

Table S1. Selective pressure analysis on SARS-CoV-2 delta variant
Italian protein coding sub-sets genomes

	<i>nsp1</i>
Positively selected sites (w for sites > 1) HYPHY software	62 (P, S); 87 (E, D); 94 (G, S, V)
Negatively selected sites (w for sites < 1) HYPHY software	16 (L), 35 (V), 105 (G), 116 (V), 160 (N)
	<i>nsp2</i>
Positively selected sites (w for sites > 1) HYPHY software	27 (R,C); 81 (K,N), 89 (E,K), 129 (P,L,S), 155 (D, G), 159 (A, V), 263 (S, F), 318 (A, V), 339 (G,S), 485 (V, I), 496 (Q, P, H)
Negatively selected sites (w for sites < 1) HYPHY software	8 (N); 20 (C); 101 (I); 154 (G); 179 (Y); 236 (C); 308 (V); 311 (V); 312 (K); 339 (G, S); 340 (A, V); 425 (V); 457 (E); 560 (I)
	<i>nsp3</i>
Positively selected sites (w for sites > 1) HYPHY software	126 (S, L); 384 (K, N); 862 (L,F); 1228 (P, L); 1791 (L, F)
Negatively selected sites (w for sites < 1) HYPHY software	9 (D), 12 (V), 21 (V), 75 (L), 89 (L), 119 (E), 237 (T), 249 (H), 363 (N), 390 (K), 438 (Y), 466 (P), 506 (N), 534 (A), 567 (T), 622 (D), 629 (T), 646 (R), 667 (A), 694 (K), 714 (D), 717 (V), 806 (D), 881 (Y), 884 (A), 891 (N), 918 (F), 952 (Y), 955 (T), 978 (Y), 988 (M, G), 989 (M, S), 1089 (F), 1095 (D), 1107 (F), 1117 (I), 1141 (F), 1159 (P), 1181 (N), 1188 (N), 1210 (L), 1224 (E), 1254 (V), 1377 (P), 1416 (L), 1520 (F), 1528 (I), 1622 (G), 1649 (D), 1672 (I), 1698 (H), 1730 (K), 1828 (V), 1846 (E), 1859 (Y), 1860 (N), 1885 (V).
	<i>nsp4</i>
Positively selected sites (w for sites > 1)	204 (T, I), 279 (D, N), 295 (T, I), 296 (C, F)

HYPHY software

Negatively selected sites (w for sites < 1) 43 (I), 66 (N), 89 (P), 140 (I), 144 (D), 192 (V), 222 (R), 223 (H), 258 (V), 273 (Q), 290 (V), 318 (N), 337 (F), 378 (T), 390 (F), 410 (S),

HYPHY software 416 (A), 443 (R), 445 (L)

nsp5

Positively selected sites (w for sites > 1) /

HYPHY software

Negatively selected sites (w for sites < 1) 187 (D)

HYPHY software

nsp6

Positively selected sites (w for sites > 1) 2 (A, V), 6 (T, I), 27 (Q, R), 37 (L, F)

HYPHY software

Negatively selected sites (w for sites < 1) 16 (L), 179 (V), 183 (M, I), 200 (F), 229 (C), 259 (L)

HYPHY software

nsp7

Positively selected sites (w for sites > 1) /

HYPHY software

Negatively selected sites (w for sites < 1) 9 (T)

HYPHY software

nsp8

Positively selected sites (w for sites > 1) /

HYPHY software

Negatively selected sites (w for sites < 1) 185 (I)

HYPHY software	
	<i>nsp9</i>
Positively selected sites (w for sites > 1)	/
HYPHY software	
Negatively selected sites (w for sites < 1)	112 (L)
HYPHY software	
	<i>nsp10</i>
Positively selected sites (w for sites > 1)	/
HYPHY software	
Negatively selected sites (w for sites < 1)	34 (G), 48 (H), 59 (P)
HYPHY software	
	<i>nsp11</i>
Positively selected sites (w for sites > 1)	/
HYPHY software	
Negatively selected sites (w for sites < 1)	/
HYPHY software	
	<i>nsp12</i>
Positively selected sites (w for sites > 1)	46 (A, S), 61 (E, D, K), 95 (A, S), 141 (T, I), 197 (R, Q), 323 (P, L), 384 (S, P), 463 (M, I), 822 (Q, H), 838 (L, I)
HYPHY software	
Negatively selected sites (w for sites < 1)	37 (I), 39 (N), 59 (K,N), 61 (E,D,K), 83 (E), 168 (N), 177 (N,K), 212 (L), 217 (Y), 221 (D), 235 (D), 273 (Y), 275 (F), 291 (D), 301 (C),
HYPHY software	
	308 (L), 326 (F), 340 (F), 369 (K), 428 (F), 450 (I), 458 (Y), 463 (M, I), 495 (V), 541 (Q), 569 (R), 599 (H), 606 (Y), 608 (D), 657 (N), 691 (N), 700 (V), 701 (T), 702 (A), 713 (N), 752 (H), 760 (D), 765 (C), 769 (T), 770 (Y), 872 (H), 875 (Q), 885 (L), 891 (L), 894 (E), 910 (D).
HYPHY software	
	<i>nsp13</i>

