

**Supplementary Table S2.** SARS-CoV-2 PSS supported by multiple lines of evidence. For each site, the amino acid of the genome of reference is represented, followed by mutations and the date of their first record, according to COV2var database.

Protein	PSS	Reference a.a. → mutation(s) (first recording)
S	5	L → F (01/2020)
	9	P → S (03/2020); L (03/2020)
	18	L → F (01/2020); R (03/2020)
	19	T → P (04/2020); R (03/2020); I (03/2020)
	67	A → S (03/2020); V (01/2020)
	70	V → I (05/2020); F (03/2020)
	77	K → T (08/2020)
	83	V → A (05/2020)
	95	T → A (03/2020); N (04/2020); I (01/2020)
	97	K → E (04/2020); T (06/2020); R (04/2020); N (03/2020)
	98	S → P (05/2020); F (01/2020)
	138	D → H (03/2020); Y (01/2020)
	142	G → S (03/2020); D (03/2020); V (03/2020)
	145	Y → N (05/2020); H (03/2020); D (03/2020)
	146	H → N (04/2020); Y (03/2020); L (04/2020); Q (04/2020)
	147	K → E (06/2020); T (06/2020); I (05/2020); N (04-10/2020)
	152	W → R (03-04/2020); L (03/2020); C (01/2020)
	157	F → S (03/2020); L (02/2020)
	212	L → I (08/2020); S (04/2020)
	213	V → L (03/2020); E (11/2020); A (04/2020); G (08/2020)
	222	A → V (02/2020)
	250	T → A (03/2020); I (03/2020)
	251	P → S (04/2020); H (02/2020); L (03/2020)
	252	G → S (03/2020); D (05/2020); V (04/2020)
	253	D → N (04/2020); Y (03/2020); A (03/2020); G (01/2020)
	368	L → I (05/2020)
	371	S → P (04/2020); F (04/2020)
	376	T → A (11/2020)
	385	T → I (04/2020)
	408	R → I (01/2020); S (09/2020)
	417	K → T (04/2020); N (02/2020)
	440	N → K (03-05/2020)
	444	K → T (02/2021); R (03/2020); M (01/2021); N (04/2020-01/2021)
	445	V → L (12/2020); F (04/2020); A (04/2020)
	446	G → S (04/2020); D (05/2020); V (03/2020)
	452	L → M (04/2020); Q (03/2020); R (01/2020)
	460	N → S (04/2020); K (10/2020)
	477	S → N (01/2020); I (03/2020); R (04/2020)
	484	E → K (02/2020); Q (03/2020); A (03/2020); G (04/2020)
	486	F → I (09/2020); L (04/2020); V (07/2020); S (12/2020)
	490	F → L (03/2020); V (05/2020); S (04/2020)
	493	Q → R (04/2020); L (05/2020)
	498	Q → R (04/2020)
	501	N → Y (02/2020); T (03/2020)
	505	Y → H (04/2020)
	614	D → N (03/2020); G (01/2020)
	655	H → Y (01/2020)

