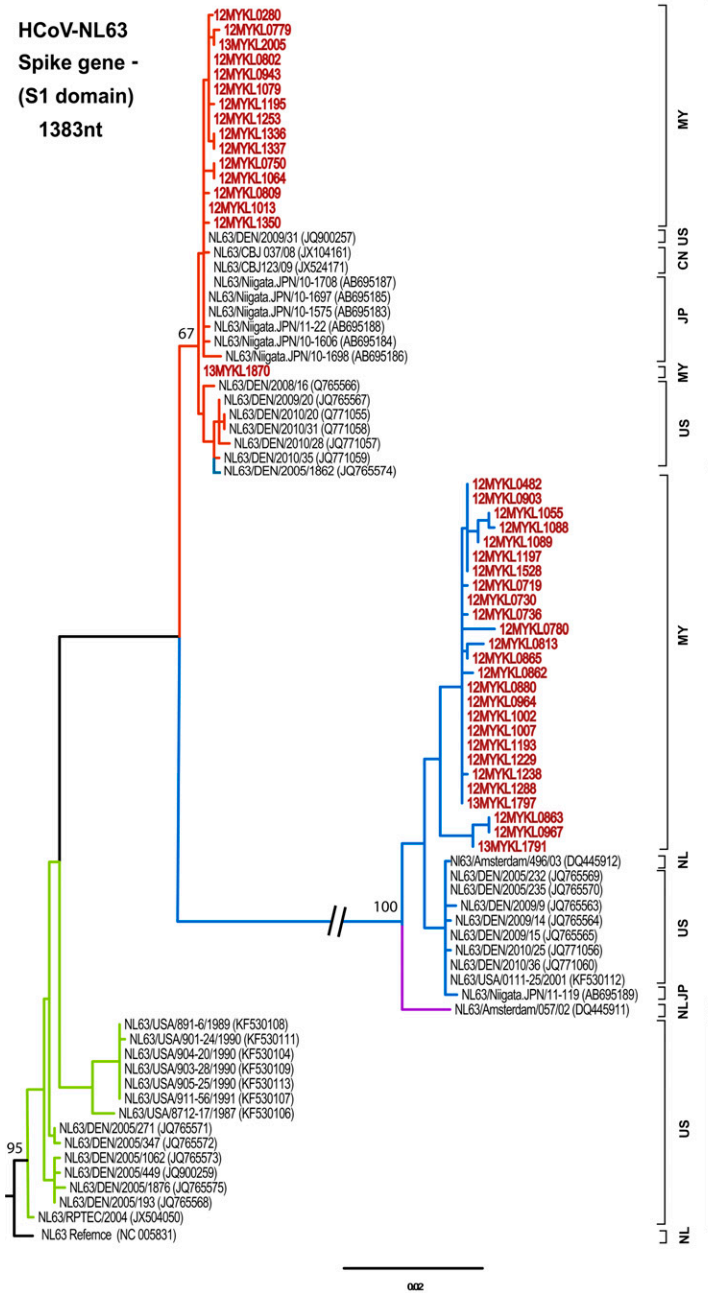
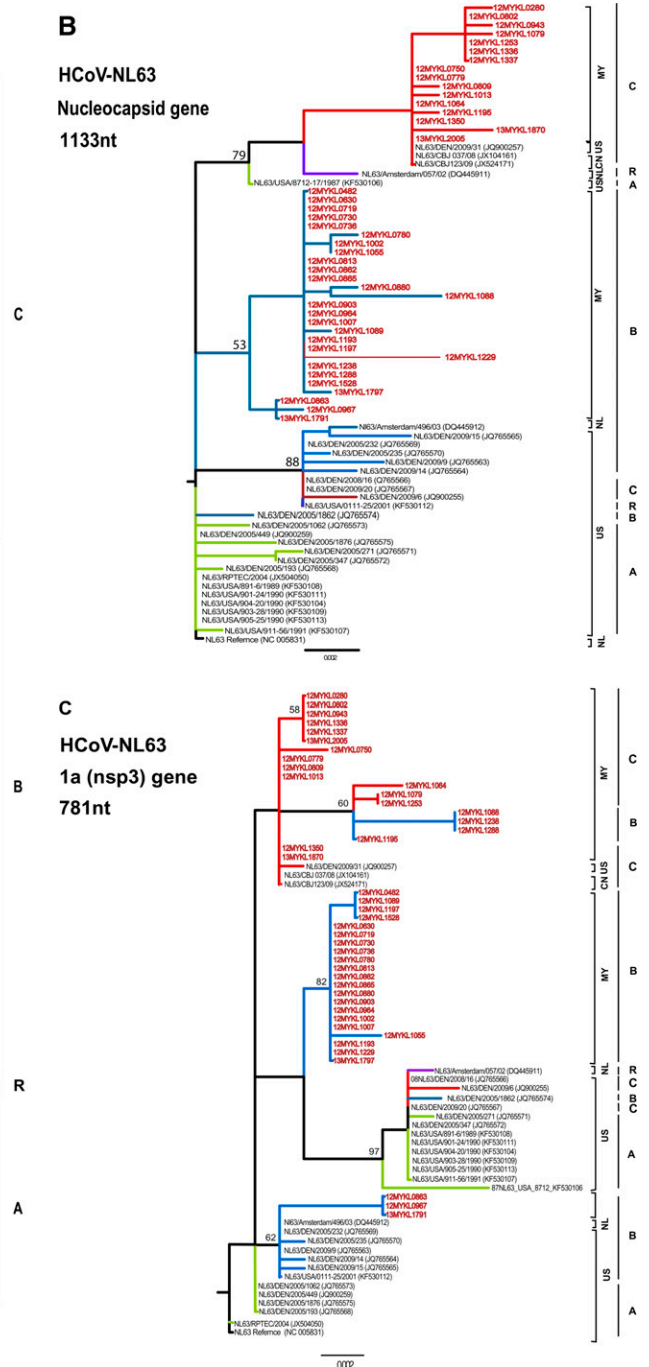


