Phylogeography of Influenza A(H3N2) Virus in Peru, 2010–2012

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It remains unclear whether lineages of influenza A(H3N2) virus can persist in the tropics and seed temperate areas. We used viral gene sequence data sampled from Peru to test this source–sink model for a Latin American country. Viruses were obtained during 2010–2012 from influenza surveillance cohorts in Cusco, Tumbes, Puerto Maldonado, and Lima. Specimens positive for influenza A(H3N2) virus were randomly selected and underwent hemagglutinin sequencing and phylogeographic analyses. Analysis of 389 hemagglutinin sequences from Peru and 2,192 global sequences demonstrated interseasonal extinction of Peruvian lineages. Extensive mixing occurred with global clades, but some spatial structure was observed at all sites; this structure was weakest in Lima and Puerto Maldonado, indicating that these locations may experience greater viral traffic. The broad diversity and co-circulation of many simultaneous lineages of H3N2 virus in Peru suggests that this country should not be overlooked as a potential source for novel pandemic strains.

Worldwide, influenza virus causes substantial illness and death and considerable public health costs (*1*). Like other countries, Peru experiences a significant number of influenza cases (*2*,*3*). The epidemiology of influenza virus in tropical and low- to middle-income countries and the role they play in global influenza ecology remains unclear (*4*). One outstanding question is whether a global source–sink dynamic exists. In the source–sink model, countries have putative tropical sources of influenza characterized by year-round (or multiannual) transmission, local persistence of influenza lineages, and relatively high genetic diversity. Then, it is postulated, that influenza lineages migrate and seed seasonal epidemics in cooler temperate regions, where they experience interseasonal extinction (*5*). Determining if and where this source–sink dynamic exists is of major importance because the results could guide targeted influenza surveillance for vaccine recommendations, pandemic planning, and prediction of novel strains (*4*,*6*).

Most analyses of whether a global source population exists have focused on East and Southeast Asia, in part because several pandemic and seasonal epidemics appear to have originated in those areas (*7*–*11*). Because of the lower availability of local influenza sequence data from tropical Latin America, relatively little is known about the possible role that region plays in global influenza dynamics (*12*). Nonmolecular epidemiologic studies have hinted at climate-driven patterns of influenza virus spread in South America; for example, diffusion of influenza activity from tropical to temperate areas has been noted in Brazil (*13*). Peru's diverse climates make it an ideal location to test aspects of the source–sink model in Latin America, particularly because some tropical areas in Peru are known to experience year-round influenza activity (*14*). In recent years, prospective community-based influenza-like illness (ILI) surveillance cohorts were established in multiple regions of Peru, providing a unique opportunity to examine the epidemiology of human influenza virus (*15*).

Our study objectives were to determine whether 1) a source–sink influenza dynamic exists within Peru, including the existence of genetically diverse hubs and virus lineage persistence between seasons; 2) Peru could act as a global source for influenza virus lineages that could seed temperate regions; and 3) influenza virus is circulating within Peru in a closed system. We also sought to compare the spatial dynamics of influenza A(H3N2) virus across the 4 climatically and demographically diverse Peruvian sites.

We based our analysis on human influenza A(H3N2) virus because, over a long-term scale, it is the best represented lineage in sequence databases, and it has caused regular seasonal influenza epidemics in both hemispheres, including in Latin America (*16*,*17*). Although much attention has been paid to the study of pandemic influenza A(H1N1) pdm09 virus (*18*), H3N2 virus remains a significant cause of influenza in Peru, is a dominant seasonal influenza A

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DOI: http://dx.doi.org/10.3201/eid2108.150084

virus subtype in other regions of the world, and causes substantial illness and death in Peru and beyond. A key aspect of this study is that we obtained samples from diverse ecologies and populations, including viruses from large urban and semirural locations and diverse altitudes and climates, and the distance between study sites was sufficient to allow spatial analysis. In addition, the prospective cohort studies involved continuous, active, year-round surveillance that enabled capture of any interseasonal strains.

Materials and Methods

Study Setting, Enrolment Criteria, and Field Procedures

In 2009, the United States Navy Medical Research Unit No. 6 (NAMRU-6), the Centers for Disease Control and Prevention (CDC), and the Peruvian Ministry of Health established a community-based prospective ILI cohort (Proyecto Influenza) in 4 ecologically distinct regions of Peru. Sites were chosen to represent the diverse ecologies, climates, and population structure in Peru. Lima, on the central desert coast, is Peru's capital and largest city and a transport hub for the rest of the nation. Lima has a population of 8,348,400 persons and a temperate climate with little rain (*19*). Puerto Maldonado, in the southern Amazon Basin, has a population of 89,500 persons. The city has high annual rainfall and a warm, humid climate year-round (*19*). Cusco is a high-altitude (3,200 meters) city in the southern Andes Mountains. This southern highlands city has a population of 420,030 persons (*19*). Tumbes is a northern equatorial coastal city of 157,760 persons (*19*).

Enrollment criteria and field procedures were as described elsewhere (*15*). In brief, during 2010–2012, households were selected from each study site by using a computer-based randomization process. An adult head and all residents of the household were eligible for enrollment. Participants were assessed 3 times per week for the development of ILI. For children <5 years of age, ILI was defined as sudden onset of fever (≥38°C) and cough, sore throat, or coryza. For persons ≥5 years of age, ILI was defined as sudden onset of fever (≥38°C) with cough, sore throat, or both. We administered a household enrolment form in which sociodemographic and risk factor data were collected. Nasal and throat swab samples for virus identification were obtained from persons with signs meeting the ILI case definition; a rapid influenza test was performed so that immediate medical referral could be made if necessary.

Ethical Approval

The NAMRU-6 Institutional Review Board approved the study. Informed written consent was obtained at the time of enrolment from each adult participant and from a parent or guardian of children. NAMRU-6 participation was under protocol NMRCD.2009.005, which is in compliance with all applicable US federal regulations governing the protection of human subjects.

Detection of Influenza Virus in Nasal or Throat Swab Specimens

Nucleic acid was extracted from nasal and throat swab specimens in universal transport media by using the QIAamp Viral RNA Isolation Kit (QIAGEN, Valencia, CA, USA). Reverse transcription PCR (RT-PCR) for influenza detection, including subtype, was performed by using primers and probes from the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (Influenza Reagent Resource, CDC, Atlanta, GA, USA). Original respiratory samples were then stored at −80°C at NAMRU-6 Peru.

Identification of Sequences for Phylogenomic Analyses and Generation of Sequence Data

Over the study period, we randomly selected 100 H3N2 virus–positive (RT-PCR cycle threshold <29) specimens from each study site (400 total). Original respiratory specimens were sent (at −80°C) from NAMRU-6 Peru to the J. Craig Venter Institute (Rockville, MD, USA) for extraction and hemagglutinin (HA) gene sequencing. GenBank accession numbers for the consensus sequences are available in online Technical Appendix Table 1 (http://wwwnc.cdc.gov/EID/article/21/8/15-0084-Techapp1.pdf). Viral RNA was isolated by using the ZR 96 Viral RNA Kit (Zymo Research Corporation, Irvine, CA, USA). The influenza A virus genomic RNA segments were simultaneously amplified from purified RNA (3 mL) by using a multisegment RT-PCR strategy (*20,21*). Amplicons were sequenced by using the Nextera DNA Sample Preparation Kit Library construction and the Illumina MiSeq version 2 platform (both from Illumina, Inc., San Diego, CA, USA) or the Ion Xpress Plus Fragment Library Kit and the Ion Torrent PGM platform (both from Thermo Fisher Scientific, Waltham, MA, USA). The sequence reads were sorted by barcode and trimmed, and chimeric influenza virus sequences and noninfluenza sequences were removed. The next-generation sequencing reads were then mapped to the best matching reference virus by using the CLC Bio Assembly Cell 3.0 program clc_ref_assemble_long (http://www.clcbio.com/products/clc-assembly-cell/) (*22*). At loci where next-generation sequencing platforms agreed on a variation (as compared with the reference sequence), the reference sequence was updated to reflect the difference. A final mapping of all next-generation sequences to the updated reference sequences was then performed.

Collation of Background Sequence Data, Alignment, and Evolutionary Model Selection

Global background H3N2 HA sequences were obtained from the National Institute of Allergy and Infectious

Disease Influenza Research Database (IRD; http://www.fludb.org/brc/home.spg?decorator=influenza) (*23*) and the Global Initiative on Sharing Avian Influenza Data EpiFlu Database (http://platform.gisaid.org/epi3/frontend#f989c). Sequences for viruses obtained during January 2004–August 2013 from the following regions were sampled (nos. in parentheses indicate no. of sequences): South America, excluding Peru (193); Australia, New Zealand, and Oceania, excluding Hawaii (259); East and Southeast Asia (374); Middle East/Central Asia, including Russia (110); Europe (235); Central America and the Caribbean (116); Mexico (27); Canada (234); the United States, including Hawaii (549); and Africa (79). In addition, 16 sequences for strains collected in Peru during 2006–2013 were obtained through IRD or the EpiFlu Database. A total of 2,192 background sequences were selected (online Technical Appendix Tables 2–4).

To improve phylogenetic resolution, only complete or near-complete HA sequences (containing at least the entire HA1 region) were included. For geographic regions with an abundance of full HA1 sequences in GenBank (e.g., Asia, United States), intermittent sequences were manually selected from a list sorted by country in the IRD. For underrepresented geographic regions (e.g., Africa, South America), all available full HA1 sequences were included to overcome ascertainment bias. Accession numbers (GenBank and EpiFlu Database) for these comparator sequences are shown in online Technical Appendix Tables 2–4.

