

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

<http://flusurver.bii.a-star.edu.sg/> or directly from **GISAID EpiFlu™** (in near future)



## 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 (including the recent H7N9!) and novel reassortant swine flu H3N2v.**

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

Paste your protein or nucleotide FASTA sequence(s) into the text area below. ([Sample FASTA sequences: 2009 H1N1 NA and HA](#))

OR upload your protein or nucleotide sequences in a FASTA file

No file chosen

The server can **automatically** determine the type of input (either protein or nucleotide) and the closest reference sequence among current vaccine strains to compare. Also mixtures of genes/proteins (e.g. HA and NA or all genes of the same patient) can be provided as input. To compare with more remotely related sequences/strains, it is possible to select a specific reference strain by choosing below.

Compare with:

Additional settings:

☒ ignore low quality bases for nucleotide input (indicated by lower case, except for all lower case sequences)

(estimated time needed: ~2 seconds per sequence in automatic mode)



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Paste  
sequence  
data here!

Prepared by:  
Aeron Hurt  
Sebastian Maurer-Stroh

Contact:  
[sebastianms@bii.a-star.edu.sg](mailto:sebastianms@bii.a-star.edu.sg)

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

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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)<br><a href="#">find closest related sequences</a> | 99.360        | <a href="#">100.000</a> | 3           | <p>V106I, N248D, H275Y<br/><a href="#">show in structure</a></p> <p>NA drug sensitivity positions:<br/>26, 0, 1<br/>Reduced sensitivity or resistance!</p> |

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

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Tachyon 11364 hits

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

Time: 15.89s

Hit Seq Filter:  Databases: ☒ All ☐ PDB ☐ RefSeq ☐ SwissProt/UniProtKB Limit: ☒ 250 ☐ 1000 ☐ None

| Rank | Score   | FASTA | BLAST                      | Hit  |
|------|---------|-------|----------------------------|--|
| 1    | 1.0     | GFBAT | gi 251748198 gb ACT10319.1 | neuraminidase [Influenza A virus (A/Hong Kong/2369/2009(H1N1))]            |
| 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/FFD/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/23669/2009(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/248/2009(H1N1))]             |

Find closest reference strain and database hits!

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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)<br><a href="#">find closest related sequences</a> | 99.360        | <u>100.000</u>    | 3           | <a href="#">V106I</a> , <a href="#">N248D</a> , <a href="#">H275Y</a><br><a href="#">show in structure</a><br>NA drug sensitivity positions:<br><a href="#">26</a> , <a href="#">0</a> , <a href="#">1</a><br>Reduced sensitivity or resistance! |

```
>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  MNPNQKIITIGSVCHTIGHANLILQIGNIISIIVISHSIQLGNQNIETCNQSVITYENNT 200
          MNPNQKIITIGSVCHTIGHANLILQIGNIISIIVISHSIQLGNQNIETCNQSVITYENNT
Sbjct: 1   MNPNQKIITIGSVCHTIGHANLILQIGNIISIIVISHSIQLGNQNIETCNQSVITYENNT 60
```

```
Query: 201 VVNQTYVNISNTNFAAGQSVSVKLAGNSLCPVSGHAIYSKDNSIRIGSKGDVFIREF 380
          VVNQTYVNISNTNFAAGQSVSVKLAGNSLCPVSGHAIYSKDNSIRIGSKGDVFIREF
Sbjct: 61  VVNQTYVNISNTNFAAGQSVSVKLAGNSLCPVSGHAIYSKDNSIRIGSKGDVFIREF 120
```

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

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

```
Query: 741  VMTDGPSDGQASYKIFRIEKGKIVKSEVHNPNTTYECCSCYPDSSEITCVRDNNVHGSN 920
          VMTDGPB+QASYKIFRIEKGKIVKSEVHNPNTTYECCSCYPDSSEITCVRDNNVHGSN
Sbjct: 241 VMTDGPBNGQASYKIFRIEKGKIVKSEVHNPNTTYECCSCYPDSSEITCVRDNNVHGSN 300
```

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

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

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Genetics Institute ([BII](#)), Singapore  
 Medicina Genomica ([INMEGEN](#)), Mexico

Check alignment to reference hit!

