:10) Aligned. Score: 99.9203
Sequences (1:11) Aligned. Score: 99.761
Sequences (1:12) Aligned. Score: 99.9203
Sequences (1:13) Aligned. Score: 99.761
Sequences (1:14) Aligned. Score: 99.5219
Sequences (1:15) Aligned. Score: 99.6813
Sequences (1:16) Aligned. Score: 99.8406
Sequences (1:17) Aligned. Score: 98.4861
Sequences (2:3) Aligned. Score: 99.8406
Sequences (2:4) Aligned. Score: 99.761

Sequences (2:5) Aligned. Score: 99.3625
Sequences (2:6) Aligned. Score: 99.8406
Sequences (2:7) Aligned. Score: 99.8406
Sequences (2:8) Aligned. Score: 99.761
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Sequences (2:12) Aligned. Score: 99.8406
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Sequences (2:14) Aligned. Score: 99.761
Sequences (2:15) Aligned. Score: 99.761
Sequences (2:16) Aligned. Score: 99.761
Sequences (2:17) Aligned. Score: 98.7251
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Sequences (3:8) Aligned. Score: 99.9203
Sequences (3:9) Aligned. Score: 100
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Sequences (3:16) Aligned. Score: 99.9203
Sequences (3:17) Aligned. Score: 98.5657
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Sequences (4:6) Aligned. Score: 99.9203
Sequences (4:7) Aligned. Score: 99.9203
Sequences (4:8) Aligned. Score: 100
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Sequences (4:15) Aligned. Score: 99.6813
Sequences (4:16) Aligned. Score: 99.8406
Sequences (4:17) Aligned. Score: 98.4861
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Sequences (5:7) Aligned. Score: 99.5219
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Sequences (6:10) Aligned. Score: 100

Sequences (6:11) Aligned. Score: 99.6813
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Sequences (6:17) Aligned. Score: 98.5657
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Guide tree file created: [clustalw.dnd]

There are 16 groups
Start of Multiple Alignment

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Group 1: Sequences: 2 Score:20831
Group 2: Sequences: 2 Score:20824
Group 3: Sequences: 2 Score:20849
Group 4: Sequences: 3 Score:20850
Group 5: Sequences: 4 Score:20851
Group 6: Sequences: 2 Score:20856
Group 7: Sequences: 3 Score:20846
Group 8: Sequences: 4 Score:20848
Group 9: Sequences: 8 Score:20848
Group 10: Sequences: 9 Score:20850
Group 11: Sequences: 11 Score:20831
Group 12: Sequences: 12 Score:20782
Group 13: Sequences: 2 Score:20826
Group 14: Sequences: 14 Score:20819
Group 15: Sequences: 16 Score:20810
Group 16: Sequences: 17 Score:20674
Alignment Score 1063793

CLUSTAL-Alignment file created [clustalw.aln]

clustalw.aln

CLUSTAL 2.1 multiple sequence alignment

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AY274119.3      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
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AY338174.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY714217.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
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AP006561.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY291315.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY310120.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY282752.2      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY427439.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY502924.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AH012999.2      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY508724.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
AY654624.1      MFIFLLFLLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFL
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AY502924.1 GTSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKN
AH012999.2 GTSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKN
AY508724.1 GTSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKN
AY654624.1 GTSWFITQRNFFSPQIITTDNTFVSGKCDVVIGIINNTVYDPLQPELDSFKEELDKYFKN
AY613952.1 GTSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKN
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AY278554.2 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY648300.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY274119.3 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY463060.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY338174.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY714217.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY345988.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AP006561.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY291315.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY310120.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY282752.2 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
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AY508724.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY654624.1 HTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
AY613952.1 HTSPDVLGDISGINASVVNIQEEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYVWL
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AY274119.3 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY463060.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY338174.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY714217.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY345988.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AP006561.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY291315.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY310120.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY282752.2 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
AY427439.1 GFIAGLIAIVMTIILCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT
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clustalw.dnd