Positively selected sites (w for sites > 1)	77 (P, L), 89 (V, I)	
HYPHY software		
Negatively selected sites (w for sites < 1)	32 (D), 34 (V), 47 (P, L), 60 (V), 75 (H), 93 (Y), 139 (K), 151 (I), 177 (N), 234 (P), 258 (I), 311 (H), 318 (C), 323 (K), 336 (A), 360 (V),	
HYPHY software	401 (D), 420 (E), 446 (A, P), 462 (K), 521 (V)	
		<i>nsp14</i>
Positively selected sites (w for sites > 1)	46 (P, L), 289 (R, H), 374 (S, F), 394 (A, V)	
HYPHY software		
Negatively selected sites (w for sites < 1)	93 (G), 103 (T), 156 (G), 182 (V), 212 (R), 224 (Y), 232 (G), 235 (Y), 279 (C), 382 (C), 383 (L), 402 (D), 410 (N), 424 (H) , 428 (T)	
HYPHY software		
		<i>nsp15</i>
Positively selected sites (w for sites > 1)	80 (A, V), 81 (A, V)	
HYPHY software		
Negatively selected sites (w for sites < 1)	39 (D), 45 (N), 84 (V), 85 (I), 116 (C), 137 (A), 145 (E)	
HYPHY software		
		<i>nsp16</i>
Positively selected sites (w for sites > 1)	9 (V, I), 34 (A, V), 215 (P, L, T)	
HYPHY software		
Negatively selected sites (w for sites < 1)	15 (Y), 17 (M, I), 45 (A), 55 (N), 56 (T), 66 (R), 93 (T), 107 (A), 116 (A), 155 (G), 167 (V), 170 (K), 199 (A), 237 (I), 250 (F), 266 (Q), 277 (K)	
HYPHY software		
		<i>spike</i>
Positively selected sites (w for sites > 1)	5 (L, F), 70 (V, I, F), 95 (T, I), 142 (G, D, Y, H, V), 222 (A, S, V), 367 (V, L, H, F), 452 (L, R), 501 (N, Y) , 613 (Q, H), 614 (D, G), 677 (Q, H), 681 (P,R),	

HYPHY software 950 (D, N), 1104 (V, L), 1128 (V, L), 1219 (G, V, C)

Negatively selected sites (w for sites < 1)
HYPHY software 32 (F), 102 (R), 106 (F), 137 (N, K), 234 (N), 296 (L), 302 (T), 312 (I), 346 (R), 395 (V), 400 (F), 410 (I), 432 (C), 477 (S), 603 (N), 649 (C), 665 (P), 707 (Y), 732 (T), 760 (C), 856 (N), 935 (Q), 1061 (V), 1065 (V), 1119 (N), 1122 (V), 1230 (V), 1239 (S), 1257 (D)

ORF3a

Positively selected sites (w for sites > 1)
HYPHY software 41 (L, I, F), 110 (A, S, V)

Negatively selected sites (w for sites < 1)
HYPHY software 22 (D), 101 (L)

E

Positively selected sites (w for sites > 1)
HYPHY software /

Negatively selected sites (w for sites < 1)
HYPHY software /

M

Positively selected sites (w for sites > 1)
HYPHY software 82 (I, T)

Negatively selected sites (w for sites < 1)
HYPHY software 53 (F), 88 (V), 121 (N), 203 (N)

ORF6

Positively selected sites (w for sites > 1) HYPHY software	/
Negatively selected sites (w for sites < 1) HYPHY software	16 (L)
ORF7a	
Positively selected sites (w for sites > 1) HYPHY software	/
Negatively selected sites (w for sites < 1) HYPHY software	69 (D)
ORF8	
Positively selected sites (w for sites > 1) HYPHY software	/
Negatively selected sites (w for sites < 1) HYPHY software	46 (Y)
N	
Positively selected sites (w for sites > 1) HYPHY software	9 (Q, L, H)
Negatively selected sites (w for sites < 1) HYPHY software	13 (P), 35 (A), 110 (F), 128 (D), 154 (N), 158 (V), 297 (D), 298 (Y), 302 (P), 329 (T)
ORF 10	
Positively selected sites (w for sites > 1) HYPHY software	/

Negatively selected sites (w for sites < 1) /

HYPHY software