A

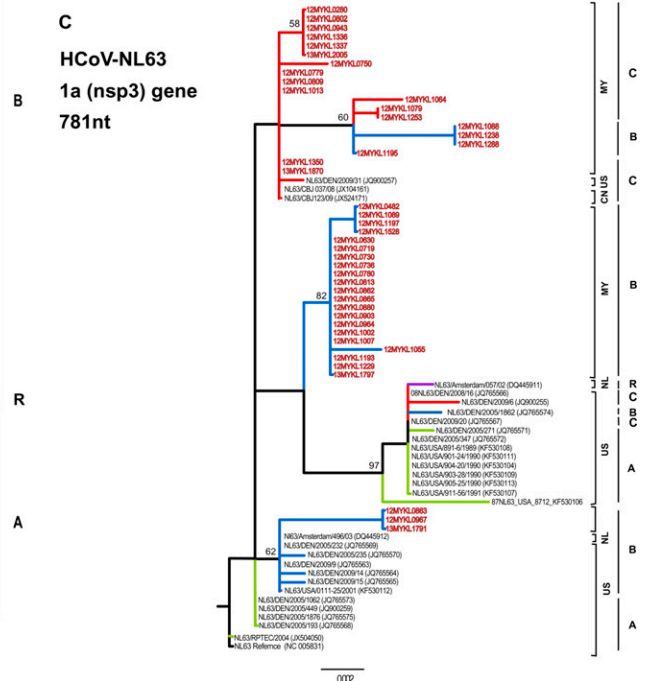
**HCoV-NL63
Spike gene -
(S1 domain)
1383nt**

