5. Eldin C, Melenotte C, Mediannikov O, Ghigo E, Million M, Edouard S, et al. From Q fever to *Coxiella burnetii* infection: a paradigm change. Clin Microbiol Rev. 2017;30:115–90. https://doi.org/10.1128/CMR.00045-16

6. Fournier P-E, Marrie TJ, Raoult D. Diagnosis of Q fever. J Clin Microbiol. 1998;36:1823–34. https://doi.org/10.1128/JCM.36.7.1823-1834.1998

7. Sahu R, Rawool DB, Vinod VK, Malik SV, Barbudhde SB. Current approaches for the detection of *Coxiella burnetii* infection in humans and animals. J Microbiol Methods. 2020;179:106087. https://doi.org/10.1016/j.mimet.2020.106087

8. Way Rose BM, Allender MC. Health assessment of wild eastern box turtles (*Terrapene carolina carolina*) in east Tennessee. J Herpetological Med Surg. 2011;21:107. https://doi.org/10.5818/1529-9651-21.4.107

9. Archer GA, Phillips CA, Adamovicz L, Band M, Byrd J, Allender MC. Detection of copathogens in free-ranging eastern box turtles (*Terrapene carolina carolina*) in Illinois and Tennessee. J Zoo Wildl Med. 2017;48:1127–34. https://doi.org/10.1638/2017-0148R.1

10. Klee SR, Tyczka J, Ellerbrok H, Franz T, Linke S, Baljer G, et al. Highly sensitive real-time PCR for specific detection and quantification of *Coxiella burnetii*. BMC Microbiol. 2006;6:2. https://doi.org/10.1186/1471-2180-6-2

Address for correspondence: William E. Sander, Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign, 1008 W Hazelwood Dr, Urbana, IL 61801-3028, USA; email: wsander@illinois.edu

---

**Reassortant Influenza A(H1N1)pdm09 Virus in Elderly Woman, Denmark, January 2021**

Jakob N. Nissen, Sophie J. George, Charlotte K. Hjulsager, Jesper S. Krog, Xiaohui C. Nielsen, Tina V. Madsen, Klara M. Andersen, Tyra G. Krause, Lasse S. Vestergaard, Lars E. Larsen, Ramona Trebbien

Author affiliations: Statens Serum Institut, Copenhagen, Denmark (J.N. Nissen, C.K. Hjulsager, J.S. Krog, K.M. Andersen, T.G. Kause, L.S. Vestergaard, R. Trebbien); University of Copenhagen, Copenhagen (S.J. George, L.E. Larsen); Zealand University Hospital, Koege, Denmark (X.C. Nielsen, T.V. Madsen)

DOI: https://doi.org/10.3201/eid2712.211361

A case of human infection with influenza A(H1N1)pdm09 virus containing a nonstructural gene highly similar to Eurasian avian-like H1Nx swine influenza virus was detected in Denmark in January 2021. We describe the clinical case and report testing results of the genetic and antigenic characterizations of the virus.

Human infection with swine influenza A virus (IAV) had not previously been detected in Denmark, but sporadic cases have been reported from other countries (1). We report the identification of a case of zoonotic swine influenza infection in Denmark during a low-activity influenza season.

The variant IAV was detected by the National Influenza Center at Statens Serum Institut (Copenhagen, Denmark), as part of routine surveillance. A sputum sample was collected on January 21, 2021, in Zealand, Denmark, from a female patient in her 70s with various concurrent conditions, including a chronic respiratory disease, who was admitted to hospital after 2 days of moderate influenza-like symptoms: fever (39°C), coughing, sore throat, and difficulty breathing. The patient sample was positive for IAV in analyses at the local hospital microbiology laboratory; remaining sample material was submitted to the National Influenza Center, which confirmed it positive for influenza A(H1N1)pdm09 (Appendix, https://wwwnc.cdc.gov/EID/article/27/12/21-1361-App1.pdf).

We performed whole genome sequencing on the virus (2), and named it A/Denmark/1/2021 (vH1N1), and submitted to GISAID (https://www.gisaid.org; accession no. EPI_ISL_909652). BLAST (https://blast.ncbi.nlm.nih.gov/Blast.cgi) and phylogenetic analyses revealed that all segments except the nonstructural gene belonged to influenza A(H1N1)pdm09 clade 1A.3.3.2 (3), which is most similar (97%–98% nt identity) to viruses collected from swine in France and Germany in 2014 and 2015 (Table; Figure). The nonstructural gene was most similar (95%) to Eurasian avian-like H1Nx swine influenza viruses of clade 1C. No segments had a near-exact match to sequences in GenBank or GISAID, and all were distinct from the seasonal vaccine strain, A/Guangdong-Maonan/SWL1536/2019 (Table).

