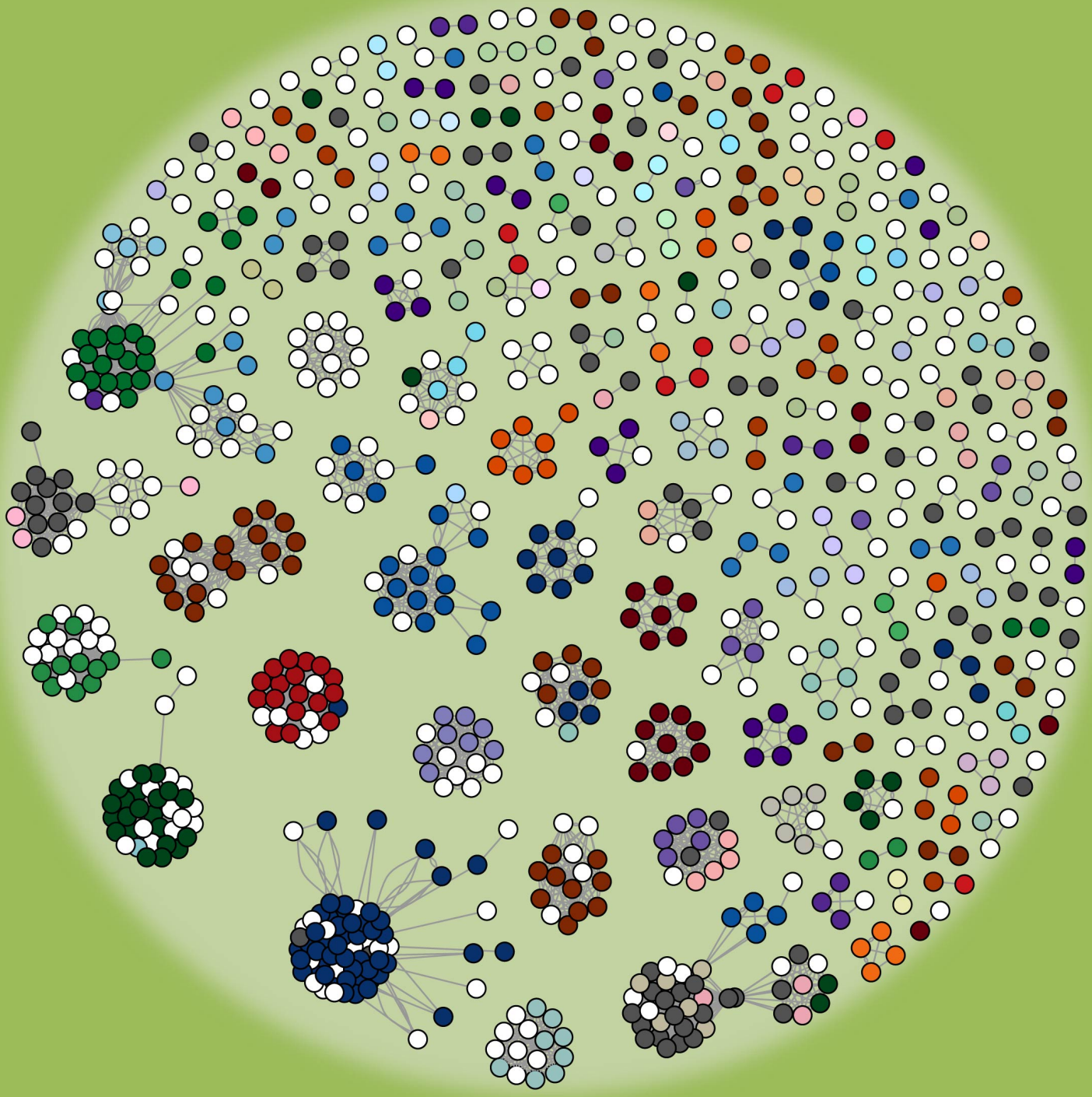
14th Australian Influenza Symposium

11-12 November 2021

Virtual Forum



Welcome

The WHO Collaborating Centre for Reference and Research on Influenza is delighted to welcome you to the **14th Australian Influenza Symposium 2021**, which this year will be held as a virtual event. We would especially like to thank all of the speakers for agreeing to present their work at the symposium. Finally, we wish to acknowledge the following:

Symposium Organising Committee:
WHO Collaborating Centre for Reference and Research on Influenza:

- Prof. Ian Barr
- Dr. Miku Kuba

WHO Collaborating Centre for Reference and Research on Influenza VIDRL

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

We are especially thankful for the financial support from:

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Virtual Event Organiser:

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Acknowledgement of Country:
In the spirit of reconciliation the WHO Collaborating Centre for Reference and Research on Influenza, VIDRL and the Doherty Institute, acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea and community. We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.