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Select tree menu ▼

Exec

CLUSTALW Result

Supplementary Material 4 Sequence Alignment of HuCoVHKU1 Isolates

[\[clustalw.aln\]](#)[\[clustalw.dnd\]](#)[\[readme\]](#)

Select tree menu ▾

Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

Sequence format is Pearson

Sequence 1: NC_006577.2 1356 aa
Sequence 2: AY884001 1351 aa
Sequence 3: DQ339101.1 1351 aa
Sequence 4: DQ415896 1356 aa
Sequence 5: DQ415897 1351 aa
Sequence 6: DQ415898 1351 aa
Sequence 7: DQ415899 1351 aa
Sequence 8: DQ415900 1356 aa
Sequence 9: DQ415901 1356 aa
Sequence 10: DQ415902 1351 aa
Sequence 11: DQ415903 1356 aa
Sequence 12: DQ415904 1356 aa
Sequence 13: DQ415905 1356 aa
Sequence 14: DQ415906 1356 aa
Sequence 15: DQ415907 1356 aa
Sequence 16: DQ415908 1356 aa
Sequence 17: DQ415909 1356 aa
Sequence 18: DQ415910 1356 aa
Sequence 19: DQ415911 1351 aa
Sequence 20: DQ415912 1351 aa
Sequence 21: DQ415913 1351 aa
Sequence 22: DQ415914 1356 aa
Sequence 23: MK167038.1 1351 aa
Sequence 24: MH940245.1 1351 aa
Sequence 25: LC315650.1 1356 aa
Sequence 26: LC315651.1 1352 aa
Sequence 27: KY983584.1 1356 aa
Sequence 28: KY674921.1 1352 aa
Sequence 29: KY674941.1 1356 aa
Sequence 30: KY674942.1 1356 aa
Sequence 31: KY674943.1 1356 aa
Sequence 32: KT779555.1 1356 aa
Sequence 33: KT779556.1 1356 aa
Sequence 34: KF686341.1 1356 aa
Sequence 35: KF686340.1 1356 aa
Sequence 36: KF686343.1 1356 aa
Sequence 37: KF686344.1 1356 aa
Sequence 38: KF686346.1 1356 aa
Sequence 39: KF430201.1 1355 aa

Start of Pairwise alignments

Aligning...

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Sequences (1:4) Aligned. Score: 99.9263
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Sequences (36:38) Aligned. Score: 99.9263
Sequences (36:39) Aligned. Score: 99.5572
Sequences (37:38) Aligned. Score: 99.41
Sequences (37:39) Aligned. Score: 99.0406
Sequences (38:39) Aligned. Score: 99.631
Guide tree file created: [clustalw.dnd]

There are 38 groups
Start of Multiple Alignment

Aligning...

Group 1:	Sequences: 2	Score:22539
Group 2:	Sequences: 2	Score:22559
Group 3:	Sequences: 3	Score:22563
Group 4:	Sequences: 4	Score:22565
Group 5:	Sequences: 5	Score:22565
Group 6:	Sequences: 6	Score:22566
Group 7:	Sequences: 7	Score:22566
Group 8:	Sequences: 9	Score:22544
Group 9:	Sequences: 10	Score:22554
Group 10:	Sequences: 11	Score:22552
Group 11:	Sequences: 2	Score:22570
Group 12:	Sequences: 13	Score:22551
Group 13:	Sequences: 2	Score:22562
Group 14:	Sequences: 15	Score:22524
Group 15:	Sequences: 2	Score:22568
Group 16:	Sequences: 3	Score:22568
Group 17:	Sequences: 4	Score:22568
Group 18:	Sequences: 5	Score:22568
Group 19:	Sequences: 6	Score:22568
Group 20:	Sequences: 7	Score:22558
Group 21:	Sequences: 8	Score:22458
Group 22:	Sequences: 23	Score:22508
Group 23:	Sequences: 2	Score:22561
Group 24:	Sequences: 3	Score:22523
Group 25:	Sequences: 26	Score:22493
Group 26:	Sequences: 2	Score:22462
Group 27:	Sequences: 2	Score:22365
Group 28:	Sequences: 4	Score:22297
Group 29:	Sequences: 2	Score:22417
Group 30:	Sequences: 6	Score:22288
Group 31:	Sequences: 2	Score:22467
Group 32:	Sequences: 3	Score:22467
Group 33:	Sequences: 4	Score:22461