Because of the suspected swine origin of the case virus, we used whole-genome sequencing to retrospectively analyze 68 IAVs with a hemagglutinin (HA) gene belonging to clade 1A.3.3.2 sampled from swine herds in Denmark during 2020–2021. Nine of the samples, collected April 2020–January 2021 from ≥7 different herds in different parts of Denmark, including Zealand, contained the same
gene constellation as the case virus (98.9%–99.4% nt identity). This finding suggests that the virus from the human case originated from swine in Denmark.

The patient and her husband reside in the countryside, <2 km from a medium-sized farm with finisher pigs. Because of coronavirus disease pandemic restrictions, she had not been in close contact with other persons or been close to the pig farm. Both the patient and her husband, who had no signs of illness, were vaccinated against seasonal influenza in October or November 2020. European General Data Protection Regulation (https://gdpr.eu) restrictions on reporting personally identifiable information prevent revealing additional information about the patient or the farm.

Veterinary authorities in Denmark collected nose swab samples from 68 pigs at the neighboring farm on February 1, 2021, according to standard procedures. All samples tested negative by PCR for IAV. Because of the high prevalence of influenza-positive herds in Denmark, we could not be confident potential seropositive swine were infected by the virus in question, so we did not take blood samples. However, we therefore could not exclude previous virus circulation in the herd, because swabs were taken 11 days after virus detection in the patient. According to the Danish Meteorological Institute, the patient’s residence was downwind of the pig herd most days preceding clinical symptoms.

Most of the case virus genes were derived from influenza A(H1N1)pdm09, which has been circulating in the human population of Denmark since 2009. However, the HA gene is different from that of the strains currently circulating (4), and it is therefore difficult to predict the level of immunity in the human population against this virus. Antigenic characterization (5) showed no or very poor cross-reactivity to all reference antiserum used for analysis (Appendix Table 1), and the HA gene contained several more mutations at antigenic sites compared with the seasonal vaccine strain (Appendix Figure). Therefore, vaccine effectiveness of the 2020–2021 seasonal influenza vaccine against the variant virus has been assessed as low.

Neuraminidase inhibition tests showed no reduction of oseltamivir or zanamivir inhibition, and the viral genome contains no known antiviral mutations except the V27A mutation in the M2 gene, known from most other H1N1 viruses circulating in human and swine (6,7). We identified no amino acid changes presumed to be related to increased risk of human infection (8), but further in vitro and in vivo analyses are planned to explore this possibility.

Because national coronavirus disease pandemic restrictions limited interpersonal contact, there

---

### Table. Percentage identity similarity between gene and protein segments of influenza virus isolate A/Denmark/1/2021 (vH1N1) from a patient in Denmark and reference viruses from GISAID*

| A/Denmark/1/2021 (vH1N1) segment | A/swine/Luedinghausen/21728/2015† | A/California/07/2009‡ | A/Guangdong-Maonan/SWL1536/2019¶ | A/swine/Denmark/3797–4/2020§ |
|---------------------------------|---------------------------------|----------------------|----------------------------------|-------------------------------|
| Amino acid                      |                                 |                      |                                  |                               |
| PB2                             | 98.7                            | 97.5                 | 97.6                             | 100                           |
| PB1                             | 99.5                            | 99.3                 | 98.7                             | 99.9                          |
| PA                              | 98.9                            | 98.0                 | 98.3                             | 99.6                          |
| PA-X                            | 98.7                            | 97.4                 | 97.0                             | 99.6                          |
| HA                              | 97.3                            | 92.0                 | 91.9                             | 99.3                          |
| NP                              | 99.0                            | 99.0                 | 98.2                             | 100                           |
| NA                              | 97.9                            | 95.1                 | 91.9                             | 99.8                          |
| M1                              | 98.8                            | 98.4                 | 97.6                             | 100                           |
| M2                              | 96.9                            | 96.9                 | 93.8                             | 100                           |
| NS1                             | 76.5                            | 77.4                 | 74.7                             | 99.5                          |
| NEP                             | 85.1                            | 86.0                 | 85.1                             | 99.2                          |
| Nucleotide                      |                                 |                      |                                  |                               |
| PB2                             | 98.0                            | 96.1                 | 94.7                             | 99.8                          |
| PB1                             | 96.8                            | 95.9                 | 93.8                             | 99.2                          |
| PA                              | 98.0                            | 96.7                 | 95.4                             | 99.4                          |
| HA                              | 97.3                            | 94.4                 | 93.0                             | 99.4                          |
| NP                              | 97.4                            | 96.4                 | 94.5                             | 99.4                          |
| NA                              | 97.4                            | 96.1                 | 93.7                             | 99.5                          |
| MP                              | 97.8                            | 97.4                 | 95.9                             | 99.9                          |
| NS                              | 80.2                            | 80.3                 | 80.3                             | 99.8                          |

