

Accessing the FluSurver in GISAID

Please send questions and feedback to:
flusurver@gisaid.org

The FluSurver team is located in Singapore and our working day for fast replies may be shifted depending on your local time zone.



Bioinformatics
Institute



First steps: find, select and add isolates to analyze from the EpiFlu™ database

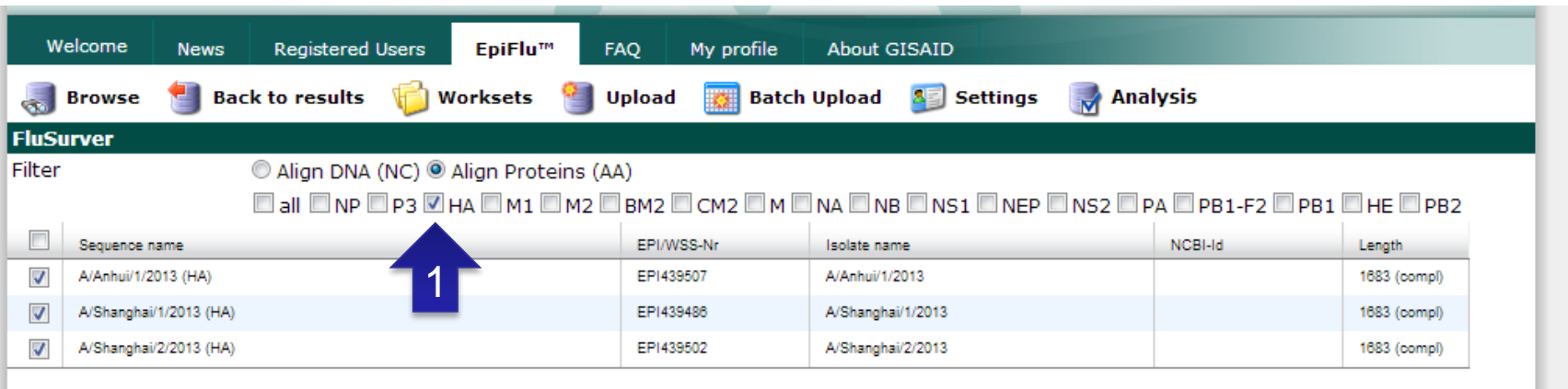
The screenshot shows the GISAID EpiFlu™ web interface. At the top, there's a header with the GISAID logo, copyright information (© 2008 - 2013 | The GISAID Foundation | Terms of Use | Contact | System Requirements), and flags for China and the UK. Below the header is a navigation bar with tabs: Welcome, News, Registered Users, EpiFlu™, FAQ, My profile, and About GISAID. Underneath is a secondary navigation bar with icons and labels: Browse, Back to results, Worksets, Upload, Batch Upload, Settings, and Analysis. The main content area is titled 'Released files' and contains a table with columns: Name, Isolate ID, Subtype, Host, Collection date, Passage, PB2, PB1, PA, HA, NP, NA, MP, and I. The table lists three isolates, all of which are selected with checkmarks in the first column. Below the table is a pagination bar showing 'Total: 3 isolates' and navigation links: '<< first < prev 1 next > last >>'. A search bar is labeled 'Search in results'. At the bottom, there are buttons for 'Go back', 'Help', 'Copy to...', 'Add to analysis', and 'Download'. A blue arrow points to the 'Add to analysis' button.

After selecting strains on the left, click add to analysis **1**

This screenshot shows a 'Choose analysis' dialog box overlaid on the EpiFlu™ interface. The dialog has a title bar 'Choose analysis' and two main sections. The first section, 'Alignment', has a sub-header 'Align DNA or Proteins' and a list of third-party servers. The second section, 'List of third party servers', contains a single entry: 'FluSurver' with a sub-label 'FluSurver'. A blue arrow points to the 'FluSurver' entry. The background shows the same 'Released files' table as the previous screenshot, but it is partially obscured by the dialog box.

2 Select "FluSurver"

Next steps: Select proteins to analyze[1] , e.g. HA, then click on continue [2], wait for submission form to load and then click “Analyze with FluSurver” [3].



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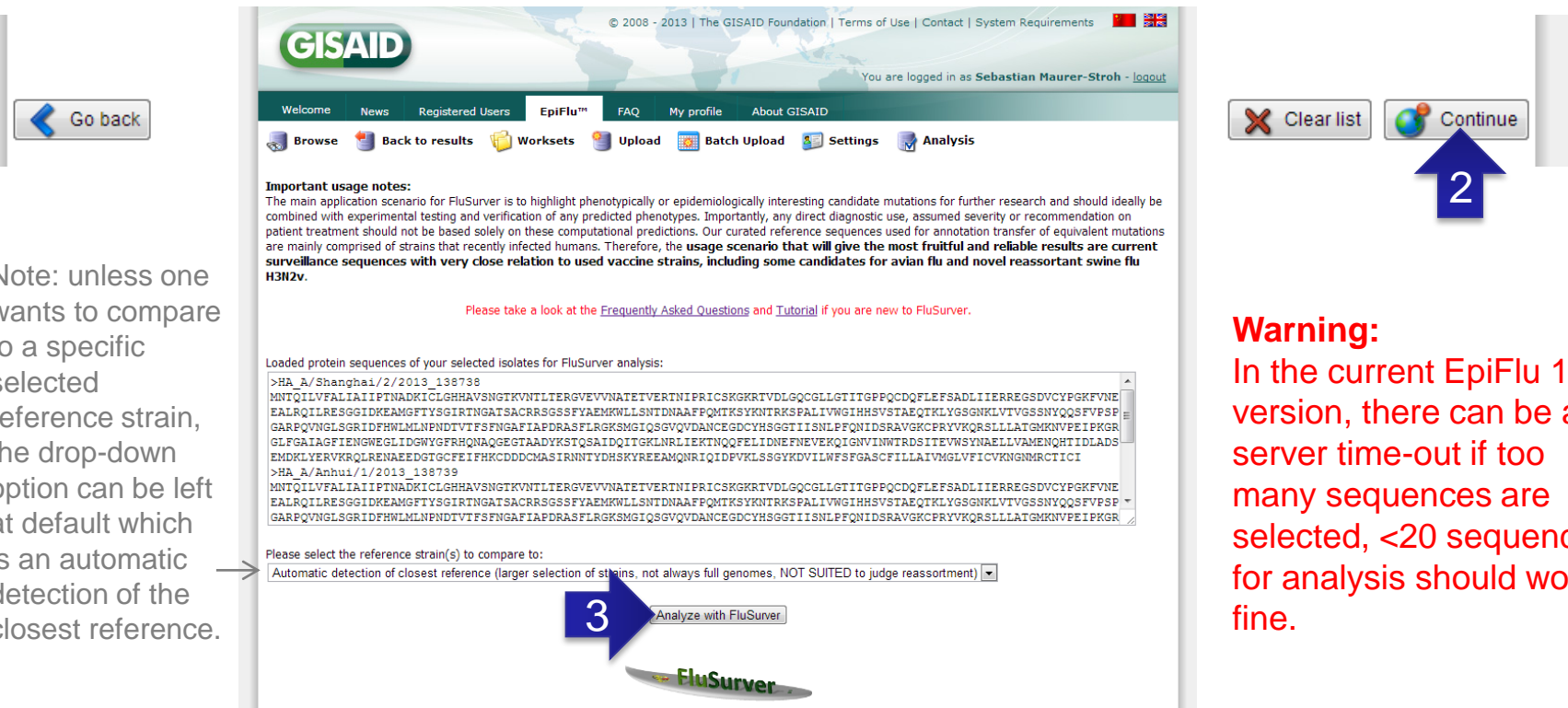
Browse Back to results Worksets Upload Batch Upload Settings Analysis

FluSurver

Filter ☐ Align DNA (NC) ☒ Align Proteins (AA)

☐ all ☐ NP ☒ P3 ☒ HA ☐ M1 ☐ M2 ☐ BM2 ☐ CM2 ☐ M ☐ NA ☐ NB ☐ NS1 ☐ NEP ☐ NS2 ☐ PA ☐ PB1-F2 ☐ PB1 ☐ HE ☐ PB2

<input type="checkbox"/>	Sequence name	EPI/WSS-Nr	Isolate name	NCBI-Id	Length
<input checked="" type="checkbox"/>	A/Anhui/1/2013 (HA)	EPI439507	A/Anhui/1/2013		1883 (compl)
<input checked="" type="checkbox"/>	A/Shanghai/1/2013 (HA)	EPI439488	A/Shanghai/1/2013		1883 (compl)
<input checked="" type="checkbox"/>	A/Shanghai/2/2013 (HA)	EPI439502	A/Shanghai/2/2013		1883 (compl)



Go back

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Important usage notes:
The main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing and verification of any predicted phenotypes. Importantly, any direct diagnostic use, assumed severity or recommendation on patient treatment should not be based solely on these computational predictions. Our curated reference sequences used for annotation transfer of equivalent mutations are mainly comprised of strains that recently infected humans. Therefore, the **usage scenario that will give the most fruitful and reliable results are current surveillance sequences with very close relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu H3N2v.**

Please take a look at the [Frequently Asked Questions](#) and [Tutorial](#) if you are new to FluSurver.

Loaded protein sequences of your selected isolates for FluSurver analysis:

```
>HA_A/Shanghai/2/2013_198738
MNTQILVFALIAIIPINADKICLGHAVSNGTKVNTLTERGVEVVNATETVERTNIPRICSGKGRITVDLGQGLLGTITGFPQCQDFLEFSADLIERREGSDVCYFGKRVNE
EALRQILRESGGIDKEAMGFTYSGIRTINGATSACRRSGSSFYAEMKWLSTNDNAAFPQMTKSYKNTKRSFALIVNGIHHSVSTAEQTKLYGSGNKLTVGSSNYQQSFVPSF
GARFQVNLGSGRIDFWHMLNPNNDTVTFSGNFIAPDRASFLRGKSMGIQSGVQVDANCEGDCYHSGGTIIISNLPFQNDISRAVGKCPRYVKRSLLLATGMKNVFEIPKGR
GLFGAIAAGFIENGWGLIDGWYGRHQAQEGTAADYKSTQSAIDQITGKLNRLIEKTNQGFELIDNEFNEVEKQIGNVINWTRDSITEVNSYNAELLVAMENQHTIDLADS
EMDKLYERVKRQLRENAEEDGTGCFEIFHKCDDDCMASIRNNTYDHSKYREEMQNRQIDPFVKLSGGYKDVILWFSFGASCIFLLAIVMGLVFCVKNGNMRCITCI
>HA_A/Anhui/1/2013_138739
MNTQILVFALIAIIPINADKICLGHAVSNGTKVNTLTERGVEVVNATETVERTNIPRICSGKGRITVDLGQGLLGTITGFPQCQDFLEFSADLIERREGSDVCYFGKRVNE
EALRQILRESGGIDKEAMGFTYSGIRTINGATSACRRSGSSFYAEMKWLSTNDNAAFPQMTKSYKNTKRSFALIVNGIHHSVSTAEQTKLYGSGNKLTVGSSNYQQSFVPSF
GARFQVNLGSGRIDFWHMLNPNNDTVTFSGNFIAPDRASFLRGKSMGIQSGVQVDANCEGDCYHSGGTIIISNLPFQNDISRAVGKCPRYVKRSLLLATGMKNVFEIPKGR
```

Please select the reference strain(s) to compare to:
Automatic detection of closest reference (larger selection of strains, not always full genomes, NOT SUITED to judge reassortment) ▼

Analyze with FluSurver

FluSurver

Clear list Continue

Note: unless one wants to compare to a specific selected reference strain, the drop-down option can be left at default which is an automatic detection of the closest reference.