Group 34: Sequences: 5 Score:22446
Group 35: Sequences: 6 Score:22442
Group 36: Sequences: 12 Score:22272
Group 37: Sequences: 13 Score:22036
Group 38: Sequences: 39 Score:20303
Alignment Score 5911267

CLUSTAL-Alignment file created [clustalw.aln]

clustalw.aln

CLUSTAL 2.1 multiple sequence alignment

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NC_006577.2      MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415910        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415896        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415909        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415904        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415905        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415907        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415914        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415906        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415903        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415908        MLLIIFILPTTLAVIGDFNCTNFAINDLNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415900        MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
DQ415901        MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KT779555.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNST
KT779556.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNST
KY674941.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KY674942.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KY674943.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF686341.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF686340.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF686346.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF686343.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF430201.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNST
LC315650.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KF686344.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSYGLGTYIILDRVYLNTT
KY983584.1      MLLIIFILPTTLAVIGDFNCTNFAINDKNTTVPRISEYVVDVSHGLGTYIILDRVYLNTT
AY884001        MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
MH940245.1      MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
LC315651.1      MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
KY674921.1      MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415902        MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415911        MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415897        MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415899        MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415913        MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415912        MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ415898        MFLIIFILPTTLAVIGDFNCTNSFINDYNTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
DQ339101.1     MFLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
MK167038.1     MLLIIFILPTTLAVIGDFNCTNSFINHYNKTIPRISEDVVDVSLGLGTYIVLNRVYLNTT
*.***** **.*.***** *****.*****.*****
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NC_006577.2 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415910 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415896 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415909 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415904 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415905 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415907 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415914 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415906 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415903 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415908 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415900 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
DQ415901 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KT779555.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KT779556.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KY674941.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KY674942.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KY674943.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF686341.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF686340.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF686346.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF686343.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF430201.1 ILFTGYFPKSGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
LC315650.1 ILFTGYFPKAGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KF686344.1 ILFTGYFPKAGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
KY983584.1 ILFTGYFPKAGANFRDLSLKGTTYLSTLWYQKPFLLSDFNNGIFSRVKNTKLYVNKTYLSE
AY884001 LLFTGYFPKSGANFRDLALKGSKYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
MH940245.1 LLFTGYFPKSGANFRDLALKGSKYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
LC315651.1 LLFTGYFPKSGANFRDLALKGSTYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
KY674921.1 LLFTGYFPKSGANFRDLALKGSIFLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415902 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415911 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415897 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415899 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415913 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415912 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ415898 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
DQ339101.1 LLFTGYFPKSGANFRDLALKGSIYLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
MK167038.1 LLFTGYFPKSGANFRDLALKGSITLSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNITYLSE
:*****:**** *:***: :*****: *****: *****: ****

NC_006577.2 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415910 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415896 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415909 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415904 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415905 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415907 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415914 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415906 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415903 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415908 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415900 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
DQ415901 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE
KT779555.1 FSTIVIGSVFINNSYTIIVVQPHNGVLEITACQYTMCEYPHTICKSKGSSRNESWHFDKSE

DQ415909 TG VYDLSGFTVKPVATVHRRIPDLPDCIDIKWLN NFNVPSPLNWERKIFSNCN FN LSTLL
DQ415904 TG VYDLSGFTVKPVATVHRRIPDLPDCIDIKWLN NFNVPSPLNWERKIFSNCN FN LSTLL
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KF686344.1 TG VYDLSGFTVKPVATVHRRIPDLPDCIDIKWLN NFNVPSPLNWERKIFSNCN FN LSTLL
KY983584.1 TG VYDLSGFTVKPVATVHRRIPDLPDCIDIKWLN NFNVPSPLNWERKIFSNCN FN LSTLL
AY884001 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
MH940245.1 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
LC315651.1 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
KY674921.1 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ415902 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ415911 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ415897 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ415899 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ415913 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
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DQ415898 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
DQ339101.1 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
MK167038.1 TG VYDLSGFTVKPVATVYRRIPNLPDCIDINWLN NVSVPSPLNWERKIFSNCN FN LSTLL
*****.***.*****.***.*****.*****.*****.*****.*****.*****