Untranslated regions were trimmed, and duplicate sequences were removed, resulting in a final dataset of 2,581 sequences 1,639–1,700 nt in length; 1 partial sequence was 1,324 nt long. A second dataset of 389 sequences (1,700 nt long) was constructed for viruses from Peru. All sequences were aligned before inspection by using the MUSCLE algorithm in MEGA5.2 and hand-edited for final correction (*24*). A best-fit model of nucleotide substitution (general time-reversible with a gamma-distributed rate variation among sites and a proportion of invariant sites) was selected by using jModelTest2 software (*25*).

Global Phylogenetic Analysis

A maximum-likelihood tree of all 2,581 H3 sequences was inferred by using RAxML software version 7.26 (*26*). Statistical robustness was tested by nonparametric bootstrap resampling analysis (500 replicates). Inferred maximum-likelihood trees were viewed and annotated by using FigTree software (http://tree.bio.ed.ac.uk/software/figtree/).

Bayesian Analyses of Peruvian Sequences

We analyzed 389 HA time-stamped sequences (i.e., labeled with the time of sampling to the nearest day) for viruses from Peru by using the Bayesian Markov chain Monte Carlo method in BEAST (*27*); the results enabled inference of the time-scale of the viruses' epidemiologic histories. For this analysis, we selected a Bayesian skyline demographic model was selected and, assuming a strict molecular clock rate (under a uniform prior), we selected the Hasegawa-Kishino-Yano nucleotide substitution model with a discrete-gamma distribution in place of other, more complex models that likely overparameterized the data. The analysis was run by using a 500,000,000-step Markov chain, sampling every 50,000 states. A 10% burn-in was removed, and statistical convergence was determined by parameter values with effective sample size values >200. The posterior distribution of trees was summarized as the maximum clade credibility tree, as generated by using TreeAnnotator version 1.75 (http://beast.bio.edu.ac.uk/TreeAnnotator/) and visualized by using FigTree.

For viruses from Peru, the posterior distribution of HA trees from BEAST was also used to assess the strength of geographic clustering in the data by using the phylogeny-trait association test available in the Bayesian Tip-association Significance testing package (*28*). For this analysis, each sequence was given a geographic code reflecting its place of origin. The overall statistical significance of geographic clustering of all Peruvian sequences by location was determined by calculating observed and expected association index and parsimony score statistics for the entire Peruvian sequence dataset, where the null hypothesis is that clustering by geographic location is not more than that expected by chance. In addition, the maximum clade statistic was used to compare the strength of clustering at each location by calculating the expected and observed mean clade size from each of the 4 study locations. A significance level of $p<0.05$ was used in all cases.

Results

Of the 400 H3N2 PCR–positive specimens selected from the NAMRU-6 repository, 389 HA segments were successfully sequenced (online Technical Appendix Table 1). The distribution of successfully sequenced H3N2 HA genes by year and location relative to other co-circulating influenza virus subtypes in the study period is presented in Table 1. Well-distributed sampling in all sites for all years was impossible because of differences in specimen quality and because overall H3N2 virus activity in the cohorts was considerably less overall during 2011–2012 than in 2010, partly due to the dominance of influenza B virus in 2012. Thus, the sampling was skewed toward 2010 and toward fewer sequences for Cusco and Puerto Maldonado in 2012 and Tumbes in 2011.

Phylogenetic analysis of the 389 study sequences for viruses from Peru and 2,192 global HA sequences revealed extensive geographic mixing (Figures 1, 2; fully labeled

Table 1. Distribution of sequenced influenza A(H3N2) virus strains, compared with all confirmed cases of influenza and influenza-like illness, Peru, 2010–2012

Year, location	No. sequenced influenza A(H3N2) strains*	No. other strains or illnesses				
		All H3N2	Influenza A(H1N1) pdm09	Influenza B	Influenza illness	Influenza-like illness
2010						
All	227	414	138	306	858	1,716
Lima	41	95	38	96	229	458
Cusco	31	42	63	74	179	358
Tumbes	92	155	25	83	263	526
Puerto Maldonado	63	122	12	53	187	374
2011						
All	105	219	36	16	271	542
Lima	13	35	6	1	42	84
Cusco	65	101	2	0	103	206
Tumbes	2	17	11	14	42	84
Puerto Maldonado	25	66	17	1	84	168
2012						
All	57	87	57	233	377	754
Lima	27	45	29	48	122	244
Cusco	0	7	7	74	88	176
Tumbes	28	42	18	18	78	156
Puerto Maldonado	2	38	3	93	134	268
2010–2012						
All	389	1,485	462	1110	3057	6,114

*Strains sequenced during this phylogeographic study of influenza A(H3N2) virus in Peru.

tree in the online Technical Appendix Figure). Perhaps the most notable observation from this analysis was the interseasonal extinction of virus clades from Peru in all regions of the country, even in a tropical region where molecularly confirmed year-round influenza transmission has been noted (*14*). In addition, the phylogeny showed extensive global mixing of H3N2 viruses, with co-circulation of clades from Peru with those from all Northern and Southern Hemisphere regions, including in countries in Latin and North America, Africa, Europe, Central Asia, and East

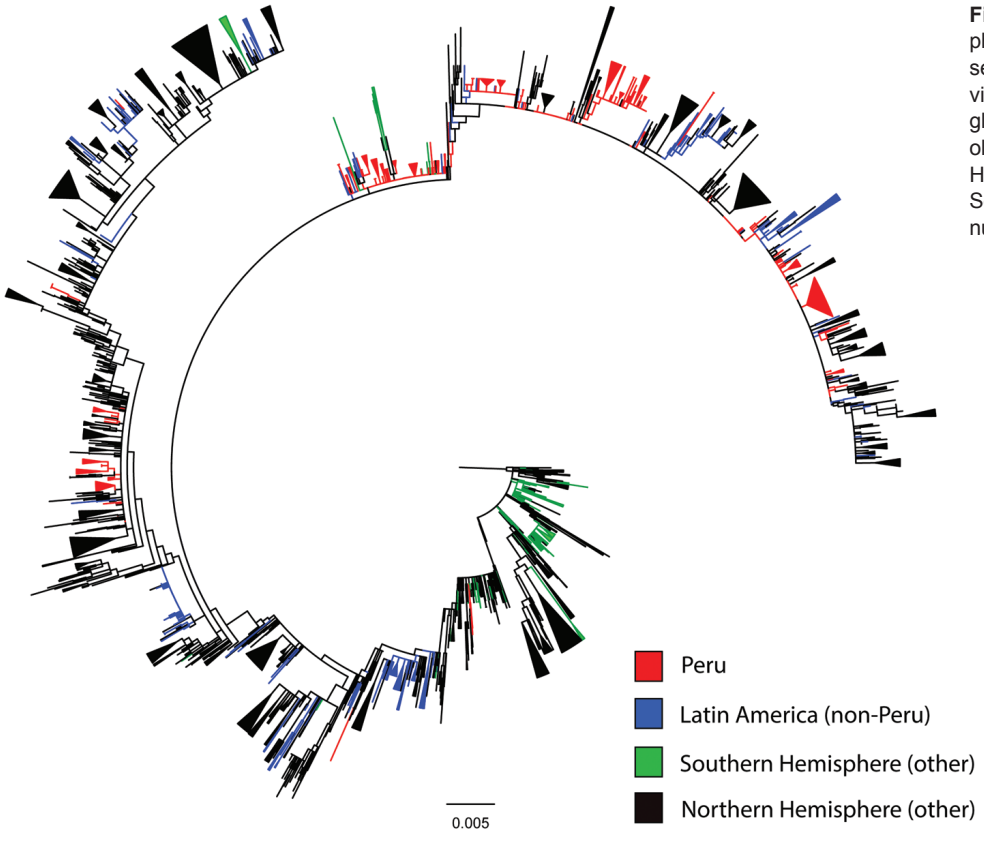

Figure 1. Maximum-likelihood phylogeny of hemagglutinin sequences of influenza A(H3N2) viruses from Peru and other global locations, rooted with the oldest available sequence (A/Hong Kong/CUHK52390/2004). Scale bar indicates number of nucleotide substitutions per site.