Warning:
In the current EpiFlu 1.0 version, there can be a server time-out if too many sequences are selected, <20 sequences for analysis should work fine.

EpiFlu™ 2.0 – In near Future

GISAID Welcome John Doe

GISAID published: 34,593 viruses with 89,498 Sequences Total count: 113,361 viruses with 393,536 Sequences

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Personal Worksheet

Virus Name

[Delete Entry](#)
[Clear List](#)
[Select All](#)
[Deselect All](#)

	Name	Segment	Segment accession #	Length
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	NS	EPI1880	890
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	PB1	EPI1874	2274
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	HA	EPI1876	1686
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	NP	EPI1877	1501
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	NA	EPI1878	1413
<input type="checkbox"/>	A/chicken/77/Jiangxi/2014	PB2	EPI1873	2280
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	M	EPI1887	982
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	PA	EPI1883	2151
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	NS	EPI1888	823
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	HA	EPI1884	1704
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	NP	EPI1885	1497
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	PB1	EPI1882	2274
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	PB2	EPI1881	2280
<input type="checkbox"/>	A/duck/Jiangxi/95/2014	NA	EPI1886	1380
<input type="checkbox"/>	A/Galicia/1786/2014	HA	EPI1907	1040
<input type="checkbox"/>	A/Hong Kong/308/2014	PB2	EPI498034	2280
<input type="checkbox"/>	A/Hong Kong/308/2014	NA	EPI498036	1401
<input type="checkbox"/>	A/Hong Kong/308/2014	PB1	EPI498035	2274
<input type="checkbox"/>	A/Hong Kong/308/2014	PA	EPI498033	2151
<input type="checkbox"/>	A/Hong Kong/308/2014	M	EPI498032	982

Back **1** 2 3 ... 5 Forward

Export selected

Blast Nucleotide

Blast Protein

Analyze with FluSurver

Align Sequences

View Tree

Slight change in appearance of menu options in new version

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FluSurver

The main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing and verification of any predicted phenotypes. Importantly, any direct diagnostic use, assumed severity or recommendation on patient treatment should not be based solely on these computational predictions. Our curated reference sequences used for annotation transfer of equivalent mutations are mainly comprised of strains that recently infected humans. Therefore, the usage scenario that will give the most fruitful and reliable results are current surveillance sequences with very close relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu H3N2v. Please take a look at the [Frequently Asked Questions](#) and [Tutorial](#) if you are new to FluSurver. There is also a [special note for using FluSurver results in publications](#).

Result for comparison with reference selection: H7N7_Human_2003_Netherlands219 [Back to Reference Selection](#)

Query	Best reference hit	% AA identity	% length coverage	# mutations	List of mutations
HA_A/Anhui/1/2013_138739	HA A/Netherlands/219/2003(H7N7) find closest related sequences	96.071	98.418	22	V18I , S20I , V63I , T137A , T150A , D190S , I195V , G202V , T205A , I218V , Q242L , I252M , E286G , N314D , E328R , R347G , T419N , R423K , M436I , N464D , I515M , A550V show in structure
HA_A/Shanghai/1/2013_138737	HA A/Netherlands/219/2003(H7N7) find closest related sequences	96.071	98.418	22	V18I , S20I , V63I , T137A , T150A , A153S , D190N , I195V , T205A , I218V , P237T , I252M , E286G , N292D , H299Y , N314D , E328R , R347G , R423K , M436I , N464D , I515M show in structure
HA_A/Shanghai/2/2013_138738	HA A/Netherlands/219/2003(H7N7) find closest related sequences	96.071	98.418	22	V18I , S20I , V63I , T137A , T150A , D190S , I195V , G202V , T205A , I218V , Q242L , I252M , E286G , N314D , E328R , R347G , T419N , R423K , M436I , N464D , I515M , A550V show in structure

[Right-click here to save/download mutation report table for archiving or import to Excel](#)

[Back to Reference Selection](#)

For each of the query sequences, there are six columns of information generated in the result summary page. From here, users may proceed to look at the query sequence's alignment to the reference strain, get more information on each mutation, generate a structural view of all the mutations in the query sequence ("show in structure") or view a summary of the mutations in a table to download (at end of results).

More details on browsing the results further can be found online at:
<http://flusurver.bii.a-star.edu.sg/help/tutorialpage.html#part2>



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Result for comparison with reference selection: **H7N7_Human_2003_Netherlands219** [Back to Reference Selection](#)

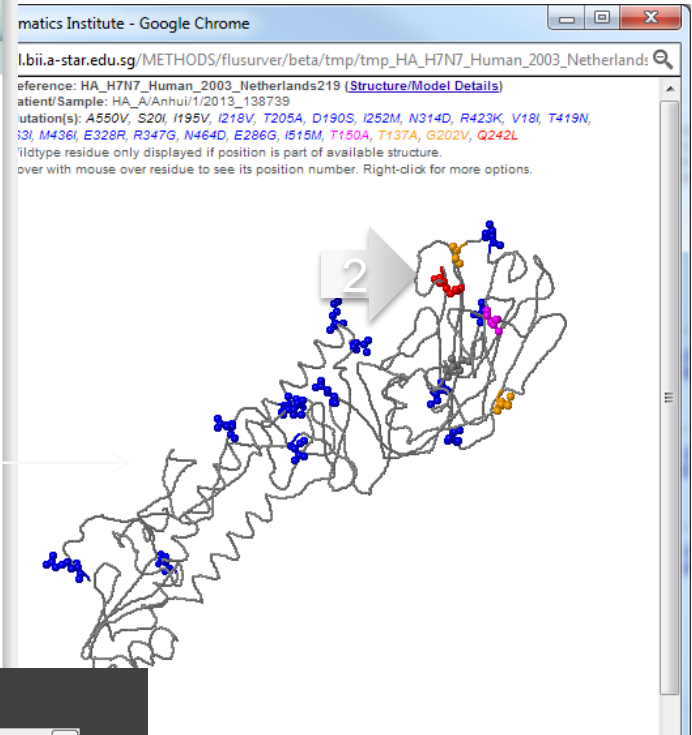
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HA_A/Shanghai/1/2013_138737	A/Netherlands/219/2003(H7N7) find closest related sequences	96.071	98.418	22	V18I , S20I , V63I , T137A , T150A , A153S , D190N , I195V , T205A , I218V , P27T , I262M , E286G , N292D , H295Y , N314D , E328R , R347G , R423K , M436I , N464D , I515M show in structure
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Choose nearest server location: [Singapore](#) [Mexico](#)
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Co-hosted by Instituto Nacional de Medicina Genómica
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Mutation Effect Analysis Example



mendel.bii.a-star.edu.sg/METHODS/flusurver/beta/EFFECTS/HA

Protein: HA
Influenza type: Human H3N2 (N/A)
Mutation (as in paper): Q226L
neutral AA: Q
neg. eff. AA: L
Effect: host specificity shift

Comment:
Increasing affinity of receptor-binding to SA₂,6Gal and decreasing affinity to SA₂,3Gal (Table1.).
[Literature reference](#)
(Mutation Q226L in the paper is at an equivalent position of the mutation in your query)

HA Q242L

Key to alternative position numbering:

240	FluSurver numbering (absolute as in 2009 H1N1 pandemic)
HA1 226	Classical H3N2 strain numbering
HA1 223	Classical H1N1 strain numbering
Chosen reference:	HA_H7N7_Human_2003_Netherlands219
Position in reference:	242
AA in reference:	Q
AA in query:	L

A mutation at the position equivalent to HA 242 has been reported in the literature to be related to [antigenic drift / escape mutant and host specificity shift and other](#).

A combination of mutations including the position equivalent to HA 242 has been reported in the literature to be related to [host specificity shift](#).

As seen in resolved structures of proteins from related strains, the HA position equivalent to your mutation is involved in:

- [host cell receptor binding](#)
- [antibody recognition sites](#)

[See all interactions for this position](#)

[Back to Reference Selection](#)

1. H7N9 HA example: closest annotated reference strain in FluSurver was an H7 from an outbreak in the Netherlands in 2003. With 96% identity, or 22 mutations, this is close enough for first interpretation.
2. The structure view shows that the highlighted red and orange mutations are located in the host receptor binding pocket.
3. The "red" Q242L mutation is equivalent to Q226L (in H3 numbering) which has been reported to increase 2,6 host receptor affinity, which is one important factor why this avian strain can infect humans.

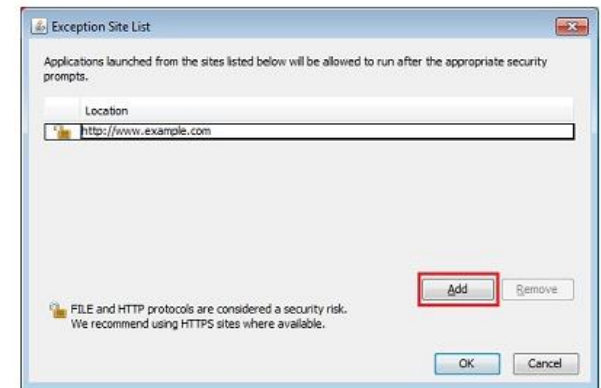
Troubleshooting

- I cannot see the structural view!
 - The structural view uses a free Java program called Jmol which requires:
 - a recent version of the free Java Runtime Environment to be installed (<http://java.com/en/download/>)
 - accepting the security certificate when prompted.
 - If needed, add “http://mendel.bii.a-star.edu.sg” and “http://flusurver.bii.a-star.edu.sg” to list of trusted sites in the Java configure settings as shown on the right (We have protected the code of the Jmol version used on our server so it cannot be modified by any unauthorized third parties)



Steps to Add URLs to the Exception Site list

- Go to the Java Control Panel (On Windows Click Start and then Configure Java)
- Click on the Security tab
- Click on the Edit Site List button
- Click Add in the Exception Site List window



- Click in the empty field under the Location field to enter the URL

Example: <http://www.example.com>
(URL should begin with <http://> or <https://>)

- Answers to more frequently asked questions:
<http://flusurver.bii.a-star.edu.sg/help/faq.html>
- If there are any access problems via GISAID and urgent analysis is needed, you can also use our general site (<http://flusurver.bii.a-star.edu.sg/>) but this version does not include statistics of GISAID sequences!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier



The main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing and verification of any predicted phenotypes. Importantly, any direct diagnostic use, assumed severity or recommendation on patient treatment should not be based solely on these computational predictions. Our curated reference sequences used for annotation transfer of equivalent mutations are mainly comprised of strains that recently infected humans. Therefore, **the usage scenario that will give the most fruitful and reliable results are current surveillance sequences with very close relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu H3N2v.** Please take a look at the [Frequently Asked Questions](#) and [Tutorial](#) if you are new to FluSurver. There is also a [special note for using FluSurver results in publications](#).