	658	$N \rightarrow D$ (03/2020); S (09/2020)
	680	$S \rightarrow F$ (03/2020)
	681	$P \rightarrow S$ (03/2020); H (01/2020); R (05/2020); L (03/2020)
	764	$N \rightarrow K$ (01/2020)
	950	$D \rightarrow N$ (03/2020)
	1147	$S \rightarrow L$ (03/2020)
	1219	$G \rightarrow C$ (01/2020); V (03/2020)
N	3	$D \rightarrow H$ (03/2020); Y (03/2020); V (03/2020); E (03/2020)
	9	$Q \rightarrow L$ (04/2020); H (03/2020)
	24	$T \rightarrow A$ (10/2020); N (02/2020); I (03/2020)
	25	$G \rightarrow C$ (03/2020); D (04/2020); V (03/2020)
	28	$Q \rightarrow R$ (03/2020); H (03/2020)
	32	$R \rightarrow C$ (03/2020); H (03/2020)
	33	$S \rightarrow G$ (01/2020); C (10/2020); N (03/2020); I (03/2020)
	63	$D \rightarrow N$ (03/2020); Y (03/2020); G (06/2020)
	67	$P \rightarrow S$ (01/2020); L (03/2020)
	90	$A \rightarrow T$ (03/2020); S (03/2020); V (04/2020)
	135	$T \rightarrow A$ (06/2020); I (03/2020)
	136	$E \rightarrow D$ (04/2020)
	178	$G \rightarrow S$ (03/2020); V (07/2020)
	199	$P \rightarrow S$ (02/2020); L (01/2020)
	202	$S \rightarrow C$ (02/2020); N (01/2020); T (02/2020); I (03/2020)
	204	$G \rightarrow R$ (01-03/2020); A (04/2020); V (02/2020)
	205	$T \rightarrow N$ (05/2020); I (01/2020)
	215	$G \rightarrow S$ (02/2020); C (03/2020); V (03/2020)
	218	$A \rightarrow T$ (06/2020); S (03/2020); V (03/2020)
	219	$L \rightarrow F$ (04/2020)
	235	$S \rightarrow F$ (01/2020)
	238	$G \rightarrow S$ (04/2020); C (03/2020); D (09/2020); V (03/2020)
	241	$Q \rightarrow K$ (05/2020); L (03/2020)
	343	$D \rightarrow H$ (03/2020); G (06/2020)
	365	$P \rightarrow S$ (02/2020); L (03/2020)
	368	$P \rightarrow S$ (03/2020); L (01/2020)
	376	$A \rightarrow T$ (02/2020); V (04/2020)
	377	$D \rightarrow Y$ (01/2020); A (03/2020); G (03/2020)
	379	$T \rightarrow A$ (05/2020); I (02/2020)
	383	$P \rightarrow S$ (02/2020); L (02/2020)
	391	$T \rightarrow I$ (01/2020)
	413	$S \rightarrow R$ (06/2020); I (03/2020)
M	2	$A \rightarrow T$ (03/2020); S (01/2020); V (03/2020)
	3	$D \rightarrow N$ (05/2020); Y (03/2020); G (02/2020)
	4	$S \rightarrow F$ (01/2020)
	6	$G \rightarrow C$ (03/2020)
	30	$T \rightarrow I$ (04/2020)
	34	$L \rightarrow F$ (03/2020)
	63	$A \rightarrow T$ (01/2020); S (05/2020)
	69	$A \rightarrow S$ (03/2020); V (03/2020)
	70	$V \rightarrow I$ (03/2020); L (05/2020); F (03/2020)
	82	$I \rightarrow V$ (08/2020); T (03/2020); S (08/2020)
	155	$H \rightarrow Y$ (03/2020)

E	9	$T \rightarrow A$ (04/2020); I (03/2020)
NSP1	24	$R \rightarrow C$ (02/2020); L (03/2020)
	28	$V \rightarrow I$ (04/2020); L (03/2020)
	62	$P \rightarrow S$ (03/2020)
	76	$A \rightarrow V$ (04/2020)
	87	$E \rightarrow D$ (03/2020)
	100	$S \rightarrow N$ (05/2020)
	110	$H \rightarrow Y$ (03/2020); R (04/2020)
	135	$S \rightarrow N$ (01/2020); R (08/2020)
	137	$G \rightarrow S$ (03/2020); C (03/2020); D (03/2020); V (02/2020)
NSP2	27	$R \rightarrow L$ (03/2020)
	31	$A \rightarrow T$ (03/2020); V (02/2020)
	36	$S \rightarrow T$ (09/2020); Y (08/2020); F (02/2020)
	101	$I \rightarrow V$ (03/2020)
	112	$K \rightarrow N$ (03/2020)
	164	$C \rightarrow F$ (04/2020)
	225	$A \rightarrow D$ (06/2020); V (04/2020)
	339	$G \rightarrow S$ (01/2020); C (04/2020); D (03/2020)
	419	$A \rightarrow V$ (03/2020)
	466	$W \rightarrow L$ (04/2020); C (02/2020)
NSP3	485	$V \rightarrow I$ (03/2020)
	10	$D \rightarrow N$ (04/2020); Y (04/2020)
	24	$T \rightarrow I$ (04/2020)
	149	$A \rightarrow V$ (03/2020)
	175	$G \rightarrow S$ (02/2020); C (03/2020); D (05/2020)
	183	$T \rightarrow I$ (03/2020)
	218	$D \rightarrow E$ (02/2020)
	733	$I \rightarrow V$ (03/2020); T (04/2020)
	1228	$P \rightarrow S$ (03/2020); L (03/2020)
	1250	$T \rightarrow I$ (01/2020)
NSP4	1412	$I \rightarrow T$ (03/2020)
	92	$A \rightarrow V$ (04/2020)
	94	$V \rightarrow A$ (08/2020)
	264	$L \rightarrow F$ (02/2020)
	327	$T \rightarrow A$ (05/2020); I (12/2019)
	438	$L \rightarrow I$ (08/2020); F (01/2020); P (01/2020)
NSP5	492	$T \rightarrow A$ (04/2020); I (01/2020)
	104	$V \rightarrow I$ (04/2020)
NSP6	132	$P \rightarrow S$ (03/2020); H (01/2020); L (03/2020)
	2	$A \rightarrow V$ (03/2020)
	11	$H \rightarrow Y$ (03/2020); Q (04/2020)
	37	$L \rightarrow F$ (01/2020)
	162	$I \rightarrow V$ (07/2020); T (03/2020)
	182	$V \rightarrow I$ (03/2020); F (05/2020)
	195	$E \rightarrow D$ (01/2020)
NSP7	197	$C \rightarrow F$ (04/2020)
	NA	NA
NSP8	17	$T \rightarrow A$ (03/2020)
	24	$Q \rightarrow R$ (04/2020); H (04/2020)

