Influenza Updates

The newsletter of the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne

@WHOCCFluMelb

Volume 10, Issue 1, May 2021

Preparation for the upcoming influenza season

Winter and the influenza season is fast approaching over the next few months across many southern hemisphere countries. However, ongoing mitigation strategies implemented across many countries to address the COVID-19 pandemic will likely continue to result in a significantly reduced influenza season. This is likely to remain unchanged until restrictions are lifted. This means that any sample you are able to send to us will be vital in our continued surveillance efforts.

With this in mind, please note the following points:

- Please send us your samples as soon as possible after collection, as they are most useful when they have been collected recently
- We accept both viral isolates and/or original clinical specimens
- We need to receive samples by the end of August at the very latest (and preferably earlier) in order to process them in time for the Consultation.
- The WHO Shipping Fund Project (SFP) is available to assist National Influenza Centres in covering the cost of shipping samples to WHO Collaborating Centres up to four times per year. It is recommended that one of the shipments be in July to mid-August. If you have any questions about shipping samples or would like information about accessing the WHO Shipping Fund, please contact us at *whoflu@influenzacentre.org*.

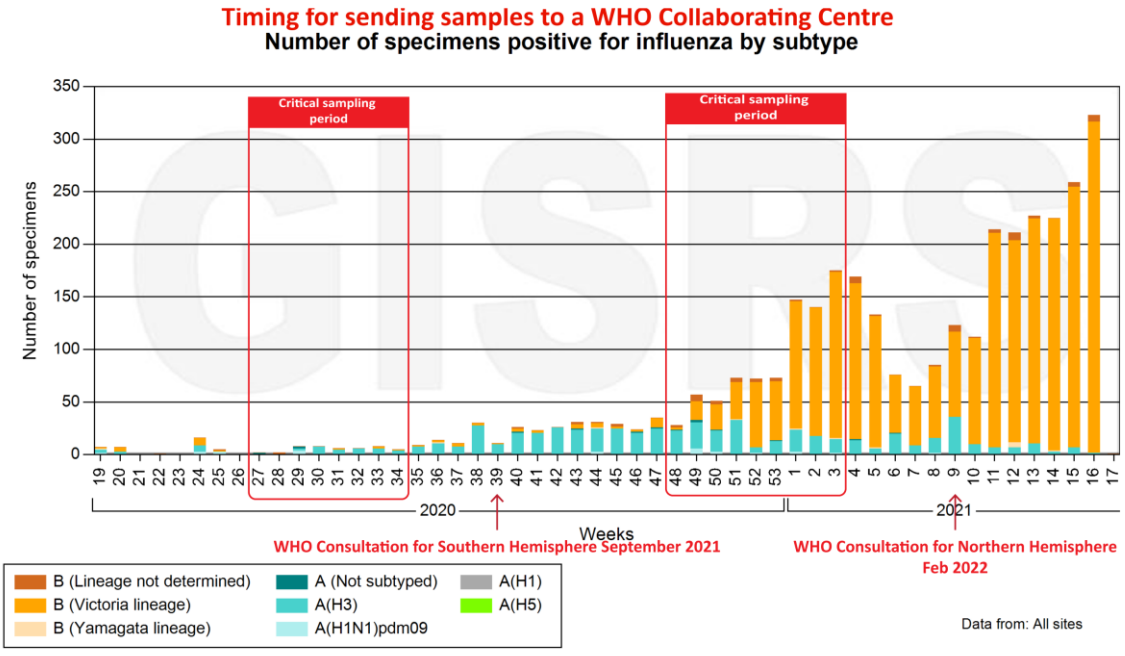


Figure adapted from FluNet: https://apps.who.int/flumart/Default?ReportNo=3&WHORegion= Western Pacific Region of WHO

WHO Collaborating Centre for Reference and Research on Influenza VIDRL

Doherty Institute

The University of Melbourne

The Royal Melbourne Hospital

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

Recommendations for Northern Hemisphere 2021-2022 vaccine announced

The WHO Consultation on the Composition of Influenza Vaccines for the northern hemisphere 2021-2022 was held as a virtual Consultation on 26 February 2021. Following the Consultation, WHO made the following recommendation:

