Non-random reassortment in human influenza A viruses

Raul Rabadan, Arnold J. Levine, Michael Krasnitza

Institute for Advanced Study, Einstein Dr., Princeton, NJ, USA. *Correspondence*: Raul Rabadan, Institute for Advanced Study, Einstein Dr., Princeton, NJ 08540, USA. Email: rabadan@ias.edu, krasnitz@ias.edu a*These two authors have contributed equally to this work.

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Background The influenza A virus has two basic modes of evolution. Because of a high error rate in the process of replication by RNA polymerase, the viral genome drifts via accumulated mutations. The second mode of evolution is termed a shift, which results from the reassortment of the eight segments of this virus. When two different influenza viruses co-infect the same host cell, new virions can be released that contain segments from both parental strains. This type of shift has been the source of at least two of the influenza pandemics in the 20th century (H2N2 in 1957 and H3N2 in 1968).

Objectives The methods to measure these genetic shifts have not yet provided a quantitative answer to questions such as: what is the rate of genetic reassortment during a local epidemic? Are all possible reassortments equally likely or are there preferred patterns?

Methods To answer these questions and provide a quantitative way to measure genetic shifts, a new method for detecting reassortments from nucleotide sequence data was created that does not rely upon phylogenetic analysis. Two different sequence

databases were used: human H3N2 viruses isolated in New York State between 1995 and 2006, and human H3N2 viruses isolated in New Zealand between 2000 and 2005.

Results Using this new method, we were able to reproduce all the reassortments found in earlier works, as well as detect, with very high confidence, many reassortments that were not detected by previous authors. We obtain a lower bound on the reassortment rate of 2–3 events per year, and find a clear preference for reassortments involving only one segment, most often hemagglutinin or neuraminidase. At a lower frequency several segments appear to reassort *in vivo* in defined groups as has been suggested previously *in vitro*.

Conclusions Our results strongly suggest that the patterns of reassortment in the viral population are not random. Deciphering these patterns can be a useful tool in attempting to understand and predict possible influenza pandemics.

Keywords Genetic shift, human flu, influenza A, reassortment.

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Introduction

There are fundamentally several reasons why the influenza A virus is able to infect human populations and repeatedly evade the hosts' immune systems. The first reason is a high mutation rate which results from the poor fidelity of the RNA-dependent RNA polymerization and the lack of editing and repair processes. This results in the accumulation of mutations in the surface proteins of the virus that can change the antigenic properties of the virus (antigenic drift). The other mechanism of evolution of influenza relies upon the fact that the influenza A virus contains eight separate chromosomes, or segments, that encode 11 proteins. When two different influenza viruses co-infect the same host cell, new viral particles can be created, containing segments from both parental strains. This process, known as reassortment, can change the genome sequence of a virus rapidly and extensively. Such genetic reassortments between viruses infecting different hosts have been responsible for two of the three pandemics of the 20th century, the H2N2 Asian flu in 1957 and the H3N2 Hong Kong flu in 1968. Reassortment is an important evolutionary mechanism within human influenza A viruses. ^{1–4}

The influenza A virus is composed of eight segments, so that, *a priori*, there can be 256 possible reassortants produced from a pair of parental strains. Are all of these reassorted viruses equally likely to occur? This question was addressed *in vitro* by M. Lubeck, P. Palese, and J. Schulman in 1979⁵. They analyzed 40 reassortant viruses derived from A/PR/8/34(H1N1) and A/HK/8/68(H3N2) in the laboratory. Interestingly, they found strong correlations among the segregation of segments 1, 2, and 3, 1 and 5, and 3 and 8. This experiment had some limitations: it was not clear whether these correlations were universal, or only a property of a particular pair of influenza strains. Second, the patterns of reassortment observed *in vitro*, in cell culture,

are not subject to immunoselection or other forces that may act *in vivo* or in human hosts. Understanding the patterns of reassortment of viral populations in human hosts can provide valuable information about the evolution of the influenza virus and perhaps even hints about its packaging structure.

Here, we construct a simple statistical method to estimate the likelihood that two pairs of segments from two strains have both evolved from the same parental strain (and therefore, that no reassortment has occurred). Traditionally, reassortments have been detected by constructing phylogenetic trees for the whole genome, as well as for each viral segment, and looking for strains that have segments on different branches of their respective trees (see, for instance, 1-4,6-7). However, there are several problems with this approach. The structure of a phylogenetic tree depends on the method used to construct it (such as maximum parsimony, maximum likelihood, and others). Mutational biases that are known to exist in influenza replication, and the possible variability of evolutionary rates over time and at different branches⁹ of the tree make accurate phylogenetic analysis very challenging. While the inherent uncertainties can be overcome to some extent by validation algorithms such as bootstrapping, they will still make it difficult to detect all but the most extreme cases of reassortment. Worse, when many reassortments have occurred, it may be difficult to even construct a meaningful genome tree. Luckily, if our only goal is detecting likely reassortments, there is no need to go through the intermediate step of tree inference. Our direct approach avoids all these complications, and can be applied given the sequences of just two virus isolates. This method is completely insensitive to mutational bias and variable evolutionary rates, as long as different segments of the same strain drift at roughly the same rate. Because the uncertainties involved in phylogenetic analysis are sidestepped, we are able to detect many more reassortments than have been observed in previous

We apply the algorithm to two human influenza A H3N2 data sets: in 581 strains from the New York area from 1995 to 2006 and 399 strains from New Zealand from 2000 to 2005. Similar analysis can be performed for other human strains and other hosts (e.g., avian H5N1) (R. Rabadan, A.J. Levine & H. Robins, submitted for publication).

Methods

The basic idea of this method is as follows: let us consider two strains v_a and v_b and two of their segments s_i and s_j . We can compute the number of differences in nucleotide sequence between s_{ia} and s_{ib} and between s_{ja} and s_{jb} . Let us denote them as d_{abi} and d_{abj} . If there are no reassortments

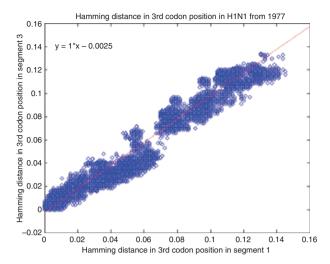


Figure 1. Hamming distance in third codon position between human H1N1 influenza strains (237 cases of human H1N1 from 1977 to 2006) in segment 1 versus segment 3. The red line is the best line fit to the data.

these numbers should be proportional to each other. If the two s_i segments are very similar and the two s_j segments are very different (with a defined low p-value), there has been a reassortment.

As an example of this method, in Figure 1 we show the pairwise third codon position Hamming distance in segment 1 versus segment 3 for 237 human H1N1 influenza strains isolated from 1977 to 2006. The red line is the best fit to these data. From these data, it is clear that the pairwise Hamming distance in segment 1 is roughly proportional to pairwise Hamming distance in segment 3, i.e., the distances are roughly equal after rescaling by the length of the segment. This is an example of genetic drift (which occurs equally among segments) with time. If instead, we take the third codon position Hamming distance in segment 1 versus segment 2 for human H3N2 influenza strains in New York State (208 sequences from 2000 to 2003), we can see that there are clearly points lying significantly off the diagonal, indicating a possible reassortment. Most of the points that reside off the diagonal come from pairs containing a single strain, A/New York/11/2003(H3N2) [in the second part of Figure 2 the pairs of sequences that contain A/New York/11/2003(H3N2) are marked in red]. In Figure 3 randomized 'segments' are generated by permuting the third codon positions of segments 1 and 2 (in red). As expected, these randomized segments all lie along the diagonal creating a background or non-reassorted distribution.