NC_006577.2 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415910 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415896 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415909 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415904 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415905 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415907 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415914 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415906 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415903 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415908 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415900 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
DQ415901 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
KT779555.1 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
KT779556.1 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
KY674941.1 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
KY674942.1 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS
KY674943.1 RLVHTDSFSCNNFDESKIYGSCFKSIVLDKFAIPNSRRSDLQLGSSGFLQSSNYKIDTTS

DQ415899 SSCQLYYSLPLVNVTTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVNSDFPCADPS
DQ415913 SSCQLYYSLPLVNVTTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVNSDFPCADPS
DQ415912 SSCQLYYSLPLVNVTTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVNSDFPCADPS
DQ415898 SSCQLYYSLPLVNVTTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVNSDFPCADPS
DQ339101.1 SSCQLYYSLPLVNVTTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVNSDFPCADPS
MK167038.1 SSCQLYYSLPAINVTINNYNPSSWNRRYGFNFNLSSHSVYRYCFVSNNTFCPCAKPS
***** :*****:** *****.* :** :**** :***** ***** *

NC_006577.2 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415910 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415896 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415909 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415904 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415905 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415907 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415914 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415906 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415903 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415908 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415900 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
DQ415901 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KT779555.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KT779556.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KY674941.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KY674942.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KY674943.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KF686341.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KF686340.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KF686346.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KF686343.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
KF430201.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DHTDWCRCCLPDPITAYDPRSCSQKKS
LC315650.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DRTDWCRCCLPDPITAYDPRSCSQKKS
KF686344.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DRTDWCRCCLPDPITAYDPRSCSQKKS
KY983584.1 FASSCKSHKPPSASCPIGTNYRSCST-TVL DRTDWCRCCLPDPITAYDPRSCSQKKS
AY884001 VVNSCVKSKPLSAICPAGTKYRHCIDL-TLVVNWRCRCCLPDP ISTYSPNTCPQKKVV
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DQ415896 VVGGEHCAGFGVDEEKGVL DGSYVNSCLCSTDAFLGWSYDTCVSNRNCNIFSNF ILNGI
DQ415909 VVGGEHCAGFGVDEEKGVL DGSYVNSCLCSTDAFLGWSYDTCVSNRNCNIFSNF ILNGI
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DQ415898	FFICCTGCGSACFSKCHNCCDEYGGHNDVFIKASHDD
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Select tree menu ▼

Exec

CLUSTALW Result

Supplementary Material 5 Sequence Alignment of HuCoVNL63 Isolates

[\[clustalw.aln\]](#)[\[clustalw.dnd\]](#)[\[readme\]](#)

Select tree menu ▾

Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

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Guide tree file created: [clustalw.dnd]
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There are 41 groups
Start of Multiple Alignment

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Aligning...
Group 1: Sequences: 2 Score:22405
Group 2: Sequences: 2 Score:22399
Group 3: Sequences: 4 Score:22341
Group 4: Sequences: 2 Score:22390
Group 5: Sequences: 3 Score:22393
Group 6: Sequences: 4 Score:22394
Group 7: Sequences: 5 Score:22395
Group 8: Sequences: 6 Score:22395
Group 9: Sequences: 7 Score:22395
Group 10: Sequences: 8 Score:22396
Group 11: Sequences: 9 Score:22396
Group 12: Sequences: 10 Score:22396
Group 13: Sequences: 11 Score:22396
Group 14: Sequences: 12 Score:22396
Group 15: Sequences: 13 Score:22396
Group 16: Sequences: 14 Score:22396
Group 17: Sequences: 2 Score:22374
Group 18: Sequences: 16 Score:22320
Group 19: Sequences: 2 Score:22384
Group 20: Sequences: 3 Score:22383
Group 21: Sequences: 4 Score:22390
Group 22: Sequences: 5 Score:22392
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Group 23:	Sequences: 6	Score:22393
Group 24:	Sequences: 7	Score:22393
Group 25:	Sequences: 8	Score:22394
Group 26:	Sequences: 24	Score:22377
Group 27:	Sequences: 25	Score:22369
Group 28:	Sequences: 2	Score:22336
Group 29:	Sequences: 27	Score:22268
Group 30:	Sequences: 28	Score:22274
Group 31:	Sequences: 32	Score:22280
Group 32:	Sequences: 2	Score:22388
Group 33:	Sequences: 3	Score:22388
Group 34:	Sequences: 4	Score:22376
Group 35:	Sequences: 36	Score:22152
Group 36:	Sequences: 2	Score:22381
Group 37:	Sequences: 3	Score:22304
Group 38:	Sequences: 4	Score:22305
Group 39:	Sequences: 2	Score:22376
Group 40:	Sequences: 6	Score:22271
Group 41:	Sequences: 42	Score:21909