Result for comparison with reference selection: auto

[Back to Reference Selection](#)

Query	Best reference hit	% AA identity	% length coverage	# mutations	List of mutations
A/Singapore/GN285/2009(H1N1)	NA A/California/07/2009(H1N1) find closest related sequences	99.360	100.000	3	<p>V106I, N248D, H275Y show in structure</p> <p>NA drug sensitivity positions: 26, 0, 1 Reduced sensitivity or resistance!</p>

[Right-click here to save/download mutation report table for archiving or import to Excel](#)

[Back to Reference Selection](#)

Tachyon 11364 hits

Time: 15.89s

Length: 469 Views: [Plain](#) | [Jalview](#) | [Raw](#) Downloads: [FASTA](#) | [MAFFT](#) | [Raw](#) Params: internal, NCBI NR-24070523 sequer

Rank	Score	FASTA	BLAST	ANNIE	UniProt	Hit Seq	Filter	Databases	Limit
1	1.0	GFBAT				gi 251748198 gb ACT10319.1 neuraminidase [Influenza A virus (A/Hong Kong/2369/2009(H1N1))]		All PDB RefSeq SwissProt/UniProtKB	250 1000 None
2	0.9914	GFBAT				gi 300117086 gb ADJ67981.1 neuraminidase, partial [Influenza A virus (A/Perth/262/2009(H1N1))]			
3	0.98718	GFBAT				gi 326320245 gb ADZ53143.1 neuraminidase [Influenza A virus (A/Hong Kong/FPD/2009(H1N1))]			
4	0.98294	GFBAT				gi 291219999 gb ADD84685.1 neuraminidase [Influenza A virus (A/Mexico/InDRE797/2010(H1N1))]			
5	0.97872	GFBAT				gi 251833646 gb ACT22016.1 neuraminidase [Influenza A virus (A/Osaka/180/2009(H1N1))]			
6	0.97872	GFBAT				gi 294544923 gb ADF10109.1 neuraminidase [Influenza A virus (A/Ontario/25913/2009(H1N1))]			
7	0.97872	GFBAT				gi 294544441 gb ADF10049.1 neuraminidase [Influenza A virus (A/Ontario/10016/2009(H1N1))]			
8	0.97872	GFBAT				gi 299781814 gb ADJ40477.1 neuraminidase [Influenza A virus (A/Netherlands/2445b/2009(H1N1))]			
9	0.97872	GFBAT				gi 325451706 gb ADZ13521.1 neuraminidase [Influenza A virus (A/Lyon/48.49/2009(H1N1))]			
10	0.97872	GFBAT				gi 294611208 gb ADF27356.1 neuraminidase [Influenza A virus (A/Taiwan/6663/2009(H1N1))]			
11	0.97872	GFBAT				gi 326320207 gb ADZ53124.1 neuraminidase [Influenza A virus (A/Hong Kong/23369/2009(H1N1))]			
12	0.97872	GFBAT				gi 425786025 gb AFX96841.1 neuraminidase [Influenza A virus (A/Viet Nam/12032005/2009(H1N1))]			
13	0.97872	GFBAT				gi 316986112 gb ADU76312.1 neuraminidase [Influenza A virus (A/England/00380009/2009(H1N1))]			
14	0.97872	GFBAT				gi 295147036 gb ADF80503.1 neuraminidase [Influenza A virus (A/Seoul/1870/2009(H1N1))]			
15	0.97872	GFBAT				gi 307071034 gb ADN24718.1 neuraminidase, partial [Influenza A virus (A/Canada-AB/RV2828/2009(H1N1))]			
16	0.97872	GFBAT				gi 296840062 gb ADN24401.1 neuraminidase [Influenza A virus (A/Guangzhou/238/2009(H1N1))]			

Find closest reference strain and database hits!

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[Back to Reference Selection](#)

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```
>NA_H1N1_Human_2009_California07
gi|229396469|gb|ACQ63272|neuraminidase[Influenza A virus
(A/California/07/2009(H1N1))] USA20090409
Length = 469
```

```
Score = 989 bits (2558), Expect = 0.0
Identities = 466/469 (99%), Positives = 469/469 (100%)
Frame = +3
```

```
Query: 21  MNPNQKIITIGSVCHTIGHANLILQIGNIISIVISHSIQLGNQNIETCNQSVITYENNT 200
          MNPNQKIITIGSVCHTIGHANLILQIGNIISIVISHSIQLGNQNIETCNQSVITYENNT
Sbjct: 1   MNPNQKIITIGSVCHTIGHANLILQIGNIISIVISHSIQLGNQNIETCNQSVITYENNT 60
```

```
Query: 201 VVNQTYVNISNTNFAAGQSVVSKLAGNSSLCPVSGHAIYSKDNSIRIGSGDVFVIREP 380
          VVNQTYVNISNTNFAAGQSVVSKLAGNSSLCPVSGHAIYSKDNSIRIGSGDVFVIREP
Sbjct: 61  VVNQTYVNISNTNFAAGQSVVSKLAGNSSLCPVSGHAIYSKDNSVRIGSGDVFVIREP 120
```

```
Query: 381 FISCSPLECRFTFFLTQALLNDKHSNGTIKDRSPYRTLMSCPIGEVPSPYNSRFESVAWS 560
          FISCSPLECRFTFFLTQALLNDKHSNGTIKDRSPYRTLMSCPIGEVPSPYNSRFESVAWS
Sbjct: 121 FISCSPLECRFTFFLTQALLNDKHSNGTIKDRSPYRTLMSCPIGEVPSPYNSRFESVAWS 180
```

```
Query: 561 ASACHDGINWLITIGISGPDNGAVAVLYKNGIITDTIKSWMMNILLRTQESACVNGSCFT 740
          ASACHDGINWLITIGISGPDNGAVAVLYKNGIITDTIKSWMMNILLRTQESACVNGSCFT
Sbjct: 181 ASACHDGINWLITIGISGPDNGAVAVLYKNGIITDTIKSWMMNILLRTQESACVNGSCFT 240
```

```
Query: 741 VMTDGPSDGQASYKIFRIEKGKIVKSEVMNAPNTTYECCSCYPDSSEITCVRDNNVHGSN 920
          VMTDGPB+QQASYKIFRIEKGKIVKSEVMNAPNTTYECCSCYPDSSEITCVRDNNVHGSN
Sbjct: 241 VMTDGPBNGQASYKIFRIEKGKIVKSEVMNAPNTTYECCSCYPDSSEITCVRDNNVHGSN 300
```

```
Query: 921 RPUVSFNQMLEYQIGYICSGIFGDNPPNDKTSQCPVSSNGANGVKGFSFKYNGNVWIG 1100
          RPUVSFNQMLEYQIGYICSGIFGDNPPNDKTSQCPVSSNGANGVKGFSFKYNGNVWIG
Sbjct: 301 RPUVSFNQMLEYQIGYICSGIFGDNPPNDKTSQCPVSSNGANGVKGFSFKYNGNVWIG 360
```

