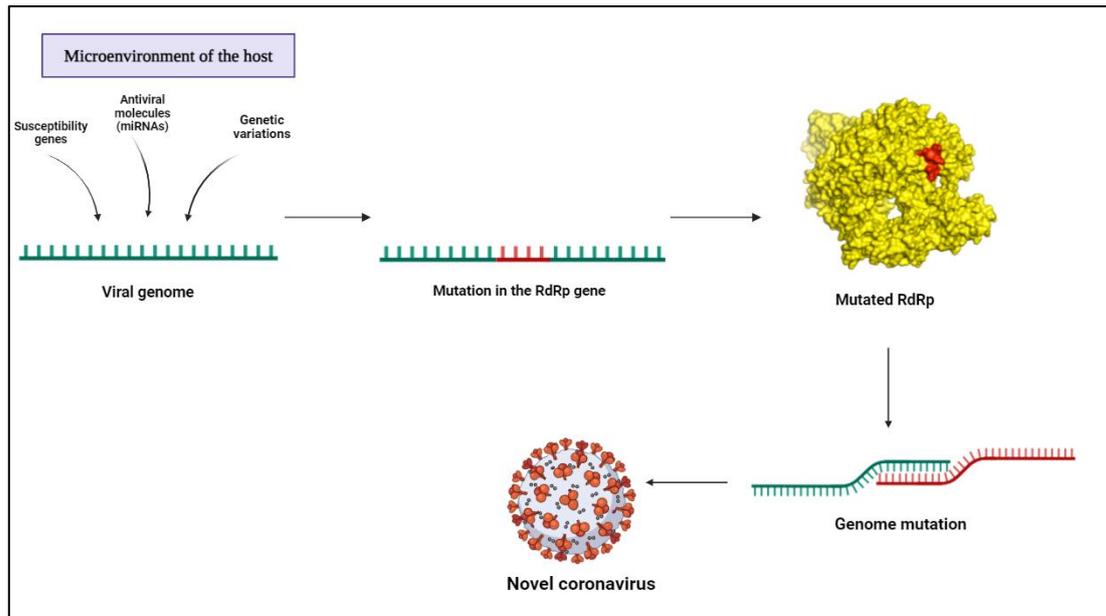
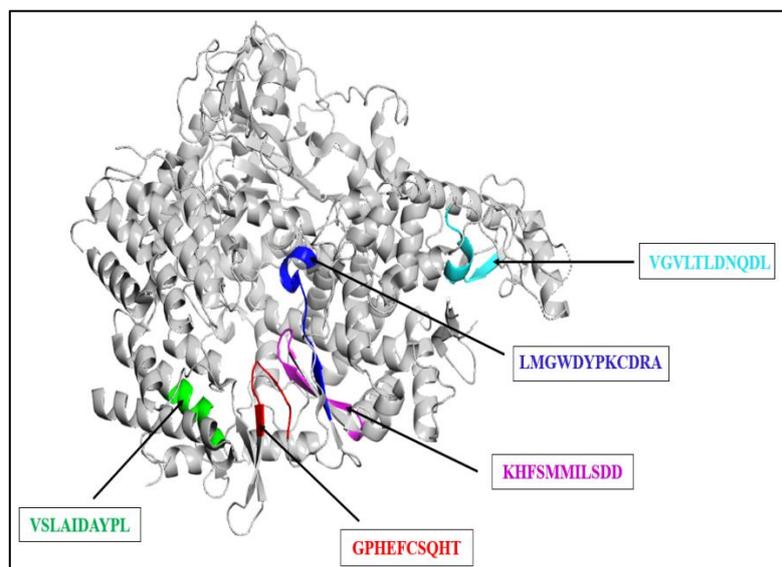