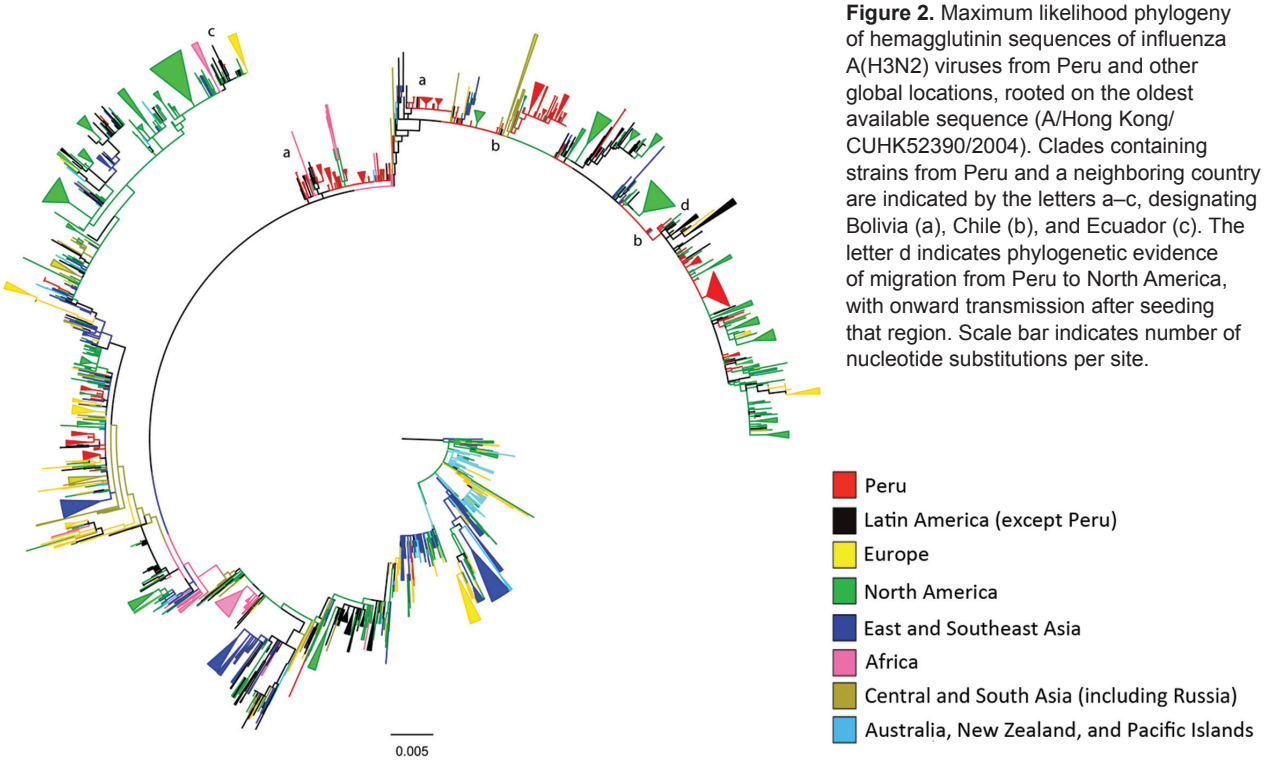

Figure 2. Maximum likelihood phylogeny of hemagglutinin sequences of influenza A(H3N2) viruses from Peru and other global locations, rooted on the oldest available sequence (A/Hong Kong/CUHK52390/2004). Clades containing strains from Peru and a neighboring country are indicated by the letters a–c, designating Bolivia (a), Chile (b), and Ecuador (c). The letter d indicates phylogenetic evidence of migration from Peru to North America, with onward transmission after seeding that region. Scale bar indicates number of nucleotide substitutions per site.

and Southeast Asia. In one instance, onward transmission of virus was noted after migration from Peru to the United States (Figure 2, section d).

Viruses from each study location in Peru formed weak to moderately supported clades with sequences for viruses from other localities (bootstrap values were usually <70% but occasionally >80%), reflecting a relative lack of phylogenetic resolution in the data at this scale (online Technical Appendix Figure). In contrast, smaller but often better supported clades (frequently with bootstrap values >70%) containing H3 virus sequences from multiple locations in Peru were observed (online Technical Appendix Figure).

Closer examination of the phylogenetic analysis of sequences for viruses from Latin America showed evidence for the presence of weakly supported sublineages consisting predominantly of strains from Peru but also containing strains from Chile and Bolivia (Figure 2); this finding is indicative of viral traffic between these border-sharing countries. Analysis of clustering with strains from Ecuador was limited by a paucity of sequences, but evidence of strongly supported clustering with strains from Peru was found (Figure 2). In addition, strains from Peru fell into some weakly supported multinational sublineages containing strains from Brazil, Venezuela, Paraguay, Nicaragua, Colombia, Argentina, and Mexico, which suggests H3N2 viral traffic throughout the Americas (online Technical Appendix Figure).

Analyzed separately, the maximum clade credibility tree (Figure 3) for strains from Peru showed substantial HA diversity each year; many clades co-circulated at each location. The smaller-sized locations of Tumbes, Puerto Maldonado, and Cusco had a wide range of co-circulating clades, similar to those of larger travel hubs, such as Lima (Table 2). This analysis also showed a short time to most common recent ancestor (mean 3.8 y, 95% highest posterior density 3.1–4.6 y), as has been shown for most other studied localities (*5*,*29*). A similarly short mean time to most recent common ancestor (1.6 y, 95% highest posterior density 1.1–2.1 y) was obtained for 2010, the most sampled year, providing the most precise single-season estimate.

To determine the phylogeographic structure in the data, we performed phylogeny-trait association tests (Table 3). For strains from Peru, the results confirmed a stronger spatial clustering of sequences at all sites than would be expected by chance alone ($p<0.01$), but the results also showed clear evidence of some viral traffic among sampling locations, as noted in the phylogenetic analysis. Furthermore, the maximum clade statistic was significant ($p = 0.009$) in all 4 study sites, reflecting predominantly local evolution in these localities. Differences in the observed and expected maximum clade values tentatively suggested that Lima exhibited the least structure (i.e., most mixing; difference of 5.50) and Tumbes the strongest spatial structure (difference of 10.33) (Table 3).

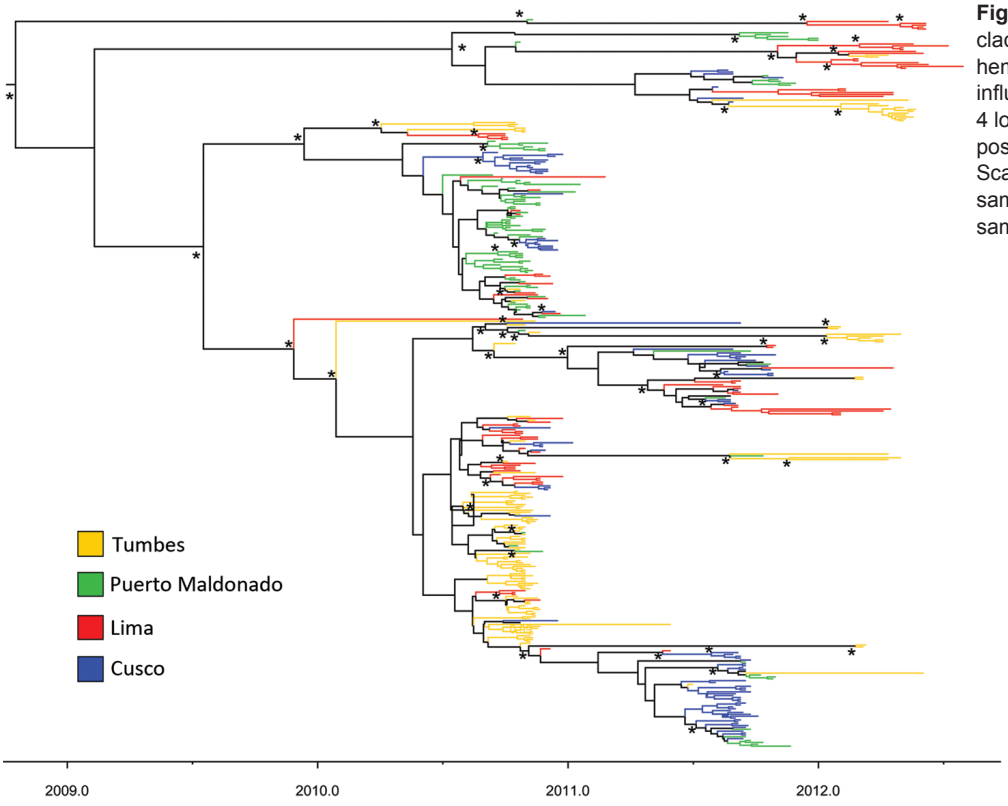

Figure 3. Time-scaled maximum clade credibility phylogeny of hemagglutinin sequences for influenza A(H3N2) viruses from 4 locations in Peru. *Indicates posterior probabilities >0.9. Scale bar refers to year of sampling to indicate time of sampling for each virus.

Discussion

Our phylogenetic analysis showed that the level of international H3N2 viral traffic was high and that mixing of Peruvian HA sequences with those from multiple regions of the world was rapid and widespread (Figures 1, 2). These findings support a continuous H3N2 gene flow in and out of Peru rather than a local closed system in which viruses evolve entirely within the country. Mixing of viruses between all study sites in Peru and other countries may also suggest gene flow in and out of Peruvian locations outside the main air-transport hub of Lima. However, such a conclusion comes with a strong caveat because we may not have sampled all Lima source lineages that seed peripheral locations in the country. Of note, we found evidence of H3N2 virus migration between Peru and its neighbors, although this conclusion was limited by a relative paucity of sequences from these other Latin American countries.

At each study site in Peru, we found multiple co-circulating clades of influenza virus that regularly underwent extinction (Figures 1, 2), suggesting that much of the genetic diversity of viruses in Peru results from global lineages that pass through the country, rather than from local evolution associated with long-term local persistence. In particular, all sampled strains, even those from tropical Peruvian sites like Tumbes and Puerto Maldonado, underwent extinction rather than persisted over time, thus regularly halting local evolution of imported influenza viruses. That the time to most common recent ancestor of the whole sample (mean 3.8 y) was much shorter than the known history of H3N2 virus in Peru is also consistent with the idea that the influenza virus gene pool in Peru is being frequently replenished from other regions.

Our findings are consistent with those of studies in countries with temperate regions, such as Australia, New Zealand, and countries in North America, which showed regular introduction of new H3N2 virus lineages and seeding of local seasonal epidemics rather than the interseasonal persistence of lineages (*29–31*). Such studies have similarly revealed that the genetic diversity of seasonal influenza in temperate locales primarily results from the ongoing introduction of genetically divergent lineages during seasonal epidemics (*5*,*30–32*).

In contrast, interseasonal persistence of H3N2 influenza virus has been documented in subtropical and tropical

Table 2. Number of circulating influenza A(H3N2) virus clades, Peru, 2010–2012*

Location	No. clades circulating, by year		
	2010	2011	2012
Lima	8	6	5
Puerto Maldonado	6	4	0
Cusco	4	9	0
Tumbes	13	1	5

*Data are derived from the phylogenetic tree in Figure 3.