It is recommended that **quadrivalen**t vaccines for use in the 2021-2022 northern hemisphere influenza season contain the following:

Egg-based:

- an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an A/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Cell– or recombinant-based:

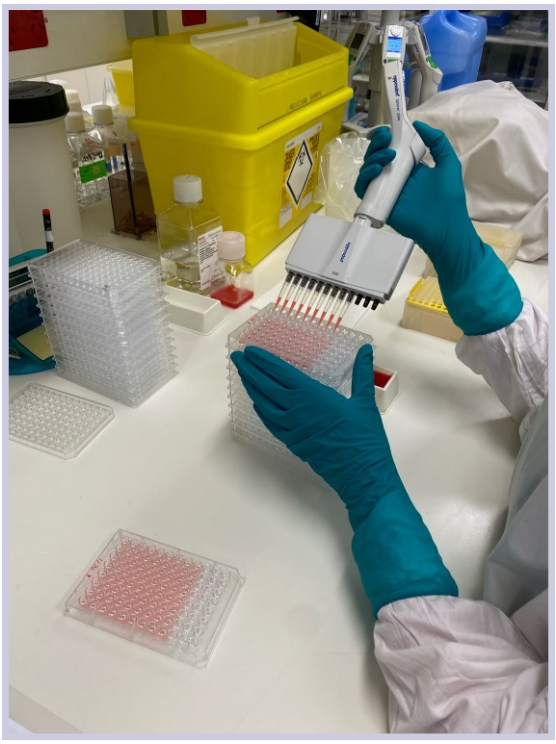
- an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;
- an A/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

The composition of trivalent influenza vaccines is recommended to include the A(H1N1)pdm09, A(H3N2), and the B Victoria lineage viruses.

The recommendations for the northern hemisphere 2021-2022 vaccine includes a change in the A(H1N1)pdm09 and A(H3N2) components of the egg-based vaccine compared to the previous vaccine recommendations for the southern hemisphere 2020. The changes in the recommended A(H1N1)pdm09 and A(H3N2) components reflect increasing proportions of circulating virus that were similar to these updated strains, compared to previous vaccine viruses. More details about the most recent recommendations can be found here.

Contribution of National Influenza Centres to the vaccine recommendations

We thank everyone who has sent us influenza samples prior to the Consultation. Your viruses provide essential data on recently circulating strains and help to inform the choice of recommended vaccine strains. We are especially pleased that the most recently added A(H1N1)pdm09 virus, A/Victoria/2570/2019, was originally submitted to us by **The Alfred Hospital** in Melbourne. In addition, the most recently added A(H3N2) virus, A/Cambodia/e0826360/2020, was originally submitted to us by **Institut Pasteur du Cambodge** in Cambodia.



In this context, we would like to acknowledge the contribution and critical role played by WHO National Influenza Centres and other submitting laboratories in providing influenza samples to WHO Collaborating Centres, not only for the purposes of analysis and surveillance, but also for the provision of potential vaccine candidates. Please continue to send us your samples. The need for constant surveillance remains as the influenza virus continues to circulate and evolve.

Global virus tracker - 'Where I Work' series

Centre Director Kanta Subbarao was featured in an article that is part of the '**Where I Work**' series published by Nature.

In the article, she discusses her ongoing work with respiratory viruses, in particular SARS-CoV-2 and influenza, and also of her changing work environment during this ongoing pandemic.

Read the article here.

(Image credit: Daniel Mahon for *Nature*)

Upcoming meetings and conferences

COVID-19, Influenza and RSV: Surveillance-informed prevention and treatment

19-21 October 2021

The conference will address the evolution, epidemiology and impact of SARS-CoV-2, influenza, RSV and other respiratory viruses, implications for surveillance strategies and progress on vaccines, antivirals, immunomodulators, and other countermeasures.

To view the preliminary program, click here.
For abstract submission and registration, click here.