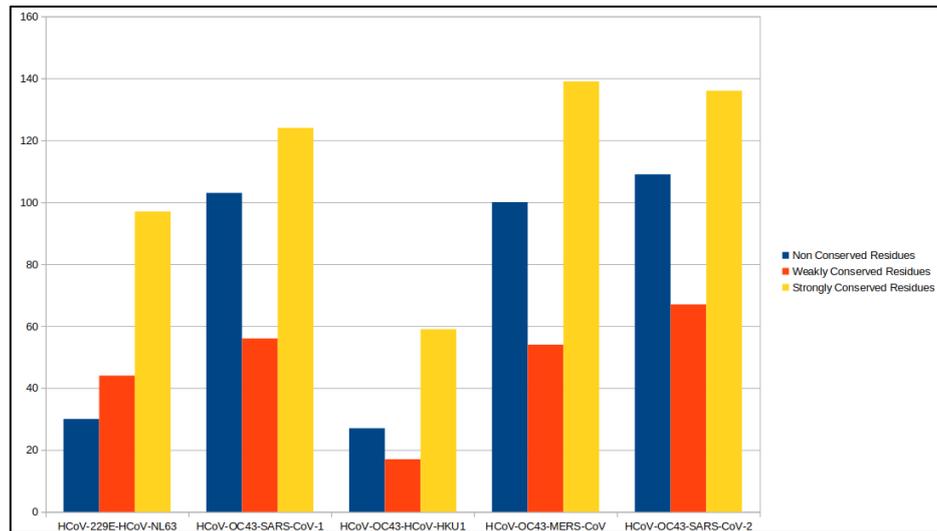
Supplementary Files



Supp Figure 1. Microenvironmental factors of host leading to mutation in the RdRp gene causing evolution of coronaviruses.



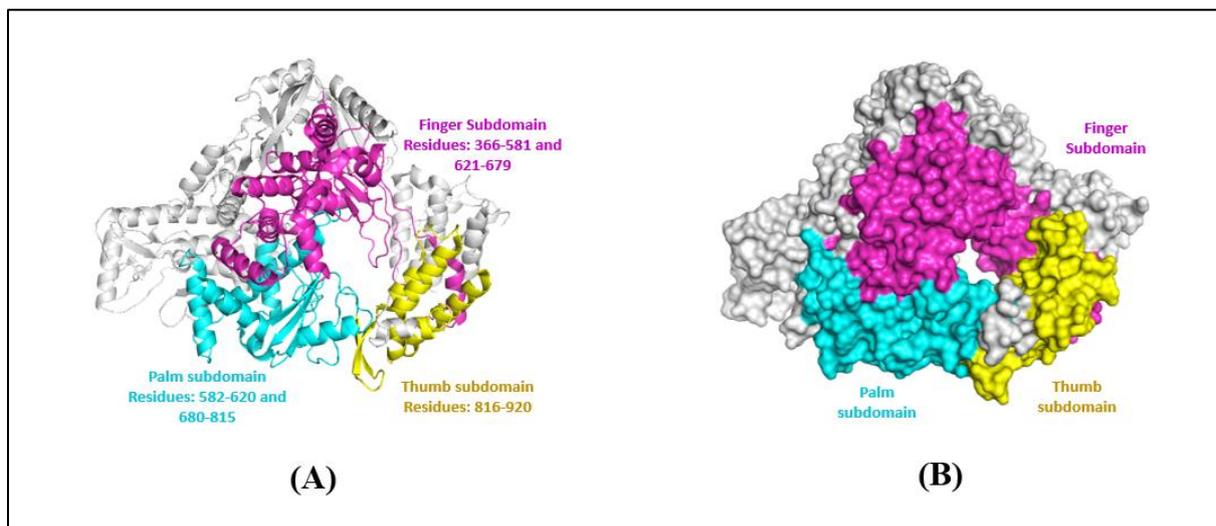
Supp Figure 2. Cartoon model of conserved regions of human coronavirus RdRp. Finger subdomain (Blue), palm subdomains (Blue, magenta, red), thumb subdomain (green)



Supp Figure 3. Graphical representation of mutation types observed in the RdRp protein

[*Non-Conserved Residues *Weakly conserved residues (somewhat similar properties)

*Strongly/highly conserved residues (Similar chemical properties)]