```
Query: 1101 RTKSISSRNQFEMIWDNGWTGTDNNFSIKQDIVGNEWSGYSGFVQPELTGLDCIRP 1280
          RTKSISSRNQFEMIWDNGWTGTDNNFSIKQDIVGNEWSGYSGFVQPELTGLDCIRP
```

[download mutation report table for archiving or import to Excel](#)

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atics Institute ([BI](#)), Singapore
Medicina Genomica ([INMEGEN](#)), Mexico

Check alignment to reference hit!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

Color	Interest level	Remarks
Black	0 (least significant)	No known effects
Green	0	Common
Blue	1	At site of interaction
Orange	2	At site known to be involved in drug-binding, alter host-specificity.
Red	3 (most significant)	At site known to alter virulence, cause drug resistance, reverses premature STOP codon in PB1-F2.

FluSurver

Testing candidate mutations for further research and should ideally be combined with experimental testing. Any prediction or recommendation on patient treatment should not be based solely on these computational predictions. The results are based on a comparison of strains that recently infected humans. Therefore, the usage scenario that will give the most accurate results is for vaccine strains, including some candidates for avian flu and novel reassortant swine flu. There is also a [special note for using FluSurver results in publications](#).

auto

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entity % length coverage # mutations

List of mutations

V106I, N248D, H275Y
[show in structure](#)

100 100.000 3

NA drug sensitivity positions:
26, 0, 1

Reduced sensitivity or resistance!

[Download report table for archiving or import to Excel](#)

[Reference Selection](#)

Singapore
ca (INMEGEN), Mexico

Check list of mutations!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing of predicted severity or recommendation on patient treatment should not be based solely on these computational predictions. The results are mainly comprised of strains that recently infected humans. Therefore, **the usage scenario that will give the most relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu** if you are new to FluSurver. There is also a [special note for using FluSurver results in publications](#).

mutation selection: auto [Back to Reference Selection](#)

% AA identity	% length coverage	# mutations	List of mutations
99.360	100.000	3	V106I, H244S, H275Y show in structure NA drug sensitivity positions: 26, 0, 1 Reduced sensitivity or resistance!

[Load mutation report table for archiving or import to Excel](#)

[Back to Reference Selection](#)

Institute (BII), Singapore
 Influenza Genomics (INMEGEN), Mexico

NA H275Y

Key to alternative position numbering:

FluSurver numbering	Classical H3N2 strain numbering	Classical H1N1 strain numbering
275	(absolute as in 2009 H1N1 pandemic)	275

Chosen reference: NA_H1N1_Human_2009_California07
 Position in reference: 275
 AA in reference: H
 AA in query: Y

Mutation NA H275Y already occurred 197 times (2.48% of all samples with NA sequence) in 27 countries. The first strain with this mutation, collected in May 2009, was A/Mexico city/CIA10/2009(H1N1). The mutation most recently occurred in strain A/Rio Grande Do Sul/887/2012(H1N1), collected in June 2012. ([see map](#))

[See detailed global statistics for this position](#)

A mutation at the position equivalent to NA 275 has been reported in the literature to be related to [mild drug resistance and strong drug resistance](#).

A combination of mutations including the position equivalent to NA 275 has been reported in the literature to be related to [strong drug resistance](#).

As seen in resolved structures of proteins from related strains, the NA position equivalent to your mutation is involved in:

- [drug binding](#)

[See all interactions for this position](#)

Based on FoldX structural stability calculations H275Y is predicted to be strongly destabilizing which could represent a fitness disadvantage (ddG = 4.55 kcal/mol)

[PubMed search for this mutation \(including alternative numbering\)](#)

Click on mutation of interest for details!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidates

NA H275Y

Key to alternative position numbering:

FluSurver numbering	Classical H3N2 strain numbering	Classical H1N1 strain numbering
275	(absolute as in 2009 H1N1 pandemic)	274
274		275

Chosen reference: NA_H1N1_Human_2009_California07

Position in reference: 275

AA in reference: H

AA in query: Y

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[PubMed search for this mutation \(including alternative numbering\)](#)

FluSurver

Map of cities with the NA H275Y mutation

The city with **red** label indicates first appearance of the mutation. City with **yellow** label indicate later appearance of the mutation. The city with the most recent appearance of the mutation has the **green** label. Number in the label indicates frequency of occurrence of the mutation in that city. A dot in the label indicates that there are 10 or more occurrences in that city.

As there are too many cities with viral isolates carrying this mutation, cities with number of occurrences below 2 are not labeled in the map above.

Map of countries with the NA H275Y mutation

Number of occurrences

Countries without data: 1 44

Region	# Occ.	Date of collection(YYYYMMDD)
Sheffield	1	20110105
Catalonia	1	20091126
North Carolina	2	20091016
Kurume	35	20100118
Thailand	4	20100104
Sydney	8	20100916
Denmark	2	20090809
Seoul	4	20091100
Kyoto	4	20091204

Check for geographic occurrence pattern!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing

NA H275Y

Key to alternative position numbering:

275	FluSurver numbering (absolute as in 2009 H1N1 pandemic)
274	Classical H3N2 strain numbering
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AA in reference: H

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[See detailed global statistics for this position](#)

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[PubMed search for this mutation \(including alternative numbering\)](#)

FluSurver

logically interesting candidate mutations for further research and should ideally be combined with experimental testing. Assumed severity or recommendation on patient treatment should not be based solely on these computational predictions. The results are mainly comprised of strains that recently infected humans. Therefore, **the usage scenario that will give the most relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu** if you are new to FluSurver. There is also a [special note for using FluSurver results in publications](#).

selection: auto

[Back to Reference Selection](#)

% AA identity	% length coverage	# mutations	List of mutations
99.360	100.000	3	V106I, N244S, H275Y show in structure
			NA drug sensitivity positions: 26, 0, 1 Reduced sensitivity or resistance!

[Load mutation report table for archiving or import to Excel](#)

[Back to Reference Selection](#)

Mutation statistics for NA at position 275

AA	# Occ.	%	Geo Distribution	Co-occurrences
X	8	0.10		
Y	197	2.48	(geo)	(co-occur)
-	13	0.16		
H	7740	97.26	reference aa	reference aa
ALL	7958	100.00		

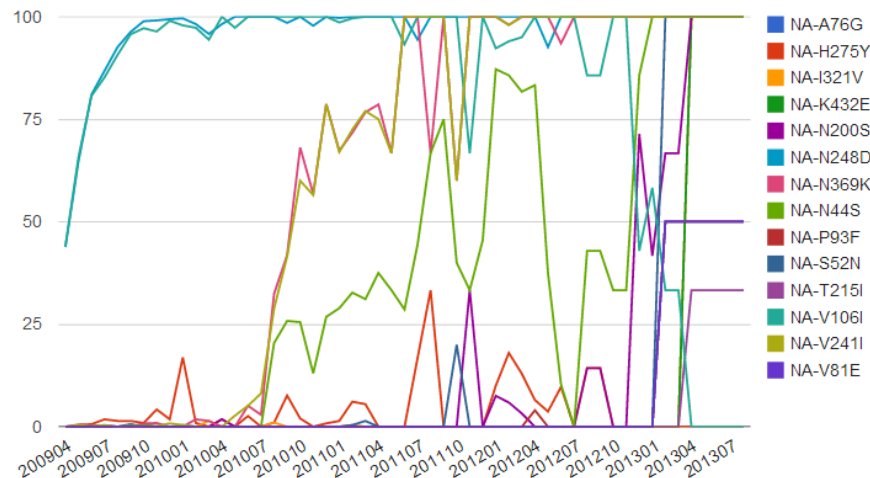
Sequences were compared to reference strain A/California/07/2009(H1N1) [AGM53851](#).
 Last updated on Sep 02nd 2013 by Raphael Tze Chuen Lee

Above are the occurrences of all amino acid residues at position 275 in NA. For statistics of all position in NA in this subtype click here: [H1N1 NA mutations table](#)