Table 3. Results of phylogeny-trait association testing for influenza A(H3N2) viruses in Peru, 2010–2012*

	Association index (95% CI)†			Parsimony scores (95% CI)†			Mean maximum clade size (95% CI)‡			
Location	Observed	Expected	p value§	Observed	Expected	p value§	Observed	Expected	p value¶	Difference#
All	8.53 (7.25–9.81)	33.02 (31.52–34.56)	<0.001	73.72 (70.00–77.00)	211.00 (205.65–217.36)	<0.001	–	–		–
Lima	–	–		–	–		8.04 (6.0–10.0)	2.6 (2.18–3.16)	0.009	5.44
Cusco	–	–		–	–		12.4 (12.0–15.0)	2.82 (2.36–3.44)	0.009	9.58
Puerto Maldonado	–	–		–	–		8.2 (6.0–14.0)	2.7 (2.28–3.45)	0.009	5.50
Tumbes	–	–		–	–		13.68 (10.0–22.0)	3.35 (2.76–4.99)	0.009	10.33

*Results were determined by a Bayesian analysis of phylogeographic structure. p values correspond to the proportion of trees from the null distribution equal to, or more extreme than, the median posterior of the statistic.
†Association index and parsimony scores only determined for all locations combined.
‡Maximum clade size statistics only determined for each specific location.
§p<0.001 confirms a stronger observed spatial clustering of sequences from Peru at all sites than would be expected by chance alone.
¶p = 0.009 reflects predominantly local evolution in the 4 locations.
#Difference between observed and expected clade size.

locations like Hong Kong and Southeast Asia (*7*,*8*,*10*). A more recent study has shown evidence for multiyear pandemic influenza A(H1N1)pdm09 strain persistence in tropical areas of western Africa that are relatively isolated (*33*). In contrast, an analysis of H3N2 virus persistence over a 15-year period in subtropical China did not demonstrate interseasonal persistence, and the sample size in that study was much larger than that in our study (*9*).

Our findings did not offer support to a source–sink dynamic within Peru, and they also indicate that Peru is an unlikely common tropical source of persistent lineages that seed other countries in Latin America or the rest of the world. Instead, our findings are more consistent with a shifting metapopulation model of H3N2 virus, such that the virus may pass through any region for a variable amount of time rather than perpetually circulating in fixed locations in the tropics and consistently seeding temperate regions each year (*11*,*34*). Such a shifting metapopulation model may also explain why some studies show apparent persistence in some tropical and subtropical locations over certain years and others do not (*7*–*9*,*33*). This model is also compatible with the existence of temporary source populations in locations throughout the world. Indeed, we provide some phylogenetic evidence that Peru may occasionally, but not consistently, act as a temporary source, spreading virus from Peru to another country, from which onward transmission continues (Figure 2, section d).

H3 virus sequences for viruses from Peru also exhibited some clustering by sampling location, a finding consistent with semilocalized seasonal H3N2 virus epidemics in each region of Peru (Figure 3), although with migration between localities. Such semilocalized epidemics have been observed in other areas (*29*). These data also provided some evidence for weaker spatial clustering in Lima compared with other localities. This evidence is not surprising because Lima has the largest population and, thus, movement of humans around, in, or out of the city would generally be expected to be greater than in other areas. In this context it is perhaps surprising that Puerto Maldonado, the least populous site, had a similar strength of spatial clustering. This locality has been characterized by rapid population growth, likely due to widespread mining and associated activities (*35*). Hence, it is possible that frequent human movement in and out of this location is creating more diffusion of influenza virus. In addition, the true population of this area may be considerably higher than suggested by official statistics.

These findings have implications for public health practice in Peru and Latin America. For example, they suggest that future novel strains of influenza virus may enter Peru at multiple locations rather than just through its major air-transport hub (Lima) (*36*). Moreover, the rapid diffusion of influenza virus throughout Peru, even in the more remote regions, also serves as a potent reminder of how quickly influenza virus can disseminate. We identified Lima and Puerto Maldonado as possible diffusion hubs for influenza virus; perhaps both cities could be prioritized for heightened influenza surveillance if a novel influenza subtype is introduced into Peru.

Although Peru does not appear to be a global source population for influenza viruses, the diversity and cocirculation of many simultaneous lineages of H3N2 virus in the country means that it should not be overlooked as a potential source for novel pandemic strains, particularly given that there is some evidence of high-risk animal farming practices and low biosecurity in this country (*37*). Similarly, the rapid, widespread, and unpredictable migration of global strains into Peru and widespread global mixing shown in this study emphasize that vaccine recommendations in either hemisphere

need to be based on well distributed, widespread global H3N2 virus sampling from as many sentinel laboratories as possible (*6*).

Acknowledgments

We thank all participants and households who enrolled in this study, and we thank Sebastian Loli for his assistance. We gratefully acknowledge the authors and originating and submitting laboratories of the sequences from the Global Initiative on Sharing Avian Influenza Data EpiFlu Database that were used as comparator sequences for this research; accession numbers are listed in online Technical Appendix Table 4.

The study was funded by the CDC; the National Institutes of Health, Fogarty International Center; and the US Department of Defense Global Emerging Infections Surveillance (grant no. I0082_09_LI). Sequencing was performed by the J. Craig Venter Institute as a partner to the National Institute of Allergy and Infectious Disease's Influenza Genome Sequencing Project. E.C.H. is supported by a National Health and Medical Research Council fellowship from the Australian government (AF30).

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References

1. Fineberg HV. Pandemic preparedness and response–lessons from the H1N1 influenza of 2009. N Engl J Med. 2014;370:1335–42. http://dx.doi.org/10.1056/NEJMra1208802
2. Forshey BM, Laguna-Torres VA, Vilcarromero S, Bazan I, Rocha C, Morrison AC, et al. Epidemiology of influenza-like illness in the Amazon Basin of Peru, 2008–2009. Influenza Other Respir Viruses. 2010;4:235–43. http://dx.doi.org/10.1111/j.1750-2659.2010.00139.x
3. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. Influenza Other Respir Viruses. 2009;3:253–6. http://dx.doi.org/10.1111/j.1750-2659.2009.00111.x
4. Viboud C, Alonso WJ, Simonsen L. Influenza in tropical regions. PLoS Med. 2006;3:e89. http://dx.doi.org/10.1371/journal.pmed.0030089
5. Rambaut A, Pybus OG, Nelson MI, Viboud C, Taubenberger JK, Holmes EC. The genomic and epidemiological dynamics of human influenza A virus. Nature. 2008;453:615–9. http://dx.doi.org/10.1038/nature06945
6. Russell CA, Jones TC, Barr IG, Cox NJ, Garten RJ, Gregory V, et al. Influenza vaccine strain selection and recent studies on the global migration of seasonal influenza viruses. Vaccine. 2008;26(Suppl 4):D31–4. http://dx.doi.org/10.1016/j.vaccine.2008.07.078
7. Bahl J, Nelson MI, Chan KH, Chen R, Vijaykrishna D, Halpin RA, et al. Temporally structured metapopulation dynamics and persistence of influenza A H3N2 virus in humans. Proc Natl Acad Sci U S A. 2011;108:19359–64. http://dx.doi.org/10.1073/pnas.1109314108
8. Le MQ, Lam HM, Cuong VD, Lam TT, Halpin RA, Wentworth DE, et al. Migration and persistence of human influenza A viruses, Vietnam, 2001–2008. Emerg Infect Dis. 2013;19:1756–65. http://dx.doi.org/10.3201/eid1911.130349
9. Cheng X, Tan Y, He M, Lam TT, Lu X, Viboud C, et al. Epidemiological dynamics and phylogeography of influenza virus in southern China. J Infect Dis. 2013;207:106–14. http://dx.doi.org/10.1093/infdis/jis526
10. Tang JW, Ngai KL, Lam WY, Chan PK. Seasonality of influenza A(H3N2) virus: a Hong Kong perspective (1997–2006). PLoS ONE. 2008;3:e2768. http://dx.doi.org/10.1371/journal.pone.0002768
11. Russell CA, Jones TC, Barr IG, Cox NJ, Garten RJ, Gregory V, et al. The global circulation of seasonal influenza A (H3N2) viruses. Science. 2008;320:340–6. http://dx.doi.org/10.1126/science.1154137
12. Nelson MI, Balmaseda A, Kuan G, Saborio S, Lin X, Halpin RA, et al. The evolutionary dynamics of influenza A and B viruses in the tropical city of Managua, Nicaragua. Virology. 2014;462–463:81–90. http://dx.doi.org/10.1016/j.virol.2014.05.025
13. Alonso WJ, Viboud C, Simonsen L, Hirano EW, Daufenbach LZ, Miller MA. Seasonality of influenza in Brazil: a traveling wave from the Amazon to the subtropics. Am J Epidemiol. 2007;165:1434–42. http://dx.doi.org/10.1093/aje/kwm012
14. Laguna-Torres VA, Gomez J, Ocana V, Aguilar P, Saldarriaga T, Chavez E, et al. Influenza-like illness sentinel surveillance in Peru. PLoS ONE. 2009;4:e6118. http://dx.doi.org/10.1371/journal.pone.0006118
15. Razuri H, Romero C, Tinoco Y, Guezala MC, Ortiz E, Silva M, et al. Population-based active surveillance cohort studies for influenza: lessons from Peru. Bull World Health Organ. 2012;90:318–20.
16. Cox NJ, Subbarao K. Global epidemiology of influenza: past and present. Annu Rev Med. 2000;51:407–21. http://dx.doi.org/10.1146/annurev.med.51.1.407
17. The pink book. Influenza: epidemiology and prevention of vaccine-preventable diseases. Influenza virus [cited 2013 Nov 1]. http://www.cdc.gov/vaccines/pubs/pinkbook/flu.html#flu
18. Cheng VC, To KK, Tse H, Hung IF, Yuen KY. Two years after pandemic influenza A/2009/H1N1: what have we learned? Clin Microbiol Rev. 2012;25:223–63. http://dx.doi.org/10.1128/CMR.05012-11
19. Instituto Nacional de Estadistica e informatica [cited 2013 Oct 1]. http://www.inei.gob.pe
20. Zhou B, Donnelly ME, Scholes DT, St George K, Hatta M, Kawaoka Y, et al. Single-reaction genomic amplification accelerates sequencing and vaccine production for classical and swine origin human influenza a viruses. J Virol. 2009;83:10309–13. http://dx.doi.org/10.1128/JVI.01109-09
21. Zhou B, Wentworth DE. Influenza A virus molecular virology techniques. Methods Mol Biol. 2012;865:175–92. http://dx.doi.org/10.1007/978-1-61779-621-0_11
22. White paper on reference assembly in CLC Assembly Cell 3.0. May 10, 2010 [cited 2013 Nov 1]. http://www.clcbio.com/wp-content/uploads/2012/09/white_paper_on_reference_assembly_on_the_CLC_Assembly_Cell.pdf
23. Squires RB, Noronha J, Hunt V, Garcia-Sastre A, Macken C, Baumgarth N, et al. Influenza Research Database: an integrated bioinformatics resource for influenza research and surveillance. Influenza Other Respir Viruses. 2012;6:404–16. http://dx.doi.org/10.1111/j.1750-2659.2011.00331.x
24. Tamura K, Peterson D, Peterson N, Stecher G, Nei M, Kumar S. MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. Mol Biol Evol. 2011;28:2731–9. http://dx.doi.org/10.1093/molbev/msr121

