

Additional file 2 – Estimation of divergence time

In the study by Donnelly et al. (2003), the mean incubation time based on 1425 cases in Hong Kong was 6.4 days and the mean time from onset of clinical symptoms to admission to a hospital was 3 – 5 days, with a longer period earlier in the epidemic [1]. The propagation time during cell culture was likely 5-7 days [2, 3]. Therefore, for those isolates without certain infection and isolate dates, we used 7 days for incubation, 5 days for admission to a hospital, and 7 days for cell culture.

TOR2:

Toronto index patient 1 (or patient F) was infected and linked to index patient A on February 21, 2003 in Hong Kong [4]. TOR2 was the primary contact of patient 1. He was admitted to hospital on March 7 and died on March 13, 2003 in Toronto [5]. The specimen might be collected between March 7 and March 13, thus, it took 15 – 21 days since February 21, 2003.

CDC Urbani:

The patient was the primary contact of Vietnam index patient B. He was admitted to the hospital on March 11 and died on March 29, 2003 in Bangkok [6, 7]. The specimen might be collected between March 11 and March 29, thus, it took 19 – 37 days since February 21, 2003.

TW1:

The first SARS patient in Taiwan was admitted to the hospital on March 8, 2003 and the virus culture succeeded on April 19, 2003. So, the divergence time is likely to be 16 – 48 days since February 21, 2003 [8].

Five Singaporean isolates (SIN2500, SIN2677, SIN2679, SIN2748, and SIN2774):

SIN2500 was the primary index patient in Singapore and directly linked to index patient A in Hong Kong. SIN2677, SIN 2748, SIN2774, and SINxxxx (this patient was unavailable) were the four primary contacts and SIN2679 was the secondary contact of SINxxxx [9]. For those isolates, all patients have “history of close contact with another patient with SARS or travel to a region with documented community transmission of SARS within 10 days of onset of symptoms”, and clinical samples are “obtained from the patients between 0 and 11 days after of onset of symptoms” (see [9]). Therefore, the time for the SIN2500 was estimated to be between 7 days (mean incubation time) and 21 (10 + 11) days. Because of the close clinical relationship, we estimated the minimum incubation period 2 days [10] for SIN2677, SIN2748, SIN2774, and SINxxxx, and maximum 13 (2 + 11) days. For SIN2679, the estimated range is likewise to be 2 and 13 days from SINxxxx.

CUHK-W1, CUHK-Su10, and HKU-39849

Before we finished the data analysis, we did not find a formal report of the clinical relationship and sample isolation dates for these three isolates. The specimens were probably isolated before April 2, two weeks before the sequences were released in mid-April, 2003. Therefore, we used the divergence time from 12 days (7 incubation days + 5 hospital admission days) to 41 days (February 21 to April 2, 2003). Recently, we learned that CUHK-W1 was isolated on March 24, 2003 and CUHK-Su10 was isolated on March 13, 2003 (Personal Communication, The Chinese SARS Molecular Epidemiology Consortium). The dates were close to the median values of our estimates. Because the isolation dates have not been formally published, we still used our estimated range of the time.

The estimated divergence time between each pair of sequences is shown in Table S1 and S2 and the proportion of nucleotide difference is shown in Table S3.

Table S1: Low estimate of divergence time between each pair of sequences.

	TOR2	Urbani	CUHK-W1	CUHK-Su10	HKU-39849	SIN2500	SIN2677	SIN2679	SIN2748	SIN2774
TOR2										
Urbani	34									
CUHK-W1	27	31								
CUHK-Su10	27	31	24							
HKU-39849	27	31	24	24						
SIN2500	22	26	19	19	19					
SIN2677	24	28	21	21	21	16				
SIN2679	26	30	23	23	23	18	16			
SIN2748	24	28	21	21	21	16	14	16		
SIN2774	24	28	21	21	21	16	14	16	14	
TW1	31	35	28	28	28	23	25	27	25	25

Table S2: High estimate of divergence time between each pair of sequences.

	TOR2	Urbani	CUHK-W1	CUHK-Su10	HKU-39849	SIN2500	SIN2677	SIN2679	SIN2748	SIN2774
TOR2										
Urbani	58									
CUHK-W1	62	78								
CUHK-Su10	62	78	82							
HKU-39849	62	78	82	82						
SIN2500	42	58	62	62	62					
SIN2677	50	66	70	70	70	31				
SIN2679	59	75	79	79	79	40	49			
SIN2748	50	66	70	70	70	31	36	49		
SIN2774	50	66	70	70	70	31	36	49	36	
TW1	69	85	89	89	89	69	77	86	77	77

Table S3: The proportion of nucleotide difference between each pair of sequences ($\times 10^{-3}$).

	TOR2	Urbani	CUHK-W1	CUHK-Su10	HKU-39849	SIN2500	SIN2677	SIN2679	SIN2748	SIN2774
TOR2										
Urbani	0.24									
CUHK-W1	0.37	0.40								
CUHK-Su10	0.17	0.27	0.34							
HKU-39849	0.37	0.47	0.61	0.40						
SIN2500	0.14	0.24	0.37	0.17	0.37					
SIN2677	0.17	0.27	0.40	0.20	0.40	0.10				
SIN2679	0.14	0.24	0.37	0.17	0.37	0.14	0.17			
SIN2748	0.10	0.20	0.34	0.14	0.34	0.03	0.07	0.10		
SIN2774	0.17	0.27	0.40	0.20	0.40	0.10	0.14	0.17	0.07	
TW1	0.10	0.20	0.34	0.14	0.34	0.10	0.14	0.10	0.07	0.14

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