Check if there are other mutations at same position!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

Frequency of mutation over time



The line chart above shows the frequency of mutations in NA over time. Only mutations that were present in more than 30 percent of circulating strains in any of the months were represented in the line chart. Please note that the frequency of mutation in the most recent months tends to fluctuate as the database are still being populated.

Accession	Protein	Strain	WildtypeAA	Position	MutatedAA	Frequency	Date of collection(YYYYMMDD)	Remarks
ACY03001	NA	(A/Italy/137/2009(H1N1))	M	1	L	1	20090700	(co-occur)
ACU68826	NA	(A/Poland/303/2009(H1N1))	N	2	I	4 (geo)	20090710	(co-occur)
AFB77614	NA	(A/Kenya/071/2010(H1N1))	N	2	H	2 (geo)	20101129	(co-occur)
ACR08462	NA	(A/New York/3099/2009(H1N1))	N	2	S	1	20090429	(co-occur)
ACZ96222	NA	(A/Texas/44313703/2009(H1N1))	P	3	S	2 (geo)	20090831	(co-occur)
AGQ02440	NA	(A/Pernambuco/120924/2012(H1N1))	P	3	Q	1	20121002	(co-occur)
ACX66671	NA	(A/Lorestan/1599/2009(H1N1))	N	4	K	5 (geo)	20090727	(co-occur)
ADR32078	NA	(A/Jiangsu/S62/2009(H1N1))	N	4	T	5 (geo)	20091110	(co-occur)
AEG94621	NA	(A/Hualong/SWL1313/2009(H1N1))	N	4	I	2 (geo)	20091118	(co-occur)
AGI54909	NA	(A/South Carolina/29/2009(H1N1))	Q	5	R	3 (geo)	20090723	(co-occur)
ADK90313	NA	(A/Lisboa/60/2009(H1N1))	Q	5	H	2 (geo)	20090914	(co-occur)
ACY30121	NA	(A/Italy/161/2009(H1N1))	Q	5	K	2 (geo)	20090700	(co-occur)
ADY46355	NA	(A/Singapore/ON975/2009(H1N1))	Q	5	P	3 (geo)	20090706	(co-occur)
ADD84500	NA	(A/Xian/001/2009(H1N1))	K	6	N	7 (geo)	20090903	(co-occur)
ADG42646	NA	(A/California/VRDL89/2009(H1N1))	K	6	R	4 (geo)	20091017	(co-occur)
ADV17285	NA	(A/Thailand/CU-B2357/2010(H1N1))	K	6	E	3 (geo)	20100420	(co-occur)
ADX96969	NA	(A/Lima/WRAIR8689F/2009(H1N1))	K	6	M	1	20090627	(co-occur)
ADK87312	NA	(A/Qingdao/1215/2009(H1N1))	K	6	T	1	20090912	(co-occur)
AFB77614	NA	(A/Kenya/071/2010(H1N1))	I	7	V	1	20101129	(co-occur)

Check for temporal occurrence patterns!

ch and should ideally be combined with experimental testing should not be based solely on these computational predictions. ns. Therefore, the usage scenario that will give the most candidates for avian flu and novel reassortant swine flu ate for using FluSurver results in publications.

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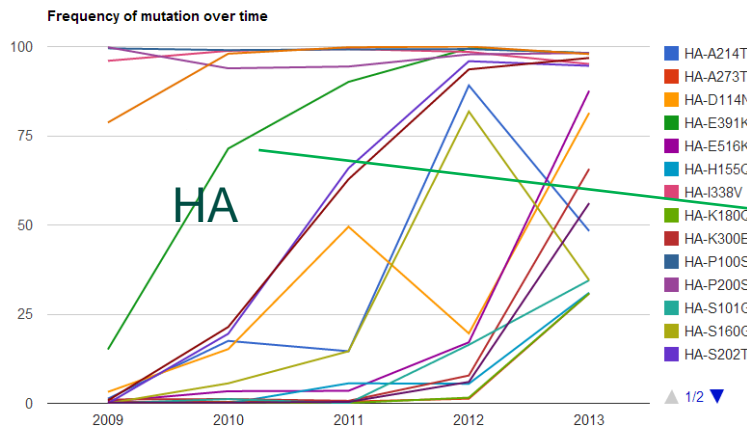
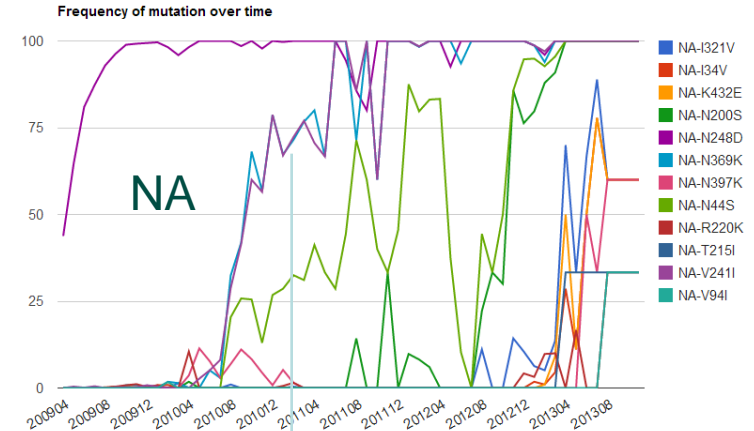
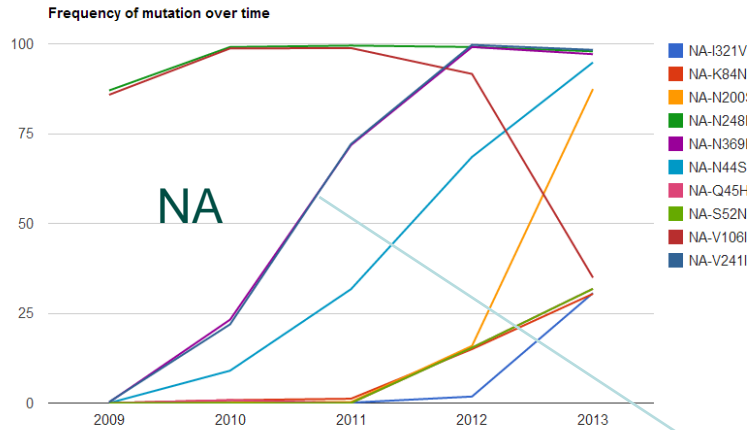
Mutation statistics for NA at position 275

AA	# Occ.	%	Geo Distribution	Co-occurrences
X	8	0.10		
Y	197	2.48	(geo)	(co-occur)
-	13	0.16		
H	7740	97.26	reference aa	reference aa
ALL	7958	100.00		

Sequences were compared to reference strain A/Columbia/07/2009(H1N1) [AGM53851](#).
Last updated on Sep 02nd 2013 by Raphael Tze Chuen Lee

Above are the occurrences of all amino acid residues at position 275 in NA. For statistics of all position in NA in this subtype click here: [H1N1_NA_mutations_table](#)

Mutation frequency pattern highlights relevant changes



New H275Y permissive mutations

Hurt *et al.* J Infect Dis. 2012 Jul 15;206(2):148-57.

Butler *et al.* PLoS Pathog. 2014 Apr 3;10(4):e1004065.

Change in pH-dependency of fusion

Maurer-Stroh *et al.* PLoS Curr. 2010 Jun 1;2:RRN1162.

Cotter *et al.* PLoS Pathog. 2014 Jan;10(1):e1003831.

Example H1N1pdm in FluSurver

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

Country	Strain	PB2	PB1	PB1-F2	PA	HA	NP	NA	M1	M2	NS1	NS2	Date of collection(YYYYMMDD)
Taiwan	(A/Taiwan/7336/2009(H1N1))	-	-	-	-	A26T P100S P200S S220T I338V E391K	-	V106I N248D H275Y	-	-	-	-	20091105
Japan	(A/Kurume/R8/2010(H1N1))	-	-	-	-	-	-	V53A V80M S82P V106I N248D H275Y Y282H	-	-	-	-	20100118
South Korea	(A/Daejeon/1871/2009(H1N1))	-	-	-	-	K39R N73S P100S S145P G172E P200S S220T I338V	-	A88T V106I I117M N248D H275Y	-	-	-	-	20091215
United Kingdom	(A/England/94840152/2009(H1N1))	-	-	-	-	P100S P200S S220T I338V	-	V106I N248D H275Y E482K	-	-	-	-	20091119
Japan	(A/Kurume/N8/2010(H1N1))	-	-	-	-	-	-	V80M S82P V106I N248D H275Y	-	-	-	-	20100118
United Kingdom	(A/England/00380015/2009(H1N1))	-	-	-	-	P100S P200S S220T I338V	-	V106I N248D H275Y E482K	-	-	-	-	20091117
USA	(A/California/21/2012(H1N1))	-	-	-	-	S86T P100S K136N S160G P200S S220T A214T S220T D239G N277D I338V F347L E391K S468N V537A	-	A20V G41R N44S V106I V241I N248D H275Y N369K	V80I	S13N	-	-	20120220
Viet Nam	(A/Viet Nam/835/2009(H1N1))	-	-	-	P224S	P100S P200S S220T I338V	V100I	V106I N248D H275Y	-	-	L115F I123V	-	20090727
Mexico	(A/Mexico/INDRE3354/2012(H1N1))	-	-	-	-	S86T P100S S160G P200S S220T A214T S220T N277D I338V E391K S468N V537A	-	G41R N44S S95I V106I V241I N248D H275Y N369K	-	-	-	-	20120208
Japan	(A/Kurume/N1/2010(H1N1))	-	-	-	-	-	-	V80M S82P V106I N248D H275Y	-	-	-	-	20100118
USA	(A/Bethesda/NIH108-D14/2009(H1N1))	R591Q	K736G	-	V14I P224S K718Q	A15T P100S P200S S220T I338V E391K F432L	V100I V270I V444I	V106I N248D H275Y	-	-	I123V	-	20091105
Japan	(A/Kurume/L19/2010(H1N1))	-	-	-	-	-	-	V80M S82P V106I N248D H275Y	-	-	-	-	20100118
China	(A/Haishu/SWL110/2010(H1N1))	-	-	-	-	P100S S179N P200S S220T I338V	-	V106I N248D H275Y	-	-	-	-	20100104
Germany	(A/Munich/INS541/2011(H1N1))	R299K V344M I354L N456S	V645I	-	P224S N321K I330V M548I	P100S D114N P200S S220T I338V E391K S468N	V100I	V106I V241I N248D K280R H275Y I321V N369K	V80I	-	I123V	-	20110218
Canada	(A/Canada-AB/RV2828/2009(H1N1))	-	M82V N158S	-	P224S	P100S P200S S220T T258I I338V	-	V106I N248D H275Y V394I	-	-	-	-	20090804
USA	(A/Texas/33/2012(H1N1))	-	-	-	-	S86T P100S S160G P200S S220T A214T S220T N277D I338V E391K S468N V537A	-	G41R N44S V106I L127W V241I N248D H275Y N369K	V80I	S13N	-	-	20120312
USA	(A/Texas/48/2012(H1N1))	-	-	-	-	S86T P100S S160G P200S S220T A214T S220T N277D I338V E391K S468N V537A	-	G41R N44S S95N V106I V241I N248D H275Y N369K	V80I	S13N	-	-	20120316
United Kingdom	(A/England/00380020/2009(H1N1))	-	-	-	-	P100S P200S S220T I338V	-	V106I N248D H275Y E482K	-	-	-	-	20091120
USA	(A/North Carolina/59/2009(H1N1))	-	-	-	-	P100S V169I P200S S220T P288Q I312V I338V	-	V106I V234I N248D H275Y	-	P25T	-	-	20091107
Spain	(A/Catalonia/NS7382/2009(H1N1))	-	-	-	-	P100S S179N P200S S220T T249A I338V G411D	-	V106I N248D H275Y	-	-	-	-	20091128

reported in the literature to be related to **strong drug resistance**.

As seen in resolved structures of proteins from related strains, the NA position equivalent to your mutation is involved in:

- **drug binding**

[See all interactions for this position](#)

Based on FoldX structural stability calculations H275Y is predicted to be strongly destabilizing which could represent a fitness disadvantage ($\Delta\Delta G = 4.55$ kcal/mol)

[PubMed search for this mutation \(including alternative numbering\)](#)

[Read mutation report table for archiving or import to Excel](#)

[Click to Reference Selection](#)

Reduced sensitivity or resistance!

Mutation statistics for NA at position 275

AA	# Occ.	%	Geo Distribution	Co-occurrences
X	8	0.10		
Y	197	2.48	(geo)	(co-occur)
-	13	0.16		
H	7740	97.26	reference aa	reference aa
ALL	7958	100.00		

Sequences were compared to reference strain A/California/07/2009(H1N1) [AGM53851](#).
Last updated on Sep 02nd 2013 by Raphael Tze Chuen Lee

Above are the occurrences of all amino acid residues at position 275 in NA. For statistics of all position in NA in this subtype click here: [H1N1 NA mutations table](#)