25. Darriba D, Taboada GL, Doallo R, Posada D. jModelTest 2: more models, new heuristics and parallel computing. Nat Methods. 2012;9:772. http://dx.doi.org/10.1038/nmeth.2109
26. Stamatakis A, Ludwig T, Meier H. RAxML-III: a fast program for maximum likelihood–based inference of large phylogenetic trees. Bioinformatics. 2005;21:456–63. http://dx.doi.org/10.1093/bioinformatics/bti191
27. Drummond AJ, Suchard MA, Xie D, Rambaut A. Bayesian phylogenetics with BEAUti and the BEAST 1.7. Mol Biol Evol. 2012;29:1969–73. http://dx.doi.org/10.1093/molbev/mss075
28. Parker J, Rambaut A, Pybus OG. Correlating viral phenotypes with phylogeny: accounting for phylogenetic uncertainty. Infect Genet Evol. 2008;8:239–46. http://dx.doi.org/10.1016/j.meegid.2007.08.001
29. Nelson MI, Simonsen L, Viboud C, Miller MA, Taylor J, George KS, et al. Stochastic processes are key determinants of short-term evolution in influenza a virus. PLoS Pathog. 2006;2:e125. http://dx.doi.org/10.1371/journal.ppat.0020125
30. Holmes EC, Ghedin E, Miller N, Taylor J, Bao Y, St George K, et al. Whole-genome analysis of human influenza A virus reveals multiple persistent lineages and reassortment among recent H3N2 viruses. PLoS Biol. 2005;3:e300. http://dx.doi.org/10.1371/journal.pbio.0030300
31. Nelson MI, Simonsen L, Viboud C, Miller MA, Holmes EC. Phylogenetic analysis reveals the global migration of seasonal influenza A viruses. PLoS Pathog. 2007;3:1220–8. http://dx.doi.org/10.1371/journal.ppat.0030131
32. Lavenu A, Leruez-Ville M, Chaix ML, Boelle PY, Rogez S, Freymuth F, et al. Detailed analysis of the genetic evolution of influenza virus during the course of an epidemic. Epidemiol Infect. 2006;134:514–20. http://dx.doi.org/10.1017/S0950268805005686
33. Nelson MI, Njouom R, Viboud C, Niang MN, Kadjo H, Ampofo W, et al. Multiyear persistence of 2 pandemic A/H1N1 influenza virus lineages in west Africa. J Infect Dis. 2014;210:121–5. http://dx.doi.org/10.1093/infdis/jiu047
34. Lemey P, Rambaut A, Bedford T, Faria N, Bielejec F, Baele G, et al. Unifying viral genetics and human transportation data to predict the global transmission dynamics of human influenza H3N2. PLoS Pathog. 2014;10:e1003932. http://dx.doi.org/10.1371/journal.ppat.1003932
35. Asner GP, Llactayo W, Tupayachi R, Luna ER. Elevated rates of gold mining in the Amazon revealed through high-resolution monitoring. Proc Natl Acad Sci U S A. 2013;110:18454–9. http://dx.doi.org/10.1073/pnas.1318271110
36. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. PLoS ONE. 2011;6:e21287. http://dx.doi.org/10.1371/journal.pone.0021287
37. McCune S, Arriola CS, Gilman RH, Romero MA, Ayvar V, Cama VA, et al. Interspecies interactions and potential Influenza A virus risk in small swine farms in Peru. BMC Infect Dis. 2012;12:58. http://dx.doi.org/10.1186/1471-2334-12-58

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Article DOI: http://dx.doi.org/10.3201/eid2108.150084

Phylogeography of Influenza A(H3N2) Virus in Peru, 2010–2012

Technical Appendix

Technical Appendix Figure. Maximum-likelihood phylogeny of hemagglutinin sequences from Peru and other regions of the world, temporally rooted (A/Hong Kong/CUHK52390/2004). All tip labels are included and nodes are annotated by bootstrap (http://wwwnc.cdc.gov/eid/images/15-0084 TechApp-F.jpg). Fine detail may be viewed using the zoom function in PDF viewer software. Colored tip labels refer to global regions in the context of Peruvian taxa: Peru (red), Asia including East Asia and SE Asia (deep blue), Europe (yellow), North America including USA (excluding Hawaii), Mexico and Canada (green), Caribbean and Central/South America excluding Peru (black), Africa (pink), Australia, New Zealand and Oceania (including Hawaii) (light blue), Middle East/Central Asia/South Asia and Russia (brown). Nodes and branches have not been assigned a geographic location.

Technical Appendix Table 1. Accession numbers of Peruvian strains sequenced from this study

Accession nos.						
CY160276.1	CY160768.1	CY161240.1	CY161736.1	CY162224.1	CY162704.1	CY163184.1
CY160281.1	CY160776.1	CY161248.1	CY161744.1	CY162232.1	CY162712.1	CY163192.1
CY160288.1	CY160784.1	CY161256.1	CY161752.1	CY162240.1	CY162720.1	CY163200.1
CY160296.1	CY160792.1	CY161264.1	CY161760.1	CY162248.1	CY162728.1	CY163208.1
CY160304.1	CY160800.1	CY161272.1	CY161768.1	CY162256.1	CY162736.1	CY163216.1
CY160312.1	CY160808.1	CY161280.1	CY161776.1	CY162264.1	CY162744.1	CY163224.1
CY160320.1	CY160816.1	CY161288.1	CY161784.1	CY162272.1	CY162752.1	CY163240.1
CY160328.1	CY160824.1	CY161296.1	CY161792.1	CY162280.1	CY162760.1	CY163248.1
CY160336.1	CY160832.1	CY161304.1	CY161800.1	CY162288.1	CY162768.1	CY163256.1
CY160344.1	CY160840.1	CY161312.1	CY161808.1	CY162296.1	CY162776.1	CY163264.1
CY160352.1	CY160848.1	CY161320.1	CY161816.1	CY162304.1	CY162784.1	CY163272.1
CY160360.1	CY160856.1	CY161328.1	CY161824.1	CY162312.1	CY162792.1	CY163280.1
CY160368.1	CY160864.1	CY161336.1	CY161832.1	CY162320.1	CY162800.1	CY163288.1
CY160376.1	CY160872.1	CY161344.1	CY161840.1	CY162328.1	CY162808.1	CY163296.1
CY160384.1	CY160880.1	CY161352.1	CY161848.1	CY162336.1	CY162816.1	CY163304.1
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CY160400.1	CY160896.1	CY161368.1	CY161864.1	CY162352.1	CY162832.1	CY163320.1
CY160408.1	CY160904.1	CY161376.1	CY161872.1	CY162360.1	CY162840.1	CY163328.1
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Technical Appendix Table 2. Background GenBank sequences for the Pacific Islands, Americas, and Europe