There have been many estimations of the evolutionary rates in influenza, ^{10–13} but to avoid as much as possible dealing with selection pressures, we consider only third codon positions. It has been widely reported that segments 4 and 6, that are coding for hemagglutinin (HA) and neuraminidase (NA), evolve at a higher rate than the rest of the

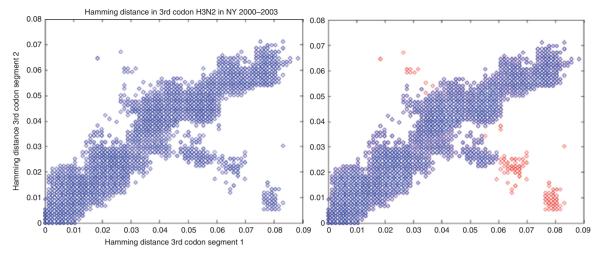


Figure 2. Hamming distance in third codon position between human H3N2 influenza strains in the New York state (208 sequences from 2000 to 2003) in segment 1 versus segment 2. In red are the pairs of sequences that contain A/New York/11/2003(H3N2).

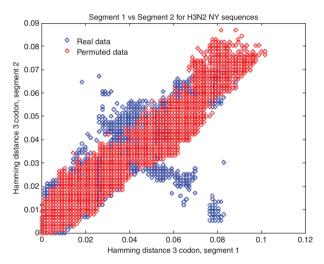


Figure 3. Hamming distance in third codon position between human H3N2 influenza strains in the New York state (208 sequences from 2000 to 2003) in segment 1 versus segment 2. If we create new segments by randomly permuting the third codon positions of both segments together, we create a new distribution (in red is one example). If there are no reassortments the permuted distribution and the real one should be similar (around the diagonal).

segments. The higher evolutionary rate is mainly because of positive selection in the two proteins. HA and NA are the two viral proteins that can be found in the lipid envelope of the virion and are recognized by the host immune system. By taking into account third codon positions we factorize out the pressure of positive selection. In Figure 4, we have represented the Hamming distance in 581 H3N2 viral sequences isolated in the State of New York between 1995 and 2006. We can observe that the evolutionary rates in third codon position of segment 1 versus segment 4 and segment 2 versus segment 4 are very similar, i.e., the points

are near the slope 1 line. Interestingly enough, if we try to find the line through the origin that better fit these data, we found that has a slope smaller than one (0.845 for segment 1 versus segment 4, and 0.904 for segment 2 versus segment 4), i.e., the HA gene seems to evolve slightly slower than PB2 or PB1. This can be easily seen by looking at Figure 4. This smaller rate for segment 4 versus segments 1 and 2 is probably because of the reassortment that can be seen on the right of both figures. Similar results are found in NA, suggesting that the positive selection is driving the higher evolutionary rates in these segments.

To calculate the likelihood of reassortment we perform the following steps:

- 1 Our null hypothesis is that given two strains A and B and two segments i and j, there is a single strain C such that C_i is the common ancestor of A_i and B_i , and C_j is the common ancestor of A_i and A_i .
- **2** We assume that third codon positions evolve at the same average rate and therefore sample from a common distribution in all segments. Then, the probability of observing d_{abi} and d_{abi} follows the hypergeometric distribution:

$$P(d_i, L_i + L_j, L_i, d_i + d_j) = \frac{\begin{pmatrix} L_i \\ d_i \end{pmatrix} \begin{pmatrix} L_i \\ d_j \end{pmatrix}}{\begin{pmatrix} L_i + L_j \\ d_i + d_j \end{pmatrix}}$$

The p-value of observing a difference of no more than d_1 will be the cumulative hypergeometric distribution. Here L_1 and L_2 are the lengths of the two segments in amino acid space (i.e., the counts of third codon positions). How accurate is the assumption that all segments evolve at the same average rate? Using sequence data from the two databases, we have performed pairwise segment comparisons as in Figure 1 to estimate the ratios between their evolutionary

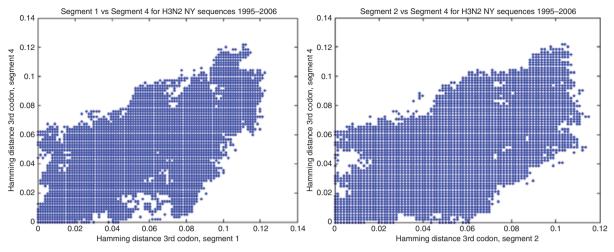


Figure 4. The evolutionary rate in different segments is similar if we take into account the changes in third codon positions. In this figure is represented the Hamming distance in third codon position between every pair of viruses found in New York State between 1995 and 2006 (581 sequences). On the left is shown the distance in third codon position in segment 1 versus segment 4, and on the right segment 2 versus segment 4. It can be appreciated that most of the points are along the slope 1 line, indicating similar rates between the different segments.

rates. For segments 1–6 we obtain values close to one. Segments 7 and 8 have a relatively higher proportion of conserved sites and evolve at somewhat slower rates. For these segments, we have rescaled the effective length L by a correction factor to account for the slower rate of drift. This is in part because of the fact that these segments have two open reading frames that overlap. We verified that correcting effective segment lengths by factors of 0.8-1.2 resulted in mild changes to the p-values which did not affect the results in Table 1.

- 3 To account for population structure, we use the initial, or raw, p-value obtained above as a statistic. We create a randomized background population with the same structure by randomly permuting the third codon positions between the two segments, using the same permutation in each strain. We use the distribution of raw p-values from this permuted population as a background distribution from which we compute the true p-value for the raw p-value statistic.
- 4 Deviations from the null hypothesis are reflected in lower p-values. One has to correct for multiple hypotheses. We take a Bonferroni correction as a conservative first approximation. This will eliminate false-positives.
- 5 Consistency condition: the procedure can be repeated with every pair of segments and one can check if the result is consistent: if i and j have not reassorted and j and k have not reassorted then i and k have not reassorted.

Results

To illustrate the application of the method, let us consider the following example. Note: for every pair of segments an index 0 or 1 is adopted:

- 0 means that two segments come from the same distribution, i.e., there was no reassortment.
- 1 means that one of the two segments reassorted. Example:
 - 63 A/New York/11/2003(H3N2).
 - 1 A/New York/28/2003(H3N2).

0	1	1	1	1	1	1	1
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0

By comparing with the rest of the database it is easy to see that A/New York/11/2003(H3N2) is a reassortant [it was isolated in 10/31/2003 from an 8-year-old boy in Suffolk County (Long Island)]. Only segment 1 has reassorted.