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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)<br><a href="#">find closest related sequences</a> | 99.360        | <a href="#">100.000</a> | 3           | <div style="border: 2px solid red; padding: 5px;"> <a href="#">V106I</a>, <a href="#">N248D</a>, <a href="#">H275Y</a><br/> <a href="#">show in structure</a> </div> <p>NA drug sensitivity positions:<br/> <a href="#">26</a>, <a href="#">0</a>, <a href="#">1</a><br/>           Reduced sensitivity or resistance!</p> |

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

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Check list of mutations!

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Back to Reference Selection

| % AA identity | % length coverage | # mutations | List of mutations  |
|---------------|-------------------|-------------|--|
| 99.360        | 100.000           | 3           | <a href="#">V106I, H245Q, H275Y</a><br><a href="#">show in structure</a><br>NA drug sensitivity positions:<br>26, 0, 1<br>Reduced sensitivity or resistance! |

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

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

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                 | Classical H3N2 strain numbering     | 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](#).

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[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 \(including alternative numbering\)](#)

**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

**NA H275Y**

Key to alternative position numbering:

|     |  |
|-----|--|
| 275 | FluSurver numbering<br>(absolute as in 2009 H1N1 pandemic) |
| 274 | Classical H3N2 strain numbering                            |
| 275 | Classical H1N1 strain numbering                            |

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 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 \(including alternative numbering\)](#)

**FluSurver**

Biologically 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](#).

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

| % AA identity | % length coverage | # mutations | List of mutations  |
|---------------|-------------------|-------------|--|
| 99.360        | 100.000           | 3           | <a href="#">V106I, H249G, H275Y</a><br><a href="#">show in structure</a> |

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

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

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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 |                  |                |

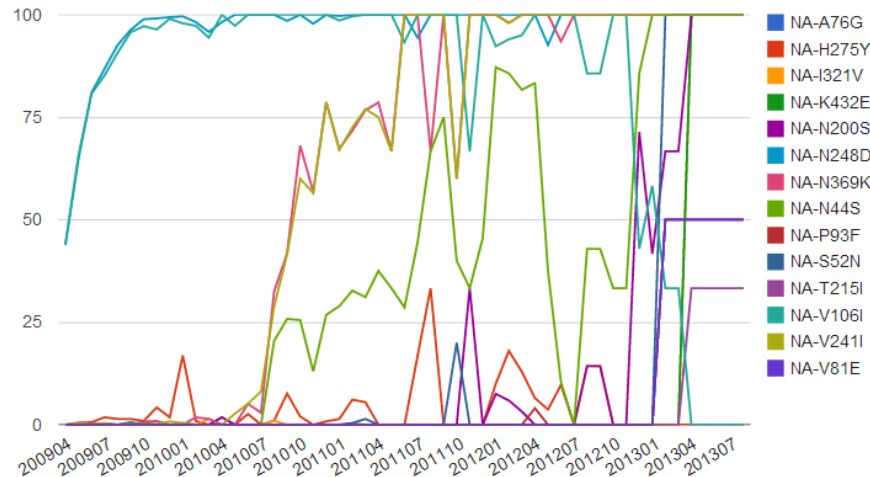
Sequences were compared to reference strain A/California/07/2009(H1N1) [AGM53851](#).  
Last updated on Sep 02nd 2013 by Raphael Tze Chuen Lee

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) |
| AEL94621  | 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/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](#)



# 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 M549I | 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                     |
|                |                                    |                         |            |        |                         | T14I A26T P100S D114N P200S S220T R222K I233V  |                   |   |      |      |             |     |                              |

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  
 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 \(including alternative numbering\)](#)

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 US National Library of Medicine National Institutes of Health

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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 influenza AND (neuraminidase OR NA) AND (H275Y OR H274Y)

Display Settings: Summary, 20 per page, Sorted by Pub Date

Send to:

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 |
|---------------------|-------------------------------------|---------------------------------|---------------------------------|
| 275                 |                                     | 274                             | 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](#).