Australian Society for Microbiology Virology Special Interest Group Online Meeting

ASM Virology Special Interest Group
Online Meeting Announcement

The Australian Society for Microbiology
bringing Microbiologists together

Tuesday June 15, 7-8.15 PM AEST

Invited speaker:
Assoc. Professor Sheena Sullivan, Doherty Institute

Long-term SARS-CoV-2 antibody responses in a cohort of returned cruise ship passengers

Head Epidemiologist Sheena Sullivan will be speaking as part of ASM Virology's monthly meeting.

For registration details, click here.

FEMS Best Article of 2020 Award

FEMS Microbiology Reviews, fuaa026, 44, 2020, 631–644

doi: 10.1093/femsre/fuaa026
Advance Access Publication Date: 16 July 2020
Review Article

REVIEW ARTICLE

Wild birds as reservoirs for diverse and abundant gamma- and deltacoronaviruses

Michelle Wille[1,*,†] and Edward C. Holmes[2,†]

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One sentence summary: Although wild birds are hosts to numerous species of gammacoronaviruses and deltacoronaviruses, some of which infect domestic birds or are able to spill-over into mammals, we reveal the limitations to our current understanding of their diversity, ecology and evolution.

Editor: Blossom Damania
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ABSTRACT

Wild birds interconnect all parts of the globe through annual cycles of migration with little respect for country or continental borders. Although wild birds are reservoir hosts for a high diversity of gamma- and deltacoronaviruses, we have little understanding of the ecology or evolution of any of these viruses. In this review, we use genome sequence and ecological data to disentangle the evolution of coronaviruses in wild birds. Specifically, we explore host range at the levels of viral genus and species, and reveal the multi-host nature of many viral species, albeit with biases to certain types of avian host. We conclude that it is currently challenging to infer viral ecology due to major sampling and technical limitations, and suggest that improved assay performance across the breadth of gamma- and deltacoronaviruses, assay standardization, as well as better sequencing approaches, will improve both the repeatability and interpretation of results. Finally, we discuss cross-species virus transmission across both the wild bird – poultry interface as well as from birds to mammals. Clarifying the ecology and diversity in the wild bird reservoir has important ramifications for our ability to respond to the likely future emergence of coronaviruses in socioeconomically important animal species or human populations.

Keywords: avian coronavirus; *Coronaviridae*; coronavirus; deltacoronavirus; gammacoronavirus; infectious bronchitis virus; IBV; wild birds

Wille M, Holmes EC. Wild birds as reservoirs for diverse and abundant gamma- and deltacoronaviruses. FEMS Microbiol Rev. 2020 Sep 1;44(5):631-644. doi: 10.1093/femsre/fuaa026. Pubmed Link

Michelle Wille's article, '***Wild birds as reservoirs for diverse and abundant gamma- and deltacoronaviruses***' was chosen as the Best Article of 2020 by the journal Federation of European Microbiological Studies (FEMS) Microbiology Reviews.

This review investigates the prevalence of coronaviruses in wild birds, and highlights the importance of surveillance in managing viral pathogens that may become a risk to the human population in the future.

Read the full article here.

Featured Research Article

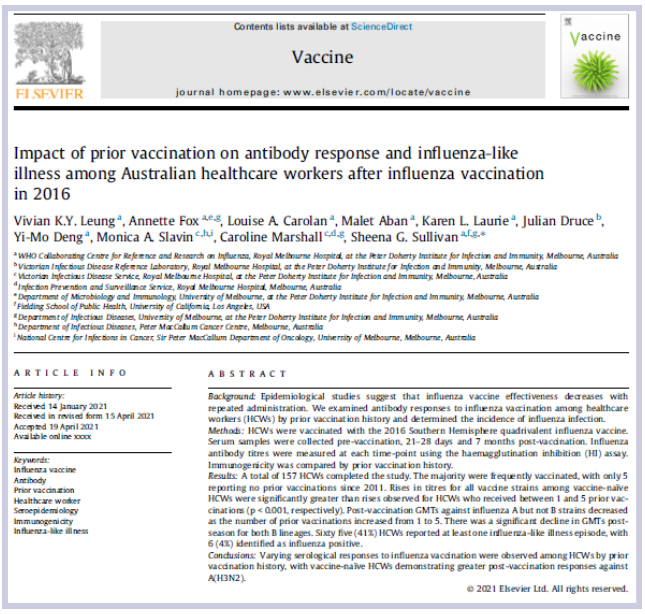
'Impact of prior vaccination on antibody response and influenza-like illness among Australian healthcare workers after influenza vaccination in 2016'