Check for co-occurring mutations!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidates

NA H275Y

Key to alternative position numbering:

FluSurver numbering	(absolute as in 2009 H1N1 pandemic)	Classical H3N2 strain numbering	Classical H1N1 strain numbering
275			
274			
275			

Chosen reference: NA_H1N1_Human_2009_California07

Position in reference: 275

AA in reference: H

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[PubMed search for this mutation \(including alternative numbering\)](#)

Known effect(s) of mutations at position equivalent to your mutation:

Protein: NA
Influenza type: Human H1N1 (2006)
Mutation (as in paper): H274Y
neutral AA: H
neg. eff. AA: Y
Effect: strong drug resistance (drug name in comments)

Comment:
Tamiflu but not Relenza resistance (Table 3)
[Literature reference](#)
(Mutation H274Y in the paper is at an equivalent position of the mutation in your query)

PubMed search results:

Antimicrob Agents Chemother. 2008 Sep;52(9):3284-92. doi: 10.1128/AAC.00555-08. Epub 2008 Jul 14.

Surveillance for neuraminidase inhibitor resistance among human influenza A and B viruses circulating worldwide from 2004 to 2008.

Sheu TG, Devde VM, Okomo-Adhiambo M, Garten RJ, Xu X, Bright RA, Butler EN, Wallis TR, Klimov AI, Gubareva LV. Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.

PubMed search results for influenza AND (neuraminidase OR NA) AND (H275Y OR H274Y):

Results: 1 to 20 of 239

1. [Neuraminidase inhibitor susceptibility surveillance of influenza viruses circulating worldwide during the 2011 Southern Hemisphere season.](#)
Okomo-Adhiambo M, Sleeman K, Lysén C, Nguyen HT, Xu X, Li Y, Klimov AI, Gubareva LV. Influenza Other Respi Viruses. 2013 Sep;7(5):645-58. doi: 10.1111/irv.12113. Epub 2013 Apr 10. PMID: 23575174 [PubMed - in process] [Related citations](#)
2. [Functional and structural analysis of influenza virus neuraminidase n3 offers further insight into the mechanisms of oseltamivir resistance.](#)
Li Q, Qi J, Wu Y, Kiyota H, Tanaka K, Suhara Y, Ohnishi H, Suzuki Y, Vavricka CJ, Gao GF. J Virol. 2013 Sep;87(18):10016-24. doi: 10.1128/JVI.01129-13. Epub 2013 Jul 3. PMID: 23824808 [PubMed - in process] [Related citations](#)

Check for associated literature!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting changes

NA H275Y

Key to alternative position numbering:

FluSurver numbering	(absolute as in 2009 H1N1 pandemic)	Classical H3N2 strain numbering	Classical H1N1 strain numbering
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Chosen reference: NA_H1N1_Human_2009_California07

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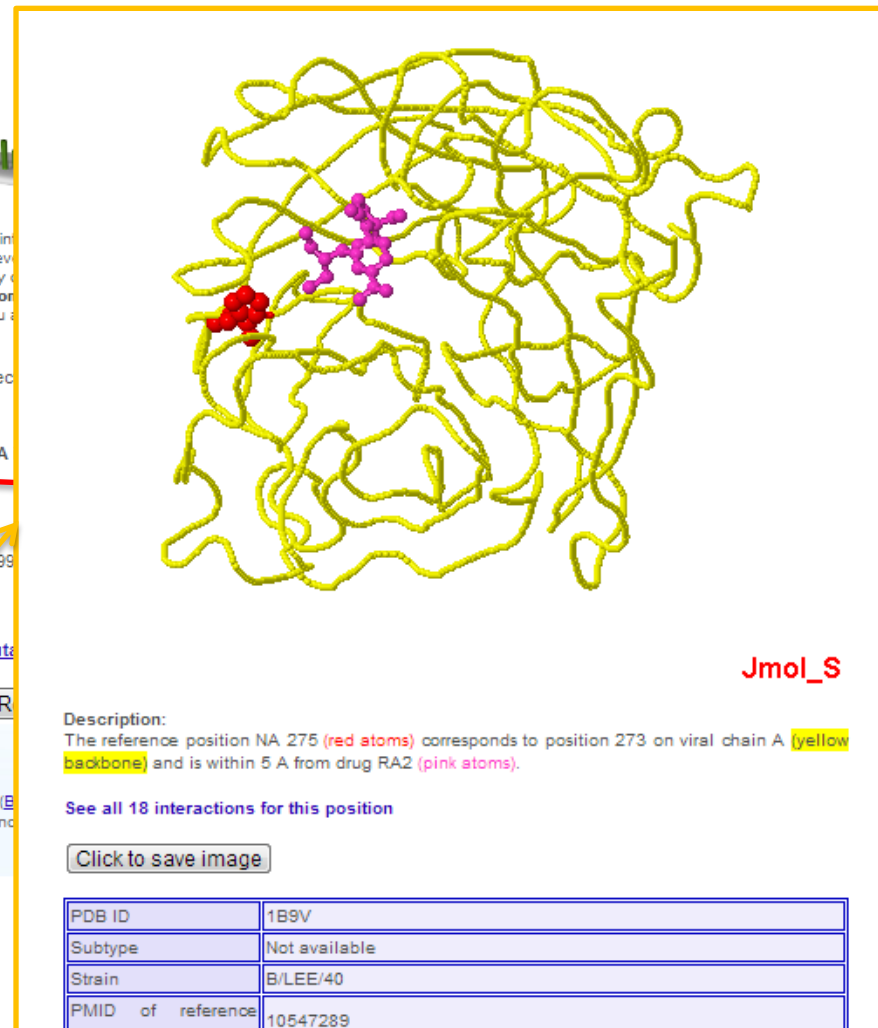
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- [drug binding](#)

[See all interactions for this position](#)

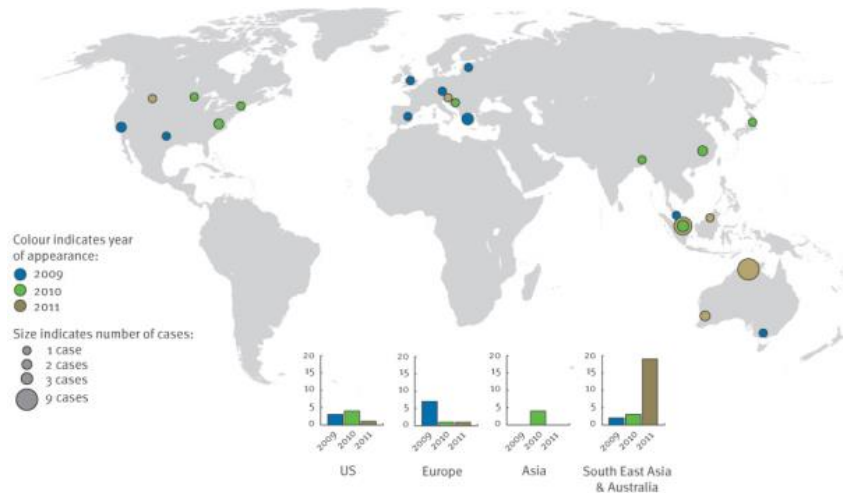
Based on FoldX structural stability calculations H275Y is predicted to be strongly destabilizing which could represent a fitness disadvantage (ddG = 4.55 kcal/mol)

[PubMed search for this mutation \(including alternative numbering\)](#)

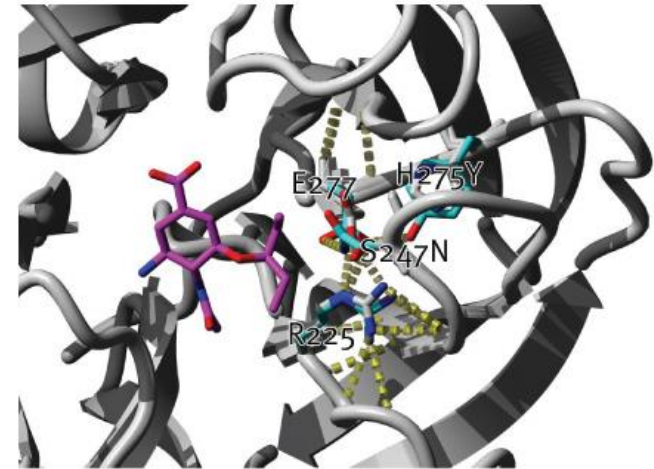


Check for structural interactions!

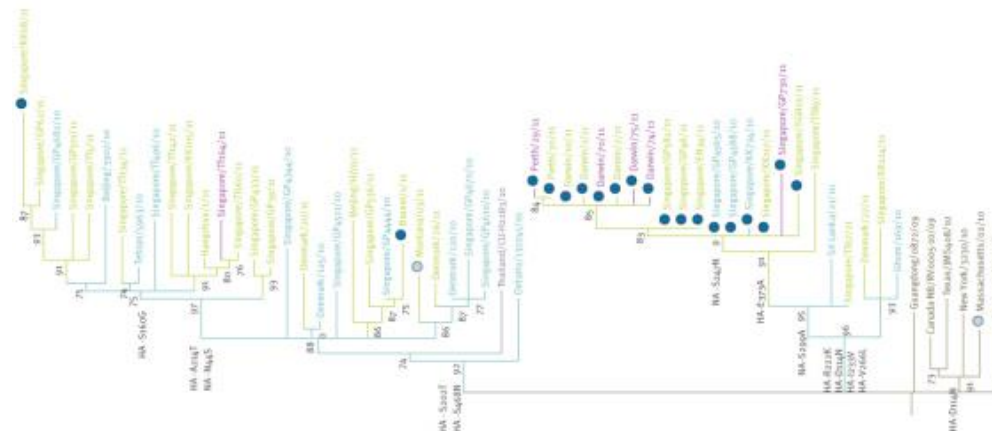
New drug sensitivity altering mutation NA S247N



Global occurrence of new variant



Structural context of mutation



Phylogenetic context of new variant

Found circulating in 10% of samples in Singapore and 30% of samples in Northern Australia in early 2011.

Experimentally measured increase of IC₅₀ for Tamiflu by 6-fold and Relenza by 3-fold but **normally administered dose of drugs still sufficient.**

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

main application scenario for FluSurver is to highlight phenotypically or epidemiologically interesting candidate mutations for further research and should ideally be combined with experimental testing. The predicted severity or recommendation on patient treatment should not be based solely on these computational predictions. The results are mainly comprised of strains that recently infected humans. Therefore, **the usage scenario that will give the most relation to used vaccine strains, including some candidates for avian flu and novel reassortant swine flu** if you are new to FluSurver. There is also a [special note for using FluSurver results in publications](#).

mutation selection: auto [Back to Reference Selection](#)

% AA identity	% length coverage	# mutations	List of mutations
99.360	100.000	3	V106I, H245G, H275Y show in structure

NA drug sensitivity positions:
 26.0.1
 Reduced sensitivity or resistance!

[Download mutation report table for archiving or import to Excel](#)

[Back to Reference Selection](#)

Institute (BII), Singapore
 Genomics (INMEGEN), Mexico

NA H275Y

Key to alternative position numbering:

FluSurver numbering	Classical H3N2 strain numbering	Classical H1N1 strain numbering
275	(absolute as in 2009 H1N1 pandemic)	274

Chosen reference: NA_H1N1_Human_2009_California07
 Position in reference: 275
 AA in reference: H
 AA in query: Y

Mutation NA H275Y already occurred 197 times (2.48% of all samples with NA sequence) in 27 countries. The first strain with this mutation, collected in May 2009, was A/Mexico city/CIA10/2009(H1N1). The mutation most recently occurred in strain A/Rio Grande Do Sul/887/2012(H1N1), collected in June 2012. ([see map](#))

[See detailed global statistics for this position](#)

A mutation at the position equivalent to NA 275 has been reported in the literature to be related to [mild drug resistance](#) and [strong drug resistance](#).

A combination of mutations including the position equivalent to NA 275 has been reported in the literature to be related to [strong drug resistance](#).

As seen in resolved structures of proteins from related strains, the NA position equivalent to your mutation is involved in:

- [drug binding](#)

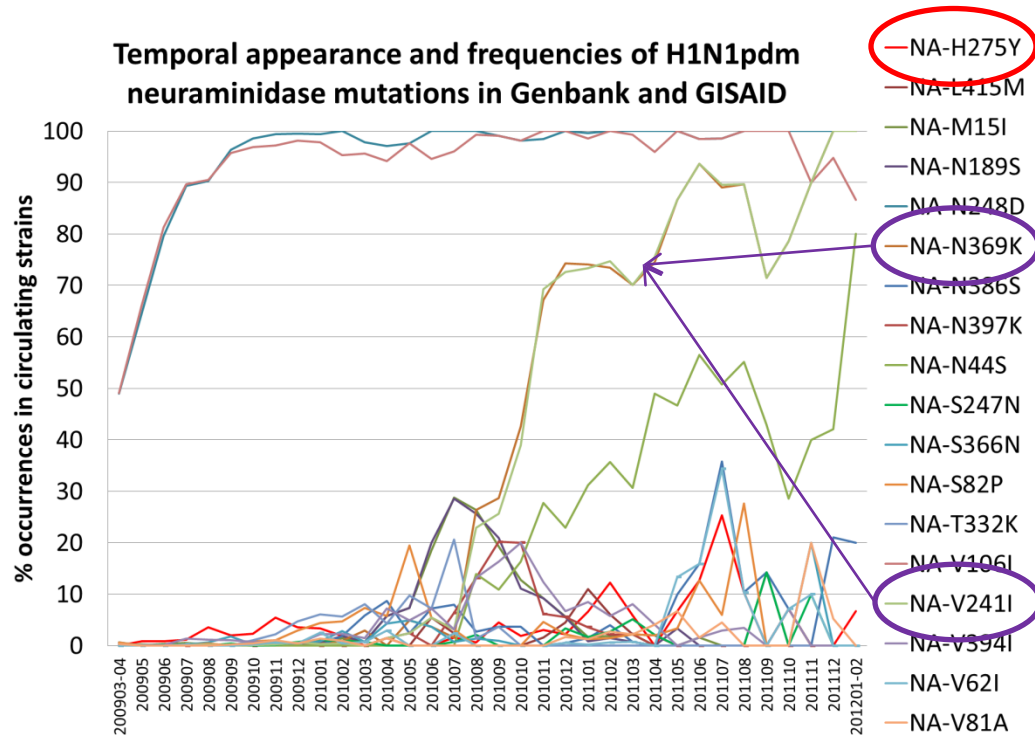
[See all interactions for this position](#)

Based on FoldX structural stability calculations H275Y is predicted to be strongly destabilizing which could represent a fitness disadvantage (ddG = 4.55 kcal/mol)

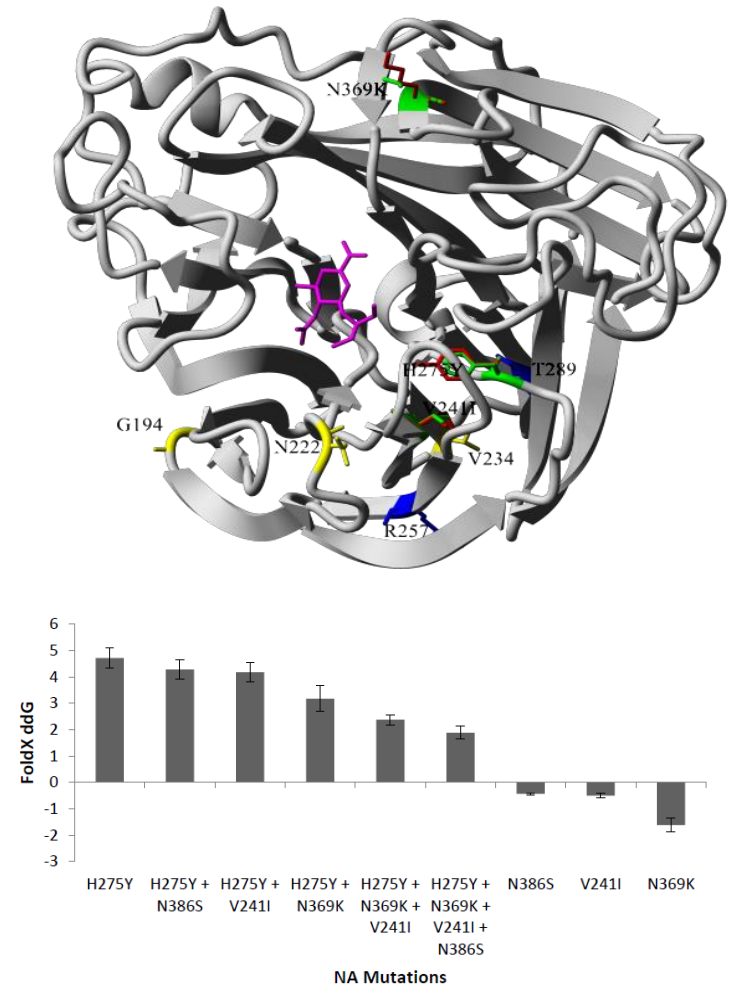
[PubMed search for this mutation \(including alternative numbering\)](#)

Check for stability
or passage effect
(if available)!

Frequency rise points to role of permissive mutations



FoldX predicts increase in structural stability for mutations that were increasing in frequency and were fixed in Newcastle strains.

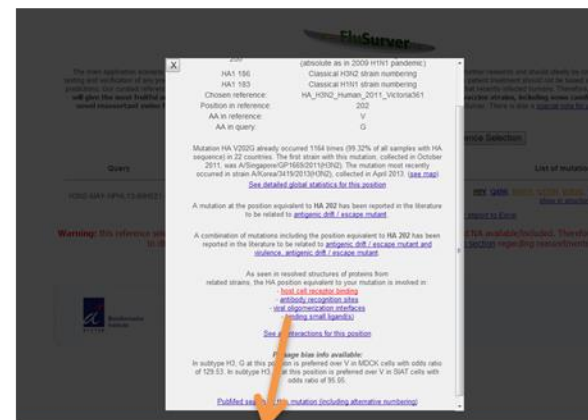
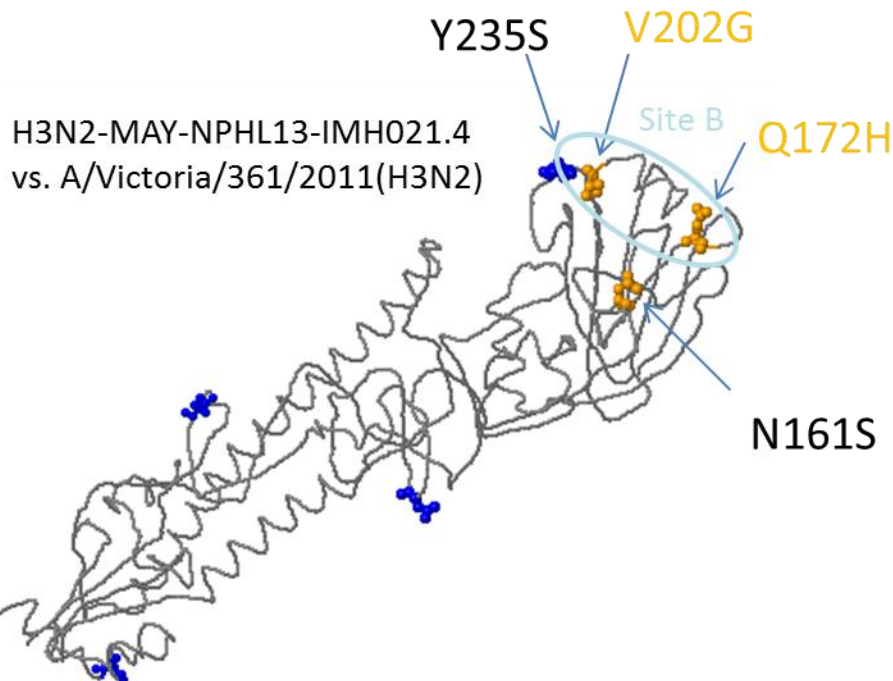


Hurt AC, Hardie K, Wilson NJ, Deng YM, Osbourn M, Leang SK, Lee RT, Iannello P, Gehrig N, Shaw R, Wark P, Caldwell N, Givney RC, Xue L, Maurer-Stroh S, Dwyer DE, Wang B, Smith DW, Levy A, Booy R, Dixit R, Merritt T, Kelso A, Dalton C, Durrheim D, Barr IG.

Characteristics of a widespread community cluster of H275Y oseltamivir-resistant A(H1N1)pdm09 influenza in Australia.

J Infect Dis. 2012 Jul 15;206(2):148-57.

Current H3N2 strains have HA passage bias mutations in antigenic sites



As seen in resolved structures of proteins from related strains, the HA position equivalent to your mutation is involved in:

- [host cell receptor binding](#)
- [antibody recognition sites](#)
- [viral oligomerization interfaces](#)
- [binding small ligand\(s\)](#)

V202G

[See all interactions for this position](#)

Passage bias info available:

