## Supplementary Methods

### Subjects

This study included three independent case-control populations. The first one (called 'Beijing community population' in current study) consists of 352 patients with SARS who were infected in community and recruited from Xiaotangshan Hospital (Beijing, China) and 392 control subjects who were blood donors recruited before the outbreak. The enrollment criterion had been described in detail previously[1]. Thirteen cases and 165 controls had to be excluded because their DNA had been depleted in the original study; therefore, the present sample had a total of 339 cases and 227 controls. No differences were observed in terms of the age and sex distribution between the 352 and the remaining 339 cases, and, between the 392 and the remaining 227 controls. Of the remaining 339 case patients, 52 had comorbid conditions. Of the 287 case patients without comorbid conditions, 19 were patients with severe SARS, who were identified by their admissions to intensive care units or deaths, and the remaining 268 were patients with mildly symptomatic SARS. For the 339 patients, the male/female ratio was 1.2, and the mean age was 32.3 years (range, 15-77 years). For the remaining 227 age-, sex-, and ethnicity-matched healthy control subjects; the male/female ratio was 1.5, and the mean age was 29.8 years (range, 17-62 years).

The second population (called 'Beijing health care worker population' in current study), consisting of 66 patients with SARS and 64 control subjects, was recruited from Beijing Wujing Hospital (Beijing, China). The patients were health care workers infected in hospital during the course of duty, and the controls were also health care workers who had worked in SARS wards but remained disease-free and were confirmed to be seronegative for SARS. The enrollment criterion had been described in detail previously[2]. In present study, only 42 cases and 40 controls were included because the other DNAs had been depleted in the original study. No significant differences were observed in terms of the age and sex distribution between the

66 and the remaining 42 cases (mean age, 28.4 and 29.4 years, respectively; male/female ratio, 1.1 and 1.2, respectively), and, between the 64 and the remaining 40 controls (mean age, 29.6 and 29.3 years, respectively; male/female ratio, 1.9 and 2.6, respectively).

The third population (called 'Tianjin population' in current study), consisting of 60 patients with SARS and 129 control subjects, was recruited from Wujing Medical College at Tianjin (Tianjin, China). All the patients were infected in community, and the controls contained 85 blood donors and 44 health care workers who had worked in SARS wards but remained disease-free and were confirmed to be seronegative for SARS. The enrollment criterion had been described in detail previously[3]. More men ($\chi^2$ = 5.71, $P$ = 0.017) and higher mean age ($P$ = 0.013, $t$ test) were presented in the 60 cases compared with 129 control subjects (mean age, 34.6 and 25.8 years, respectively; male/female ratio, 0.5 and 1.1, respectively).

**Polymorphism genotyping**

The PCR fragment containing the VNTR polymorphism was generated using L-SIGN-forward and L-SIGN-reverse primers (**Supplementary Table 2 online)** in a reaction mixture of 15 μl containing 10-20 ng genomic DNA, 0.25 mM dNTPs, 1.5 mM $MgCl_2$, 200 pM of each primer and 1 unit (U) Ex Taq DNA polymerase (TaKaRa, Otsu, Shiga). The reaction was carried out at 94ºC for 2 min, 32 cycles of denaturing at 94ºC for 30 s, annealing at 56.5ºC for 30 s and extension at 72ºC for 40 s, and final extension at 72ºC for 10 min. The amplified products were separated by 2% agarose gel electrophoresis. The length of alleles was determined using marker standards and genotypes were expressed as number-of-repeat combinations. Genotyping was performed in a blind manner that the performers did not know subjects' case/control status. For quality control, a 15% masked, random sample of cases and controls was tested twice by different people and all results were 100% concordance. Some samples were also confirmed by direct sequencing. As an over-calling of homozygous 5/5

genotype, under-calling of 7/7 and heterozygous 7/5 was observed in Beijing Community SARS patients and may have thus contributed to the Hardy-Weinberg disequilibrium, we confirmed all 18 samples with 5/5 genotype and 20 samples randomly selected from the 175 samples with 7/7 genotype in Beijing Community SARS group by direct sequencing. All the 48 samples with 7/5 genotype in Beijing Community SARS group were also confirmed by 2% agarose gel electrophoresis by different people.

**Statistical analysis**

Allele and genotype frequencies for the polymorphism were determined by direct gene counting, and the fitness to Hardy-Weinberg equilibrium was tested using the Markov chain method implemented in the GENEPOP software package (available at: http://wbiomed.curtin.edu.au/genepop/). Comparisons of sex distribution between patient and control groups were performed by use of the $\chi^2$ test. Differences of mean age between the groups were analyzed by use of an unpaired *t* test. Comparison of allele or genotype frequencies was done using the CLUMP program (available at: http://www.mds.qmw.ac.uk/statgen/dcurtis/software). Genetic association for heterozygote and homozygote genotype with the SARS risk was assessed by use of logistic regression using SPSS software (version 9.0; SPSS Inc., Chicago, IL), and the odds ratio (OR) and 95% confidential interval (c.i.) were calculated and adjusted for age and gender, where it was appropriate. An association was considered significant at a *P* value of less than 0.05, and all statistical tests were two-sided.

**URLs.** Hardy-Weinberg Exact Test, available at http://wbiomed.curtin.edu.au/genepop/; CLUMP program, available at http://www.mds.qmw.ac.uk/statgen/dcurtis/software.

**GenBank accession number.** Genomic sequence of *L-SIGN*, AC008812.7

## References


1. Zhang, H. *et al*. *J*. *Infect*. *Dis*. **192**, 1355-1361 (2005).

2. Wang, H.W. *et al*. *Zhonghua Liu Xing Bing Xue Za Zhi* **26**, 574-577 (2005).

3. Zhang, K.J. *et al*. *Acta Academiae Medicinae CPAPF* **14**, 435-438 (2005).