Featuring Vivian Leung, Annette Fox, Louise Carolan, Malet Aban, Yi-Mo Deng, and Sheena Sullivan from the Centre

Published online in *Vaccine* this May, the article describes the differences in the antibody response elicited between cohorts of healthcare workers. The workers were grouped depending on the frequency of prior influenza vaccination before the commencement of the study.

Particularly for A(H3N2), the antibody response was stronger in those with no prior history of vaccination.

Read the full article here.



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Impact of prior vaccination on antibody response and influenza-like illness among Australian healthcare workers after influenza vaccination in 2016

Vivian K.Y. Leung[a], Annette Fox[a,e,g], Louise A. Carolan[a], Malet Aban[a], Karen L. Laurie[a], Julian Druce[b], Yi-Mo Deng[a], Monica A. Slavin[c,h,i], Caroline Marshall[c,d,g], Sheena G. Sullivan[a,f,g,*]

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ABSTRACT

Background: Epidemiological studies suggest that influenza vaccine effectiveness decreases with repeated administration. We examined antibody responses to influenza vaccination among healthcare workers (HCWs) by prior vaccination history and determined the incidence of influenza infection.
Methods: HCWs were vaccinated with the 2016 Southern Hemisphere quadrivalent influenza vaccine. Serum samples were collected pre-vaccination, 21–28 days and 7 months post-vaccination. Influenza antibody titres were measured at each time-point using the haemagglutination inhibition (HI) assay. Immunogenicity was compared by prior vaccination history.
Results: A total of 157 HCWs completed the study. The majority were frequently vaccinated, with only 5 reporting no prior vaccinations since 2011. Rises in titres for all vaccine strains among vaccine-naïve HCWs were significantly greater than rises observed for HCWs who received between 1 and 5 prior vaccinations ($p < 0.001$, respectively). Post-vaccination GMTs against influenza A but not B strains decreased as the number of prior vaccinations increased from 1 to 5. There was a significant decline in GMTs post-season for both B lineages. Sixty five (41%) HCWs reported at least one influenza-like illness episode, with 6 (4%) identified as influenza positive.
Conclusions: Varying serological responses to influenza vaccination were observed among HCWs by prior vaccination history, with vaccine-naïve HCWs demonstrating greater post-vaccination responses against A(H3N2).

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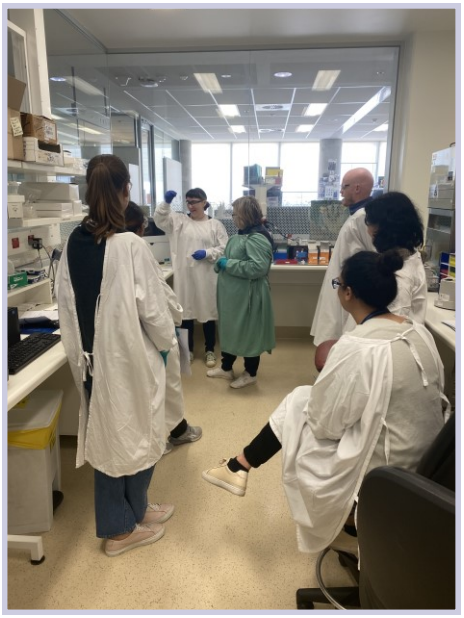
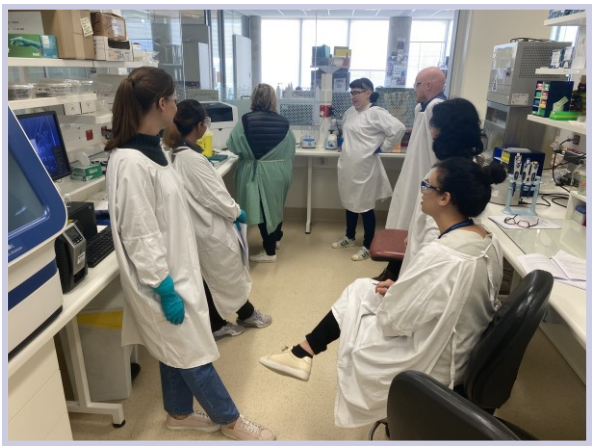
Leung VKY, Fox A, Carolan LA, Aban M, Laurie KL, Druce J, Deng YM, Slavin MA, Marshall C, Sullivan SG. Impact of prior vaccination on antibody response and influenza-like illness among Australian healthcare workers after influenza vaccination in 2016. Vaccine. 2021 May 10:S0264-410X(21)00483-7. doi: 10.1016/j.vaccine.2021.04.036 . Pubmed Link