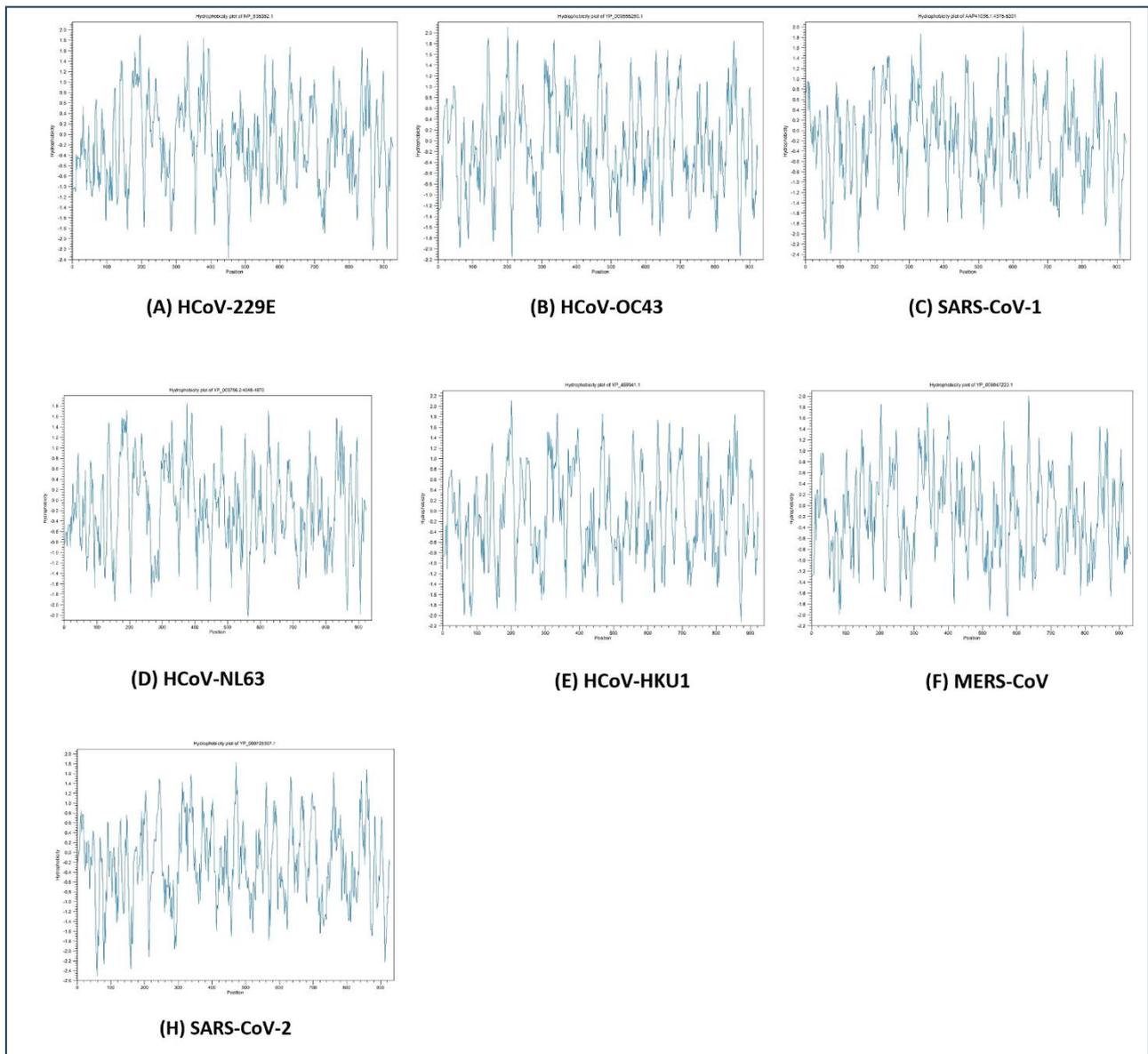


Supp Figure 4: 3D structure of SARS-CoV-2 RNA-dependent RNA polymerase (PDB ID:

6M71). (A) Cartoon model (B) Surface model of RdRp protein in a cupped right-handed

