

Supplementary Table S1. Strains/isolates and NCBI accession numbers of analyzed MERS-CoV and lineage C Betacoronaviruses.

Strain/isolate name		Accession ID
NeoCoV	*	KC869678
BtVs-BetaCoV/SC2013	*	KJ473821
Pi-BatCoV HKU5	*	NC_009020
BtCoV/133/2005	*	NC_008315
Ty-BatCoV HKU4	*	NC_009019
EriCoV/2012-216	*	KC545386
EriCoV/2012-174	*	KC545383
Human betaCoV 2c EMC/2012	*	JX869059
MERS CoV isolate Wadi-Ad-Dawasir_1_2013	*	KJ156881
MERS CoV isolate FRA/UAE	*	KF745068
MERS CoV isolate Riyadh_1_2012	*	KF600612
MERS CoV isolate Hafr-Al-Batin_1_2013	*	KF600628
MERS CoV isolate Al-Hasa_17_2013	*	KF600647
MERS CoV strain Hu/Oman_2285_2013		KT156560
MERS CoV strain Hu/Oman_2874_2013		KT156561
MERS CoV isolate MERS-CoV/KOR/KNIH/002_05_2015		KT029139
MERS CoV strain Hu/Riyadh_KSA_2959_2015		KT026453
MERS CoV strain Hu/Riyadh_KSA_4050_2015		KT026454
MERS CoV strain ChinaGD01		KT006149
MERS CoV strain Hu/Riyadh-KSA-2345/2015		KR011263
MERS CoV strain Hu/Riyadh-KSA-2343/2015		KR011264
MERS CoV strain Hu/Riyadh-KSA-2466/2015		KR011265
MERS CoV strain Hu/Riyadh-KSA-2049/2015		KR011266
MERS CoV isolate Hu-France (UAE) - FRA1_1627-2013_BAL_Sanger		KJ361500
MERS CoV isolate Hu-France - FRA2_130569-2013_InSpu_Sanger		KJ361502
MERS CoV isolate Camel/UAE/D1164.9/2014		KP719927
MERS CoV isolate Camel/UAE/D1164.10/2014		KP719928
MERS CoV isolate Camel/UAE/D1164.11/2014		KP719929
MERS CoV isolate Camel/UAE/D1164.14/2014		KP719930
MERS CoV isolate Camel/UAE/D1339/2014		KP719931
MERS CoV isolate Camel/UAE/D1243.12/2014		KP719932
MERS CoV isolate Camel/UAE/D1209/2014		KP719933
MERS CoV isolate England/4/2013		KM210277
MERS CoV isolate England/3/2013		KM210278
MERS CoV isolate Florida/USA-2_Saudi Arabia_2014		KP223131
MERS CoV strain Abu Dhabi_UAE_8_2014		KP209306
MERS CoV strain Abu Dhabi_UAE_18_2014		KP209307
MERS CoV strain Abu Dhabi_UAE_16_2014		KP209308
MERS CoV strain Abu Dhabi_UAE_30_2014		KP209309
MERS CoV strain Abu Dhabi/Gayathi_UAE_2_2014		KP209310
MERS CoV strain Abu Dhabi_UAE_33_2014		KP209311
MERS CoV strain Abu Dhabi_UAE_9_2013		KP209312
MERS CoV strain Abu Dhabi_UAE_26_2014		KP209313
MERS CoV isolate Jeddah_C7149/KSA/2014-04-05		KM027255
MERS CoV isolate Jeddah_C7569/KSA/2014-04-03		KM027256
MERS CoV isolate Jeddah_C7770/KSA/2014-04-07		KM027257
MERS CoV isolate Jeddah_C8826/KSA/2014-04-12		KM027258
MERS CoV isolate Jeddah_C9055/KSA/2014-04-14		KM027259

MERS CoV isolate Jeddah_C10306/KSA/2014-04-20	KM027260
MERS CoV isolate Makkah_C9355/KSA/Makkah/2014-04-15	KM027261
MERS CoV isolate Riyadh_2014KSA_683/KSA/2014	KM027262
MERS CoV isolate England/2/2013	KM015348
MERS CoV strain Indiana/USA-1_Saudi Arabia_2014	KJ813439
MERS CoV isolate Camel/Qatar_2_2014	KJ650098
MERS CoV isolate KSA-CAMEL-505	KJ713295
MERS CoV isolate KSA-CAMEL-378	KJ713296
MERS CoV isolate KSA-CAMEL-503	KJ713297
MERS CoV isolate KSA-CAMEL-363	KJ713298
MERS CoV isolate KSA-CAMEL-376	KJ713299
MERS CoV isolate MERS-CoV-Jeddah-Camel-1	KF917527
MERS CoV isolate MERS-CoV-Jeddah-human-1	KF958702
MERS CoV isolate KFU-HKU 13	KJ650295
MERS CoV isolate KFU-HKU 19Dam	KJ650296
MERS CoV isolate KFU-HKU 1	KJ650297
MERS CoV isolate Jeddah_1_2013	KJ556336
MERS CoV isolate NRCE-HKU205	KJ477102
MERS CoV isolate Al-Hasa_25_2013	KJ156866
MERS CoV isolate Riyadh_9_2013	KJ156869
MERS CoV isolate Hafr-Al-Batin_6_2013	KJ156874
MERS CoV isolate Hafr-Al-Batin_2_2013	KJ156910
MERS CoV isolate Riyadh_14_2013	KJ156934
MERS CoV isolate Riyadh_5_2013	KJ156944
MERS CoV isolate Taif_1_2013	KJ156949
MERS CoV isolate Riyadh_4_2013	KJ156952
MERS CoV isolate Qatar3	KF961221
MERS CoV isolate Qatar4	KF961222
MERS CoV isolate Riyadh_3_2013	KF600613
MERS CoV isolate Bisha_1_2012	KF600620
MERS CoV isolate Al-Hasa_12_2013	KF600627
MERS CoV isolate Buraidah_1_2013	KF600630
MERS CoV isolate Al-Hasa_19_2013	KF600632
MERS CoV isolate Al-Hasa_21_2013	KF600634
MERS CoV isolate Al-Hasa_16_2013	KF600644
MERS CoV isolate Al-Hasa_15_2013	KF600645
MERS CoV isolate Al-Hasa_18_2013	KF600651
MERS CoV isolate Riyadh_2_2012	KF600652
MERS CoV isolate Al-Hasa_4_2013	KF186564
MERS CoV isolate Al-Hasa_3_2013	KF186565
MERS CoV isolate Al-Hasa_2_2013	KF186566
MERS CoV isolate Al-Hasa_1_2013	KF186567
MERS CoV strain Munich	KF192507
Human betaCoV 2c Jordan-N3/2012	KC776174
Human betaCoV 2c England-Qatar/2012	KC667074
BetaCoV England 1	KC164505