Pacific Islands	Eastern United States	Western United States	Canada and Alaska, USA	Mexico, Central America, and Caribbean	Europe	South America
CY130191	KF789944	KC893099	KC882748	CY088899	HQ880599	HM628693
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CY147307	KF789560	KF790275	KC892853	CY070951	JX518887	CY093415
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CY147309	KC892934	KF790514	KF790407	CY073869	CY114509	JN872405
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KC535402	KF790032	KC882493	KC892629	CY098081	CY114553	JN872407
KC535444	KC883362	CY141180	KF790118	CY088995	CY093391	JN872408
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KC882762	KC883000	KC513479	KC892601	CY074763	JX913019	JN872414
KC882769	KC535302	KC513482	KF790391	CY074731	JX913027	KF142477
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KC892459	KC883275	KC535428	KC883402	CY088907	JX913003	JN872415
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	KC535396	KC535295	KF790184	CY074827	KC488827	JN872424
	KC882692	KC882908	KF790195	CY074875	KC488826	JN872411
	KC893147	KF789627	KF790238	CY074891	KC135510	HM628692
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	CY134638	KC882651	CY134659	CY088987	CY093567	JN872428
	CY134648	KC883338	CY147301	CY088867	CY093575	JN872419
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	KC892544	KF789840	KF598717	CY092289	KC135504	JX679214
	CY141185	KC883292	KF598718	CY088939	KC135500	EU716428
	CY141186	KC892367	KF598719	CY074675	KC135508	CY121632
	CY141187	KC883093	KF598720	CY074707	JN940429	EU716426
	CY141188	KC892829	KF598721	CY089003	JN940431	EU716429
	CY141189	KF789739	KF598722	CY074835	KC135506	
	CY141190	KC892985	KF598723	CY070935	KC135502	
	CY141191	KC892850	KF598724	CY074867	KC135498	
	CY141192	KC882777	KF598725	CY074899	JN940427	
	CY141193	KC882784	KF598702	CY074819	CY114538	
	CY141194	KC892253	KF598728	CY088883	CY114558	
	CY141195	CY120885	KF598703	CY074923	JX978743	
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	CY141197	KC892677	KF598704	CY088931	JX978737	
	CY141199	KC892655	KF598730	CY074691	KC488807	
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	KF142471	KF789927	KF598712	CY088782	KC488823	
	KC883203	KF789534	KF598713	CY074811	JX978776	
	KF790330	CY091581	KF598714	CY093117	CY114548	
	KC893107	CY092281	CY111004	CY092297	KC135512	
	KC893166	CY092265	KF551068	CY088923	JQ988045	
	KF789614	CY092273	KC526207	CY070927	CY110774	
	KF790532	KF199854	CY111005	CY098065	CY110775	
	KF789660	CY068081	KC526208	CY074883	CY110776	
	KC882545	KC882579	CY111007	CY089019	KC488817	
	KC883261	KC882584	CY111006	CY074715		

Pacific Islands	Eastern United States	Western United States	Canada and Alaska, USA	Mexico, Central America, and Caribbean	Europe	South America
	KC882523	KF790512	KC526210	CY088963		
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	KC892576	KC893012	KF551069	CY103791		
	KC892723	KF789646	KC526211	CY074755		
	KC882447	KC882644	CY111011	CY074787		
	KC892236	KF789567	KC526212	CY074723		
	KC892696	KC892376	CY111009	CY093375		
	KF789664	KC883221	KC526213	CY093471		
	KF789667	KC883246	CY111010	CY093479		
	CY141209	KC892462	KC526214	CY093503		
	CY141210	KC892968	KF551070	CY093511		
	CY141211	KC892227	CY111013	CY093519		
	KF790187	KC893064	CY110990	CY093527		
	KF790524	KC892859	CY110991	CY093535		
	KF789674	KF790214	CY110992	CY093543		
	KC893110	KF789637	CY110993	CY093551		
	KC893183	KF789799	CY110994	CY093559		
	KC893180	KF789828	KF551072	CY093447		
	KF790135	KC892812	CY110995	CY093423		
	KC892456	KF790454	CY110996	CY093431		
	KF789949	KC535447	CY110997	CY093439		
	KC535419	KF790503	CY110998			
	KC883129	KC882764	CY110999			
	KF790039	KC883336	KF551074			
	KC882652	KF789550	CY111000			
	KC883156	KF790036	KF551075			
	KF790362	KC883408	CY111001			
	KC882606	KC882609	CY111002			
	KC892889	KC883086	CY111003			
	KC883137	KC892361	KF551067			
	KC882836	KC892635	KF551076			
	KC892978	KC892600	KF551077			
	KC892573	KC892608	KF551078			
	KC892719	KC892845	KC526204			
	KC892896	KC892879	KC526205			
	KC892758	KC892876	KC526206			
	CY070967	KC892874	JQ658890			
	CY072214	KC892871	JQ658925			
	CY134640	KC892206	JQ658889			
	CY134641	KC892221	JQ658891			
	CY134643	KC892392	JQ658892			
	CY134644	KC892224	JQ658901			
	CY134645	KC893067	JQ658895			
	CY134646	KF790242	JQ658896			
	CY134647	KF789590	JQ658898			
	CY134650	KF789759	JQ658899			
	CY134651	CY141215	JQ658897			
	CY134652	CY141216	JQ658903			
	CY134653	KF790329	JQ658900			
	CY134654	KC882914	JQ658902			
	CY134661	KC892370	JQ658921			
	CY134686	KC883443	JQ658907			
	CY141220	KF790461	JQ658904			
	CY141221	KC892552	JQ658923			
	CY141222	KF790473	JQ658913			
	CY141223	KC882900	JQ658914			
	CY141224	KF790457	JQ658908			
	CY141225	KC892508	JQ658909			
	CY141226	KF789731	JQ658910			
	CY141227	KC892822	JQ658911			
	CY141228	KF790019	JQ658912			
	CY141229	KC883415	JQ658927			
	CY141230	KC892209	JQ658926			
	CY141231	KF790023	JQ658920			
	CY141232	KC883095	JQ658918			
	CY141234	KC892954	JQ658919			
	CY141235	KF789767	JQ658915			
	CY141239	KC892751	JQ658916			
	CY141240	KF790323	JQ658917			
	CY141241	KF790384	JQ658893			
	CY141242	KC893072	JQ658894			
	CY141243	KF789656	JQ658905			

Pacific Islands	Eastern United States	Western United States	Canada and Alaska, USA	Mexico, Central America, and Caribbean	Europe	South America
	CY141244	KF789977	JQ658906			
	CY141245	KC882772	JQ658924			
	CY141246	KC892358	JQ658888			
	CY141247	KC892549	KF598738			
	CY141248	KC883084	KF598743			
	KF789982	KC892931	KF761498			
	KF790180	KC882793	KF761499			
	KF790282	KC893047	KF761500			
	KF790236	KC892198	KF761501			
	KF790277	KC892212	KF761503			
	KF790258	KF790432	KF761505			
	KF790278	KC892960	KF761506			
	KF789822	KF789752	KF761507			
	KF790419	KF790077	KF761508			
	KF790394	KC535372	KF761509			
	CY084334	KC535405	KF761510			
	KC882595	KC892815	KF761511			
	KC893087	KC882736	KF761512			
	KF790201	KC882775	KF761513			
	KF790138	KC882917	KF685747			
	KF789613	KF790331				
	KC883240	KC883394				
	KF789728	KF789544				
	KF789842	KF789847				
	KC892471	KC883407				
	KC892555	KC892352				
	KC892193	KC892355				
	KC892279	KC883099				
	KC882431	KC892379				
	KC892156	KC892388				
	KC892177	KC892444				
	KC892149	KC892802				
	KC882577	KC892504				
	KC892976	KC892618				
	KC892524	KC892885				
	KF789582	KC892882				
	KF789770	KC892675				
	CY141249	CY120883				
	CY141250	CY141276				
	CY141251	CY141277				
		CY141278				
		CY141279				
		CY141280				
		CY141281				
		CY141282				
		KC892241				
		KC892665				
		KF790001				
		KF790167				
		KF790516				
		KF789753				
		KF789818				
		KF789826				

Technical Appendix Table 3. GenBank background sequences Asia, Australia, New Zealand, and Africa

Middle East and Central Asia	Australia and New Zealand	China, including Hong Kong	Singapore	Africa	Northeast Asia
KC865653	CY090869	CY091827	JX437710	CY062337	AB796432
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KC865649		CY091843	KF014130	CY062340	CY147295
KC865651		CY091845	JX437712	CY062341	CY147296
KC865613		CY099953	JX437713	CY062342	CY147298
KC865621		HQ664924	JX437714	CY062343	CY147300
KC865619		HQ664914	JX437715	CY062344	CY147303
KC709818		HQ664931	JX437716	CY062345	CY147294
KC865609		CY050136	JX437717	CY062346	CY147302
CY116636		CY050138	KF014203	CY062349	CY147311
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CY116640		CY050104	JX437719	CY062351	HQ703352
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KC865655		CY050108	KF014205	JQ396181	
KC865657		CY050110	KF014131	JQ396183	
KC865659		CY050111	KF014206	JQ396184	
KC865661		CY050115	KF014132	JQ396185	
KC865663		CY050123	KF014133	KF451872	
KC865615		CY050125	KF014207	KF451873	
KC865617		CY050127	KF014208	KF451875	
KC865623		CY050128	JX437720	KF451876	
KC865625		CY050089	KF014209	KF451877	
KC865627		CY050090	KF014134	KF451878	
KC865629		CY050091	KF014135	KF451880	
KC865631		CY050093	KF014210	KF451881	
KC865633		CY050095	KF014136	KF451882	
KC865635		CY050097	KF014211	KF451883	
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KC865641		JN256732	KF014212	KF451885	
KC865643		CY106912	KF014138	JQ396182	
KC865645		JN256733	KF014213	KC999473	
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		CY106920	KF014139	KC999474	
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		CY106944	KF014140	KC999476	
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		JN256740	KF014143		
		CY115824	KF014219		
		JN256741	KF014220		
		CY106984	KF014144		
		JN256742	JX437842		
		CY106992	KF014145		
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			KF014146		
			KF014222		
			KF014147		
			JX437722		
			KF014223		
			KF014224		
			KF014148		
			KF014225		
			KF014149		
			KF014226		
			KF014150		
			KF014227		
			KF014151		
			KF014228		
			KF014152		
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			CY124153		
			CY124155		
			CY124157		