*GISAID, https://www.gisaid.org. PB1/PB2, polymerase basic protein 1/2; PA, polymerase acidic protein; HA, hemagglutinin; NP, nucleoprotein; NA, neuraminidase; MP/M1/M2, matrix protein 1/2; NS/NS1; nonstructural protein; NEP, nuclear export protein
†GISAID accession EPI_ISL_504870.
‡GISAID accession EPI_ISL_227813.
¶GISAID accession EPI_ISL_377080.
§GISAID accession EPI_ISL_1673688.
were only 46 confirmed influenza cases in Denmark during the 2020–2021 season, and transmission of the variant virus was considered negligible. The Danish Patient Authority did not identify any person-to-person swine influenza transmission, and no further public health response measures were enacted.

The effects of the most recent swine influenza pandemic and the extensive diversity and reassortment in swine influenza viruses indicate the obvious zoonotic potential of these viruses (9,10). Therefore, more attention should be given to routine detection and control of swine influenza viruses.

Acknowledgments
We thank laboratory technicians Mille Weissman Poulsen, Carina Bøgh Folsing, Jesper Rønn, Sari Mia Dose, and Sophia Rasmussen for technical assistance in the laboratory.

This work was conducted as part of the national influenza surveillance in Denmark, which is funded by the government.

About the Author
Dr. Nissen is a postdoctoral researcher at the National Influenza Center, Statens Serum Institut, Copenhagen,
Denmark. With a background in genomics and bioinformatics, he focuses on bioinformatic tool development and the prediction of the zoonotic potential of influenza viruses.

References

1. Dürrwald R, Wedde M, Biere B, Oh D-Y, Heßler-Klee M, Geidel C, et al. Zoonotic infection with swine A/H1_N1 influenza virus in a child, Germany, June 2020. Euro Surveill. 2020;25:2001638. https://doi.org/10.2807/1560-7917.ES.2020.25.42.2001638

2. Trebbien R, Pedersen SS, Vorborg K, Franck KT, Fischer TK. Development of oseltamivir and zanamivir resistance in influenza A(H1N1)pdm09 virus, Denmark, 2014. Euro Surveill. 2017;22:30445. https://doi.org/10.2807/1560-7917.ES.2017.22.3.30445

3. Anderson TK, Macken CA, Lewis NS, Scheuermann RH, Van Reeth K, Brown IH, et al. A phylogeny-based global nomenclature system and automated annotation tool for H1 hemagglutinin genes from swine influenza A viruses. MSphere. 2016;1:e00275–16. https://doi.org/10.1128/mSphere.00275-16

4. Melidou A, Pereyaslov D, Hungnes O, Prosenc K, Alm E, Adlhoch C, et al.; WHO European Region influenza surveillance network; WHO European Region Influenza Surveillance Network author list. Virological surveillance of influenza viruses in the WHO European Region in 2019/20—impact of the COVID-19 pandemic. Euro Surveill. 2020;25:2001822. https://doi.org/10.2807/1560-7917.ES.2020.25.46.2001822

5. World Health Organization Global Influenza Surveillance Network. Manual for the laboratory diagnosis and virological surveillance of influenza. Geneva: The Organization; 2011.