In subtype H3, G at this position is preferred over V in MDCK cells with odds ratio of 129.53. In subtype H3, G at this position is preferred over V in SIAT cells with odds ratio of 95.05.

Q172H

As seen in resolved structures of proteins from related strains, the HA position equivalent to your mutation is involved in:

- [host cell receptor binding](#)
- [antibody recognition sites](#)
- [binding small ligand\(s\)](#)
- is involved in [binding host protein\(s\)](#)
- [viral oligomerization interfaces](#)

[See all interactions for this position](#)

Passage bias info available:

In subtype H3, H at this position is preferred over Q in SIAT cells with odds ratio of 67.59.

Same isolate but different passage
(A/SINGAPORE/22/2012 NPHL: GP1187-2012)

GISAID ID	Submitter	Passage	Mutations relative to Victoria/361
EPI_ISL_128750	WHO CC Melbourne via NPHL	MDCK0, MDCK1	H9Y, Q49R, N161S, Q172H, V202G, Y235S, N294K
EPI_ISL_135838	US CDC via WHO CC Melbourne	E4/E1	H9Y, Q49R, N161S, N294K

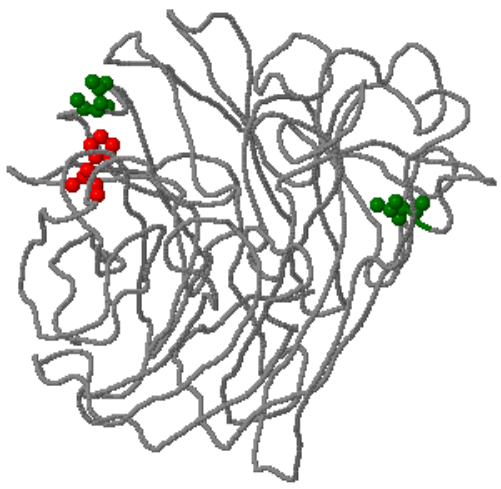
FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

Reference: NA_H1N1_Human_2009_California07 ([Structure/Model Details](#))
 Patient/Sample: A/Singapore/GN285/2009(H1N1)
 Mutation(s): **N248D**, **V106I**, **H275Y**
 Wildtype residue only displayed if position is part of available structure.
 Hover with mouse over residue to see its position number. Right-click for more options.

The main application is for the visualization and verification of any protein structure. Our curated reference structures are **fruitful and reliable**.
 H3N2v. P

Que

A/Singapore/GN2



Jmol_S

[See interactions of position NA 248 in related structures.](#)
[See interactions of position NA 106 in related structures.](#)
[See interactions of position NA 275 in related structures.](#)

[Click to save image](#)

er research and should ideally be combined with experimental testing. Treatment should not be based solely on these computational predictions. For humans, Therefore, **the usage scenario that will give the most** some candidates for avian flu and novel reassortant swine flu. [Special note for using FluSurver results in publications.](#)

[e Selection](#)

# mutations	List of mutations
3	V106I, N248D, H275Y show in structure

NA drug sensitivity positions:
26, 0, 1
 Reduced sensitivity or resistance!

[Import to Excel](#)

View all mutations together in structure or homology model of reference strain!

FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

Reference: NA_H1N1_Human_2009_California07
 Patient/Sample: A/Singapore/GN285/2009(H1N1)
 Mutation(s): N248D, V106I, H275Y
 Wildtype residue only displayed if position is part of available structure.
 Hover with mouse over residue to see its position number. Right-click for more options.

The main application is for the verification of any prediction. Our curated reference sequences are fruitful and reliable. H3N2v. P

Que

A/Singapore/GN2

Bioinforma
Institute

Information of the template of 3NSS used to model NA_H1N1_Human_2009_California07

PDB ID	3NSS
Subtype	H1N1
Strain	A/CALIFORNIA/04/2009
Structure Title	THE 2009 PANDEMIC H1N1 NEURAMINIDASE N1 LACKS THE 150-CAVITY IN ITS ACTIVE SITES
PMID of Reference	Not Available
Viral Protein	NEURAMINIDASE
Corresponding Chain	A

Information of the alignment of NA_H1N1_Human_2009_California07 with 3NSS

Identity	Alignment Length	E-Value	Bit Score
100.00	388	0.0	797

Alignment of NA_H1N1_Human_2009_California07 with 3NSS used for structural modeling

	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	
_aln.pos	3NSS	SVELAGNSSL	CFVSGWAIYSK	DNSVRIGSGKGV	VFVIREPFISCS	FLECRITFFLT	QGALLNDKHSNGT	IKDRSPYRTIM	SCPIGEVFS	FPYNSRFES	VAWSASACHD	GINWLTIGIS	GFDNGAV	VLKYNIGI	ITDTIKSRWN	NILRTQES
NA_H1N1_2009_CALIFORNIA07	SVELAGNSSL	CFVSGWAIYSK	DNSVRIGSGKGV	VFVIREPFISCS	FLECRITFFLT	QGALLNDKHSNGT	IKDRSPYRTIM	SCPIGEVFS	FPYNSRFES	VAWSASACHD	GINWLTIGIS	GFDNGAV	VLKYNIGI	ITDTIKSRWN	NILRTQES	
_consrvd																

	160	170	180	190	200	210	220	230	240	250	260	270	280	290	300
_aln.pos	3NSS	ACVNGSCFTT	WMDGSPNGQ	ASVYKIFRIE	RGRKIVKSV	EMNAPHYH	VEECSCV	PDSEITCV	CRDNNHGS	NRFWISFM	QWLEYQ	IGVICS	SGIFGDN	FRPDKTIG	SCGFVS
NA_H1N1_2009_CALIFORNIA07	ACVNGSCFTT	WMDGSPNGQ	ASVYKIFRIE	RGRKIVKSV	EMNAPHYH	VEECSCV	PDSEITCV	CRDNNHGS	NRFWISFM	QWLEYQ	IGVICS	SGIFGDN	FRPDKTIG	SCGFVS	NGANGV
_consrvd															

	310	320	330	340	350	360	370	380	390
_aln.pos	3NSS	GTNNFISIKQ	DIIVGINES	GYSGSFVQ	HPELTGLD	CIKPCFW	VELIRGR	FEENTINT	SGSSIS
NA_H1N1_2009_CALIFORNIA07	GTNNFISIKQ	DIIVGINES	GYSGSFVQ	HPELTGLD	CIKPCFW	VELIRGR	FEENTINT	SGSSIS	FCGVNS
_consrvd									

See interactions of position NA 248 in related structures.
 See interactions of position NA 106 in related structures.
 See interactions of position NA 275 in related structures.

Click to save image

Jmol_S

Check source and template similarity of structure/homology model!

FluSurver – an online tool to make sequence analysis and mutation effect prediction easier

Check drug summary table!

The main application scenario for FluSurver is to help in the selection and verification of any predicted phenotypes. Importantly, our curated reference sequences used for annotation are of high quality and **fruitful and reliable results are current surveillance data**. Please take a look at the [FluSurver H3N2v](#). Please take a look at the [FluSurver H3N2v](#).

Known effect(s) of mutations at position equivalent to your mutation:

Protein: NA
Influenza type: Human H1N1 (2006)
Mutation (as in paper): H274Y
neutral AA: H
neg. eff. AA: Y
Effect: strong drug resistance (drug name in comments)

Comment:
Tamiflu but not Relenza resistance (Table 3)
Literature reference
(Mutation H274Y in the paper is at an equivalent position of the mutation in your query)

NCBI Resources How To

PubMed.gov: PubMed Advanced

Display Settings: Abstract

Antimicrob Agents Chemother. 2008 Sep;52(9):3284-92. doi: 10.1128/AAC.00555-08. Epub 2008 Jul 14.

Surveillance for neuraminidase inhibitor resistance among human influenza A and worldwide from 2004 to 2008.

Sheu TG, Deyde VM, Okomo-Adhiambo M, Garten RJ, Xu X, Bright RA, Butler EN, Wallis TR, Klimov AI, Gubareva LV. Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia.

Residue	Type	Ref.num.	Effect annotation	Close to drug in 3D structure (<5Å)
V116	wt	116 (N2)	sensitive	-
R118	wt	118 (N2)	no known effect (common wildtype AA)	3D
E119	wt	119 (N2)	sensitive	3D
L134	wt	134 (N2)	no known effect (common wildtype AA)	3D
Q136	wt	136 (N2)	sensitive	-
D151	wt	151 (N2)	sensitive	3D
Y155	wt	155 (N2)	sensitive	-
R156	wt	156 (N2)	no known effect (common wildtype AA)	3D
S180	wt	179 (N2)	no known effect (common wildtype AA)	3D
I223	wt	222 (N2)	sensitive	3D
L224	wt	223 (N2)	no known effect (common wildtype AA)	3D
R225	wt	224 (N2)	sensitive	3D
T226	wt	225 (N2)	no known effect (common wildtype AA)	3D
Q227	wt	226 (N2)	sensitive	-
E228	wt	227 (N2)	sensitive	3D
G245	wt	244 (N2)	no known effect (common wildtype AA)	3D
P246	wt	245 (N2)	no known effect (common wildtype AA)	3D
S247	wt	246 (N2)	sensitive	3D
N248D	mt	247 (N2)	no known effect (mt)	3D
H275Y	mt	274 (N2)	effect	3D
E277	wt	276 (N2)	sensitive	3D
R293	wt	292 (N2)	sensitive	3D
N344	wt	347 (N2)	no known effect (common wildtype AA)	3D
G345	wt	348 (N2)	no known effect (common wildtype AA)	3D
G348	wt	351 (N2)	no known effect (common wildtype AA)	3D
R368	wt	371 (N2)	sensitive	3D
G401	wt	405 (N2)	no known effect (common wildtype AA)	3D