* strain used in the branch-site analysis.

Supplementary Table S2. List of positively selected sites detected in branch-site tests.

nsp	Relative Position ^a	Absolute Position ^b	Selected Branch
nsp1	S110	S110	Branch 16
nsp2	C190	C383	Branch 23
nsp2	D225	D418	Branch 23
nsp2	V257	V450	Branch 23
nsp2	L321	L514	Branch 23
nsp2	N388	N581	Branch 16
nsp2	A490	A693	Branch 23
nsp2	V568	V761	Branch 23
nsp3	R42	R895	Branch 23
nsp3	S49	S902	Branch 16
nsp3	C91	C944	Branch 16
nsp3	K365	K1218	Branch 23
nsp3	M370	M1223	Branch 23
nsp3	L406	L1259	Branch 23
nsp3	V421	V1274	Branch 23
nsp3	V448	V1301	Branch 23
nsp3	C482	C1335	Branch 23
nsp3	I503	I1356	Branch 23
nsp3	M517	M1370	Branch 23
nsp3	N536	N1389	Branch 23
nsp3	M723	M1576	Branch 23
nsp3	R730	R1583	Branch 23
nsp3	R812	R1665	Branch 23
nsp3	Q830	Q1683	Branch 16
nsp3	S947	S1800	Branch 16
nsp3	Q1009	Q1862	Branch 23

nsp3	Y1035	Y1888	Branch 16
nsp3	T1080	T1933	Branch 16
nsp3	P1107	P1960	Branch 23
nsp3	Y1160	Y2013	Branch 23
nsp3	R1228	R2081	Branch 23
nsp3	G1295	G2148	Branch 23
nsp3	K1361	K2214	Branch 23
nsp3	A1386	A2239	Branch 16
nsp3	W1454	W2307	Branch 23
nsp3	G1459	G2312	Branch 23
nsp3	Q1467	Q2320	Branch 23
nsp3	S1666	S2519	Branch 17
nsp3	S1797	S2650	Branch 23
nsp3	C1815	C2668	Branch 16
nsp3	A1845	A2698	Branch 23
nsp3	N1871	N2724	Branch 23
nsp4	N6	N2746	Branch 23
nsp4	G15	G2755	Branch 23
nsp4	G202	G2942	Branch 16
nsp4	C345	C3085	Branch 16
nsp4	G453	G3193	Branch 23
nsp4	K480	K3220	Branch 23
nsp5	H8	H3255	Branch 23
nsp5	Q86	Q3333	Branch 23
nsp5	V132	V3379	Branch 23
nsp5	V256	V3503	Branch 23
nsp6	K5	K3558	Branch 23
nsp8	N149	N4077	Branch 16

nsp10	S61	S4298	Branch 23
nsp12	T272	T4649	Branch 16
nsp12	N387	N4764	Branch 23
nsp12	G779	G5156	Branch 23
nsp13	A505	A5815	Branch 23
nsp14	T228	T6136	Branch 23
nsp14	S284	S6192	Branch 23
nsp14	S371	S6279	Branch 23
nsp15	S305	S6737	Branch 23
nsp16	N138	N6913	Branch 23
nsp16	T151	T6926	Branch 23
nsp16	T214	T6989	Branch 23
nsp16	K249	K7024	Branch 23

^a The numbering refers to the position of the site relative to the specific nsp.

^b The numbering refers to the position of the site in ORF1ab (NCBI ID: JX869059).

Supplementary Table S3. List of coevolving sites.

Nsp	Site ^a	Nsp	Site ^a
nsp1	54	nsp3	1425
nsp3	75	nsp3	607
nsp3	94	nsp3	1440
nsp3	405	nsp3	1680
nsp3	546	nsp3	1783
nsp3	558	nsp3	1153
nsp12	200	nsp14	322

^a The numbering refers to the position of the site relative to the specific nsp.