6. Krumbholz A, Schmidtke M, Bergmann S, Motzke S, Bauer K, Stech J, et al. High prevalence of amantadine resistance among circulating European porcine influenza A viruses. J Gen Virol. 2009;90:900–8. https://doi.org/10.1099/vir.0.007260-0

7. Dong G, Peng C, Luo J, Wang C, Han L, Wu B, et al. Adamantane-resistant influenza a viruses in the world (1902–2013): frequency and distribution of M2 gene mutations. PLoS One. 2015;10:e0119115. https://doi.org/10.1371/journal.pone.0119115

8. GISAID. FluServer: real-time surveillance of influenza mutations [cited 2021 Mar 29]. https://flusurver.bii.a-star.edu.sg

9. Neumann G, Noda T, Kawaoka Y. Emergence and pandemic potential of swine-origin H1N1 influenza virus. Nature. 2009;459:931–9. https://doi.org/10.1038/nature08157

10. Henritzi D, Petric PP, Lewis NS, Graaf A, Pessia A, Starick E, et al. Surveillance of European domestic pig populations identifies an emerging reservoir of potentially zoonotic swine influenza A viruses. Cell Host Microbe. 2020;28:614–627.e6. https://doi.org/10.1016/j.chom.2020.07.006

Address for correspondence: Ramona Trebbien, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark; email: ratr@ssi.dk

Correction: Vol. 27, No. 10

The name of author Xiaohui Wang was misspelled in Emergomyces orientalis Emergomyces Diagnosed by Metagenomic Next-Generation Sequencing (D. He et al.). The article has been corrected online (https://wwwnc.cdc.gov/eid/article/27/10/21-0769_article).
Reassortant Influenza A(H1N1)pdm09 Virus in Elderly Woman, Denmark, January 2021

Appendix

Methods for Virus Detection and Analysis

We collected sputum samples and analyzed them at the local hospital microbiology laboratory with the SARS-CoV-2 Flu (A+B) & RSV array (CerTest Biotec, https://www.certest.es) on the BD MAX System (Becton Dickinson, https://www.bd.com) and the Xpert Xpress Flu/RSV assay on the GeneXpert XVI system (Cepheid, https://www.cepheid.com). Subsequently, the National Influenza Center analyzed remaining sample materials using in-house real-time reverse transcription PCR to detect the matrix-, H1pdm09-, and N1pdm09-gene segments. For whole genome sequencing, a one-tube RT-PCR approach was used (1), and libraries for sequencing on the Miseq platform (Illumina, https://www.illumina.com) were prepared using the Nextera XT DNA preparation kit (Illumina) (2).

References

1. Zhou B, Donnelly ME, Scholes DT, St George K, Hatta M, Kawaoka Y, et al. Single-reaction genomic amplification accelerates sequencing and vaccine production for classical and Swine origin human influenza a viruses. J Virol. 2009;83:10309–13. PubMed https://doi.org/10.1128/JVI.01109-09

2. Trebbien R, Pedersen SS, Vorborg K, Franck KT, Fischer TK. Development of oseltamivir and zanamivir resistance in influenza A(H1N1)pdm09 virus, Denmark, 2014. Euro Surveill. 2017;22:30445. PubMed https://doi.org/10.2807/1560-7917.ES.2017.22.3.30445

3. Brownlee GG, Fodor E. The predicted antigenicity of the haemagglutinin of the 1918 Spanish influenza pandemic suggests an avian origin. Philos Trans R Soc Lond B Biol Sci. 2001;356:1871–6. PubMed https://doi.org/10.1098/rstb.2001.1001
### Appendix Table 1. Results from antigenic characterization using hemagglutination inhibition assay and microneutralization assay*

| Reference virus          | A/Guangdong-Maonan/SW1636/2019 | A/Victoria/2570/19 | A/Wisconsin/588/19 | A/Denmark/3280/29 | A/Michigan/45/15 | A/California/07/09 | A/Brisbane/02/2018 |
|--------------------------|-------------------------------|-------------------|-------------------|-------------------|------------------|-------------------|-------------------|
| Hemagglutinin inhibition test results |
| A/Guangdong-Maonan/SW1636/2019 | 2560                          | 640               | 1280              | <2560             | 640              | 640               | 640               |
| A/Victoria/2570/19        |                               |                   |                   |                   |                  |                   |                   |
| A/Wisconsin/588/19        |                               |                   |                   |                   |                  |                   |                   |
| A/Denmark/3280/29         |                               |                   |                   |                   |                  |                   |                   |
| A/Michigan/45/15          |                               |                   |                   |                   |                  |                   |                   |
| A/California/07/09        |                               |                   |                   |                   |                  |                   |                   |
| A/Brisbane/02/2018        |                               |                   |                   |                   |                  |                   | 640               |
| A/Denmark/1/2021          | <20                           | <20               | <20               | <20               | 30               | <20               | <20               |
| Microneutralization results |
| A/Michigan/45/15          |                               | 640               | 120               |                   |                  |                   |
| A/California/07/09        |                               |                   | 40                | 240               |                  |                   |
| A/Guangdong-Maonan/SW1636/2019 | 7680                          |                   |                   |                   | 1280             |                   |
| A/California/07/09        |                               |                   |                   |                   |                  |                   |
| A/Denmark/1/2021          | <20                           | 20                | 20                | 20                | <20              | 1920              | 30                |

