|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Segment (Protein)** | **Position** | **Transmission** | **Amino Acid pattern** | **Top 5 shap** | **Pos selection** | **Higher mut rate** | **Protein functional domain** | **Literature** |
| **PB2** | 251 | human-human | R | X |  |  | Mid domain | Host discrimination (Cai M, 2002) |
| human-swine | R >> K |  |  |  |
| swine-human | R > K |  |  |  |
| swine-swine | R / K | X |  |  |
| 340 | human-human | K > R |  |  |  | Cap binding |  |
| human-swine | K > R |  |  |  |
| swine-human | K / R >> N | X |  |  |
| swine-swine | K / R >> N | X |  |  |
| 344 | human-human | V > M |  |  |  | Cap binding |  |
| human-swine | V > M |  | X |  |
| swine-human | V >> M | X |  |  |
| swine-swine | V >> M |  |  |  |
| 453 | human-human | S > P / H > T | X |  |  | Cap binding |  |
| human-swine | S > P > H > T | X |  |  |
| swine-human | P > S |  |  |  |
| swine-swine | P > S |  |  |  |
| 456 | human-human | N > S |  |  |  | Cap binding |  |
| human-swine | N > S |  |  |  |
| swine-human | N / S >> D > T | X |  |  |
| swine-swine | N > S > D |  |  |  |
| 684 | human-human | S > A >> T |  |  |  | NLS | Host discrimination (Griffin EF, 2023, Hayashi T, 2015) |
| human-swine | S > A | X |  |  |
| swine-human | A > S > G |  |  |  |
| swine-swine | A > S >> T / G |  |  |  |
| **PB1** | 152 | human-human | S >> L > M |  |  |  | Fingers |  |
| human-swine | S >> L > M |  | X |  |
| swine-human | S > M > L / T > K / V |  |  |  |
| swine-swine | S > M > L >> K | X | X |  |
| 175 | human-human | D / N | X |  |  | Fingers |  |
| human-swine | D / N |  |  |  |
| swine-human | D >> N |  |  |  |
| swine-swine | D >> N |  |  |  |
| 179 | human-human | I > M > V |  |  |  | Fingers/β-ribbon |  |
| human-swine | I >> M | X |  |  |
| swine-human | I / M |  |  |  |
| swine-swine | M > I |  |  |  |
| 216 | human-human | G / S |  |  |  | Fingers | Replication fidelity ( Lin RW, 2019) |
| human-swine | G / S >> N / D |  |  |  |
| swine-human | S >> G > N | X |  |  |
| swine-swine | S > G > N |  |  |  |
| 374 | human-human | A >> S | X |  |  | β-hairpin |  |
| human-swine | A > S >> E | X |  |  |
| swine-human | A >> S > E / T / V |  | X |  |
| swine-swine | A >> S |  |  |  |
| 375 | human-human | S >> N > G / D |  |  |  | β-hairpin | Host discrimination (Borkenhagen, Taubenberger JK, 2005) |
| human-swine | S >> N > D |  |  |  |
| swine-human | S >> D > E / G / N | X | X |  |
| swine-swine | S > D > N > Y > G | X |  |  |
| 433 | human-human | K >> R |  |  |  | Palm |  |
| human-swine | K > R |  |  |  |
| swine-human | R /K >> N | X |  |  |
| swine-swine | K > R | X |  |  |
| 633 | human-human | S >> N | X |  |  | Thumb |  |
| human-swine | S >> N |  |  |  |
| swine-human | S > N >> C |  |  |  |
| swine-swine | S >> N |  |  |  |
| 741 | human-human | S > A > T |  |  |  | C-term |  |
| human-swine | S >> A |  |  |  |
| swine-human | S > A >> V |  |  |  |
| swine-swine | A / S | X |  |  |
| **PB1 (PB1-F2)** | 4 | human-human | E >> G |  |  |  | N-term |  |
| human-swine | E >> G | X |  |  |
| swine-human | E >> G |  |  |  |
| swine-swine | E / G | X |  |  |
| 11 | human-human | Q >> L > R | X |  |  | N-term |  |
| human-swine | Q >> L > R > X |  |  |  |
| swine-human | Q >> R / X > L > P | X |  |  |
| swine-swine | Q / R >> L > X | X |  |  |
| 16 | human-human | X > T > I |  |  |  | N-term |  |
| human-swine | X > T > I |  |  |  |
| swine-human | T > X > I | X |  |  |
| swine-swine | I > T > X |  |  |  |