We can extract the cases involving a few reassortments, most of them singletons in the database, by taking pairs of sequences close to each other in Hamming space and demanding a p-value below the Bonferroni bound. In the following table, we summarize the different independent reassortment events that we detected in the NY and NZ databases.

Under these strict limits, we observe a lower bound on the reassortment rate of around 2–3 reassortments per year. These include only the reassortments detected between closely related sequences that for the most part were not fixed in the viral population. That means that the true reassortment rate is considerably higher than this lower bound.

Table 1. Summary of independent reassortment events detected in the New York and New Zealand databases

Pair of sequences	Segments reassorted
A/New York/658/1995(H3N2), A/New York/695/1995(H3N2)	5
A/New York/652/1995(H3N2), A/New York/672/1995(H3N2)	2, 4
A/New York/580/1996(H3N2), A/New York/564/1997(H3N2)	2
A/New York/521/1998(H3N2), A/New York/541/1998(H3N2)	1, 8 ⁶
A/New York/538/1998(H3N2), A/New York/529/1998(H3N2)	5
A/New York/525/1998(H3N2), A/New York/529/1998(H3N2)	5, 6 ⁶
A/New York/327/1999(H3N2), A/New York/249/1998(H3N2)	3, 5, 6 ⁶
A/New York/428/1999(H3N2), A/New York/240/1998(H3N2)	6 ⁶
A/New York/455/1999(H3N2), A/New York/250/1998(H3N2)	2, 6 ⁶
A/New York/177/1999(H3N2), A/New York/249/1998(H3N2)	3, 4, 7 ⁶
A/New York/155/1999(H3N2), A/New York/181/1999(H3N2)	4, 6
A/New York/138/1999(H3N2), A/New York/137/1999(H3N2)	4, 6, 7 ²
A/New York/182/2000(H3N2), A/New York/425/1999(H3N2)	3 ²
A/New York/187/2000(H3N2), A/New York/147/1999(H3N2)	3, 8
A/New York/107/2002(H3N2), A/New York/129/2002(H3N2)	4, 6, 7
A/New York/105/2002(H3N2), A/New York/91/2002(H3N2)	1, 6, 8
A/New York/88/2002(H3N2), A/New York/134/2002(H3N2)	4, 6
A/New York/11/2003(H3N2), A/New York/28/2003(H3N2)	1 ^{2,6}
A/New York/24/2003(H3N2), A/New York/22/2003(H3N2)	4, 7
A/New York/27/2003(H3N2), A/New York/34/2003(H3N2)	4, 6, 7
A/New York/18/2003(H3N2), A/New York/64/2003(H3N2)	4, 6
A/New York/214/2003(H3N2), A/New York/58/2003(H3N2)	4
A/New York/218/2004(H3N2), A/New York/462/2005(H3N2)	2, 6
A/Nelson Marlborough/1/2000(H3N2), A/Canterbury/39/2000(H3N2)	1
A/Waikato/5/2000(H3N2), A/Waikato/15/2000(H3N2)	1, 2
A/Canterbury/75/2002(H3N2), A/Canterbury/01/2002(H3N2)	8
A/Wellington/9/2002(H3N2), A/Waikato/31/2002(H3N2)	1, 2
A/Waikato/15/2003(H3N2), A/Waikato/53/2003(H3N2)	1, 4
A/Christchurch/15/2004(H3N2), A/Wellington/6/2004(H3N2)	4
A/Wellington/23/2004(H3N2), A/Tairawhiti/369/2004(H3N2)	1, 2, 4
A/Christchurch/297/2004(H3N2), A/Christchurch/184/2004(H3N2)	1

Conclusions

We propose a method to detect reassortments in influenza virus populations based on the comparison between different segments of influenza viruses. It is a simple method to quickly check if a sequence from a new virus is a reassortment in relation to the ones that are already present in public databases. Two different databases were analyzed: 581 H3N2 strains from the New York area from 1995 to 2006 and 399 H3N2 strains from New Zealand from 2000 to 2005 (see Appendix 1 for a list of the sequences used in this study). From the reassortments found involving closely related sequences, one can estimate a lower bound on the reassortment rate of 2–3 events per year. We emphasize that the true reassortment rate is likely to be much higher. There are several questions that can now be asked about the reassortments of human influenza A viruses:

• How many segments are expected to reassort? If reassortment is random we would expect a binomial distribution. It is evident from Table 1 that many reassortments involve only one segment. How significant is this? If all the

reassortments are equally probable (null hypothesis) we expect that the probability of having only one segment is P = 16/256 (there is a factor of two because of the symmetry between the two strains). The cumulative probability that 11 of the 31 reassortments involve only one segment is $P = 1.5 \times 10^{-8}$. Similarly, as we have no reassortments involving four segments we can compute the cumulative binomial $P = 5.0 \times 10^{-5}$. We conclude that reassortments *in vivo* preferentially involve only one segment. A similar bias is observed from the results obtained *in vitro* (in cell culture) of Ref. 5, with $P = 6.7 \times 10^{-4}$.

- What segments are most likely to reassort? From Table 1 we can see that segments 6 and 4 are the most frequent reassortants. A similar result can be obtained from the *in vitro* data of Ref. 5, where segments 4, 6, and 7 are often involved in reassortments.
- What are the most likely combinations of segments that reassort? There are some clear trends, for instance the 4, 6, and 7 combination appears three times $(P = 3.7 \times 10^{-8})$. The same trend appears *in vitro* in Ref. 5. Because the segments 4 and 6 encode for the HA and the NA proteins, and

these are found on the surface of the virus eliciting an immunological response from the host, it could be supposed that the frequency of detecting reassortments involving segments 4 and 6 is a result of selection. Although there might be some truth to this explanation, reassortments of these segments were also found to occur preferentially *in vitro* or in cell culture in the absence of immunoselection. This brings up the interesting possibility that the mechanisms involved in packaging these two subunits result in a greater rate of reassortment of segments 4 and 6. It is tempting to speculate that the virus has adopted a chromosome packaging structure that optimizes its chances of evading host immunity by preferentially enabling reassortments involving the two immunogenic segments (HA and NA).¹⁴

Perhaps, the most likely explanation for the other patterns of reassortment detected here and previously (e.g., segments 4, 6, and 7) is packaging bias. If, for example, some viral segments contact (hybridize) each other via RNA–RNA interactions during the virion packaging process, then they may be more likely to reassort together. This hypothesis is consistent with the similarity between the patterns observed *in vivo* and *in vitro*.