*The case variant virus was tested against a panel of reference ferret antisera of A/H1N1pdm09 viruses provided by WHO CC, Francis Crick Institute, UK. The cross-testing of viruses and antisera are indicated with the average titer-value from duplicates. A titer below 20 is considered as no reaction. Thus, in both tests there was no cross-reactivity to the A(H1N1)pdm09 vaccine virus but to some of the other A(H1N1)pdm09 viruses at low levels.
Appendix Table 2. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from GISAID’s EpiFlu Database on which this research is based. All submitters of data may be contacted directly via www.gisaid.org.

| Segment ID* | Country          | Collection date | Isolate-ID               | Isolate name                  | Originating Lab                              | Submitting Lab                              | Authors                                                                 |
|-------------|------------------|-----------------|--------------------------|-------------------------------|----------------------------------------------|----------------------------------------------|-------------------------------------------------------------------------|
| EPI1785107  | Germany          | 2015 Aug 26     | EPI_ISL_504872           | A/swine/Soegel/22071/2015     | Import from public-domain                    | Duerrwald, R.; Groth, M.; Krumholz, A.;     | Lange, J.; Philipp, A.; Zell, R.                                        |
| EPI1785091  | Germany          | 2015 May 21     | EPI_ISL_504870           | A/swine/Luedinghausen/21728/2015 | Import from public-domain                    | Duerrwald, R.; Groth, M.; Krumholz, A.;     | Lange, J.; Philipp, A.; Zell, R.                                        |
| EPI1785075  | Germany          | 2015 Apr 15     | EPI_ISL_504868           | A/swine/Diepholz/21603/2015   | Import from public-domain                    | Duerrwald, R.; Groth, M.; Krumholz, A.;     | Lange, J.; Philipp, A.; Zell, R.                                        |
| EPI1784875  | Germany          | 2014 Aug 10     | EPI_ISL_504843           | A/swine/Wachtum/20657/2014    | Import from public-domain                    | Duerrwald, R.; Groth, M.; Krumholz, A.;     | Lange, J.; Philipp, A.; Zell, R.                                        |
| EPI1784859  | Germany          | 2014 Sep 16     | EPI_ISL_504841           | A/swine/Rosendahl/20634/2014  | Import from public-domain                    | Duerrwald, R.; Groth, M.; Krumholz, A.;     | Lange, J.; Philipp, A.; Zell, R.                                        |
| EPI1201916  | Germany          | 2017 Mar 10     | EPI_ISL_304243           | A/swine/Germany/SIR1818/2017  | Friedrich-Loeffler-Institut                  | Friedrich-Loeffler-Institut                  | Henritzi, Dinah; Harder, Timm C.                                        |
| EPI1080448  | France           | 2016 Nov 14     | EPI_ISL_281884           | A/swine/France/AR9191/2016    | Friedrich-Loeffler-Institut                  | Friedrich-Loeffler-Institut                  | Henritzi, Dinah; Harder, Timm C.                                        |
| EPI1365955  | Hungary          | 2018 Dec 17     | EPI_ISL_340478           | A/Hungary/20/2019             | National Public Health Institute             | Hungarian National Center of Epidemiology   |                                                                         |
| EPI1582934  | Cameroon         | 2019 Apr 16     | EPI_ISL_388855           | A/Yaounde/19V-2830/2019       | Centre Pasteur du Cameroun                   | Crick Worldwide Influenza Centre            |                                                                         |
| EPI1542971  | Georgia          | 2019 Apr 08     | EPI_ISL_377238           | A/Georgia/749/2019            | National Centre for Disease Control and Public Health | Crick Worldwide Influenza Centre            |                                                                         |
| EPI1748982  | Latvia           | 2016 Feb 29     | EPI_ISL_219670           | A/Latvia/03–011553/2016       | State Agency, Infectology Center of Latvia   | Crick Worldwide Influenza Centre            |                                                                         |
| EPI1543082  | Slovakia         | 2019 Apr 10     | EPI_ISL_377294           | A/Trnava/535/2019             | National Public Health Institute of Slovakia | Crick Worldwide Influenza Centre            |                                                                         |
| EPI1575087  | Russian Federation| 2019 Apr 24    | EPI_ISL_387098           | A/Sakha/3–24V/2019            | State Research Center of Virology and Biotechnology | Crick Worldwide Influenza Centre            |                                                                         |