Alignment Score 7138012

CLUSTAL-Alignment file created [clustalw.aln]

clustalw.aln

CLUSTAL 2.1 multiple sequence alignment

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KY829118.1      MKLFLILLVLPLASCFFTCNSNANLSMLQLGVPDSSSTIVTGLLPPTHWFCANQSTSVVSA
KF530105.1      MKLFLILLVLPLASCFFTCNSNANLSMLQLGVPDSSSTIVTGLLPPTHWFCANQSTSVVSA
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KM055632.1      MKLFLILLVLPLASCFFTCNSNANLSMLQLGVPDSSSTIVTGLLPPTHWFCANQSTSVVSA
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Select tree menu ▼

Exec

CLUSTALW Result

Supplementary Material 6 Sequence Alignment of MERS-CoV Isolates

[\[clustalw.aln\]](#)[\[clustalw.dnd\]](#)[\[readme\]](#)

Select tree menu ▾

Exec

CLUSTAL 2.1 Multiple Sequence Alignments

Sequence type explicitly set to Protein

Sequence format is Pearson

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Start of Pairwise alignments

Aligning...

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Sequences (21:30) Aligned. Score: 99.8522
Sequences (21:31) Aligned. Score: 99.8522
Sequences (21:32) Aligned. Score: 99.7783
Sequences (21:33) Aligned. Score: 99.9261
Sequences (21:34) Aligned. Score: 99.8522
Sequences (22:23) Aligned. Score: 99.8522
Sequences (22:24) Aligned. Score: 99.9261
Sequences (22:25) Aligned. Score: 99.7044
Sequences (22:26) Aligned. Score: 99.7044
Sequences (22:27) Aligned. Score: 99.7783
Sequences (22:28) Aligned. Score: 99.8522
Sequences (22:29) Aligned. Score: 99.8522
Sequences (22:30) Aligned. Score: 99.8522
Sequences (22:31) Aligned. Score: 99.8522
Sequences (22:32) Aligned. Score: 99.7783
Sequences (22:33) Aligned. Score: 99.9261
Sequences (22:34) Aligned. Score: 99.8522
Sequences (23:24) Aligned. Score: 99.9261
Sequences (23:25) Aligned. Score: 99.7044
Sequences (23:26) Aligned. Score: 99.7044
Sequences (23:27) Aligned. Score: 99.7783
Sequences (23:28) Aligned. Score: 99.8522
Sequences (23:29) Aligned. Score: 99.8522
Sequences (23:30) Aligned. Score: 99.8522
Sequences (23:31) Aligned. Score: 99.8522
Sequences (23:32) Aligned. Score: 99.7783
Sequences (23:33) Aligned. Score: 99.9261