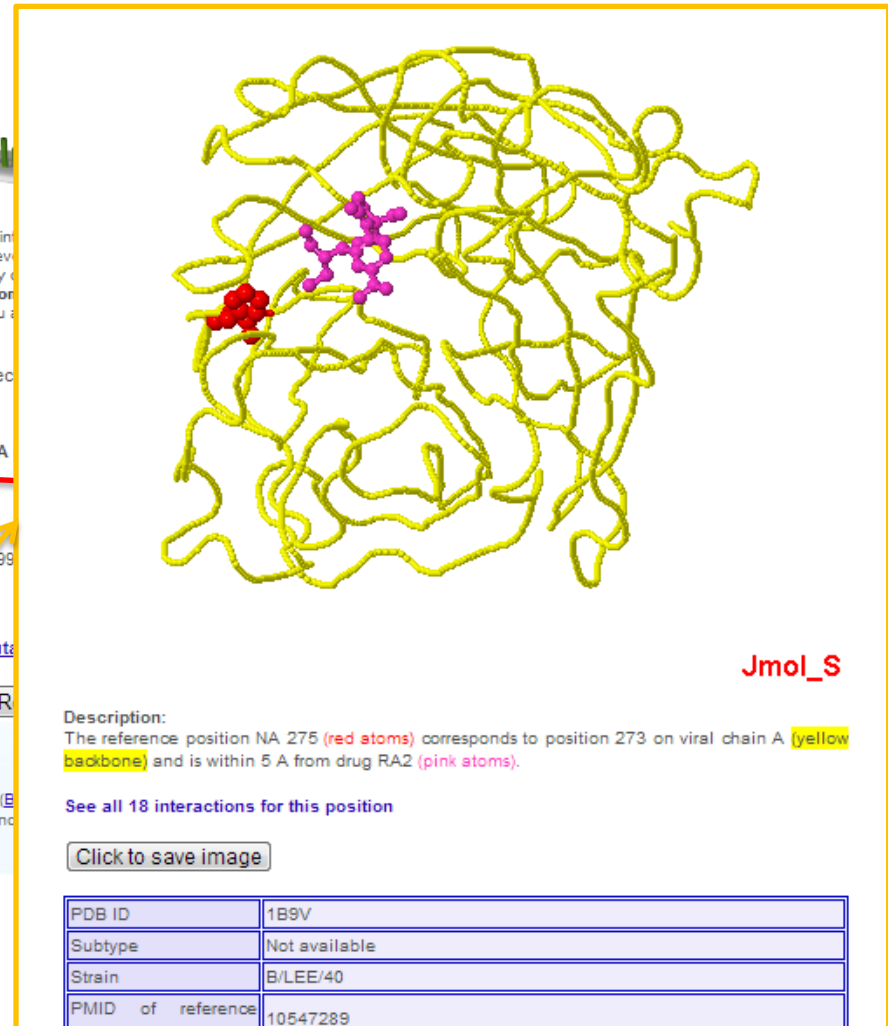
As seen in resolved structures of proteins from related strains, the NA position equivalent to your mutation is involved in:

- [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 \(including alternative numbering\)](#)



Check for structural interactions!

# 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

**NA H275Y**

Key to alternative position numbering:

|     |  |
|-----|--|
| 275 | FluSurver numbering<br>(absolute as in 2009 H1N1 pandemic) |
| 274 | Classical H3N2 strain numbering                            |
| 275 | Classical H1N1 strain numbering                            |

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 \(including alternative numbering\)](#)

FluSurver

logically 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](#).