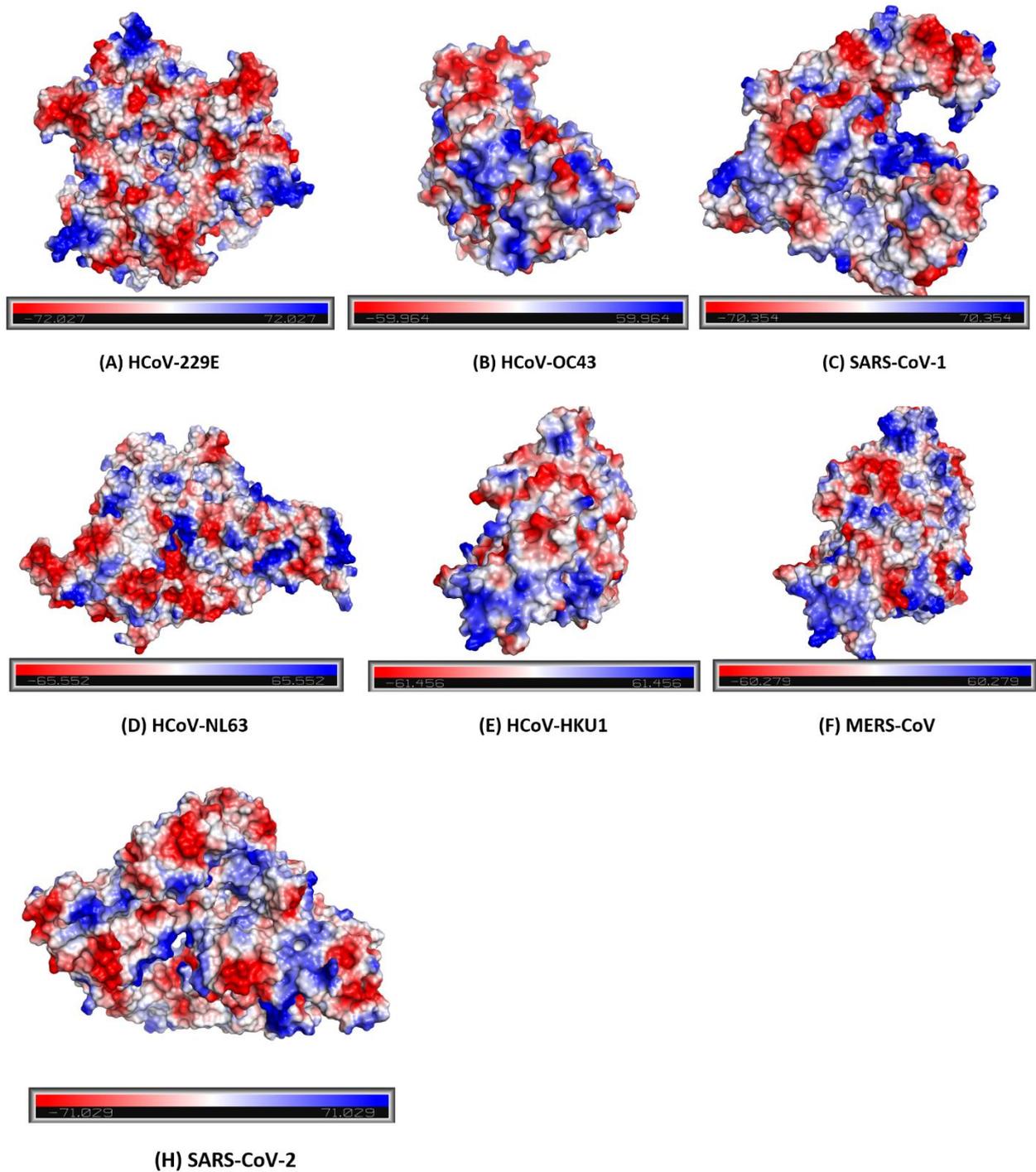
form with subdomains, Finger domain (magenta), Palm domain (Cyan), Thumb domain

(yellow)