Middle East and Central Asia	Australia and New Zealand	China, including Hong Kong	Singapore	Africa	Northeast Asia
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			CY124161		
			CY124163		
			CY124165		
			CY124167		
			CY124169		
			CY124171		
			CY124173		
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			CY124287		
			CY124291		
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			CY100093		
			CY100075		
			CY100095		
			CY100077		
			CY100097		
			CY100099		
			CY124293		
			CY100079		
			CY100081		
			CY100101		
			CY100103		

Middle East and Central Asia	Australia and New Zealand	China, including Hong Kong	Singapore	Africa	Northeast Asia
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			CY100107		
			CY100109		
			CY124295		
			CY100111		
			CY100113		
			CY100115		
			CY100117		
			CY100119		
			CY124297		
			CY124299		
			CY124301		
			KF014233		
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			KF014161		
			KF014234		
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			JX437831		
			KF014163		
			JX437832		
			KF014164		
			KF014165		
			KF014236		
			KF014237		
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			JX437834		
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			KF014177		
			JX437838		
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			KF014252		
			KF014188		
			KF014189		
			KF014253		
			KF014254		

Middle East and Central Asia	Australia and New Zealand	China, including Hong Kong	Singapore	Africa	Northeast Asia
			KF014190		
			KF014191		
			KF014255		
			JX437840		
			KF014192		
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			KF014256		
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			KF014258		
			KF014196		
			JX437841		
			KF432083		
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			CY124393		
			CY124395		
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			CY124403		
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			CY124407		
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			CY124413		
			CY124417		
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			CY124423		
			CY124429		

Middle East and Central Asia	Australia and New Zealand	China, including Hong Kong	Singapore	Africa	Northeast Asia
			CY124431		
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			CY124491		
			CY124493		
			CY124499		
			CY124501		

Technical Appendix Table 4. GISAID Reference HA H3N2 Sequences for South America*

Strain name (includes country)	Strain ID	Originating laboratory	Submitting laboratory
A/Paraguay/06/2013	EPI_ISL_149684	Central Laboratory of Public Health	CDC
A/Bolivia/902/2013	EPI_ISL_146007	CENETROP	CDC
A/Santiago/47142/2013	EPI_ISL_145682	Instituto de Salud Publica de Chile	CDC
A/Uruguay/322/2013	EPI_ISL_145680	Departamento de Laboratorio de Salud Publica	CDC
A/French Guiana/1118/2013	EPI_ISL_145679	National Influenza Center French Guiana and French Indies	CDC
A/Uruguay/396/2013	EPI_ISL_145678	Departamento de Laboratorio de Salud Publica	CDC
A/Brazil/3873/2013	EPI_ISL_145677	Instituto Adolfo Lutz	CDC
A/Valparaiso/34097/2013	EPI_ISL_145676	Instituto de Salud Publica de Chile	CDC
A/Santiago/46150/2013	EPI_ISL_145671	Instituto de Salud Publica de Chile	CDC
A/Peru/140/2013	EPI_ISL_145670	NAMRU-6	CDC
A/Santiago/36541/2013	EPI_ISL_145642	Instituto de Salud Publica de Chile	CDC
A/Santiago/35652/2013	EPI_ISL_145641	Instituto de Salud Publica de Chile	CDC
A/Venezuela/05/2013	EPI_ISL_145515	Instituto Nacional de Higiene "Rafael Rangel"	CDC
A/Brazil/265/2013	EPI_ISL_145511	Oswaldo Cruz Foundation - Ministry of Health	CDC
A/Ecuador/440/2013	EPI_ISL_145510	NAMRU-6	CDC
A/Brazil/0328/2013	EPI_ISL_145500	Instituto Adolfo Lutz	CDC
A/Brazil/0289/2013	EPI_ISL_145126	Oswaldo Cruz Foundation - Ministry of Health	CDC
A/Argentina/555/2013	EPI_ISL_145122	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/45/2013	EPI_ISL_145121	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/433/2013	EPI_ISL_145114	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/206/2013	EPI_ISL_145113	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Brazil/0328/2013	EPI_ISL_144304	Instituto Adolfo Lutz	CDC
A/Santiago/20181/2013	EPI_ISL_143262	Instituto de Salud Publica de Chile	CDC
A/Peru/114/2013	EPI_ISL_143252	NAMRU-6	CDC
A/Peru/55/2013	EPI_ISL_143251	NAMRU-6	CDC
A/Valdivia/20596/2013	EPI_ISL_142587	Instituto de Salud Publica de Chile	CDC
A/Valparaiso/14542/2013	EPI_ISL_140994	Instituto de Salud Publica de Chile	CDC
A/Buenos Aires/10435982/2012	EPI_ISL_132003	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Buenos Aires/1004423/2012	EPI_ISL_132002	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Peru/1026/2012	EPI_ISL_131270	NAMRU-6	CDC
A/Uruguay/06/2012	EPI_ISL_129661	Departamento de Laboratorio de Salud Publica	CDC
A/Peru/1339/2012	EPI_ISL_129405	NAMRU-6	CDC
A/Curico/51369/2012	EPI_ISL_129166	Instituto de Salud Publica de Chile	CDC
A/Belem/119244/2012	EPI_ISL_129163	National Influenza Center	CDC
A/Venezuela/72/2012	EPI_ISL_129162	Instituto Nacional de Higiene "Rafael Rangel"	CDC
A/Guyane/1296/2012 (A/Guadeloupe/44/2012)	EPI_ISL_129053	CRR virus Influenza region Sud	National Institute for Medical Research
A/Paraguay/32/2012	EPI_ISL_129005	Central Laboratory of Public Health	CDC
A/Puerto Montt/51699/2012	EPI_ISL_129001	Instituto de Salud Publica de Chile	CDC
A/Punta Arenas/52090/2012	EPI_ISL_128997	Instituto de Salud Publica de Chile	CDC
A/Vina Del Mar/49586/2012	EPI_ISL_128995	Instituto de Salud Publica de Chile	CDC
A/Santiago/45700/2012	EPI_ISL_128988	Instituto de Salud Publica de Chile	CDC
A/Linares/52087/2012	EPI_ISL_128987	Instituto de Salud Publica de Chile	CDC
A/Suriname/295/2012	EPI_ISL_128986	Caribbean Epidemiology Center	CDC
A/Suriname/297/2012	EPI_ISL_127834	Caribbean Epidemiology Center	CDC
A/Santiago/35234/2012	EPI_ISL_125917	Instituto de Salud Publica de Chile	CDC
A/Santiago/33977/2012	EPI_ISL_125916	Instituto de Salud Publica de Chile	CDC
A/Brazil/7920/2012	EPI_ISL_125910	Instituto Adolfo Lutz	CDC
A/Brazil/8456/2012	EPI_ISL_125906	Instituto Adolfo Lutz	CDC
A/Paraguay/37/2012	EPI_ISL_125905	Central Laboratory of Public Health	CDC
A/Paraguay/146/2012	EPI_ISL_125904	Central Laboratory of Public Health	CDC
A/Brazil/8751/2012	EPI_ISL_125902	Instituto Adolfo Lutz	CDC
A/Santiago/37926/2012	EPI_ISL_124524	Instituto de Salud Publica de Chile	CDC
A/Santiago/37126/2012	EPI_ISL_124523	Instituto de Salud Publica de Chile	CDC
A/Puerto Montt/12477/2012	EPI_ISL_119880	Instituto de Salud Publica de Chile	CDC
A/Santiago/3564/2012	EPI_ISL_119879	Instituto de Salud Publica de Chile	CDC
A/Santiago/14696/2012	EPI_ISL_119711	Instituto de Salud Publica de Chile	CDC
A/Paraguay/726/2011	EPI_ISL_102988	Central Laboratory of Public Health	CDC
A/Paraguay/216/2011	EPI_ISL_101916	Central Laboratory of Public Health	CDC
A/Bolivia/340/2011	EPI_ISL_99074	CENETROP	CDC
A/Bolivia/340/2011	EPI_ISL_99073	CENETROP	CDC
A/Bolivia/340/2011	EPI_ISL_99072	CENETROP	CDC
A/Brazil/1151/2011	EPI_ISL_99068	Instituto Adolfo Lutz	CDC