Next-Generation Sequencing (NGS) Workshop

The Molecular and Bioinformatics groups at the Centre ran an in-house training workshop titled, 'Influenza virus whole genome sequencing (WGS) using iSeq™ 100' between 11-14 May. The workshop involved training Centre staff on the use of the Illumina iSeq™ 100, as well as some data processing and analysis techniques.





Genomics Gone Viral Symposium

Centre Deputy Director Ian Barr gave a presentation titled, 'Genomics for influenza', as part of the Peter Doherty Institute's ***Genomics Gone Viral*** Symposium on 18 May.

In it, he described the importance of using Genomics-based tools to track and control influenza, listing resources such as Nextstrain and GISAID in the process.

Farewell and good luck

It is with sadness but good wishes that we announce the departure of three long-standing staff members from the Centre. We thank Jayde, Ankita, and Anthony for their significant contributions to the Centre, and wish them all the very best for their future.

Ms Jayde Simpson had been a part of the Centre as Administration Officer for the past nine years. She has contributed significantly in the day to day running of the Centre. She has now returned to her native New Zealand to enjoy a slower life on the beach.

Ms Ankita George had been a research assistant within the research division for the last two years. She has now taken on a new role as a research assistant in a Neuro-Oncology lab at the Murdoch Children's Research Institute.

Mr Anthony Leggieri had been a medical scientist with the surveillance group for the last one and a half years. He has now taken on a new role with Sonic Healthcare and Melbourne Pathology.

Recent activities at the Centre (1 January — 30 April 2021)

Below is a summary of surveillance activities at the Centre during this current reporting period. Centre activities have been relatively quiet in recent months due to decreased influenza cases resulting from social distancing and travel restriction measures implemented in response to COVID-19 across many countries. We anticipate that this decrease in the number of samples will continue while these measures are in place.

Samples received: The Centre received 23 influenza samples from the laboratories and institutions listed below during the period 1 January—30 April 2021.

AUSTRALIA: Westmead Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, SA Pathology, Australian Clinical Labs, The Department of Health and Human Services, VIDRL

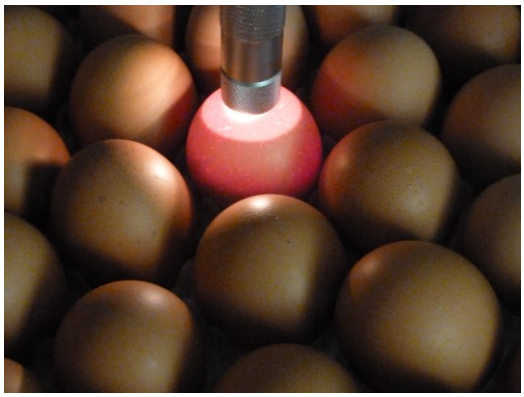
Antigenic analysis
5 viruses analysed by haemagglutination inhibition (HI) assay

Antiviral drug susceptibility
5 viruses analysed by neuraminidase inhibition (NAI) assay

Sequencing
6 viruses analysed
6HA genes
6 NA genes
6 MP genes
5 NS genes

Country of submitting laboratory	No. of viruses analysed by HI assay* A(H3N2)	No. of viruses tested by NAI assay* A(H3N2)	No. of viruses sequenced by NGS or Sanger sequencing A(H3N2)
Australia	5	5	6
Total	**5**	**5**	**6**

* *Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.*



Isolation of viruses in eggs
The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January to 30 April 2021, 7 A(H3N2) viruses were successfully isolated in eggs at the Centre.