| 27 | human-human | X > T > I |  |  |  | N-term |  |
| human-swine | X > I > T | X |  |  |
| swine-human | T > X > I |  |  |  |
| swine-swine | T > X > I |  |  |  |
| 34 | human-human | X > N > S | X |  |  | N-term |  |
| human-swine | X > S > N |  |  |  |
| swine-human | S > X > N |  |  |  |
| swine-swine | S > X > N |  |  |  |
| 45 | human-human | X > I > T |  |  |  | N-term |  |
| human-swine | X > I >> T | X |  |  |
| swine-human | I > X / T |  |  |  |
| swine-swine | T > X / I |  |  |  |
| 73 | human-human | X > R > K | X |  |  | C-term |  |
| human-swine | X > R >> K |  |  |  |
| swine-human | R > X > K |  |  |  |
| swine-swine | K > X > R |  |  |  |
| **PA** | 61 | human-human | I | X |  |  | Endonuclease |  |
| human-swine | I >> V |  |  |  |
| swine-human | I > T >> V |  |  |  |
| swine-swine | I > T > V |  |  |  |
| 85 | human-human | I / T >> N |  |  |  | Endonuclease | Polymerase activity (Bussey, 2011) |
| human-swine | I > T > N | X |  |  |
| swine-human | T >> I > N / S | X |  |  |
| swine-swine | T >> I > N > A |  | X |  |
| 208 | human-human | T >> K > S | X |  |  | Linker |  |
| human-swine | T >> K > A / S |  |  |  |
| swine-human | T / K >> R |  |  |  |
| swine-swine | K / T |  |  |  |
| 267 | human-human | P |  |  |  | C-term |  |
| human-swine | P | X |  |  |
| swine-human | P > S >> H |  |  |  |
| swine-swine | P > S >> L |  |  |  |
| 421 | human-human | S >> I > V |  |  |  | C-term | H-bond formation (Luo et al, 2017) |
| human-swine | S >> I /V |  | X | X |
| swine-human | S |  |  |  |
| swine-swine | S |  |  |  |
| 505 | human-human | I >> V | X |  |  | C-term |  |
| human-swine | I >> V |  |  |  |
| swine-human | V / I > X |  |  |  |
| swine-swine | I / V |  |  |  |
| **PA (PA-X)** | 61 | human-human | I | X |  |  | Endonuclease |  |
| human-swine | I >> V |  |  |  |
| swine-human | I > T > V |  |  |  |
| swine-swine | I > T > V |  |  |  |
| 85 | human-human | I / T >> N |  |  |  | Endonuclease |  |
| human-swine | I > T > N |  |  |  |
| swine-human | T >> I > N / S | X |  |  |
| swine-swine | T >> I > N > A | X |  |  |
| 184 | human-human | S >> N >> I |  |  |  | Endonuclease |  |
| human-swine | S >> N > G | X |  |  |
| swine-human | S > I >> T > G |  |  |  |
| swine-swine | S / I >> T / N |  |  |  |
| 206 | human-human | R / K |  | X |  | C-term | Host shutoff activity (Oishi, 2015, Hayashi 2016) |
| human-swine | R > K |  | X |  |
| swine-human | K >> R | X | X |  |
| swine-swine | K >> R |  | X |  |
| 208 | human-human | Q >> K / R |  | X |  | C-term |  |
| human-swine | Q >> K > R / P | X | X |  |
| swine-human | Q / R >> K > E / P |  | X |  |
| swine-swine | Q / R >> K |  | X |  |
|  | 210 | human-human | L >> Q > P |  | X |  | C-term |  |
|  | human-swine | L >> P > Q > R |  | X | X |
|  | swine-human | P >> L > Q > S |  | X |  |
|  | swine-swine | P >> L > Q > R |  | X |  |
| **HA (H1)** | 113 | human-human | I > A >> E > T | X | X |  | HA1 |  |
| human-swine | I >> A > T > E |  |  |  |
| swine-human | I / A > T > E > N / S |  | X |  |
| swine-swine | A > I > T > S | X |  |  |
| 137 | human-human | T > E > A > K |  | X |  | RBD |  |
| human-swine | T > A / E > K |  |  |  |
| swine-human | E / T / A > K / S > D / V | X |  |  |
| swine-swine | A > E > T |  | X |  |
| 145 | human-human | S > T / V > A |  |  |  | RBD |  |
| human-swine | S > T / V > P | X | X |  |
| swine-human | T > V > X > S > A/ L |  |  |  |
| swine-swine | T > V > S / A / I / X |  |  |  |