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Appendix 1: sequences used in this study

All sequences in this study were obtained from the Influenza Virus Resource of the National Center for Biotechnology Information (NCBI): http://www.ncbi.nlm.nih.gov/genomes/FLU/FLU.html

New York H3N2 database from 1995 to	o 2006: 581 sequences
0	A/New York/61A/2003(H3N2)
1	A/New York/28/2003(H3N2)
2	A/New York/30/2003(H3N2)
3	A/New York/32/2003(H3N2)
4	A/New York/33/2004(H3N2)
5	A/New York/34/2003(H3N2)
6	A/New York/35/2003(H3N2)
7	A/New York/36/2003(H3N2)
8	A/New York/45/2003(H3N2)
9	A/New York/47/2003(H3N2)
10	A/New York/48/2003(H3N2)
11	A/New York/50/2003(H3N2)
12	A/New York/54/2003(H3N2)
13	A/New York/60A/2003(H3N2)
14	A/New York/110/2002(H3N2)
15	A/New York/12/2003(H3N2)
16	A/New York/16/2003(H3N2)
17	A/New York/26/2003(H3N2)
18	A/New York/40/2003(H3N2)
19	A/New York/41/2003(H3N2)
20	A/New York/42/2003(H3N2)
21	A/New York/43/2003(H3N2)
22	A/New York/44/2003(H3N2)
23	A/New York/83/2001(H3N2)
24	A/New York/23/2003(H3N2)
25	A/New York/84/2001(H3N2)
26	A/New York/91/2002(H3N2)
27	A/New York/95/2002(H3N2)

28	A/New York/100/2002(H3N2)	89	A/New York/177/1999(H3N2)
29	A/New York/113/2002(H3N2)	90	A/New York/179/1999(H3N2)
30	A/New York/121/2002(H3N2)	91	A/New York/180/2000(H3N2)
31	A/New York/19/2003(H3N2)	92	A/New York/185/1999(H3N2)
32	A/New York/52/2004(H3N2)	93	A/New York/192/2003(H3N2)
33	A/New York/53/2003(H3N2)	94	A/New York/10/2004(H3N2)
34	A/New York/82/2001(H3N2)	95	A/New York/25/2003(H3N2)
35	A/New York/86/2002(H3N2)	96	A/New York/38/2003(H3N2)
36	A/New York/92/2002(H3N2)	97	A/New York/46/2003(H3N2)
37	A/New York/96/2002(H3N2)	98	A/New York/117/2002(H3N2)
38	A/New York/124/2001(H3N2)	99	A/New York/141/1999(H3N2)
39	A/New York/129/2002(H3N2)	100	A/New York/166/1999(H3N2)
40	A/New York/131/2001(H3N2)	101	A/New York/148/2000(H3N2)
41	A/New York/133/2002(H3N2)	102	A/New York/157/1999(H3N2)
42	A/New York/135/2002(H3N2)	103	A/New York/158/2000(H3N2)
43	A/New York/15/2003(H3N2)	104	A/New York/168/2000(H3N2)
44	A/New York/21/2003(H3N2)	105	A/New York/178/2000(H3N2)
45	A/New York/22/2003(H3N2)	106	A/New York/186/1999(H3N2)
46	A/New York/31/2004(H3N2)	107	A/New York/193/2003(H3N2)
47	A/New York/49/2003(H3N2)	108	A/New York/194/2003(H3N2)
48	A/New York/85/2001(H3N2)	109	A/New York/3/2003(H3N2)
49	A/New York/87/2002(H3N2)	110	A/New York/5/2004(H3N2)
50	A/New York/89/2002(H3N2)	111	A/New York/13/2003(H3N2)
51 52	A/New York/90/2002(H3N2) A/New York/103/2002(H3N2)	112 113	A/New York/14/2003(H3N2) A/New York/62A/2003(H3N2)
53	A/New York/128/2002(H3N2)	114	A/New York/93/2002(H3N2)
54	A/New York/132/2002(H3N2)	115	A/New York/111/2002(H3N2)
55	A/New York/134/2002(H3N2)	116	A/New York/111/2002(H3N2)
56	A/New York/149/1999(H3N2)	117	A/New York/55/2003(H3N2)
57	A/New York/150/2000(H3N2)	118	A/New York/59/2003(H3N2)
58	A/New York/2/2003(H3N2)	119	A/New York/64/2003(H3N2)
59	A/New York/71/2001(H3N2)	120	A/New York/67/2003(H3N2)
60	A/New York/106/2002(H3N2)	121	A/New York/160/2000(H3N2)
61	A/New York/108/2002(H3N2)	122	A/New York/138/1999(H3N2)
62	A/New York/4/2003(H3N2)	123	A/New York/165/2000(H3N2)
63	A/New York/11/2003(H3N2)	124	A/New York/189/1999(H3N2)
64	A/New York/29/2003(H3N2)	125	A/New York/198/2003(H3N2)
65	A/New York/109/2002(H3N2)	126	A/New York/1/2003(H3N2)
66	A/New York/114/2002(H3N2)	127	A/New York/6/2004(H3N2)
67	A/New York/115/2002(H3N2)	128	A/New York/7/2003(H3N2)
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69	A/New York/69/2004(H3N2)	130	A/New York/17/2003(H3N2)
70	A/New York/80/2001(H3N2)	131	A/New York/51/2003(H3N2)
71	A/New York/127/2001(H3N2)	132	A/New York/88/2002(H3N2)
72	A/New York/130/2002(H3N2)	133	A/New York/99/2002(H3N2)
73	A/New York/147/1999(H3N2)	134	A/New York/24/2003(H3N2)
74	A/New York/151/1999(H3N2)	135	A/New York/39/2003(H3N2)
75	A/New York/154/2000(H3N2)	136	A/New York/101/2002(H3N2)
76	A/New York/161/1999(H3N2)	137	A/New York/27/2003(H3N2)
77	A/New York/120/2002(H3N2)	138	A/New York/137/1999(H3N2)
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79	A/New York/163/1999(H3N2)	140	A/New York/152/2000(H3N2)
80 81	A/New York/167/1999(H3N2) A/New York/169/2000(H3N2)	141 142	A/New York/107/2002(H3N2) A/New York/74/2002(H3N2)
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84	A/New York/172/1999(H3N2)	145	A/New York/181/1999(H3N2)
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88	A/New York/176/2000(H3N2)	149	A/New York/56/2003(H3N2)