Strain name (includes country)	Strain ID	Originating laboratory	Submitting laboratory
A/Brazil/1151/2011	EPI_ISL_99067	Instituto Adolfo Lutz	CDC
A/Brazil/1151/2011	EPI_ISL_99066	Instituto Adolfo Lutz	CDC
A/Chile/72/2011	EPI_ISL_99065	Instituto de Salud Publica de Chile	CDC
A/Chile/72/2011	EPI_ISL_99064	Instituto de Salud Publica de Chile	CDC
A/Chile/64/2011	EPI_ISL_99063	Instituto de Salud Publica de Chile	CDC
A/Chile/64/2011	EPI_ISL_99062	Instituto de Salud Publica de Chile	CDC
A/Paraguay/2395/2010	EPI_ISL_99025	Central Laboratory of Public Health	CDC
A/Paraguay/2395/2010	EPI_ISL_99024	Central Laboratory of Public Health	CDC
A/Paraguay/2395/2010	EPI_ISL_99023	Central Laboratory of Public Health	CDC
A/Paraguay/2394/2010	EPI_ISL_99022	Central Laboratory of Public Health	CDC
A/Paraguay/2394/2010	EPI_ISL_99021	Central Laboratory of Public Health	CDC
A/Paraguay/2394/2010	EPI_ISL_99020	Central Laboratory of Public Health	CDC
A/Suriname/5163/2009	EPI_ISL_98967	Caribbean Epidemiology Center	CDC
A/Suriname/5163/2009	EPI_ISL_98966	Caribbean Epidemiology Center	CDC
A/Bolivia/805/2011	EPI_ISL_98825	CENETROP	CDC
A/Santiago/18456/2011	EPI_ISL_98644	Instituto de Salud Publica de Chile	CDC
A/Paraguay/210/2011	EPI_ISL_98643	Central Laboratory of Public Health	CDC
A/Santiago/18454/2011	EPI_ISL_96108	Instituto de Salud Publica de Chile	CDC
A/Santiago/14944/2011	EPI_ISL_96107	Instituto de Salud Publica de Chile	CDC
A/Santiago/13652/2011	EPI_ISL_96106	Instituto de Salud Publica de Chile	CDC
A/Peru/7111/2011	EPI_ISL_96105	NAMRU-6	CDC
A/Peru/6311/2011	EPI_ISL_96104	NAMRU-6	CDC
A/Paraguay/210/2011	EPI_ISL_96101	Central Laboratory of Public Health	CDC
A/Colombia/6459/2011	EPI_ISL_96087	Instituto Nacional de Salud de Columbia	CDC
A/Chile/64/2011	EPI_ISL_96086	Instituto de Salud Publica de Chile	CDC
A/Brazil/6078/2011	EPI_ISL_96085	Instituto Adolfo Lutz	CDC
A/Brazil/5613/2011	EPI_ISL_96084	Instituto Adolfo Lutz	CDC
A/Argentina/8823/2011	EPI_ISL_96080	CEMIC University Hospital	CDC
A/Argentina/676/2011	EPI_ISL_96079	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/566/2011	EPI_ISL_96078	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/198/2011	EPI_ISL_96077	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Brazil/6772/2011	EPI_ISL_95509		CDC
A/Argentina/179/2011	EPI_ISL_95507	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/215/2011	EPI_ISL_95505	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Santa Fe/1431/2011	EPI_ISL_94722	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Entre Rios755282/2011	EPI_ISL_94721	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Buenos Aires/10140261/2011	EPI_ISL_94720	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Chile/9920/2011	EPI_ISL_93777	Instituto de Salud Publica de Chile	CDC
A/Chile/72/2011	EPI_ISL_93776	Instituto de Salud Publica de Chile	CDC
A/Chile/64/2011	EPI_ISL_93775	Instituto de Salud Publica de Chile	CDC
A/Brazil/1151/2011	EPI_ISL_93773	Instituto Adolfo Lutz	CDC
A/Bolivia/405/2011	EPI_ISL_93772	CENETROP	CDC
A/Bolivia/401/2011	EPI_ISL_93771	CENETROP	CDC
A/Bolivia/373/2011	EPI_ISL_93770	CENETROP	CDC
A/Peru/9310/2010	EPI_ISL_89817	NAMRU-6	CDC
A/Peru/8410/2010	EPI_ISL_89816	NAMRU-6	CDC
A/Peru/7710/2010	EPI_ISL_89815	NAMRU-6	CDC
A/Peru/4010/2010	EPI_ISL_89814	NAMRU-6	CDC
A/Argentina/8409/2010	EPI_ISL_87951	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/02/2010	EPI_ISL_87950	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/01/2010	EPI_ISL_87949	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Argentina/28379/2010	EPI_ISL_85724	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28378/2010	EPI_ISL_85723	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28372/2010	EPI_ISL_85722	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28370/2010	EPI_ISL_85721	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28367/2010	EPI_ISL_85720	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28342/2010	EPI_ISL_85719	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research

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A/Argentina/28306/2010	EPI_ISL_85718	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/28302/2010	EPI_ISL_85717	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/27724/2010	EPI_ISL_85716	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Paraguay/2394/2010	EPI_ISL_85613	Central Laboratory of Public Health	CDC
A/Uruguay/2214/2010	EPI_ISL_85601	Departamento de Laboratorio de Salud Publica	CDC
A/Bolivia/1053/2010	EPI_ISL_84043	CENETROP	CDC
A/Argentina/27893/2010	EPI_ISL_83717	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/27891/2010	EPI_ISL_83716	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/27724/2010	EPI_ISL_83714	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/27895/2010	EPI_ISL_83713	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Argentina/27894/2010	EPI_ISL_83712	Instituto Nacional de Enfermedades Infecciosas	National Institute for Medical Research
A/Venezuela/07/2010	EPI_ISL_83173	Instituto Nacional de Higiene "Rafael Rangel"	CDC
A/Brazil/0791/2010	EPI_ISL_79673	Oswaldo Cruz Foundation - Ministry of Health	CDC
A/Brazil/0610/2010	EPI_ISL_79672	Oswaldo Cruz Foundation - Ministry of Health	CDC
A/Chile/8196/2010	EPI_ISL_79664	Instituto de Salud Publica de Chile	CDC
A/Colombia/6722/2010	EPI_ISL_79660	Instituto Nacional de Salud de Columbia	CDC
A/Chile/6927/2010	EPI_ISL_79330	Instituto de Salud Publica de Chile	CDC
A/Chile/6380/2010	EPI_ISL_79329	Instituto de Salud Publica de Chile	CDC
A/Chile/6278/2010	EPI_ISL_79328	Instituto de Salud Publica de Chile	CDC
A/Chile/6096/2010	EPI_ISL_79327	Instituto de Salud Publica de Chile	CDC
A/Chile/5845/2010	EPI_ISL_79326	Instituto de Salud Publica de Chile	CDC
A/Bolivia/317/2010	EPI_ISL_77796	Instituto Nacional de Laboratoriosde Salud (INLASA)	CDC
A/Colombia/7158/2009	EPI_ISL_76692	Instituto Nacional de Salud de Columbia	CDC
A/Colombia/4335/2009	EPI_ISL_69716		CDC
A/Colombia/6123/2009	EPI_ISL_66567	Instituto Nacional de Salud de Columbia	CDC
A/Bolivia/2948/2009	EPI_ISL_66561	–	CDC
A/Bolivia/2675/2009	EPI_ISL_66560	–	CDC
A/Brazil/884/2009	EPI_ISL_60770	National Influenza Center	CDC
A/Brazil/933/2009	EPI_ISL_60769	National Influenza Center	CDC
A/Brazil/1814/2009	EPI_ISL_60764	Instituto Adolfo Lutz	CDC
A/Argentina/7646/2009	EPI_ISL_60763	Instituto Nacional de Enfermedades Infecciosas	CDC
A/Paraguay/52/2009	EPI_ISL_60745	Central Laboratory of Public Health	CDC
A/Argentina/15/2009	EPI_ISL_34979	–	CDC
A/Suriname/5163/2009	EPI_ISL_34969	Caribbean Epidemiology Center	CDC
A/Venezuela/9602/2007	EPI_ISL_23342	–	CDC
A/Venezuela/8241/2007	EPI_ISL_23341	–	CDC
A/Brazil/1623/2008	EPI_ISL_23203	–	CDC
A/Brazil/1619/2008	EPI_ISL_23202	–	CDC
A/Guyane/32/2007	EPI_ISL_21966	–	CDC
A/Guyane/25/2007	EPI_ISL_21964	–	CDC
A/Guyane/13/2007	EPI_ISL_21962	–	CDC
A/Argentina/449/2007	EPI_ISL_21784	–	CDC
A/Argentina/445/2007	EPI_ISL_21783	–	CDC
A/Argentina/389/2007	EPI_ISL_21781	–	CDC
A/Argentina/3888/2007	EPI_ISL_21780	–	CDC
A/Uruguay/716/2007	EPI_ISL_21292	–	CDC
A/Uruguay/716/2007	EPI_ISL_21291	–	CDC
A/Uruguay/716/2007	EPI_ISL_21290	–	CDC
A/Peru/8307/2007	EPI_ISL_20684	–	CDC
A/Santiago/10086/2007	EPI_ISL_20677	–	CDC
A/Uruguay/0723/2007	EPI_ISL_20638	–	CDC
A/Uruguay/0710/2007	EPI_ISL_20636	–	CDC
A/Uruguay/0707/2007	EPI_ISL_20635	–	CDC
A/Argentina/501/2007	EPI_ISL_20603	–	CDC
A/Argentina/405/2007	EPI_ISL_20602	–	CDC
A/Argentina/426/2007	EPI_ISL_20601	–	CDC
A/Argentina/503/2007	EPI_ISL_20600	–	CDC
A/Argentina/117/2007	EPI_ISL_20599	–	CDC
A/Argentina/335/2007	EPI_ISL_20598	–	CDC
A/Argentina/402/2007	EPI_ISL_20596	–	CDC
A/Argentina/305/2007	EPI_ISL_20595	–	CDC
A/Argentina/146/2007	EPI_ISL_20594	–	CDC
A/Argentina/3797/2007	EPI_ISL_20590	–	CDC

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A/Argentina/3743/2007	EPI_ISL_20587	–	CDC
A/Argentina/3726/2007	EPI_ISL_20586	–	CDC
A/Argentina/3689/2007	EPI_ISL_20585	–	CDC
A/Brazil/80/2007	EPI_ISL_20577	–	CDC
A/Peru/3355/2006	EPI_ISL_20573	–	CDC
A/Peru/0128/2006	EPI_ISL_20572	–	CDC
A/Santiago/6881/2007	EPI_ISL_20544	–	CDC
A/Santiago/6421/2007	EPI_ISL_20543	–	CDC
A/Uruguay/716/2007	EPI_ISL_19048	–	CDC

*CDC, Centers for Disease Control and Prevention, Atlanta, GA, USA; NAMRU-6, United States Navy Medical Research Unit-6. The – symbol indicates missing details.