Sequences (23:34) Aligned. Score: 99.8522
Sequences (24:25) Aligned. Score: 99.7783
Sequences (24:26) Aligned. Score: 99.7783
Sequences (24:27) Aligned. Score: 99.8522
Sequences (24:28) Aligned. Score: 99.9261
Sequences (24:29) Aligned. Score: 99.9261
Sequences (24:30) Aligned. Score: 99.9261
Sequences (24:31) Aligned. Score: 99.9261
Sequences (24:32) Aligned. Score: 99.8522
Sequences (24:33) Aligned. Score: 100
Sequences (24:34) Aligned. Score: 99.9261
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Sequences (25:27) Aligned. Score: 99.6305
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Sequences (25:29) Aligned. Score: 99.7044
Sequences (25:30) Aligned. Score: 99.7044
Sequences (25:31) Aligned. Score: 99.7044
Sequences (25:32) Aligned. Score: 99.6305
Sequences (25:33) Aligned. Score: 99.7783
Sequences (25:34) Aligned. Score: 99.7044
Sequences (26:27) Aligned. Score: 99.7783
Sequences (26:28) Aligned. Score: 99.7044
Sequences (26:29) Aligned. Score: 99.7044
Sequences (26:30) Aligned. Score: 99.7044
Sequences (26:31) Aligned. Score: 99.7044
Sequences (26:32) Aligned. Score: 99.6305
Sequences (26:33) Aligned. Score: 99.7783
Sequences (26:34) Aligned. Score: 99.7044
Sequences (27:28) Aligned. Score: 99.7783
Sequences (27:29) Aligned. Score: 99.7783
Sequences (27:30) Aligned. Score: 99.7783
Sequences (27:31) Aligned. Score: 99.7783
Sequences (27:32) Aligned. Score: 99.7044
Sequences (27:33) Aligned. Score: 99.8522
Sequences (27:34) Aligned. Score: 99.7783
Sequences (28:29) Aligned. Score: 99.8522
Sequences (28:30) Aligned. Score: 99.8522
Sequences (28:31) Aligned. Score: 99.8522
Sequences (28:32) Aligned. Score: 99.7783
Sequences (28:33) Aligned. Score: 99.9261
Sequences (28:34) Aligned. Score: 99.8522
Sequences (29:30) Aligned. Score: 100
Sequences (29:31) Aligned. Score: 99.8522
Sequences (29:32) Aligned. Score: 99.7783
Sequences (29:33) Aligned. Score: 99.9261
Sequences (29:34) Aligned. Score: 99.8522
Sequences (30:31) Aligned. Score: 99.8522
Sequences (30:32) Aligned. Score: 99.7783
Sequences (30:33) Aligned. Score: 99.9261
Sequences (30:34) Aligned. Score: 99.8522
Sequences (31:32) Aligned. Score: 99.9261
Sequences (31:33) Aligned. Score: 99.9261
Sequences (31:34) Aligned. Score: 100
Sequences (32:33) Aligned. Score: 99.8522
Sequences (32:34) Aligned. Score: 99.9261
Sequences (33:34) Aligned. Score: 99.9261

Guide tree file created: [clustalw.dnd]

There are 33 groups
Start of Multiple Alignment

Aligning...

Group 1:	Sequences: 2	Score:22442
Group 2:	Sequences: 2	Score:22444
Group 3:	Sequences: 4	Score:22423
Group 4:	Sequences: 2	Score:22427
Group 5:	Sequences: 6	Score:22425
Group 6:	Sequences: 7	Score:22427
Group 7:	Sequences: 2	Score:22431
Group 8:	Sequences: 3	Score:22422
Group 9:	Sequences: 10	Score:22422
Group 10:	Sequences: 2	Score:22447
Group 11:	Sequences: 12	Score:22427
Group 12:	Sequences: 13	Score:22429
Group 13:	Sequences: 2	Score:22444
Group 14:	Sequences: 3	Score:22435
Group 15:	Sequences: 16	Score:22421
Group 16:	Sequences: 2	Score:22416
Group 17:	Sequences: 18	Score:22410
Group 18:	Sequences: 2	Score:22414
Group 19:	Sequences: 20	Score:22406
Group 20:	Sequences: 2	Score:22418
Group 21:	Sequences: 3	Score:22430
Group 22:	Sequences: 4	Score:22434
Group 23:	Sequences: 5	Score:22436
Group 24:	Sequences: 6	Score:22438
Group 25:	Sequences: 26	Score:22423
Group 26:	Sequences: 2	Score:22419
Group 27:	Sequences: 3	Score:22416
Group 28:	Sequences: 2	Score:22414
Group 29:	Sequences: 5	Score:22409
Group 30:	Sequences: 31	Score:22413
Group 31:	Sequences: 32	Score:22423
Group 32:	Sequences: 2	Score:22344
Group 33:	Sequences: 34	Score:22336