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278	A/New York/207/2004(H3N2)	339	A/New York/418/2002(H3N2)
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280	A/New York/398/1999(H3N2)	341	A/New York/424/1999(H3N2)
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293	A/New York/367/2005(H3N2)	354	A/New York/407/2002(H3N2)
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295	A/New York/384/2005(H3N2)	356	A/New York/425/1999(H3N2)
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308	A/New York/380/2004(H3N2)	369	A/New York/463/2005(H3N2)
309	A/New York/190/2004(H3N2)	370	A/New York/464/2005(H3N2)
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319	A/New York/351/2004(H3N2)	380	A/New York/440/2000(H3N2)
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324	A/New York/401/2001(H3N2)	385	A/New York/470/2004(H3N2)
325	A/New York/402/2001(H3N2)	386	A/New York/355/2004(H3N2)
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330	A/New York/408/2002(H3N2)	391	A/New York/258/2005(H3N2)
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439 A/New York/245/2004(H3N2) 500 A/New York/617/1996(H3N2) 440 A/New York/526/1997(H3N2) 501 A/New York/572/1996(H3N2) 441 A/New York/472/2004(H3N2) 502 A/New York/578/1996(H3N2) 442 A/New York/502/1998(H3N2) 503 A/New York/561/1996(H3N2) 443 A/New York/73/2004(H3N2) 504 A/New York/603/1996(H3N2) 444 A/New York/544/1998(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514		, ,		
440 A/New York/526/1997(H3N2) 501 A/New York/572/1996(H3N2) 441 A/New York/472/2004(H3N2) 502 A/New York/578/1996(H3N2) 442 A/New York/502/1998(H3N2) 503 A/New York/561/1996(H3N2) 443 A/New York/373/2004(H3N2) 504 A/New York/603/1996(H3N2) 444 A/New York/473/2003(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 509 A/New York/611/1995(H3N2) 448 A/New York/476/2003(H3N2) 510 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
441 A/New York/472/2004(H3N2) 502 A/New York/578/1996(H3N2) 442 A/New York/502/1998(H3N2) 503 A/New York/561/1996(H3N2) 443 A/New York/73/2004(H3N2) 504 A/New York/603/1996(H3N2) 444 A/New York/473/2003(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
442 A/New York/502/1998(H3N2) 503 A/New York/561/1996(H3N2) 443 A/New York/73/2004(H3N2) 504 A/New York/603/1996(H3N2) 444 A/New York/544/1998(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
443 A/New York/73/2004(H3N2) 504 A/New York/603/1996(H3N2) 444 A/New York/544/1998(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
4444 A/New York/544/1998(H3N2) 505 A/New York/606/1995(H3N2) 445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
445 A/New York/473/2003(H3N2) 506 A/New York/608/1996(H3N2) 446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)		. ,		
446 A/New York/474/2003(H3N2) 507 A/New York/609/1995(H3N2) 447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				, ,
447 A/New York/475/2003(H3N2) 508 A/New York/610/1995(H3N2) 448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				, ,
448 A/New York/476/2003(H3N2) 509 A/New York/611/1995(H3N2) 449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
449 A/New York/478/2003(H3N2) 510 A/New York/612/1995(H3N2) 450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)		* * *		
450 A/New York/498/2004(H3N2) 511 A/New York/613/1996(H3N2) 451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
451 A/New York/479/2003(H3N2) 512 A/New York/618/1995(H3N2) 452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
452 A/New York/504/1998(H3N2) 513 A/New York/619/1996(H3N2) 453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)				
453 A/New York/507/1997(H3N2) 514 A/New York/622/1996(H3N2)		, ,		
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516	A/New York/628/1995(H3N2)	577	A/New York/676/1995(H3N2)
517	A/New York/631/1996(H3N2)	578	A/New York/3/2006(H3N2)
518	A/New York/634/1996(H3N2)	579	A/New York/C4/2002(H3N2)
519	A/New York/637/1996(H3N2)	580	A/New York/7/2006(H3N2)
520	A/New York/648/1995(H3N2)	360	A/ New Tolk/ // 2000(113N2)
521	A/New York/555/1996(H3N2)		
522	A/New York/623/1995(H3N2)	New Zealand H3N	I2 database from 2000 to 2005: 399 sequences
523	A/New York/599/1996(H3N2)	0	A/Christchurch/13/2004(H3N2)
524	A/New York/602/1996(H3N2)	1	A/Christchurch/15/2004(H3N2)
525	A/New York/557/1996(H3N2)	2	A/Christchurch/14/2004(H3N2)
526	A/New York/559/1996(H3N2)	3	A/Christchurch/89/2004(H3N2)
527	A/New York/692/1995(H3N2)	4	A/Christchurch/90/2004(H3N2)
528	A/New York/695/1995(H3N2)	5	A/Christchurch/184/2004(H3N2)
529	A/New York/697/1995(H3N2)	6	A/Ashburton/280/2004(H3N2)
530	A/New York/698/1995(H3N2)	7	A/Christchurch/297/2004(H3N2)
531	A/New York/702/1995(H3N2)	8	A/Christchurch/10/2004(H3N2)
532	A/New York/703/1995(H3N2)	9	A/Christchurch/339/2004(H3N2)
533	A/New York/571/1996(H3N2)	10	A/Canterbury/382/2003(H3N2)
534	A/New York/577/1996(H3N2)	11	A/Canterbury/384/2003(H3N2)
535	A/New York/624/1996(H3N2)	12	A/Canterbury/386/2003(H3N2)
536	A/New York/632/1996(H3N2)	13	A/Canterbury/387/2003(H3N2)
537	A/New York/635/1996(H3N2)	14	A/Canterbury/390/2003(H3N2)
538	A/New York/636/1996(H3N2)	15	A/Canterbury/391/2003(H3N2)
539	A/New York/641/1996(H3N2)	16	A/Canterbury/392/2003(H3N2)
540	A/New York/658/1995(H3N2)	17	A/Canterbury/393/2003(H3N2)
541		18	A/Canterbury/394/2003(H3N2)
	A/New York/662/1995(H3N2)	19	A/Canterbury/395/2003(H3N2)
542 543	A/New York/669/1995(H3N2) A/New York/671/1995(H3N2)	20	A/Canterbury/397/2003(H3N2)
	, ,	21	A/Canterbury/398/2003(H3N2)
544 545	A/New York/672/1995(H3N2) A/New York/674/1995(H3N2)	22	A/Canterbury/399/2003(H3N2)
546	A/New York/679/1995(H3N2)	23	A/Canterbury/401/2003(H3N2)
547	A/New York/693/1995(H3N2)	24	A/Canterbury/403/2003(H3N2)
548	A/New York/647/1995(H3N2)	25	A/Canterbury/404/2003(H3N2)
549	A/New York/652/1995(H3N2)	26	A/Canterbury/405/2003(H3N2)
550	A/New York/684/1995(H3N2)	27	A/Canterbury/406/2003(H3N2)
551	A/New York/685/1995(H3N2)	28	A/Canterbury/408/2003(H3N2)
552	A/New York/687/1995(H3N2)	29	A/Canterbury/410/2003(H3N2)
553	A/New York/689/1995(H3N2)	30	A/Canterbury/411/2003(H3N2)
554	A/New York/556/1996(H3N2)	31	A/Canterbury/412/2003(H3N2)
555	A/New York/598/1996(H3N2)	32	A/Canterbury/416/2003(H3N2)
556	A/New York/639/1995(H3N2)	33	A/Canterbury/417/2003(H3N2)
557	A/New York/670/1995(H3N2)	34	A/Canterbury/418/2003(H3N2)
558	A/New York/675/1995(H3N2)	35	A/Canterbury/420/2003(H3N2)
559	A/New York/677/1995(H3N2)	36	A/Canterbury/423/2003(H3N2)
560	A/New York/682/1995(H3N2)	37	A/Canterbury/424/2003(H3N2)
561	A/New York/664/1995(H3N2)	38	A/Canterbury/427/2003(H3N2)
562	A/New York/666/1995(H3N2)	39	A/Canterbury/428/2003(H3N2)
563	A/New York/667/1995(H3N2)	40	A/Canterbury/430/2003(H3N2)
564	A/New York/668/1995(H3N2)	41	A/Canterbury/431/2003(H3N2)
		42	A/South Canterbury/433/2003(H3N2)
565	A/New York/678/1995(H3N2)	43	A/Canterbury/434/2003(H3N2)
566	A/New York/691/1995(H3N2)	44	A/Canterbury/435/2003(H3N2)
567 568	A/New York/700/1995(H3N2)	45	A/Canterbury/436/2003(H3N2)
568 560	A/New York/4/2006(H3N2)	46	A/Canterbury/437/2003(H3N2)
569 570	A/New York/554/1996(H3N2)	47	A/Canterbury/438/2003(H3N2)
570 571	A/New York/673/1995(H3N2)	48	A/Canterbury/439/2003(H3N2)
571	A/New York/683/1995(H3N2)	49	A/Canterbury/440/2003(H3N2)
572	A/New York/686/1995(H3N2)	50	A/Canterbury/441/2003(H3N2)
573	A/New York/690/1995(H3N2)	51	A/Canterbury/442/2003(H3N2)
574	A/New York/699/1995(H3N2)	52	A/Canterbury/443/2003(H3N2)
575 576	A/New York/5/2006(H3N2)	53	A/Canterbury/444/2003(H3N2)
576	A/New York/660/1995(H3N2)	55	/ / Carterbary/ 777/ 2005(115142)