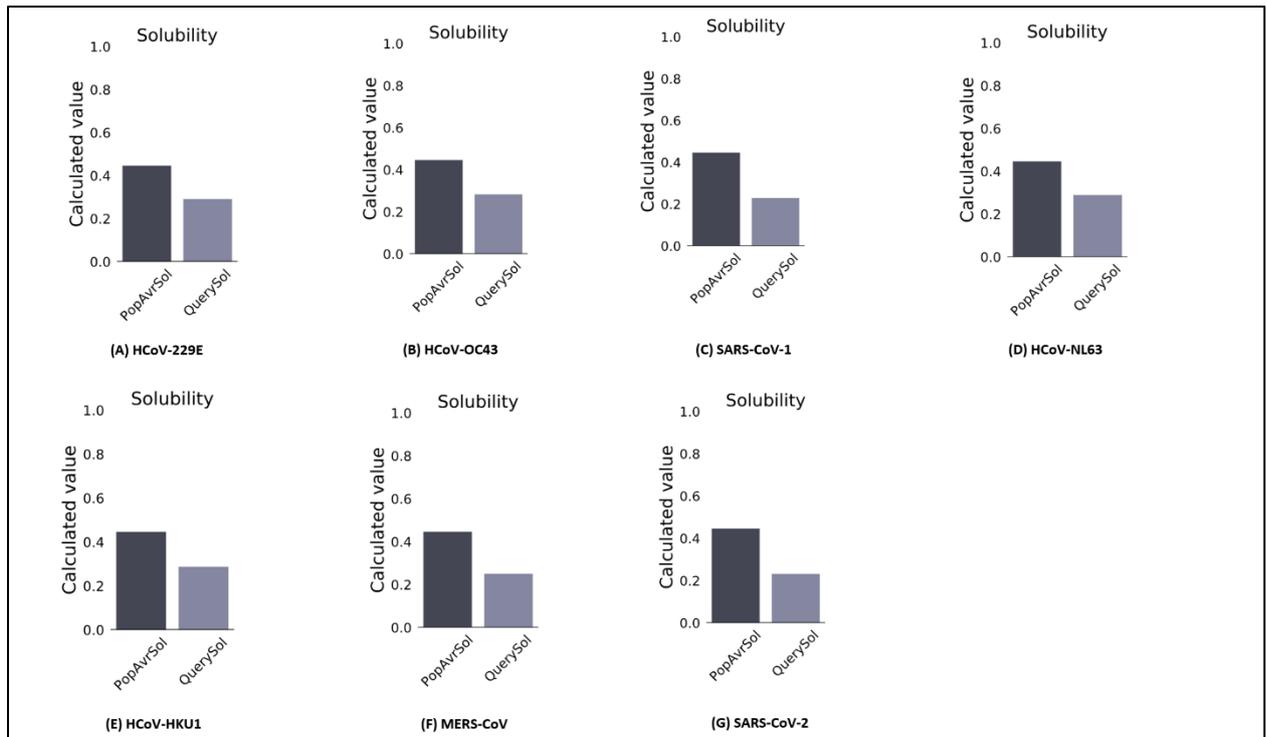


Supp Figure 5. Hydrophobicity of all human coronaviruses RdRp proteins using CLC

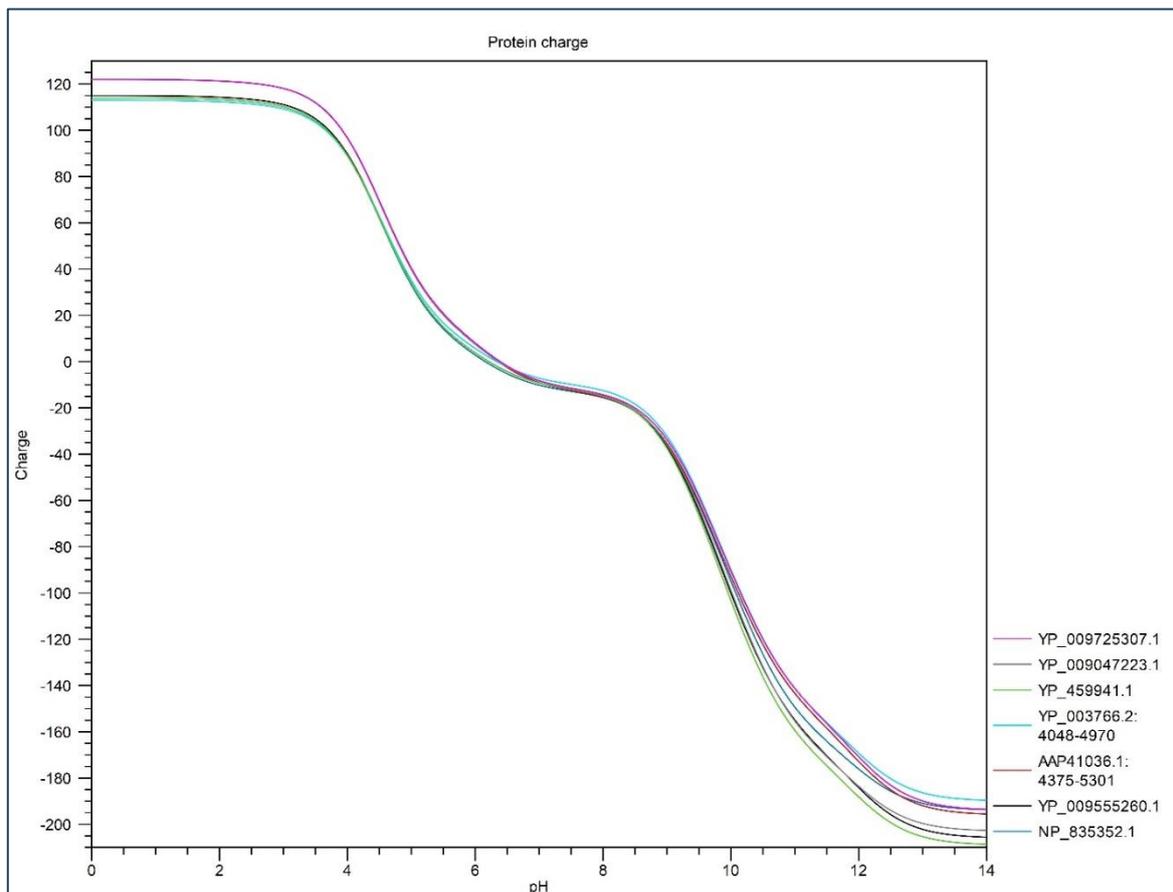
Genomics workbench 24



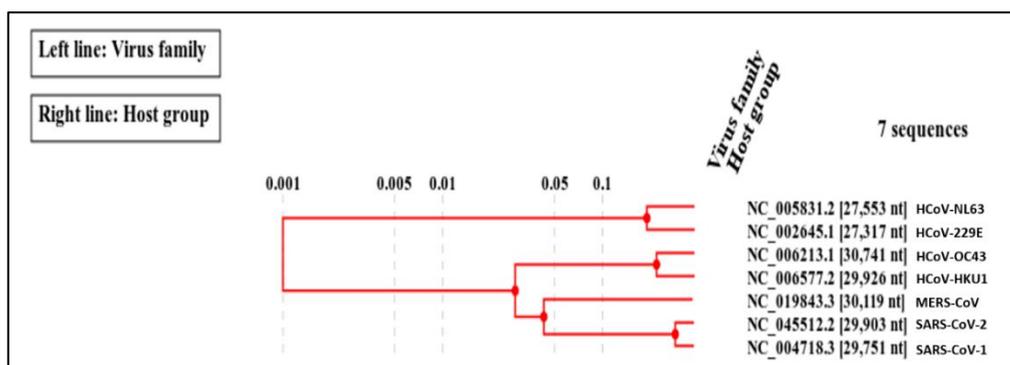
Supp Figure 6. 3D Surface representation of all Human coronavirus RdRp using PyMOL software (Red- Hydrophobic regions, Blue- Hydrophilic regions)



Supp Figure 7. Solubility of the RdRp proteins of all the 7 HCoVs



Supp Figure 8. RdRp Protein Charge v/s pH of human coronaviruses



Supp Figure 9: Phylogenetic tree of seven human coronaviruses

Supp Table 1. Human coronaviruses RdRp protein similarity

Human coronaviruses	Nucleotide sequence similarity	Amino acid Sequence Similarity
HCoV-229E-HCoV-OC43	59.54%	56%
HCoV-OC43-SARS-CoV-1	64.11%	66.20%
SARS-CoV- HCoV-NL63	61.87%	58.50%
HCoV-NL63-HCoV-HKU1	64.24%	55.50%
HCoV-HKU1-MERS-CoV	67.15%	68%
MERS-SARS-CoV-2	67.01%	71%