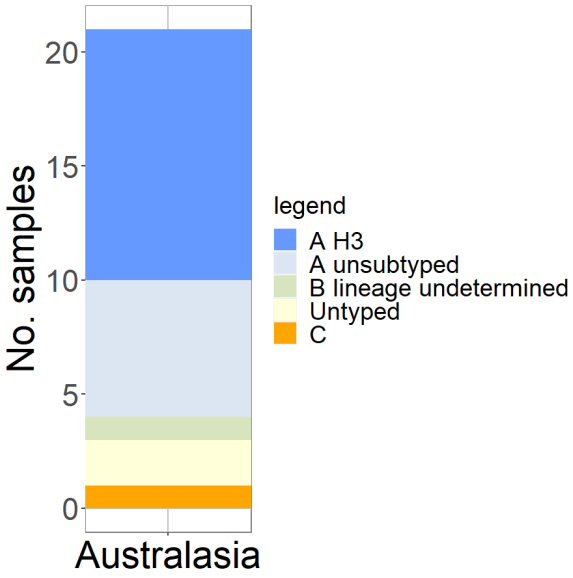
Surveillance update: Virus activity 1 January—30 April 2021

The data below are results for viruses collected between 1 January and 30 April 2021 that have been analysed at the Centre as of 25 May 2021.

Virus types/subtypes[†]

The type and subtype/lineage of 21 viruses have been determined. Of viruses analysed to date, A (H3N2) have predominated (52.4%).

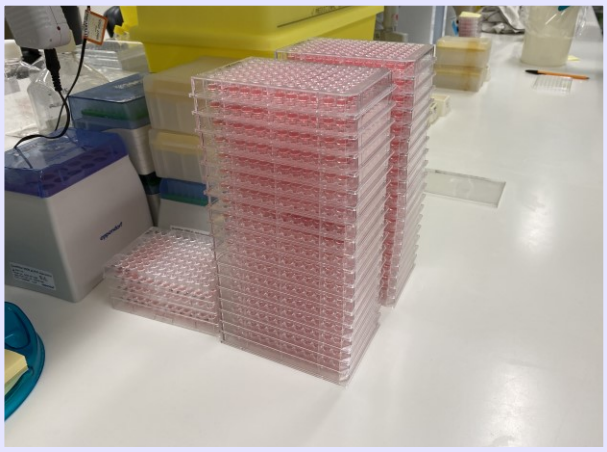
[†] *Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*



Antigenic analysis[†]

A total of 5 viruses (all A(H3N2) viruses) were tested using the haemagglutination inhibition (HI) assay. Viruses were identified as low-reactors if their titre with reference antiserum was at least 8-fold lower than the titre of the reference virus.