| 157 | human-human | A > K > N / E / T |  | X |  | RBD |  |
| human-swine | A >> E / K / T > N / V |  | X |  |
| swine-human | A > T > N > E / K > I / Q / S / V | X |  |  |
| swine-swine | A > K > T > E / V / N |  | X |  |
| 213 | human-human | A >> T |  |  |  | RBD |  |
| human-swine | A >> T |  |  |  |
| swine-human | A > T > S |  |  |  |
| swine-swine | A / T | X |  |  |
| 318 | human-human | E / K |  |  |  | HA1 |  |
| human-swine | K > E | X |  |  |
| swine-human | E >> K > Q | X |  |  |
| swine-swine | E >> K |  |  |  |
| 337 | human-human | I / V > T |  | X |  | HA1 |  |
| human-swine | V > I > T |  |  |  |
| swine-human | I >> T > V > E | X |  |  |
| swine-swine | I >> V > T | X |  |  |
| 361 | human-human | V >> I | X |  |  | FP |  |
| human-swine | V >> I |  |  |  |
| swine-human | I > V |  |  |  |
| swine-swine | I >> V |  |  |  |
|  | 390 | human-human | G > E > K |  |  |  | HA2 |  |
|  | human-swine | G > E > K |  |  | X |
|  | swine-human | G >> E / K / R |  | X |  |
|  | swine-swine | G >> R / K / E |  |  |  |
| **HA (H3)** | 9 | human-human | Y >> C / N / H > Q |  |  |  | SP |  |
| human-swine | Y >> C > H |  |  |  |
| swine-human | C > Y > H > Q | X | X |  |
| swine-swine | Y / C >> H |  |  |  |
| 47 | human-human | N >> D | X |  |  | HA1 |  |
| human-swine | N >> D > S |  | X |  |
| swine-human | D >> N |  |  |  |
| swine-swine | D >> N |  |  |  |
| 69 | human-human | D > N |  |  |  | HA1 |  |
| human-swine | D > N > S |  |  |  |
| swine-human | N >> S > K | X |  |  |
| swine-swine | N > D > S / K |  |  |  |
| 108 | human-human | K >> R / T |  |  |  | HA1 |  |
| human-swine | K >> T > E / R | X |  |  |
| swine-human | T > K > N / R |  |  |  |
| swine-swine | T > K > R > E / N | X |  |  |
| 245 | human-human | R >> I | X |  |  | RBD |  |
| human-swine | R >> I |  |  |  |
| swine-human | I > R |  |  |  |
| swine-swine | I / R |  |  |  |
| 277 | human-human | R >> Q > H | X |  |  | HA1 |  |
| human-swine | R >> Q > H |  |  |  |
| swine-human | Q >> R > H |  |  |  |
| swine-swine | Q > R > H |  |  |  |
| **NP** | 33 | human-human | I >> V | X |  |  | Body |  |
| human-swine | I >> V | X |  |  |
| swine-human | I / V |  |  |  |
| swine-swine | I > V |  |  |  |
| 53 | human-human | E >> D | X |  |  | Body | Mx1 resistance (Borkenhagen, Mänz, 2013) |
| human-swine | E >> D |  |  | X |
| swine-human | E >> D |  | X |  |
| swine-swine | E >> D |  |  |  |
| 61 | human-human | I / L | X | X |  | Body |  |
| human-swine | I >> L |  |  |  |
| swine-human | I |  |  |  |
| swine-swine | I >> L |  |  |  |
| 100 | human-human | V > I > R |  |  |  | Body | Mx1 resistance (Borkenhagen, Mänz, 2013), Affecting H-bond formation () |
| human-swine | V > I >> R |  |  |  |
| swine-human | R > I / V | X |  |  |
| swine-swine | R > V / I |  |  |  |
| 357 | human-human | K >> Q / R |  |  |  | Body | Mx1 resistance (Borkenhagen, Mänz, 2013), Affecting H-bond formation () |
| human-swine | K >> Q / R |  |  |  |
| swine-human | K >> Q |  |  |  |
| swine-swine | K > Q | X |  |  |
| 377 | human-human | S > N > I |  |  |  | Body |  |
| human-swine | N / S >> I |  |  |  |
| swine-human | I > N > S > V | X |  |  |
| swine-swine | N > I > S > V |  |  |  |
| 384 | human-human | R >> G > K |  |  |  | Body | CD8+ T-cell recognition (Rimmelzwann GF, 2004) |
| human-swine | R >> G > K | X |  |  |
| swine-human | K / R |  |  |  |
| swine-swine | R / K |  |  |  |
| 442 | human-human | T > A |  |  |  | Head |  |