	145	$T \rightarrow I$ (03/2020)
	148	$T \rightarrow A$ (03/2020); $I$ (01/2020)
NSP9	21	$T \rightarrow N$ (04/2020); $I$ (03/2020)
	24	$T \rightarrow I$ (01/2020)
	34	$T \rightarrow I$ (03/2020)
	35	$T \rightarrow I$ (03/2020)
	36	$K \rightarrow R$ (04/2020); $N$ (01/2020)
	39	$R \rightarrow K$ (04/2020)
NSP10	84	$P \rightarrow S$ (03/2020); $L$ (03/2020)
	104	$A \rightarrow T$ (06/2020); $V$ (03/2020)
	134	$R \rightarrow S$ (03/2020); $C$ (03/2020); $H$ (04/2020); $L$ (03/2020)
NSP12	323	$P \rightarrow S$ (02/2020); $L$ (01/2020)
	671	$G \rightarrow S$ (03/2020); $C$ (03/2020); $V$ (04/2020)
	694	$F \rightarrow Y$ (06/2020)
NSP13	36	$S \rightarrow P$ (02/2020)
	77	$P \rightarrow Q$ (03/2020); $L$ (02/2020)
	164	$H \rightarrow Y$ (03/2020)
	260	$D \rightarrow Y$ (01/2020)
	392	$R \rightarrow C$ (01/2020)
	460	$K \rightarrow R$ (03/2020)
NSP14	42	$I \rightarrow V$ (01/2020); $L$ (04/2020)
	43	$P \rightarrow S$ (03/2020); $L$ (01/2020)
	129	$N \rightarrow D$ (01/2020)
	374	$S \rightarrow A$ (03/2020); $F$ (03/2020)
NSP15	80	$A \rightarrow V$ (04/2020)
	259	$K \rightarrow R$ (04/2020); $N$ (04/2020)
	282	$D \rightarrow N$ (03/2020); $Y$ (04/2020); $G$ (03/2020)
NSP16	6938	$T \rightarrow I$ (03/2020)
	6949	$T \rightarrow I$ (02/2020)
	6977	$D \rightarrow Y$ (03/2020); $G$ (03/2020)
	7013	$P \rightarrow T$ (08/2020); $S$ (05/2020); $L$ (03/2020)
	7014	$R \rightarrow S$ (03/2020); $C$ (01/2020); $H$ (03/2020); $L$ (03/2020)
	7034	$P \rightarrow S$ (03/2020); $L$ (03/2020)
	7036	$Q \rightarrow H$ (03/2020)
ORF3a	26	$S \rightarrow L$ (03/2020)
	57	$Q \rightarrow H$ (01-03/2020)
	106	$L \rightarrow F$ (2/2020)
	108	$L \rightarrow V$ (04/2020); $F$ (03/2020)
	110	$A \rightarrow S$ (02/2020); $V$ (01/2020)
	155	$D \rightarrow H$ (02/2020); $Y$ (02/2020)
	172	$G \rightarrow R$ (02/2020); $C$ (03/2020); $D$ (03/2020); $V$ (01/2020)
	223	$T \rightarrow S$ (12/2020); $N$ (04/2020); $I$ (02/2020)
	224	$G \rightarrow R$ (03/2020); $C$ (02/2020); $V$ (03/2020)
	229	$T \rightarrow N$ (10/2020); $I$ (03/2020)
ORF6	NA	NA
ORF7a	45	$P \rightarrow S$ (03/2020); $L$ (02/2020)
	82	$V \rightarrow F$ (03/2020); $A$ (05/2020)
	116	$L \rightarrow F$ (01/2020)
	4	$L \rightarrow F$ (03/2020)

ORF7b	40	T → I (03/2020)
	42	H → Y (03/2020)
	43	A → T (03/2020); S (03/2020); V (01/2020)
ORF8	84	L → S (12/2019)
	100	V → L (01/2020)
	121	I → L (02/2020); F (03/2020); T (04/2020)
ORF10	NA	NA