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

| % AA identity   | % length coverage       | # mutations | List of mutations  |
|---|-------------------------|-------------|--|
| 99.360  | <a href="#">100.000</a> | 3           | <a href="#">V106I, N244S</a> <b>H275Y</b><br><a href="#">show in structure</a> |
| NA drug sensitivity positions:<br><b>26, 0, 1</b><br>Reduced sensitivity or resistance! |                         |             |  |

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

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Institute ([BII](#)), Singapore  
 Institute Genomica ([INMEGEN](#)), Mexico

Check for stability  
or passage effect  
(if available)!

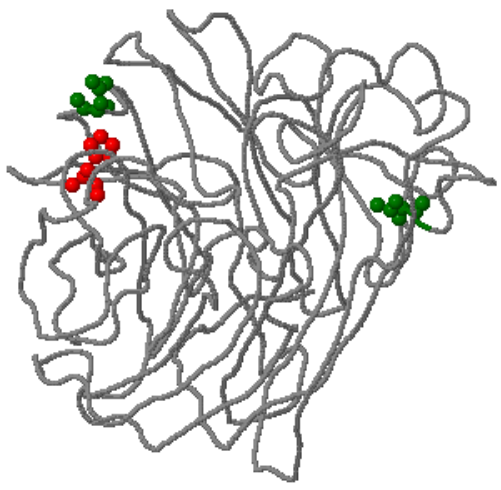
# FluSurver – an online tool to make sequence analysis and mutation detection/interpretation easier

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  
 eatment should not be based solely on these computational predictions.  
 ted 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           | <b>V106I, N248D, H275Y</b><br><a href="#">show in structure</a> |

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 |
|---------------------------|---|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|-----|
| 3NSS                      | SVELAGNSSLCPVSGWAIYSKDNVIRIGSGKGVFVIREPFISSCFLECRITFLLTQALLNDKHSNGTIDKRSFYRTIMSCPIGEVSPYNSRFESVANSASACHDGINWLTIGISGPDNGAVAVLYNGIITDTIKSRNNILRTQSEEC |    |    |    |    |    |    |    |    |     |     |     |     |     |     |
| NA_H1N1_2009_California07 | SVELAGNSSLCPVSGWAIYSKDNVIRIGSGKGVFVIREPFISSCFLECRITFLLTQALLNDKHSNGTIDKRSFYRTIMSCPIGEVSPYNSRFESVANSASACHDGINWLTIGISGPDNGAVAVLYNGIITDTIKSRNNILRTQSEEC |    |    |    |    |    |    |    |    |     |     |     |     |     |     |
| _consrvd                  | .....   |    |    |    |    |    |    |    |    |     |     |     |     |     |     |

|                           | 160  | 170 | 180 | 190 | 200 | 210 | 220 | 230 | 240 | 250 | 260 | 270 | 280 | 290 | 300 |
|---------------------------|--|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 3NSS                      | ACVNGSCFTTWMIDGSPNGQASVKIFRIEGRKIVKSVEMNAPHYHVEECSCVPSSEITCVCRDNNHGSNRPFWISFMQWLEYQIGVICSQIFGDNFRPDKTIGSCGFSVNSGANGVGFSTFYNGGVWIGRIKSISSRNGFEMINDFWGWT |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| NA_H1N1_2009_California07 | ACVNGSCFTTWMIDGSPNGQASVKIFRIEGRKIVKSVEMNAPHYHVEECSCVPSSEITCVCRDNNHGSNRPFWISFMQWLEYQIGVICSQIFGDNFRPDKTIGSCGFSVNSGANGVGFSTFYNGGVWIGRIKSISSRNGFEMINDFWGWT |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| _consrvd                  | .....  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

|                           | 310  | 320 | 330 | 340 | 350 | 360 | 370 | 380 | 390 |
|---------------------------|--|-----|-----|-----|-----|-----|-----|-----|-----|
| 3NSS                      | GTNNFISIKQDIVGINESGYSGSFVQHPFELTGLDCIRPCFWELIRGRPEENTINTSGSSISFCGVNSDTVGNWFDGAEPLPTIID |     |     |     |     |     |     |     |     |
| NA_H1N1_2009_California07 | GTNNFISIKQDIVGINESGYSGSFVQHPFELTGLDCIRPCFWELIRGRPEENTINTSGSSISFCGVNSDTVGNWFDGAEPLPTIID |     |     |     |     |     |     |     |     |
| _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.

