**Additional file 4**

**Table S3: Amino acid substitutions identified in NA of H3N2:** Amino acid substitutions were identified relative to A/Brisbane/2007 vaccine strain. The last column denotes the overall frequency of each substitution in all NA isolated during 2009-2017. N2 numbering was used for reporting substitutions.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference strain** | **AA substitution** | **2009** (%) | **2010** (%) | **2011** (%) | **2012** (%) | **2013** (%) | **2014** (%) | **2015** (%) | **2016** (%) | **Substitution Frequency (2009-2016)**  **(%)** |
| **Brisbane/2007** | Y40C |  |  | 4 | 12 |  |  |  |  | 9 |
|  | L81P |  |  | 77 | 56 | 100 | 100 | 100 | 100 | 81 |
|  | D93G |  |  | 18 | 6 | 62 | 100 | 100 | 100 | 75 |
|  | V143M |  |  | 4 | 3 |  |  | 8 | 37 | 5 |
|  | Y155F |  |  |  |  | 25 | 69 |  |  | 18 |
|  | I176M |  |  | 4 | 44 |  |  |  |  | 11 |
|  | R210K |  |  |  | 47 |  |  |  |  | 10 |
|  | E221D |  |  | 4 |  | 37 | 30 | 100 | 100 | 34 |
|  | S245N |  |  |  |  |  |  | 49 | 75 | 14 |
|  | S247T |  |  |  |  |  |  | 49 | 87 | 14 |
|  | D251V |  |  |  |  | 25 | 63 |  |  | 17 |
|  | T267K |  |  |  |  |  | 6 | 87 | 75 | 21 |
|  | S315G |  |  |  |  | 25 | 60 |  |  | 17 |
|  | D339N |  |  |  |  |  |  | 4 | 62 | 4 |
|  | S367N |  |  | 100 | 100 | 100 | 100 | 100 | 100 | 96 |
|  | K369T |  |  | 100 | 100 | 100 | 100 | 100 | 100 | 96 |
|  | I380V |  |  |  |  |  | 3 | 91 | 50 | 20 |
|  | I239T |  |  | 4 |  | 12 | 18 | 13 | 12 | 9 |
|  | N402D |  |  | 82 | 87 | 75 | 100 | 100 | 100 | 88 |
|  | G414S |  |  |  | 15 |  |  |  |  | 4 |
|  | I464L |  |  | 96 | 53 | 62 | 100 | 100 | 100 | 81 |