DISCLAIMER: This table is not suitable to unambiguously determine drug resistance but should rather serve to help selecting candidate positions/mutations that may have an effect for further experimental testing. Vicinity of a mutation to the drug in 3D structures does not automatically imply an effect on the drug and requires further careful modelling and/or experimental testing. Most of the available effect annotations refer to specific subtypes and may hence not apply exactly to your query. Please read the annotation carefully and follow up the provided links to the original literature to judge whether a similar effect on drug sensitivity for your query may be plausible.

Further research and should ideally be combined with experimental testing. Treatment should not be based solely on these computational predictions. Affected humans. Therefore, the usage scenario that will give the most interesting some candidates for avian flu and novel reassortant swine flu is a special note for using FluSurver results in publications.

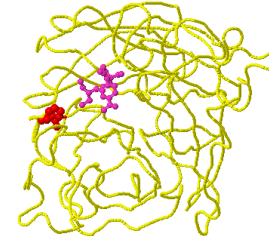
Force Selection

Force # mutations List of mutations

V106I, N248D, H275Y
[show in structure](#)

NA drug sensitivity positions:
26, 0, 1
Reduced sensitivity or resistance!

or import to Excel



Jmol_S

Description:
The reference position NA 275 (red sphere) corresponds to position 273 on viral chain A (yellow) and is within 5 Å from drug RAZ (pink sphere).

See all 18 interactions for this position

[Click to save image](#)

PDB ID	1B9V
Subtype	Not available
Strain	BL/EE/40
PMID of reference	10547289

Also useful for analysis of other segments!

Query	Best reference hit	% AA identity	% length coverage	# mutations	List of mutations
RVM4541200051 H3 clade 3B N2	M2 A/Wisconsin/67/2005(H3N2) find closest related sequences	98.780	84.536	1	V271 show in structure <div> M2 drug sensitivity positions: 16, 0, 2 Reduced sensitivity or resistance! </div>

Known effect(s) of mutations at position equivalent to your mutation:

Protein: M2
Influenza type: Duck (live poultry market) H3N2
Mutation (as in paper): V271
neutral AA: V
neg. eff. AA: I
Effect: mild drug resistance (drug name in comments)

Comment:
conferred Amantadine resistance (Table 1).

[Literature reference](#)

(Mutation V271 in the paper is at an equivalent position of the mutation in your query)

If WT residues in reference strains are associated with resistance it will be shown in drug summary table!

Summary of critical drug sensitivity positions

Residue	Type	Ref.num.	Effect annotation	Close to drug in 3D structure (<5Å)
L26	wt	26	sensitive	3D
V271	mt	27	effect	3D
A30	wt	30	sensitive	3D
N31	wt	31	effect	3D
I33	wt	33	no known effect (common wildtype AA)	3D
G34	wt	34	sensitive	3D
I35	wt	35	no known effect (common wildtype AA)	3D
H37	wt	37	no known effect (common wildtype AA)	3D
L38	wt	38	no known effect (common wildtype AA)	3D
L40	wt	40	no known effect (common wildtype AA)	3D
W41	wt	41	no known effect (common wildtype AA)	3D
I42	wt	42	no known effect (common wildtype AA)	3D
L43	wt	43	no known effect (common wildtype AA)	3D
D44	wt	44	no known effect (common wildtype AA)	3D
R45	wt	45	no known effect (common wildtype AA)	3D

Known effect(s) of mutations at position equivalent to your mutation:

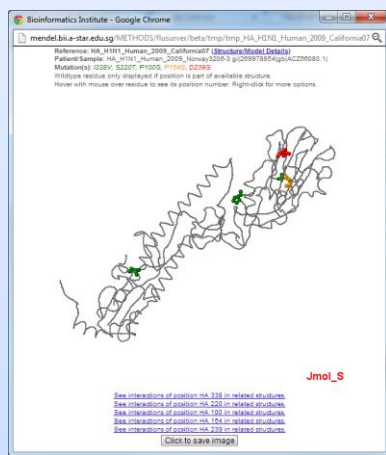
Protein: M2
Influenza type: Human H1N1 (2007)
Mutation (as in paper): S31N
neutral AA: S
neg. eff. AA: N
Effect: strong drug resistance (drug name in comments)

Comment:
Amantadine resistance (Table)

[Literature reference](#)

(Mutation S31N in the paper is at an equivalent position of the mutation in your query)

Summary of FluSurver features 2014

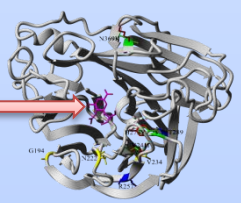


Map mutations to structure

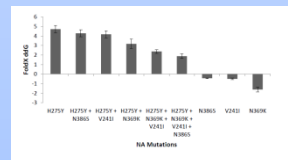
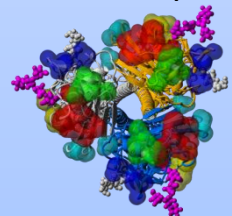
250+
reference
homology
models

1568	self/oligomerization
975	other small ligand
268	antibody
188	host protein
182	antigen-presenting MHC molecule
132	other viral protein
46	drug
45	nucleic acids
13	host cell receptor
3417	total interactions for 2062 positions

Interactions



Glycosylation site changes



FoldX stability calculations
(for high frequency
mutations in N1pdm)

Mutation numbering scheme
conversion (e.g. H3, H1, H1pdm)
and direct **PubMed** search link



Passage bias
(egg/cell adaptation)
for ~1300 mutations

Literature-curated
mutation effect database
~250 entries

mild drug resistance	19
strong drug resistance	30
virulence	68
antigenic drift / escape mutant	74
host specificity shift	21
other	12

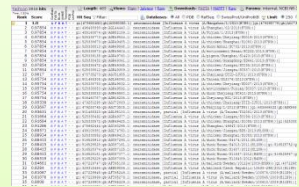
Structure

Literature

Epidemiology

Closest DB hits

Temporal pattern



Genomic co-occurrence

Regional & global occurrence



Analysis – FluSurver for Mutation Interpretation



The screenshot displays the FluSurver web application interface. The top navigation bar includes 'GISAID', 'FluSurver', and 'Mendel Institute'. The main content area is divided into several panels:

- Personal Worksheet:** Contains a table of results for comparison with reference sequence HK229_Human_2002_Netherlands219. The table has columns for Query, Best reference hit, % AA identity, % length coverage, and # mutations. It lists several queries with their corresponding best reference hits and mutation counts.
- Map of sites with the HA Q242L mutation:** A world map showing the geographic distribution of the HA Q242L mutation, with red dots indicating specific locations.
- HA Q242L:** A detailed view of the HA Q242L mutation, showing its position in the HA protein structure and its relationship to other mutations. It includes a key to alternative position numbering and a list of mutations.
- Protein: HA:** A 3D protein structure showing the location of the HA Q242L mutation, with a green arrow pointing to the specific residue.
- Comment:** A text box providing additional information about the mutation, including its effect on host specificity and its relationship to other mutations.

Important disclaimer:

FluSurver makes it very easy to link mutations with prior literature and potential phenotypic effects.

While we have placed great emphasis on avoiding false positive alerts and provide tutorials, one still needs to read the associated papers and interpret the provided evidence carefully to judge any effect realistically.

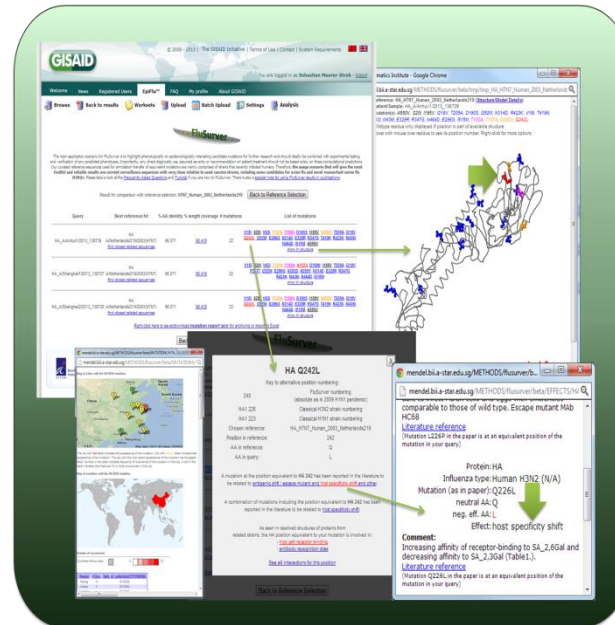
FluSurver Acknowledgements

Many current and former (*) colleagues from the A*STAR Bioinformatics Institute (BII) contribute(d) critically to its development and maintenance, including:

Sebastian Maurer-Stroh, Raphael Tze Chuen Lee, Vachiranee Limvipuvadh, Jianmin Ma, Fernanda L Sirota, Vithiagarun Gunalan, Swe Swe Thet Paing*, Narumol Doungpan*, Joy Xiang* and Frank Eisenhaber.

The FluSurver would be nothing without the valuable feedback and interaction with the influenza research and surveillance community, including especially and in chronological order:

- Genome Institute of Singapore (GIS), Singapore
- INMEGEN Mexico City, Mexico
- National Public Health Laboratory (NPHL) of the Ministry of Health, Singapore
- IAL Sao Paulo, Brazil
- WHO Collaborating Centre for Reference and Research on Influenza, Australia
- Duke-NUS Emerging Infectious Disease Programme, Singapore
- University of Melbourne, Australia
- Global Initiative for Sharing All Influenza Data (GISAID)



Fishing for Flu Mutations since 2009!

Contact: flusurver@gisaid.org