| human-swine | T >> A |  |  | X |
| swine-human | T |  |  |  |
| swine-swine | T |  | X |  |
| **NA (N1)** | 72 | human-human | T >> I |  |  |  | Stalk |  |
| human-swine | T >>I |  |  |  |
| swine-human | T >> I / N |  |  |  |
| swine-swine | T / N > I | X |  |  |
| 77 | human-human | G > R / E > I |  |  |  | Stalk |  |
| human-swine | G > I / R > E | X |  |  |
| swine-human | E / G > V > I |  |  |  |
| swine-swine | E > G > V / I > K |  |  |  |
| 79 | human-human | S > D > G > A > V |  |  |  | Stalk/Head |  |
| human-swine | S > D > G > A |  |  |  |
| swine-human | D > A > V > E / G / S / T > P | X |  |  |
| swine-swine | A / T > D > S / G > V / E |  |  |  |
| 210 | human-human | G |  |  |  | Head |  |
| human-swine | G | X | X |  |
| swine-human | G >> D > S > N |  |  |  |
| swine-swine | G > D >> N > S |  |  |  |
|  | 257 | human-human | K / R | X |  |  | Head |  |
|  | human-swine | K > R |  |  | X |
|  | swine-human | K >> R |  |  |  |
|  | swine-swine | K >> R |  |  |  |
|  | 331 | human-human | K / G > R | X |  |  | Head |  |
| human-swine | G / K > R |  |  |  |
| swine-human | G > K > R > N |  |  |  |
| swine-swine | R > G > K > N |  | X |  |
|  | 365 | human-human | I > N > T |  |  |  | Head |  |
| human-swine | I >> N > T |  |  |  |
| swine-human | T / I > N > S |  |  |  |
| swine-swine | T > I >> N | X |  |  |
|  | 389 | human-human | I > V > M > K |  |  |  | Head |  |
| human-swine | I > M / V > L |  | X |  |
| swine-human | V > M > I > T | X |  |  |
| swine-swine | V > M / I > A / L |  |  |  |
| **NA (N2)** | 52 | human-human | L >> P > F |  |  |  | Stalk |  |
| human-swine | L > P > F |  |  |  |
| swine-human | L > P / Q > F | X | X |  |
| swine-swine | L > P > T > F > Q |  |  |  |
| 336 | human-human | H > Y / N |  | X |  | Head |  |
| human-swine | H > Y > N | X |  |  |
| swine-human | H / N > R / Y > D |  |  |  |
| swine-swine | N > H / Y > D / R | X |  |  |
| 370 | human-human | S / L > F |  | X |  | Head |  |
| human-swine | S > L > F | X |  |  |
| swine-human | L / S > F |  |  |  |
| swine-swine | L > S >> F |  | X |  |
| 435 | human-human | E > R > K > A |  | X |  | Head |  |
| human-swine | E > K / R > A |  |  |  |
| swine-human | K / R > A / E | X |  |  |
| swine-swine | R > K / E > A |  |  |  |
| **MP (M1)** | 30 | human-human | D > S > G > N | X | X |  | N-term |  |
| human-swine | D > S > G > N | X |  |  |
| swine-human | G > D / S |  |  |  |
| swine-swine | D / G > S |  |  |  |
| 115 | human-human | V / I |  |  |  | Mid | Host discrimination (Borkenhagen) |
| human-swine | V > I |  |  |  |
| swine-human | V >> I | X |  |  |
| swine-swine | V >> I |  |  |  |
| 248 | human-human | M >> I | X |  |  | C-term |  |
| human-swine | M >> I | X |  |  |
| swine-human | I > M |  |  |  |
| swine-swine | I / M |  |  |  |
| **MP (M2)** | 11 | human-human | I > T |  | X |  | Ecto | Host discrimination (Borkenhagen) |
| human-swine | I > T >> F | X | X |  |
| swine-human | T > I |  | X |  |
| swine-swine | T > I |  | X |  |
| 13 | human-human | N > S |  | X |  | Ecto |  |
| human-swine | N >>S > R |  | X |  |
| swine-human | N >> S > K | X |  |  |
| swine-swine | N >> S |  | X |  |
| 19 | human-human | C >> Y |  |  |  | Ecto | Disulfide bridges in M2 tetramer Hom N, 2019) |
| human-swine | C >> Y | X |  |  |
| swine-human | Y > C | X | X |  |
| swine-swine | Y /C |  | X |  |
| 28 | human-human | I > V > A | X |  |  | TM | Host discrimination (Borkenhagen) |
| human-swine | I > V / A > D |  |  |  |