Alignment Score 4714499

CLUSTAL-Alignment file created [clustalw.aln]

clustalw.aln

CLUSTAL 2.1 multiple sequence alignment

KX034094.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ
KX034095.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ
MN723542.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ
MK462243.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ
MK052676.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ
MG546331.1	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYPQ

MN481964.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MK280984.2 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MG011351.2 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MG757604.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MH978886.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MH978887.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MN735679.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
KX034100.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
KT868868.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
KT182957.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MK462247.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MH822886.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MK858157.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
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MN481979.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MN403102.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MG757598.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
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MH371127.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
KU233362.1 MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MN723544.1 MIHSVFLLMFLLTPTESYVDVGPDSLKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
MN365232.1 MIHSVFLLMFLLTPTESYVDVGPDSLKSACIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
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MK357908.1 MIHSVFLLMFLLTPTESYVDVGPDSAKSVCIEVDIQQTFFDKTWPRPIDVSKADGIIYQP
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KX034094.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
KX034095.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MN723542.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MK462243.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MK052676.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MG546331.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MN481964.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MK280984.2 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MG011351.2 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MG757604.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
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MH978887.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MN735679.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
KX034100.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
KT868868.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
KT182957.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
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MK858157.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
MH454272.1 GRYSNITITYQGLFPYQGDHGMVVSAGHATGTTPQKLFVANYSQDVVKQFANGFVVRI
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*****.*****.*****.*****.*****.*****.*****.*****.*****.*****

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MN481964.1 LATVPHNLTITIKPLKYSYINKCSRLLSDDRTEVPQLVNNANQYSPCVSIVPSTVWEDGDY
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KT182957.1 LATVPHNLTITIKPLKYSYINKCSRLLSDDRTEVPQLVNNANQYSPCVSIVPSTVWEDGDY
MK462247.1 LATVPHNLTITIKPLKYSYINKCSRLLSDDRTEVPQLVNNANQYSPCVSIVPSTVWEDGDY
MH822886.1 LATVPHNLTITIKPLKYSYINKCSRLLSDDRTEVPQLVNNANQYSPCVSIVPSTVWEDGDY
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Exec

CLUSTAL 2.1 Multiple Sequence Alignments

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Guide tree file created: [\[clustalw.dnd\]](#)

There are 91 groups
Start of Multiple Alignment

Aligning...

Group 1:	Sequences: 2	Score:21097
Group 2:	Sequences: 2	Score:21125
Group 3:	Sequences: 4	Score:21111
Group 4:	Sequences: 2	Score:21124
Group 5:	Sequences: 3	Score:21124
Group 6:	Sequences: 4	Score:21124
Group 7:	Sequences: 5	Score:21124
Group 8:	Sequences: 6	Score:21124
Group 9:	Sequences: 7	Score:21124
Group 10:	Sequences: 8	Score:21124
Group 11:	Sequences: 9	Score:21124
Group 12:	Sequences: 10	Score:21124
Group 13:	Sequences: 11	Score:21124
Group 14:	Sequences: 12	Score:21124
Group 15:	Sequences: 13	Score:21124
Group 16:	Sequences: 14	Score:21124
Group 17:	Sequences: 15	Score:21124
Group 18:	Sequences: 16	Score:21124
Group 19:	Sequences: 17	Score:21124
Group 20:	Sequences: 18	Score:21124
Group 21:	Sequences: 19	Score:21124
Group 22:	Sequences: 20	Score:21124
Group 23:	Sequences: 21	Score:21124
Group 24:	Sequences: 22	Score:21124
Group 25:	Sequences: 23	Score:21124
Group 26:	Sequences: 24	Score:21124
Group 27:	Sequences: 25	Score:21124
Group 28:	Sequences: 26	Score:21124
Group 29:	Sequences: 27	Score:21124
Group 30:	Sequences: 28	Score:21124
Group 31:	Sequences: 29	Score:21124
Group 32:	Sequences: 30	Score:21124
Group 33:	Sequences: 31	Score:21124
Group 34:	Sequences: 32	Score:21124
Group 35:	Sequences: 33	Score:21124
Group 36:	Sequences: 34	Score:21124