54	A/Whanganui/128/2004(H3N2)	115	A/Canterbury/03/2005(H3N2)
55	A/Whanganui/129/2004(H3N2)	116	A/Canterbury/409/2003(H3N2)
56	A/Bay of Plenty/279/2004(H3N2)	117	A/Canterbury/429/2003(H3N2)
57	A/Bay of Plenty/332/2004(H3N2)	118	A/Canterbury/14/2002(H3N2)
58	A/Tairawhiti/369/2004(H3N2)	119	A/Canterbury/19/2002(H3N2)
59	A/Bay of Plenty/383/2004(H3N2)	120	A/Canterbury/20/2002(H3N2)
60	A/Whanganui/386/2004(H3N2)	121	A/Canterbury/27/2002(H3N2)
61	A/Whanganui/417/2004(H3N2)	122	A/Canterbury/29/2002(H3N2)
62	A/Canterbury/11/2004(H3N2)	123	A/Canterbury/31/2002(H3N2)
63	A/Canterbury/12/2004(H3N2)	124	A/Canterbury/33/2002(H3N2)
64	A/Canterbury/16/2004(H3N2)	125	A/Canterbury/34/2002(H3N2)
65	A/Canterbury/17/2004(H3N2)	126	A/South Canterbury/37/2002(H3N2)
66	A/Canterbury/18/2004(H3N2)	127	A/Canterbury/44/2002(H3N2)
67	A/Canterbury/19/2004(H3N2)	128	A/Canterbury/58/2002(H3N2)
68	A/Canterbury/20/2004(H3N2)	129	A/Canterbury/66/2002(H3N2)
69	A/Canterbury/21/2004(H3N2)	130	A/Canterbury/72/2002(H3N2)
70	A/Canterbury/23/2004(H3N2)	131	A/Canterbury/79/2002(H3N2)
71	A/Canterbury/24/2004(H3N2)	132	A/Canterbury/16/2005(H3N2)
72	A/Canterbury/100/2004(H3N2)	133	A/Canterbury/33/2005(H3N2)
73	A/Canterbury/101/2004(H3N2)	134	A/Canterbury/108/2004(H3N2)
74	A/Canterbury/102/2004(H3N2)	135	A/Canterbury/109/2004(H3N2)
75	A/Canterbury/103/2004(H3N2)	136	A/Canterbury/04/2002(H3N2)
76	A/Canterbury/104/2004(H3N2)	137	A/Canterbury/13/2002(H3N2)
77	A/Canterbury/105/2004(H3N2)	138	A/Canterbury/21/2002(H3N2)
78	A/Canterbury/107/2004(H3N2)	139	A/Canterbury/46/2002(H3N2)
79	A/Canterbury/201/2004(H3N2)	140	A/Canterbury/57/2002(H3N2)
80	A/Canterbury/202/2004(H3N2)	141	A/Canterbury/24/2005(H3N2)
81	A/Canterbury/205/2004(H3N2)	142	A/Canterbury/29/2005(H3N2)
82	A/Canterbury/206/2004(H3N2)	143	A/Canterbury/67/2005(H3N2)
83	A/Canterbury/207/2004(H3N2)	144	A/Canterbury/127/2005(H3N2)
84	A/Canterbury/208/2004(H3N2)	145	A/Canterbury/129/2005(H3N2)
85	A/Canterbury/209/2004(H3N2)	146	A/Canterbury/166/2005(H3N2)
86	A/Canterbury/210/2004(H3N2)	147	A/Canterbury/206/2005(H3N2)
87	A/Canterbury/303/2004(H3N2)	148	A/Canterbury/212/2005(H3N2)
88	A/Canterbury/304/2004(H3N2)	149	A/Canterbury/259/2005(H3N2)
89	A/Canterbury/311/2004(H3N2)	150	A/Canterbury/42/2000(H3N2)
90	A/Canterbury/313/2004(H3N2)	151	A/Canterbury/39/2000(H3N2)
91	A/Canterbury/315/2004(H3N2)	152	A/Canterbury/432/2003(H3N2)
92	A/Canterbury/01/2002(H3N2)	153	A/Whanganui/69/2004(H3N2)
93	A/Canterbury/02/2002(H3N2)	154	A/Tairawhiti/223/2004(H3N2)
94	A/Canterbury/05/2002(H3N2)	155	A/Canterbury/305/2004(H3N2)
95	A/Canterbury/16/2002(H3N2)	156	A/Canterbury/308/2004(H3N2)
96	A/Canterbury/18/2002(H3N2)	157	A/Canterbury/309/2004(H3N2)
97	A/Canterbury/22/2002(H3N2)	158	A/Canterbury/310/2004(H3N2)
98	A/Canterbury/35/2002(H3N2)	159	A/Canterbury/312/2004(H3N2)
99	A/Canterbury/41/2002(H3N2)	160	A/Canterbury/06/2002(H3N2)
100	A/Canterbury/47/2002(H3N2)	161	A/Canterbury/09/2002(H3N2)
101	A/Canterbury/48/2002(H3N2)	162	A/Canterbury/10/2002(H3N2)
102	A/Canterbury/49/2002(H3N2)	163	A/Canterbury/15/2002(H3N2)
	A/Canterbury/50/2002(H3N2)		A/Canterbury/60/2002(H3N2)
103 104	A/Canterbury/53/2002(H3N2)	164 165	A/Canterbury/61/2002(H3N2)
105	A/Canterbury/55/2002(H3N2)		A/Canterbury/62/2002(H3N2)
		166	
106	A/Canterbury/59/2002(H3N2)	167	A/Canterbury/64/2002(H3N2)
107	A/Canterbury/68/2002(H3N2)	168	A/Canterbury/70/2002(H3N2)
108	A/Canterbury/69/2002(H3N2)	169	A/Canterbury/76/2002(H3N2)
109	A/Canterbury/75/2002(H3N2)	170	A/Canterbury/20/2005(H3N2)
110	A/Canterbury/80/2002(H3N2)	171	A/Canterbury/64/2005(H3N2)
111	A/Canterbury/81/2002(H3N2)	172	A/Canterbury/104/2005(H3N2)
112	A/Canterbury/102/2002(H3N2)	173	A/Canterbury/186/2005(H3N2)
113	A/Canterbury/01/2005(H3N2)	174	A/Canterbury/204/2005(H3N2)
114	A/Canterbury/02/2005(H3N2)	175	A/Canterbury/220/2005(H3N2)