Suppl Table 2: Mutations present in RdRp protein of various HCoVs

Human Coronaviruses	Mutations in RdRp protein
	<p>Weakly conserved residue V10A, Y28K, A40V, V57A, D60K, A62G, C87S, N88G, T103V, S147D, T148N, D149S, N155G, N178R, C219S, G222N, Q258S, G286S, N318G, T359V, S402N, T404V, A471V, T484K, G508S, N599T, D603G, S623N, T639N, S651G, S708D, N709S, F713V, K717D, N731S, S757G, G786N, T796V, K821T, T843V, A878V, T889N, S908D, S914D</p> <p>Strongly conserved residue V35I, D39N, I43L, F63Y, Y64F, I65V, V66I, D75E, K85N, V90L, K92E, H99K, E100D, Q111H, D112N, F123Y, L125M, K131Q, D132N, E134D, F136L, I139V, E152D,</p>

HCoV-229E to HCoV-NL63	F157Y, I160V, A171S, V175I, F186L, L218V, I225V, V238I, M241L, M251V, Y284H, D292N, H297Y, E299D, I302V, L303I, S306A, V335L, A337T, T374S, V377I, K386Q, V389I, K412E, D416N, Q421R, T438A, K440N, I445V, Y450F, R455K, M458I, A467T, Q469K, V470I, A472S, S485A, I522L, S524A, I530V, A559S, F566Y, D594N, K598R, M601I, D605E, D606N, M621L, L628I, I632V, S644T, K646T, T681S, V688I, V702L, K716R, Q721R, S730T, D733E, V737I, F740Y, Q745R, S801T, A792S, E818K, N819D, I833L, I842V, I849V, K869N, E905N, H906Q, K922N, V925I
HCoV-OC43 to SARS-CoV-1	Weakly conserved residue N5T, T13V, V20T, A23G, S41K, G46A, H48F, V51T, R58E, Q68S, K85T, T103K, S109D, R136E, N137G, S155D, T158N, N173R, F182V, N183R, S188K, T190V, A193C, V199A, A225V, A234V, C253A, S287D, C321S, V378A, A381G, S382N, S399N, G400N, V419A, S487N, G564N, V581A, D595H, K603S, N607T, S643N, D646H, C668S, V797T, N802T, D819G, G820D, S848G, V849T, V866T, K875D, N893G, T905N, Q909S, S915E Strongly conserved residue L7F, N8K, S24T, I45F, N62E, D64N, F69Y, L77M, T78S, N81Q, R82H, E88N, E107D, K17Q, D138N, D144E, E153D, Q154D, I172L, K177N, R184Q, A185S, V187L, A189T, E191Q, L196M, E198D, L210I, K215N, Y222F, I241L, M244I, M247L, H249R, Y256H, V257M, N258D, N259K, F264W, V267L, Q268K, D273E, K275R, N280D, K281R, H285Y, V295I, D296N, I304L, I311V, L317F, Q328K, Y344F, K345R, I349V, D356N, L364F, D366E, L369V, L376M, I397L, L420V, L424F, L425F, D432E, T439A, T447S, N450D, K453R, K463R, L469V, E477D, Y500F, F505W, E513D, A514S, L515M, F517Y, E519D, I523L, Y524F, L532I, L535I, T588S, D596N, R599K, L601V, D606E, L625M, V629M, S630A, E639N, I662M, F685Y, S697T, M704L, N707D, I716V, Q779K, S793A, I801L, N803K, N829D, L843I, L844V, L851M, E871Q, R878H, V879L, K885R, Y888H, N889D, D890E, Q894H, I895M, I902M, S904T, D907N, K910R, F911Y, D913E, K918E, A925T, M927L
HCoV-OC43 to HCoV-HKU1	Weakly conserved residue S41N, K85T, V90I, D92S, F95V, S147C, G151D, S188N, T190V, K195T, A250V, S287G, S645G, T739N, A777V, N802, N893T Strongly conserved residue D16N, A40T, H48Y, V59I, E61D, N62D, D64N, Q68K, D76N, I79V, K82K, V106I, E107D, K117R, D118N, T120S, L141I, D144E, E153K, Q154E, T158S, V174I, V187L, A189T, K215Q, Y222F, V223I, A225T, I233V, I241M, Y256E, N259D, A260S, H285Y, Q298D, D299N, I349V, M353L, L376M, V401I, D417E, L425E, S430T, D521N, R600H, L625I, Q644H, S697T, A702S, S705A, N709H, H726N, S730T, H799N, M818I, N829D, Y867H, D913E, R923K
