Supplementary File 2. Residues examined for specific mutations involving host adaptation, virulence, pathogenicity and dominating residues differing between H1av and H1N1pdm09 origin viruses. Aa positions are numbered according to the first methionine if nothing else is indicated.

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| --- | --- | --- | --- |
| Protein and residue/aa change | Function | H1av-origin | H1N1pdm09 origin |
| PB2 |  |  |  |
| T271A | Dominant residue differ between avian- and H1N1pdm09 viruses59 | 35/36 had T1/36 had I | 85/85 had A |
| E627K | Increased viral replication and virulence84 | 0/78 | 0/48 |
| D701N | Enhance viral replication and pathogenicity of Eurasian avian like swIAV85 | 36/78 | 0/48 |
| K702R | Host-adaption; at this residue avian influenza carries lysine while most mammalian IAV carry an arginine86 | 0/78 | 0/48 |
| PB1 |  |  |  |
| V336I | Dominant residue differ between avian- and H1N1pdm09 viruses59 | 34/37 had V3/37 had I | 87/87 had I |
| PA |  |  |  |
| K356R | As above59 | 38/38 had K | 88/91 had R |
| S409N | As above59 | 5/38 had S33/38 had N | 90/91 had N1/91 had S |
| HA |  |  |  |
| T200A (H3 numbering) | Increased receptor binding affinity to the α2.6-linked sialic acid for H1N1pdm09 viruses79 | 1/78 had A | 48/48 had A |
| E190D (H3 numbering) | change in receptor specificity of avian IAV from α2.3-linked sialic acid to α2.6-linked sialic acid78 | 73/785/78 had V or S | 40/488/48 had S or G (all Hu-L) |
| G225D (H3 numbering) | As above78 | 6/7863/78 had E9/78 had T/K/N | 18/48 (14/18 was Hu-L)23/48 had N1/48 had G |
| K159, G172E, I183V, S200P, S202N, D204S, V338I and V66I | Related to the H1pdmN2sw lineage in Germany27 |  | Not specific for H1pdmN2sw. However,I173V and V466I were present in 3/12 and 1/12 of the Danish H1pdmN2sw viruses |
| NP |  |  |  |
| K48Q | Confer MxA resistance in combination with R98K and R99K for the NP protein of avian-like swine origin60 | 35/35 had Q | 92/92 had K |
| E53D | Confer MxA resistance for the NP protein of H1N1pdm09 origin61 | 35/35 had E | 10/92 had D (8/10 were H1pdmNx viruses belonging to the Hu-L cluster) |
| R98K | Confer MxA resistance in combination with K48Q and R99K for the NP protein of avian-like swine origin60 | 33/35 had K | 92/92 had R |
| R99K | Confer MxA resistance in combination with K48Q and R98K for the NP protein of avian-like swine origin60 | 31/35 had K | 90/92 had R |
| R100I/V | Confer MxA resistance for the NP protein of H1N1pdm09 origin61 and dominant residue differ between avian- and H1N1pdm09 viruses59 | 35/35 had R | 84/92 had I3/92 had M3/92 had V2/92 T/L |
| F313V | Confer MxA resistance for the NP protein of H1N1pdm09 origin61 | 35/35 had F | 91/92 had V |
| V33I | Dominant residue differ between avian- and H1N1pdm09 viruses59 | 8/35 had V27/35 had I | 91/92 had I1/92 had V |
| R100V | As above59 |  |  |
| R305K | As above59 | 35/35 had R | 91/92 had K1/92 had R |
| Q357K | As above59 | 35/35 had Q | 92/92 had K |