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176	A/Canterbury/234/2005(H3N2)	237	A/Canterbury/10/2001(H3N2)
177	A/Canterbury/235/2005(H3N2)	238	A/West Coast/32/2001(H3N2)
178	A/Canterbury/236/2005(H3N2)	239	A/Canterbury/37/2001(H3N2)
179	A/Canterbury/237/2005(H3N2)	240	A/Canterbury/44/2001(H3N2)
180	A/Canterbury/238/2005(H3N2)	241	A/West Coast/55/2001(H3N2)
181	A/Canterbury/242/2005(H3N2)	242	A/Canterbury/149/2001(H3N2)
182	A/Canterbury/260/2005(H3N2)	243	A/Canterbury/07/2001(H3N2)
183	A/Canterbury/269/2005(H3N2)	244	A/West Coast/28/2001(H3N2)
184	A/Canterbury/17/2000(H3N2)	245	A/Canterbury/43/2001(H3N2)
185	A/Canterbury/38/2000(H3N2)	246	A/Canterbury/50/2001(H3N2)
186	A/Canterbury/73/2000(H3N2)	247	A/Canterbury/140/2001(H3N2)
187	A/Canterbury/88/2000(H3N2)	248	A/Canterbury/146/2001(H3N2)
188	A/Canterbury/99/2000(H3N2)	249	A/Whanganui/127/2004(H3N2)
189	A/Canterbury/425/2003(H3N2)	250	A/Canterbury/125/2005(H3N2)
190	A/Canterbury/426/2003(H3N2)	251	A/Canterbury/06/2001(H3N2)
191	A/Canterbury/105/2005(H3N2)	252	A/Canterbury/250/2005(H3N2)
192	A/Canterbury/205/2005(H3N2)	253	A/Canterbury/36/2001(H3N2)
193	A/Canterbury/230/2005(H3N2)	254	A/Wellington/9/2000(H3N2)
194	A/Canterbury/233/2005(H3N2)	255	A/Canterbury/62/2000(H3N2)
195	A/Canterbury/248/2005(H3N2)	256	A/Dunedin/10/2002(H3N2)
196	A/Canterbury/251/2005(H3N2)	257	A/Waikato/1/2000(H3N2)
197	A/Canterbury/253/2005(H3N2)	258	A/Wellington/22/2001(H3N2)
198	A/Canterbury/255/2005(H3N2)	259	A/Waikato/5/2002(H3N2)
199	A/Canterbury/256/2005(H3N2)	260	A/Wellington/38/2002(H3N2)
200	A/Canterbury/257/2005(H3N2)	261	A/Wellington/66/2002(H3N2)
201	A/Canterbury/258/2005(H3N2)	262	A/Waikato/21/2002(H3N2)
202	A/Canterbury/266/2005(H3N2)	263	A/Dunedin/14/2002(H3N2)
203	A/Canterbury/270/2005(H3N2)	264	A/Waikato/58/2002(H3N2)
204	A/Canterbury/56/2000(H3N2)	265	A/Wellington/83/2002(H3N2)
205	A/Canterbury/68/2000(H3N2)	266	A/Wellington/84/2002(H3N2)
206	A/Canterbury/66/2000(H3N2)	267	A/Wellington/86/2002(H3N2)
207	A/Canterbury/71/2000(H3N2)	268	A/Wellington/3/2003(H3N2)
208	A/Canterbury/80/2000(H3N2)	269	A/Wellington/4/2003(H3N2)
209	A/Canterbury/81/2000(H3N2)	270	A/Waikato/1/2003(H3N2)
210	A/Canterbury/84/2000(H3N2)	271	A/Wellington/10/2003(H3N2)
211	A/Canterbury/85/2000(H3N2)	272	A/Waikato/3/2003(H3N2)
212	A/Hutt/82/2000(H3N2)	273	A/Wellington/25/2003(H3N2)
213	A/Canterbury/89/2000(H3N2)	274	A/Wellington/28/2003(H3N2)
214	A/Canterbury/93/2000(H3N2)	275	A/Waikato/61/2003(H3N2)
215	A/Canterbury/103/2000(H3N2)	276	A/Waikato/75/2003(H3N2)
216	A/Canterbury/101/2000(H3N2)	277	A/Waikato/120/2003(H3N2)
217	A/Canterbury/98/2000(H3N2)	278	A/Waikato/5/2000(H3N2)
218	A/Canterbury/90/2000(H3N2)	279	A/Waikato/1/2001(H3N2)
219	A/Canterbury/400/2003(H3N2)	280	A/Waikato/2/2002(H3N2)
220	A/Canterbury/26/2005(H3N2)	281	A/Wellington/6/2002(H3N2)
221	A/Canterbury/34/2005(H3N2)	282	A/Wellington/70/2002(H3N2)
222	A/Canterbury/124/2005(H3N2)	283	A/Dunedin/9/2002(H3N2)
223	A/Canterbury/87/2000(H3N2)	284	A/Dunedin/8/2002(H3N2)
224	A/Canterbury/96/2000(H3N2)	285	A/Wellington/71/2002(H3N2)
225	A/Canterbury/92/2000(H3N2)	286	A/Waikato/29/2002(H3N2)
226	A/Canterbury/3/2000(H3N2)	287	A/Wellington/80/2002(H3N2)
227	A/Canterbury/179/1999(H3N2)	288	A/Wellington/79/2002(H3N2)
228	A/Canterbury/1/9/1999(H3N2) A/Canterbury/2/2000(H3N2)	289	A/Waikato/52/2002(H3N2)
	A/Nelson Marlborough/1/2000(H3N2)		A/Waikato/51/2002(H3N2)
229	A/Canterbury/55/2000(H3N2)	290	,
230		291	A/Wellington/34/2003(H3N2) A/Waikato/154/2003(H3N2)
231	A/Canterbury/64/2000(H3N2) A/Canterbury/58/2000(H3N2)	292	
232		293	A/Waikato/91/2003(H3N2)
233	A/Canterbury/67/2000(H3N2)	294	A/Waikato/102/2003(H3N2)
234	A/Canterbury/61/2000(H3N2)	295	A/Walkato/150/2003(H3N2)
235	A/Port Chalmers/73(H3N2)	296 207	A/Wellington/1/2004(H3N2)
236	A/Canterbury/94/2000(H3N2)	297	A/Wellington/6/2004(H3N2)