| EPI11161425 | United States    | 2009 Apr 09     | EPI_ISL_227813           | A/California/07/2009          | Import from public-domain                    | Tan, G.; Pickett, B.; Fedorova, N.; Amedeo, P.; Isom, R.; Hu, L.; Christensen, J.; Miller, J.; Durbin, A.; Arumemi, F.; Williams, T.; Bao, Y.; Sanders, R.; Zhdanov, S.; Kiyutin, B.; Lipman, D.J.; Tatusova, T.; Hatcher, E.; Wang, J. |
| EPI1542570  | China            | 2019 Jun 17     | EPI_ISL_377080           | A/Guangdong-Maonan/SWL1536/2019 | WHO Chinese National Influenza Center       | WHO Chinese National Influenza Center       | Xiaoxu, Zeng, Yiyan, Li, Weijuan, Huang, Lei, Yang, Dayan, Wang         |
| EPI466580   | Madagascar       | 2013 May 24     | EPI_ISL_145424           | A/Madagascar/02064/2013       | Institut Pasteur de Madagascar               | National Institute for Medical Research     |                                                                         |
| Segment ID* | Country          | Collection date | Isolate-ID       | Isolate name                  | Originating Lab                                                  | Submitting Lab                                                  | Authors                                                                 |
|------------|------------------|-----------------|------------------|-------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------------|
| EPI417118  | Belgium          | 2012 Dec 07     | EPI_ISL_134397   | A/Belgium/G917/2012           | Scientific Institute of Public Health                            | National Institute for Medical Research                          |                                                                        |
| EPI346697  | Iceland          | 2011 Mar 24     | EPI_ISL_99924    | A/Iceland/59/2011             | Landspitali - University Hospital                                | National Institute for Medical Research                          |                                                                        |
| EPI417122  | Senegal          | 2012 Dec 09     | EPI_ISL_134399   | A/Dakar/20/2012               | Institut Pasteur de Dakar                                        | National Institute for Medical Research                          |                                                                        |
| EPI770076  | Japan            | 2016 Feb 01     | EPI_ISL_223792   | A/SAPPORO/18/2016             | Sapporo City Institute of Public Health                          | National Institute of Infectious Diseases                       | Takashita, Emi; Fujisaki, Seiichiro; Shirakura, Masayuki; Watanabe, Shinji; Odagiri, Takato |
| EPI347564  | Sweden           | 2011 Nov 22     | EPI_ISL_100460   | A/Stockholm/35/2011           | Public Health Agency of Sweden                                   | National Institute for Medical Research                          |                                                                        |
| EPI705858  | Hong Kong (SAR)  | 2010 Jul 16     | EPI_ISL_79623    | A/Hong Kong/2212/2010         | Government Virus Unit                                             | National Institute for Biologic Standards and Control (NIBSC)   | Nicolson, Carolyn                                                      |
| EPI319447  | Czech Republic   | 2011 Jan 18     | EPI_ISL_90718    | A/Czech Republic/32/2011      | National Institute of Public Health                              | National Institute for Medical Research                          |                                                                        |
| EPI319527  | Russian Federation| 2011 Feb 14    | EPI_ISL_90760    | A/St. Petersburg/27/2011      | WHO National Influenza Centre Russian Federation                 | National Institute for Medical Research                          |                                                                        |
| EPI466630  | South Africa     | 2013 Jun 10     | EPI_ISL_145449   | A/South Africa/3686/2013      | National Institute for Communicable Disease                     | National Institute for Medical Research                          |                                                                        |
| EPI1393451 | Norway           | 2018 Nov 27     | EPI_ISL_347404   | A/Norway/3737/2018            | WHO National Influenza Centre                                   | Crick Worldwide Influenza Centre                                |                                                                        |

*All segments are hemagglutinin.
Appendix Figure. Alignment of HA amino acid sequences of case variant virus A/Denmark/1/2021, A/California/07/2009, and seasonal vaccine strain A/Guangdong-Maonan/SWL1536/2019. The alignment is shown with H1 numbering starting after the signal peptide, and the antigenic sites Ca1, Ca2, Cb, Sa, Sb, as defined by Brownlee and Fodor (3), are indicated with shaded boxes. Mutations relative to each other have been highlighted.