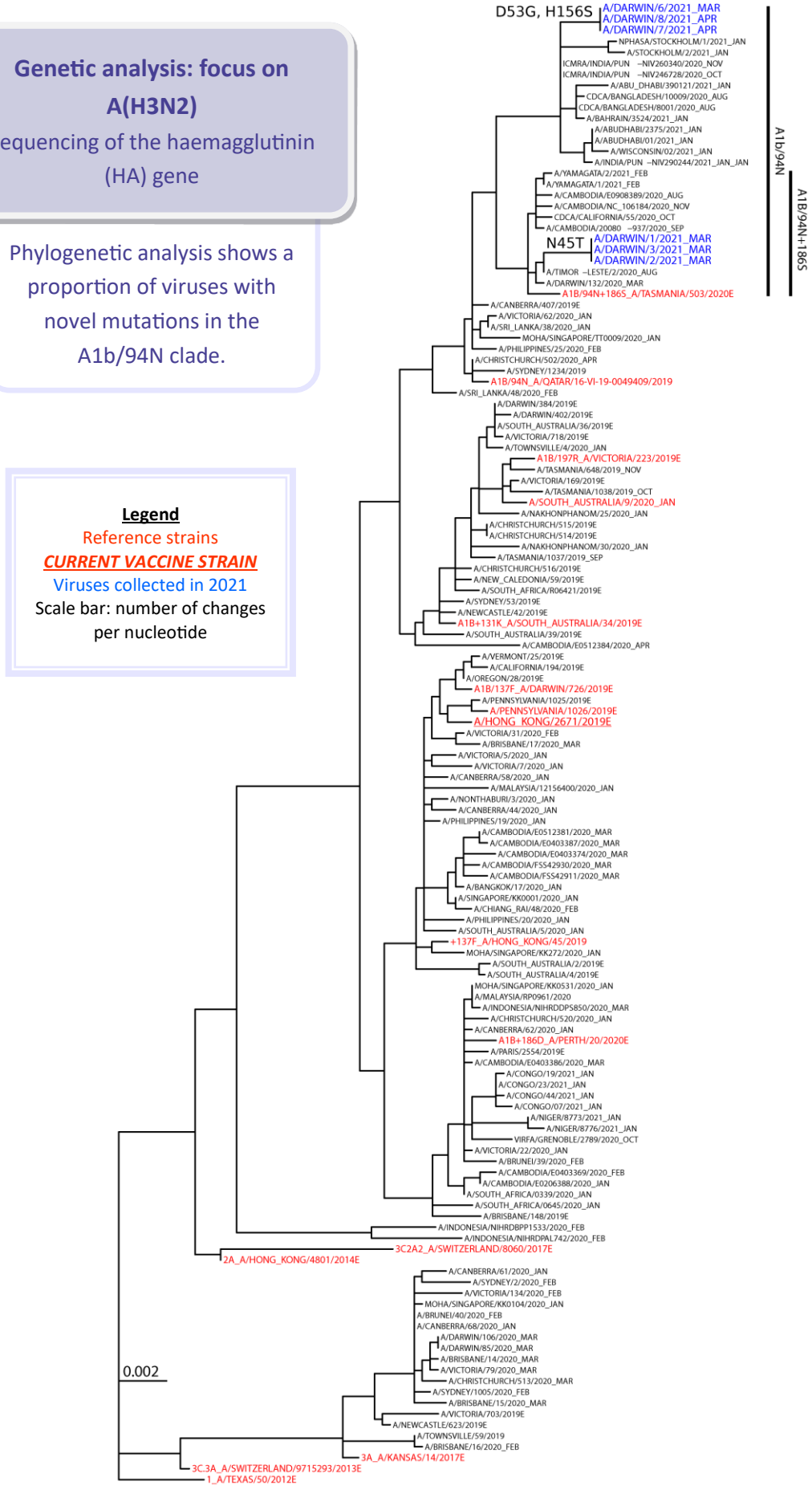
All A(H3N2) viruses tested were low reactors (8+ fold lower) to the reference strain, A/Darwin/726/2019, which is the cell equivalent of the 2021 WHO recommended southern hemisphere vaccine strain, A/Hong Kong/2671/2019.



Genetic analysis: focus on A(H3N2)

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows a proportion of viruses with novel mutations in the A1b/94N clade.



Legend

Reference strains

CURRENT VACCINE STRAIN

Viruses collected in 2021

Scale bar: number of changes per nucleotide

Antiviral drug susceptibility testing:

5 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that no viruses had highly reduced inhibition by one or more neuraminidase inhibitors (NAI).

Type/ subtype/ lineage	Oseltamivir			Peramivir			Laninamivir			Zanamivir		
	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition
A(H3N2)	9			9			9			9		
Total	**9**			**9**			**9**			**9**		

Viruses with reduced inhibition by antiviral drugs in the NAI assay undergo genetic analysis of the neuraminidase gene to detect mutations associated with the functional change. The relationship between reduced inhibition and the clinical effectiveness of a neuraminidase inhibitor is not well understood. Further studies would be required to determine whether a virus with reduced inhibition in the NAI assay is clinically resistant.

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