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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)

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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, USA.

| 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) | <a href="#">3D</a>                  |
| E119    | wt   | 119 (N2) | sensitive                            | <a href="#">3D</a>                  |
| L134    | wt   | 134 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| Q136    | wt   | 136 (N2) | sensitive                            | -                                   |
| D151    | wt   | 151 (N2) | sensitive                            | <a href="#">3D</a>                  |
| Y155    | wt   | 155 (N2) | sensitive                            | -                                   |
| R156    | wt   | 156 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| S180    | wt   | 179 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| I223    | wt   | 222 (N2) | sensitive                            | <a href="#">3D</a>                  |
| L224    | wt   | 223 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| R225    | wt   | 224 (N2) | sensitive                            | <a href="#">3D</a>                  |
| T226    | wt   | 225 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| Q227    | wt   | 226 (N2) | sensitive                            | -                                   |
| E228    | wt   | 227 (N2) | sensitive                            | <a href="#">3D</a>                  |
| G245    | wt   | 244 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| P246    | wt   | 245 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| S247    | wt   | 246 (N2) | sensitive                            | <a href="#">3D</a>                  |
| N248D   | mt   | 247 (N2) | no known effect (mt)                 | <a href="#">3D</a>                  |
| H275Y   | mt   | 274 (N2) | effect                               | <a href="#">3D</a>                  |
| E277    | wt   | 276 (N2) | sensitive                            | <a href="#">3D</a>                  |
| R293    | wt   | 292 (N2) | sensitive                            | <a href="#">3D</a>                  |
| N344    | wt   | 347 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| G345    | wt   | 348 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| G348    | wt   | 351 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| R368    | wt   | 371 (N2) | sensitive                            | <a href="#">3D</a>                  |
| G401    | wt   | 405 (N2) | no known effect (common wildtype AA) | <a href="#">3D</a>                  |

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 candidates for avian flu and novel reassortant swine flu is a special note for using FluSurver results in publications.

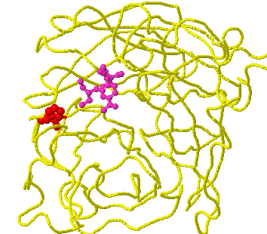
Reference Selection

Reference # 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)<br><a href="#">find closest related sequences</a> | 98.780        | <a href="#">84.536</a> | 1           | <a href="#">V271</a><br><a href="#">show in structure</a><br><div> M2 drug sensitivity positions:<br/> <a href="#">16</a>, <a href="#">0</a>, <a href="#">2</a><br/> 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                            | <a href="#">3D</a>                  |
| V271    | mt   | 27       | effect                               | <a href="#">3D</a>                  |
| A30     | wt   | 30       | sensitive                            | <a href="#">3D</a>                  |
| N31     | wt   | 31       | effect                               | <a href="#">3D</a>                  |
| I33     | wt   | 33       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| G34     | wt   | 34       | sensitive                            | <a href="#">3D</a>                  |
| I35     | wt   | 35       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| H37     | wt   | 37       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| L38     | wt   | 38       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| L40     | wt   | 40       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| W41     | wt   | 41       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| I42     | wt   | 42       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| L43     | wt   | 43       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| D44     | wt   | 44       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |
| R45     | wt   | 45       | no known effect (common wildtype AA) | <a href="#">3D</a>                  |

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)

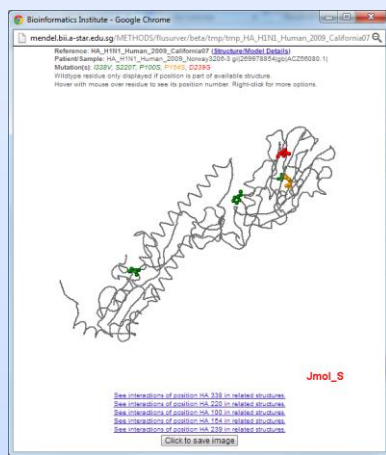
#### Comment:

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 2013

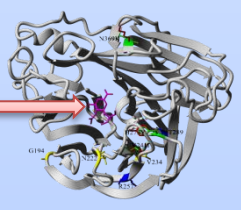


Map mutations to structure

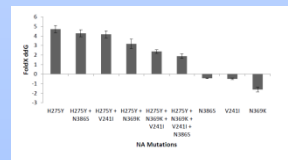
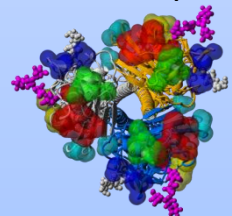
250+  
reference  
homology  
models

|      |                                       |
|------|---------------------------------------|
| 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 |

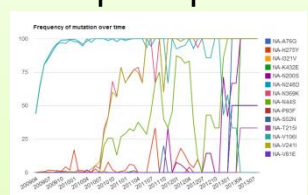
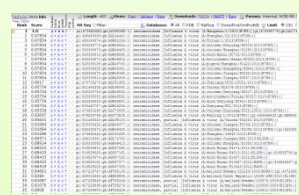
Structure

Literature

Epidemiology

Closest DB hits

Temporal pattern



Genomic co-occurrence

Regional & global occurrence



# Coming up: FluServer inside GISAID

The screenshot displays the GISAID FluServer web application interface. The main navigation bar includes links for Welcome, News, Registered Users, EpiFlu™, FAQ, My profile, and About GISAID. The user is logged in as Sebastian Maurer-Stroh.

The main application scenario for FluServer is to highlight phenotypically or epidemiologically interesting candidate mutations for further research. The interface shows a search for the HA Q242L mutation, with results for HA\_A/Anhui/1/2013\_138739, HA\_A/Shanghai/1/2013\_138737, and HA\_A/Shanghai/2/2013\_138738.

The search results table shows the following data:

| Query                       | Best reference hit            | % AA identity | % length coverage | # mutations | List of mutations   |
|-----------------------------|-------------------------------|---------------|-------------------|-------------|---|
| HA_A/Anhui/1/2013_138739    | A/Netherlands/2/19/2003(H7N7) | 96.071        | 88.418            | 22          | V18I, S20I, V63I, I137A, T199A, D190S, I185V, Q202V, T205A, I218V, Q242L, I252M, E286G, N314D, E328R, R347G, T419I, R423K, M436I, H464D, I516H, A550V |
| HA_A/Shanghai/1/2013_138737 | A/Netherlands/2/19/2003(H7N7) | 96.071        | 88.418            | 22          | V18I, S20I, V63I, I137A, T199A, A153S, D190H, I185V, T205A, I218V, P217T, I252M, E286G, N320D, H239Y, N314D, E328R, R347G, R423K, M436I, H464D, I516H |
| HA_A/Shanghai/2/2013_138738 | A/Netherlands/2/19/2003(H7N7) | 96.071        | 88.418            | 22          | V18I, S20I, V63I, I137A, T199A, D190S, I185V, Q202V, T205A, I218V, Q242L, I252M, E286G, N314D, E328R, R347G, T419I, R423K, M436I, H464D, I516H, A550V |

The interface also includes a map of the world showing the location of the mutation and a detailed view of the HA Q242L mutation. The detailed view shows the key to alternative position numbering, the mutation's location in the protein structure, and its effect on receptor binding.

**HA Q242L**

Key to alternative position numbering:

- FluServer numbering (absolute as in 2009 H1N1 pandemic)
- Classical H3N2 strain numbering
- 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 shift / 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

**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 SA<sub>2,6</sub>Gal and decreasing affinity to SA<sub>2,3</sub>Gal (Table1.).  
**Literature reference**  
 (Mutation Q226L in the paper is at an equivalent position of the mutation in your query)

Contact: [flusurver@gisaid.org](mailto:flusurver@gisaid.org)