

Table 4. List of all SNVs in S genes with multiple occurrences

Sequence alignments were generated by the method described in *Materials and Methods* as well as in the Table 2 legend. The names of the genomic sequences (from INSD/GenBank) are listed on the first column based on clusters determined by our scoring algorithm (1). All of these sequences are further divided by colored lines into subgroups (defined in the text and Fig. 1) based on their host species (human vs. palm civet) and epidemiological phases (year and early, middle, and late phases of the 2002-2003 epidemic). All of the palm civet sequences were shaded with light green.

Characteristics of the SNVs observed are listed in the top rows. From the top of the rows, they include the predicted tertiary location of the corresponding amino acid residues with respect to the computer-simulated 3D structure of the Spike (S) protein, the variant nucleotides observed at the loci, the affected codon, the resulting amino acid switches, the amino acid coordinate of the S protein, and the nucleotide coordinate of the S gene and of the genome [based on GZ02 (1)], respectively.

All 49 SNVs that are observed in more than one of the 103 S CDS sequences, i.e., two more SNVs observed than that using whole genome sequences (Table 2) are listed because more sequences were added for the analysis. One of them (nucleotide 22220) causes synonymous variation in the amino acid residue 243D, which is predicted to be partially exposed at the top of the S1 domain, whereas the other (nucleotide 23163) causes a nonsynonymous variation of amino acid residue 558F/I, which is predicted to be exposed at the side of S1 domain but not involved in receptor binding.

Different characters of the amino acid switches were labeled with different-color shadings in the corresponding row: light pink for synonymous variations, yellow for

nonsynonymous variations causing amino acid switches in the same physical-chemical group, and greenish yellow for nonsynonymous variations causing drastic amino acid switches. In the rows for individual sequences, the minor forms of the SNVs were printed with pink, and the undetermined nucleotides (N) were shaded with orange.

SNVs that contribute to the grouping of genotypes based on the predominant clustering criteria previously described (1) were further highlighted in the rows with different color shading and bolding of the letters as described for Table 2, except:

1. The 3-nt loci in the *S* gene of the 5-nt motif used to classify the major genotypes of the 2002-2003 epidemic human SARS-CoV (HP03) are shaded as reported (1), namely , positions 21721 (yellow), 22222 (blue), and 23823 (green). These variations are all emphasized with bold face.

2. The SNVs distinguishing the SARS-CoVs of the 2003-2004 epidemic (PC04 and HP04) from those of the 2002-2003 epidemic (PC03 and HP03) are shaded in light pink, of which those causing nonsynonymous variations are emphasized with bold face.

3. Compared with Table 2, nucleotides 23719 and 23785 were excluded, because the addition of more PC04 samples showed the variations within the category.

4. The SNVs distinguishing the SARS-CoV of the palm civet (PC03 and PC04) and the human patient of the 2003-2004 epidemic (HP04) from human patients of the 2002-2003 epidemic (HP03) are shaded in light blue. Because all of them cause nonsynonymous variations, they are all emphasized with bold face.

5. Compared with Table 2, nucleotide 23485 was excluded, because the addition of the GZ03-03 sample of the HP04 group showed the variation within the category.

6. Some special SNVs are illustrated:

(i) SNVs in nucleotides 22927 and 22928 cause nonsynonymous amino acid switches in the same residue, 479 of the S protein. This group of variations is emphasized with bold face and shaded with dark greenish yellow.

(ii) SNVs in nucleotides 23316 and 23317 cause the same nonsynonymous amino acid switches in the same residue, 609 of the S protein. This group of variations is emphasized with bold face and shaded with dark greenish yellow.

(iii) SNVs in nucleotides 23718 and 23719 cause nonsynonymous amino acid switches in the same residue, 743 of the S protein. This group of variations is emphasized with bold face and shaded with dark greenish yellow.

1. The Chinese SARS molecular epidemiology consortium (2004) *Science* **303**, 1666-1669.