**B**

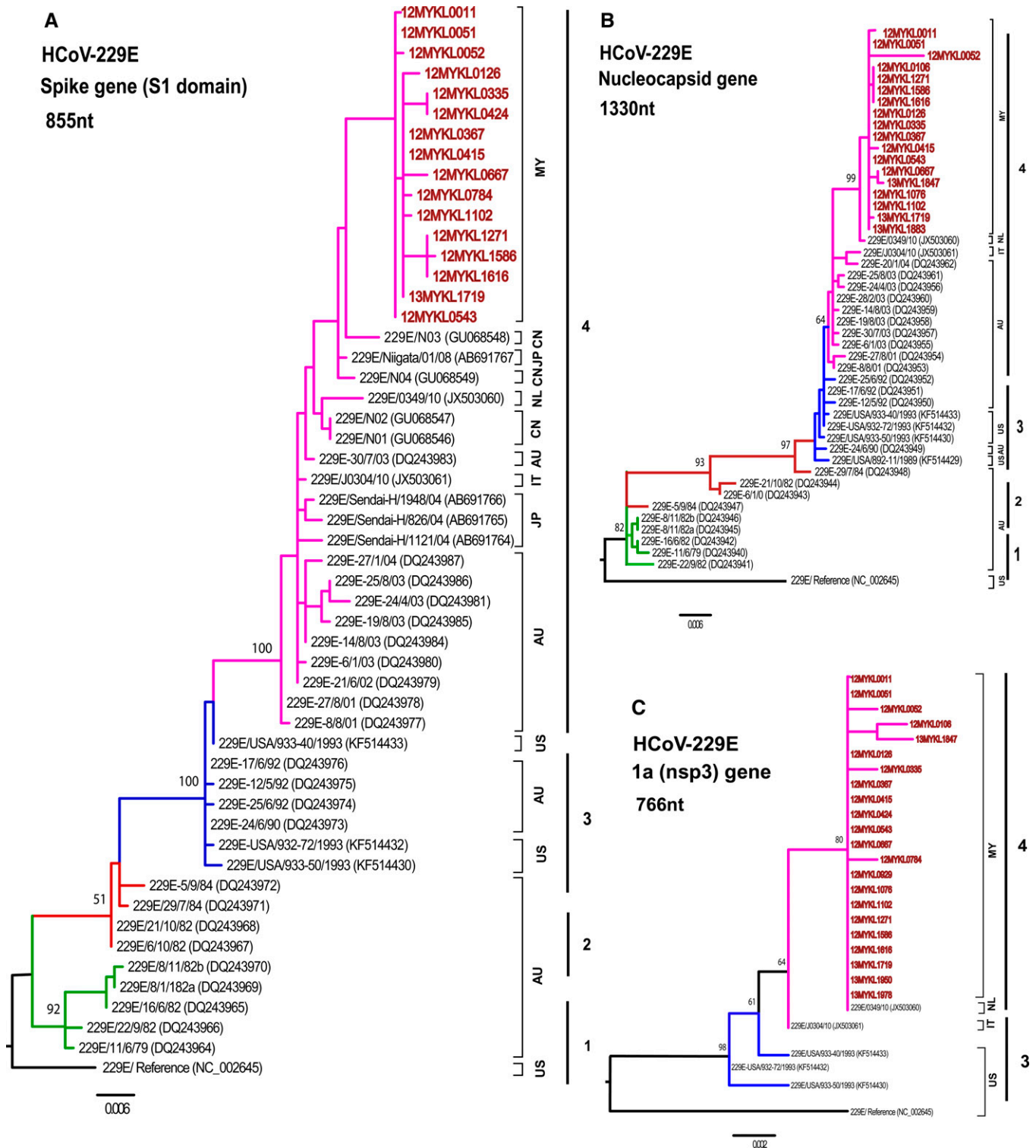
**HCoV-NL63
Nucleocapsid gene
1133nt**

**C**

**HCoV-NL63
1a (nsp3) gene
781nt**



SUPPLEMENTAL FIGURE 1. Phylogenetic analysis of the HCoV-NL63 spike, nucleocapsid, and *1a* genes. The partial spike (S1) (1,383 nucleotides), complete nucleocapsid (1,133 nucleotides), and partial *1a* (nsp3) (781 nucleotides) maximum likelihood trees were constructed using the Hasegawa–Kishino–Yano nucleotide substitution model and gamma distribution plus discrete gamma categories in phylogenetic analysis using parsimony. The HCoV-NL63 strains obtained from this study were color coded and the HCoV-NL63 genotypes A–C were indicated; green = genotype A, blue = genotype B, and red = genotype C. The recombinant genotype is indicated by purple color. Scale bars indicating genetic distance (in nucleotide substitutions per site) are shown. Each HCoV-NL63 sequence was assigned to its genotype based on the S1 phylogenetic analysis. Country codes are as follows; MY = Malaysia; US = United States; JP = Japan; NL = Netherlands; CN = China.



SUPPLEMENTAL FIGURE 2. Phylogenetic analysis of the HCoV-229E spike, nucleocapsid, and 1a genes. The partial spike (S1) (855 nucleotides), complete nucleocapsid (1,330 nucleotides), and partial 1a (nsp3) (766 nucleotides) maximum-likelihood trees were constructed using the Hasegawa–Kishino–Yano nucleotide substitution model and gamma distribution plus discrete gamma categories in phylogenetic analysis using parsimony. The HCoV-229E strains obtained from this study were color coded and the HCoV-229E groups 1–4 were indicated; green = genotype 1, red = genotype 2, blue = genotype 3, and purple = genotype 4. Scale bars indicating genetic distance (in nucleotide substitutions per site) are shown. Each HCoV-229E sequence was assigned to its genotype based on the S1 phylogenetic analysis. Country codes are as follows; MY = Malaysia; US = United States; JP = Japan; NL = Netherlands; CN = China; AU = Australia; IT = Italy.