| swine-human | I > N / A / T > D / V |  | X |  |
| swine-swine | I > T > A / D / V > N | X |  |  |
| 55 | human-human | F >> L |  |  |  | CT | Host discrimination (Borkenhagen) |
| human-swine | F >> L | X |  |  |
| swine-human | L > F > I |  |  |  |
| swine-swine | L / F |  |  |  |
| 57 | human-human | Y > H |  | X |  | CT |  |
| human-swine | Y >> H > L / N |  | X | X |
| swine-human | Y >> H |  |  |  |
| swine-swine | Y >> H |  |  |  |
| 78 | human-human | Q / K > E | X |  |  | CT | Host discrimination (Borkenhagen) |
| human-swine | Q > K > E |  |  |  |
| swine-human | Q >> K |  |  |  |
| swine-swine | Q >> K |  |  |  |
| 93 | human-human | N > S | X | X |  | CT | Phosphorylation site (Holsinger 1995) |
| human-swine | N > S |  |  | X |
| swine-human | N >> S |  |  |  |
| swine-swine | N >> S |  |  |  |
| **NS (NS1)** | 53 | human-human | D >> N > E |  |  |  | RNA-binding |  |
| human-swine | D >> N | X |  |  |
| swine-human | D > E > N |  |  |  |
| swine-swine | E > D > N |  |  |  |
| 70 | human-human | K >> E / R |  |  |  | RNA-binding | Host discrimination (Borkenhagen) |
| human-swine | K >> R |  |  |  |
| swine-human | K > E > R > G |  |  |  |
| swine-swine | E > K >> G | X |  |  |
| 73 | human-human | S >> Y | X |  |  | RNA-binding | Phosphoryla-tion site of swIAVs (Cheng J, 2019) |
| human-swine | S |  |  |  |
| swine-human | S > Y > H |  |  |  |
| swine-swine | S / Y > H |  |  |  |
| 125 | human-human | E > D > G | X |  |  | Effector | CPSF30 binding ( Hale 2010), Host discrimination (Borkenhagen) |
| human-swine | E >> D |  |  |  |
| swine-human | E > D > N |  |  |  |
| swine-swine | D / E >> N |  |  |  |
| 129 | human-human | I > V > M > T |  |  |  | Effector |  |
| human-swine | I > V > M |  |  |  |
| swine-human | I > T > M > V |  |  |  |
| swine-swine | T > I > V | X | X |  |
| 171 | human-human | Y > I / N > D > A |  | X |  | Effector |  |
| human-swine | Y > N > I > D > H |  | X |  |
| swine-human | N > D > I > E / G / Y | X | X |  |
| swine-swine | D > N > Y > G |  | X |  |
| 180 | human-human | V >> I |  | X |  | Effector |  |
| human-swine | V >> I |  | X |  |
| swine-human | V > I |  |  |  |
| swine-swine | V / I | X | X |  |
| 183 | human-human | G >> K |  |  |  | Effector | CPSF30 binding (Nogales A, 2018) |
| human-swine | G | X |  |  |
| swine-human | G > K |  |  |  |
| swine-swine | K / G |  |  |  |
| 206 | human-human | S > C > R > I / H |  | X |  | Effector |  |
| human-swine | C > R > S |  | X |  |
| swine-human | R > T > I / S > C / H | X |  |  |
| swine-swine | R / T > I > C > S |  | X |  |
| **NS (NEP)** | 26 | human-human | E >> G > K | X | X |  | N-term |  |
| human-swine | E >> G |  | X |  |
| swine-human | E > K > G |  | X |  |
| swine-swine | K / E |  | X |  |
| 40 | human-human | I > L |  |  |  | N-term | Host discrimination (Borkenhagen) |
| human-swine | I >> L | X |  |  |
| swine-human | I / L > V |  |  |  |
| swine-swine | L > I > V |  |  |  |
| 49 | human-human | V >> L > I |  |  |  | N-term |  |
| human-swine | V |  |  |  |
| swine-human | V > L > I |  |  |  |
| swine-swine | L / V | X |  |  |
| 52 | human-human | M >> T > L | X |  |  | N-term |  |
| human-swine | M |  |  |  |
| swine-human | M > T |  |  |  |
| swine-swine | T > M |  |  |  |
| 89 | human-human | A > T > I > M |  | X |  | M1-binding |  |
| human-swine | A > T > M > V > E | X |  |  |
| swine-human | I / T > A > M > L > V | X |  |  |
| swine-swine | I > A > L / M / T > V | X |  |  |