A (A) [I] (2.4 (2.004 (LI2NI2))		
A/Wellington/34/2001(H3N2)	349	A/Wellington/28/2000(H3N2)
A/Waikato/105/2001(H3N2)	350	A/Waikato/31/2002(H3N2)
A/Wellington/7/2002(H3N2)	351	A/Dunedin/12/2002(H3N2)
A/Wellington/63/2002(H3N2)	352	A/Waikato/15/2003(H3N2)
A/Waikato/155/2003(H3N2)	353	A/Waikato/108/2003(H3N2)
A/Waikato/156/2003(H3N2)	354	A/Dunedin/38/2003(H3N2)
A/Waikato/29/2003(H3N2)	355	A/Wellington/23/2004(H3N2)
A/Waikato/115/2003(H3N2)	356	A/Waikato/12/2004(H3N2)
A/Wellington/53/2003(H3N2)	357	A/Wellington/18/2004(H3N2)
A/Waikato/122/2003(H3N2)	358	A/Wellington/27/2004(H3N2)
A/Waikato/129/2003(H3N2)	359	A/Wellington/44/2004(H3N2)
A/Waikato/133/2003(H3N2)	360	A/Wellington/38/2004(H3N2)
A/Waikato/139/2003(H3N2)	361	A/Waikato/22/2004(H3N2)
A/Waikato/147/2003(H3N2)	362	A/Waikato/26/2004(H3N2)
A/Waikato/148/2003(H3N2)	363	A/Wellington/58/2004(H3N2)
A/Canterbury/97/2000(H3N2)	364	A/Waikato/35/2004(H3N2)
A/Dunedin/1/2000 (H3N2)	365	A/Waikato/43/2004(H3N2)
A/Waikato/4/2000(H3N2)	366	A/Waikato/45/2004(H3N2)
A/Waikato/7/2000(H3N2)	367	A/Wellington/62/2004(H3N2)
A/Dunedin/3/2002(H3N2)	368	A/Waikato/15/2000(H3N2)
A/Wellington/9/2003(H3N2)	369	A/Wellington/26/2000(H3N2)
3		A/Wellington/30/2000(H3N2)
A/Wellington/49/2003(H3N2)		A/Wellington/4/2004(H3N2)
A/Wellington/14/2004(H3N2)		A/Waikato/3/2004(H3N2)
3		A/Wellington/59/2004(H3N2)
<u> </u>		A/Waikato/51/2004(H3N2)
3		A/Waikato/56/2004(H3N2)
3		A/Waikato/64/2004(H3N2)
		A/Waikato/68/2004(H3N2)
3		A/Waikato/69/2004(H3N2)
		A/Waikato/71/2004(H3N2)
		A/Wellington/64/2004(H3N2)
		A/Waikato/72/2004(H3N2)
		A/Waikato/73/2004(H3N2)
		A/Waikato/1/2005(H3N2)
-		A/Wellington/1/2005(H3N2)
		A/Wellington/2/2005(H3N2)
		A/Otago/1/2005(H3N2)
		A/Wellington/3/2005(H3N2)
		A/Southland/5/2005(H3N2)
		A/Waikato/2/2005(H3N2)
* *		A/Waikato/7/2005(H3N2)
		A/Waikato/3/2005(H3N2) A/Otago/2/2005(H3N2)
3		9
_		A/Wellington/8/2005(H3N2)
* * *		A/Wellington/9/2005(H3N2)
		A/Waikato/9/2005(H3N2)
		A/Otago/4/2005(H3N2)
		A/Otago/3/2005(H3N2)
	398	A/Waikato/12/2005(H3N2)
	A/Wellington/7/2002(H3N2) A/Wellington/63/2002(H3N2) A/Waikato/155/2003(H3N2) A/Waikato/156/2003(H3N2) A/Waikato/29/2003(H3N2) A/Waikato/115/2003(H3N2) A/Wellington/53/2003(H3N2) A/Waikato/122/2003(H3N2) A/Waikato/122/2003(H3N2) A/Waikato/129/2003(H3N2) A/Waikato/133/2003(H3N2) A/Waikato/139/2003(H3N2) A/Waikato/147/2003(H3N2) A/Waikato/148/2003(H3N2) A/Canterbury/97/2000(H3N2) A/Dunedin/1/2000 (H3N2) A/Waikato/4/2000(H3N2) A/Waikato/7/2000(H3N2) A/Waikato/7/2000(H3N2) A/Waikato/7/2000(H3N2) A/Waikato/9/2003(H3N2) A/Wellington/9/2003(H3N2) A/Wellington/9/2003(H3N2)	A/Wellington/63/2002(H3N2) 351 A/Wellington/63/2002(H3N2) 352 A/Waikato/155/2003(H3N2) 353 A/Waikato/155/2003(H3N2) 354 A/Waikato/156/2003(H3N2) 355 A/Waikato/156/2003(H3N2) 355 A/Waikato/156/2003(H3N2) 356 A/Wellington/53/2003(H3N2) 357 A/Waikato/122/2003(H3N2) 358 A/Waikato/122/2003(H3N2) 359 A/Waikato/139/2003(H3N2) 360 A/Waikato/139/2003(H3N2) 361 A/Waikato/139/2003(H3N2) 362 A/Waikato/147/2003(H3N2) 362 A/Waikato/147/2003(H3N2) 363 A/Canterbury/97/2000(H3N2) 364 A/Dunedin/1/2000 (H3N2) 365 A/Waikato/74/2000(H3N2) 366 A/Waikato/7/2000(H3N2) 366 A/Waikato/7/2000(H3N2) 367 A/Dunedin/3/2002(H3N2) 369 A/Wellington/9/2003(H3N2) 370 A/Wellington/47/2003(H3N2) 371 A/Wellington/49/2003(H3N2) 371 A/Wellington/14/2004(H3N2) 372 A/Wellington/14/2004(H3N2) 373 A/Wellington/14/2004(H3N2) 374 A/Wellington/14/2004(H3N2) 375 A/Waikato/21/2004(H3N2) 376 A/Waikato/21/2004(H3N2) 377 A/Waikato/40/2004(H3N2) 377 A/Waikato/40/2004(H3N2) 377 A/Waikato/6/2004(H3N2) 377 A/Waikato/6/2004(H3N2) 377 A/Waikato/6/2004(H3N2) 379 A/Waikato/6/2004(H3N2) 381 A/Waikato/6/2004(H3N2) 381 A/Waikato/6/2004(H3N2) 381 A/Waikato/6/2004(H3N2) 382 A/Waikato/5/2001(H3N2) 383 A/Waikato/5/2001(H3N2) 383 A/Waikato/5/2001(H3N2) 384 A/Waikato/5/2001(H3N2) 385 A/Waikato/5/2001(H3N2) 385 A/Waikato/5/2001(H3N2) 386 A/Waikato/5/2001(H3N2) 386 A/Waikato/5/2001(H3N2) 387 A/Waikato/5/2001(H3N2) 383 A/Waikato/5/2000(H3N2) 384 A/Waikato/5/2001(H3N2) 385 A/Dunedin/18/2003(H3N2) 386 A/Waikato/54/2003(H3N2) 389 A/Waikato/54/2003(H3N2) 389 A/Waikato/54/2003(H3N2) 390 A/Waikato/54/2003(H3N2) 391 A/Waikato/54/2003(H3N2) 393 A/Waikato/54/2003(H3N2) 393 A/Waikato/54/2003(H3N2) 393 A/Waikato/54/2003(H3N2) 393 A/Walkato/54/2003(H3N2) 393 A/Walka