SUPPLEMENTAL TABLE 1

Evolutionary characteristics of HCoV-NL63 and HCoV-229E genotypes

Subtype-gene evolutionary rate*	Genotype	tMRCA†
NL63-Spike 4.3×10^{-4} ($2.1 - 6.6 \times 10^{-4}$)	All genotypes	1,902.2 (1,805.4–1,974.4)
	Genotype A	1,973.9 (1,961.2–1,983.8)
	Genotype B	1,995.6 (1,989.7–2,000.2)
	Genotype C	2,003.0 (1,998.6–2,006.5)
229E-Spike 3.9×10^{-4} ($1.3 - 6.5 \times 10^{-4}$)	All groups	1,956.8 (1,948.4–1,962.0)
	Group 1	1,976.6 (1,973.7–1,978.9)
	Group 2	1,981.1 (1,979.6–1,982.0)
	Group 3	1,989.0 (1,987.4–1,990.0)
	Group 4	1,996.3 (1,993.0–1,999.0)

*Estimated mean rates of evolution expressed as 10^{-4} nucleotide substitutions/site/year under a relaxed molecular clock with GTR+I substitution model and an exponential tree model. The 95% highest posterior density (HPD) confidence intervals are included in parentheses.

†Mean time of the most common ancestor (tMRCA, in calendar year). The 95% highest posterior density confidence intervals are indicated.

SUPPLEMENTAL TABLE 2

Comparison of upper respiratory tract infection symptoms severities between patients infected with HCoV-NL63 and HCoV-229E

Symptom	Severity level	HCoV-NL63	HCoV-229E	<i>P</i> value*
Sneezing	None	3	3	0.472
	Moderate	35	15	
	Severe	7	5	
Nasal discharge	None	7	4	0.051
	Moderate	33	11	
	Severe	5	8	
Nasal congestion	None	16	8	0.727
	Moderate	24	11	
	Severe	5	4	
Headache	None	22	10	0.696
	Moderate	17	8	
	Severe	6	5	
Sore throat	None	12	9	0.269
	Moderate	26	9	
	Severe	6	5	
Hoarseness of voice	None	10	8	0.172
	Moderate	34	13	
	Severe	1	2	
Muscle ache	None	17	7	0.252
	Moderate	20	15	
	Severe	7	1	
Cough	None	2	3	0.477
	Moderate	32	15	
	Severe	11	5	

**P* values < 0.05 represent significant results.