HCoV-OC43 to MERS-CoV	Weakly conserved residue S41K, V51T, R58E, D64H, Q68S, K94D, V111T, D138S, A150G, D170S, N173G, F182V, N183R, S188N, T190V, A193C, V199A, C229S, A234V, H249D, A250C, V257F, V267T, S287D, V316T, D356S, S382N, C390S, K402T, K453S, G564N, V581A, V629F, V696T, C701S, S705G, C706A, S715E, K732S, T736K, N774G, S776Q, V781T, D819G, G820D, D822G, G835S, S848G, V849T, V866T, N893G, S904C, G908S, V926T Strongly conserved residue T4S, T13S, D16N, L19I, A23S, L32F, N39K, H48Y, L49Y, V59L, E61D, N62D, K65H, F69Y, L77M, N81E, K85H, E88D, V90L, K91R, E107D, R110K, K117Q, K121E, L125M, R136Q, M140V, E153D, S155T, K159N, Y163F, I171V, K176H, R184Q, L186I, V187L, A189T, E191K, K195H, L196M, E198K, Y222F, A225T, I241L, M244V, T246S, N259K, F264W, Q268E, L276V, E277Q, N280E, H285Y, D296N, I303V, I304L, I311V, S314A, L317M, N319K, L325I, Q328K, I449L, Y360H, D366E, L368M, L369M, L376M, V378I, A381S, L384F, I397L, S399T, V401L, K407R, L420V, L424F, L425F, T439A, L465M, L469M, I484L, Q488E, I490V, Y500H, L510V, A514S, L515M, F157Y, E518Q, I523L, Y524F, L532I, L535M, F567Y, I575M, R599K, L625M, S630A, V633I, S643T, M664L, F685Y, S697T, I716V, R717K, L719M, H726N, E740K, S768A, Q779K, Q780E, S793A, I801L, N802K, N803K, M814L, V816I, Y824F, N829D, L843I, L844V, L851M, I852V, N870D, K875N, K885E, N889K, Q894H, I895M, I902M, D907N, D913E, S915A, K918R, N919D, M920L, A925T, M927L
	Weakly conserved residue K2D, N5S, T13V, V20T, A23G, S41K, G46A, H48F, V51T, R58E, G63D, Q68S, K85T, C86I, T103K, S109D, R136E, N137G, S155D, T158N, N173R, F182V, N183R, S188K, T190V, A193C, V199A, C229S, A234V, C253A, N258T, S287D, C321S, V378A, A381G, S382N, S399N, G400N, V419A, S487N, G564N, V581A, D595H, K603S, D646H, C668S, S725E, S730N, K732D, T739N, N746R, G758A, N774S, S776K, Q780S, V797T, N802T, D819G, G820D, S848G, V849T, V866T, K875D, N893G, T905N, Q909S, S915E Strongly conserved residue S1A, S24T, I45F, N62D, D64N, L66I, F69Y, L77F, T78S, N81Q, R82H, E88N, V90L, E98K, V106I, E107D, K117Q, D138N, D144E, E152D, Q154D, I172L, K177N, R184Q,

HCoV-OC43 to SARS-CoV-2	V187L, A189T, E191Q, L196M, E198N, L201I, K215N, Y222F, V223I, A225T, A226T, I233V, I241L, M244I, M247L, H249R, Y256H, N259K, F264W, V267L, Q268K, D273E, K275R, E277K, N280D, K281R, H285Y, D296N, I304L, I311V, L317F, Q328K, Y344F, K345R, I349V, D356N, L364F, D366E, L369V, L376M, I397L, Q413K, L420V, L424F, L425F, D432E, T439A, T447S, N450D, K553R, K463R, L469V, E477D, Y500F, F505W, E513D, A514S, L515M, F517Y, E519D, I523L, Y524F, L532I, L535I, T588S, D596N, R599K, L601V, I602Y, D606E, L625M, V629M, S630A, I662M, F685Y, S697T, M704L, N707D, I716V, K721H, V727L, S735T, Y741F, Y762F, K769Q, I772V, Q779K, S793A, I801L, N803K, N829D, L843I, L844V, L851M, E871Q, R878H, V879L, K885R, Y888H, N889D, D890E, Q894H, I895M, I902M, S904T, D907N, K910R, F911Y, D913E, K918E, A925T, M927L
--------------------------------	--