Group 37:	Sequences:	35	Score:21124
Group 38:	Sequences:	36	Score:21124
Group 39:	Sequences:	37	Score:21124
Group 40:	Sequences:	38	Score:21124
Group 41:	Sequences:	39	Score:21104
Group 42:	Sequences:	43	Score:21102
Group 43:	Sequences:	2	Score:21116
Group 44:	Sequences:	45	Score:21108
Group 45:	Sequences:	2	Score:21103
Group 46:	Sequences:	2	Score:21102
Group 47:	Sequences:	4	Score:21102
Group 48:	Sequences:	49	Score:21097
Group 49:	Sequences:	2	Score:21125
Group 50:	Sequences:	51	Score:21113
Group 51:	Sequences:	52	Score:21104
Group 52:	Sequences:	53	Score:21104
Group 53:	Sequences:	54	Score:21113
Group 54:	Sequences:	55	Score:21113
Group 55:	Sequences:	56	Score:21114
Group 56:	Sequences:	57	Score:21114
Group 57:	Sequences:	58	Score:21114
Group 58:	Sequences:	59	Score:21114
Group 59:	Sequences:	60	Score:21114
Group 60:	Sequences:	61	Score:21114
Group 61:	Sequences:	62	Score:21115
Group 62:	Sequences:	63	Score:21115
Group 63:	Sequences:	64	Score:21115
Group 64:	Sequences:	65	Score:21115
Group 65:	Sequences:	66	Score:21115
Group 66:	Sequences:	67	Score:21115
Group 67:	Sequences:	68	Score:21115
Group 68:	Sequences:	69	Score:21116
Group 69:	Sequences:	70	Score:21116
Group 70:	Sequences:	71	Score:21116
Group 71:	Sequences:	72	Score:21116
Group 72:	Sequences:	73	Score:21116
Group 73:	Sequences:	74	Score:21116
Group 74:	Sequences:	75	Score:21116
Group 75:	Sequences:	76	Score:21116
Group 76:	Sequences:	77	Score:21117
Group 77:	Sequences:	78	Score:21117
Group 78:	Sequences:	79	Score:21117
Group 79:	Sequences:	80	Score:21117
Group 80:	Sequences:	81	Score:21117
Group 81:	Sequences:	82	Score:21117
Group 82:	Sequences:	83	Score:21117
Group 83:	Sequences:	84	Score:21117
Group 84:	Sequences:	85	Score:21117
Group 85:	Sequences:	86	Score:21117
Group 86:	Sequences:	87	Score:21117
Group 87:	Sequences:	88	Score:21118
Group 88:	Sequences:	89	Score:21118
Group 89:	Sequences:	90	Score:21118
Group 90:	Sequences:	91	Score:21118
Group 91:	Sequences:	92	Score:20996

Alignment Score -9676132

CLUSTAL-Alignment file created [[clustalw.aln](#)]

CLUSTAL 2.1 multiple sequence alignment

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MT246472.1WashingtonStateMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT318827.1GermanyMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT396266.1NetherlandsApril	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT263074.1PeruMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
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MT371574.1CzechRepublicMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT320538.2FranceMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
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MT276598.1IsraelMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
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MT093571.1SwedenFebruary	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT304487.1OregonMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
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MT325578.1IllinoisMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
MT325591.1NorthCarolinaMarch	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHS
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 MN997409.1ArizonaJanuary
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 MT066175.1TaiwanJanuary
 MT066176.1TaiwanFebruary
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 MT240479.1PakistanMarch
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 LC542809.1JapanMarch
 MT077125.1ItalyJanuary
 MT276597.1IsraelFebruary
 MT320891.2IranMarch
 LC528233.1CruseShipFebruary
 MT256924.2ColombiaMarch
 MT126808.1BrazilFebruary
 MT372481.1MalaysiaMarch
 MT396241.1ChinaMarch

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