Cover image source: Courtney Lane - Seemann T, Lane CR, Sherry NL, Duchene S, Gonçalves da Silva A, Caly L, Sait M, Ballard SA, Horan K, Schultz MB, Hoang T, Easton M, Dougall S, Stinear TP, Druce J, Catton M, Sutton B, van Diemen A, Alpren C, Williamson DA, Howden BP. Tracking the COVID-19 pandemic in Australia using genomics. *Nat Commun.* 2020 Sep 1;11(1):4376. doi: 10.1038/s41467-020-18314-x.

Caption: Each filled dot (node) represents a Victorian coronavirus disease (COVID-19) case with a documented epidemiological link to another Victorian case. Edges (links) between nodes (cases) represent each epidemiological link. Cases are placed closer to each other within the network as the density (number) of linkages between them increases, with cases in the same epidemiological cluster forming a spatially distinct group. Cases are colored by genomic cluster; cases without a sequence included in primary analysis are colored white.

Contents

Social Media

- Social media is permitted at AIS
- WHO CC Melbourne's twitter handle is @WHOFluCCMelb
- AIS event hashtag is #AIS2021Virtual
- Please do not include any talks/slides that speakers specifically request NOT be included in social media

Program Day 1

Thursday, 11 November 2021		
9:00	Meeting opening and logistics: Ian Barr, WHO CC, Doherty Institute, Melbourne, VIC	
9:10	Opening remarks	
Plenary Session 1: COVID-19 Origins and impact | Chair: Kanta Subbarao, WHO CC, Doherty Institute, Melbourne, VIC		
9:15	Eddie Holmes; Marie Bashir Institute for Infectious Diseases & Biosecurity, University of Sydney	The Origins of SARS-CoV-2
9:45	Stanley Perlman; Department of Microbiology and Immunology, University of Iowa, USA	Animal Models for COVID-19
10:15	Jenifer Juno; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute	Host immune responses to SARS-CoV-2
10:45	*Morning tea & time to look at the pre-recorded short talks*	
Plenary Session 2: COVID-19 Epidemiology, Vaccines and Antivirals | Chair: Steve Lambert, Child Health Research Centre, University of Queensland, Brisbane, QLD		
11:15	Freya Shearer; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute	Epidemiology of COVID-19 in Australia
11:35	Sarah Cobey; Department of Ecology and Evolution, University of Chicago, USA	Epidemiological insights into the global COVID-19 pandemic
11:55	Kanta Subbarao; WHO CC for Influenza, VIDRL, Doherty Institute	SARS-CoV-2 Vaccines and Antivirals
12:15	Peter McIntyre; Department of Women's and Children's Health, University of Otago, Dunedin, NZ	SARS-CoV-2 Vaccine roll outs – the good the bad and the ugly
12:35	Jemma Geoghegan; Department of Microbiology and Immunology, University of Otago, Dunedin, NZ	Tracking COVID-19 in New Zealand using genomics
13:00	*Lunch & time to look at the pre-recorded short talks*	
Plenary Session 3: Influenza | Chair: Kirsty Short, School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, QLD		
13:30	Sheena Sullivan; WHO CC for Influenza, VIDRL, Doherty Institute	The 2020/2021 influenza seasons in Australia and what to expect in 2022
13:50	Stella Liong; School of Health and Biomedical Sciences, STEM College, RMIT University	Influenza A virus infection during pregnancy induces severe maternal vascular dysfunction and fetal growth restriction in mice
14:10	Sandra Carlson; Hunter New England Population Health	Influenza & COVID-19 digital surveillance in 2020-2021
14:30	Michelle Wille; Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney	Evolutionary ecology of avian influenza A virus in Australia
Roundtable Discussion | Chair: Kanta Subbarao, WHO CC, Doherty Institute, Melbourne, VIC		
14:55	**For discussion:** **Measures to mitigate airborne virus transmission** **Panel Members:** Kirsty Buising, Simon Joosten, Jason Monty, Lidia Morawska, Robyn Schofield	
15:30	**Day 1 concludes: time to look at the pre-recorded short talks**	

Program Day 2

Friday, 12 November 2021

Plenary Session 4: Industry – Commercial and Product Updates | Chair: Jen Kok, ICPMR Westmead Hospital, Sydney, NSW

8:30	Deb Williamson; Royal Melbourne Hospital, VIDRL, University of Melbourne, Doherty Institute	Rapid antigen testing for COVID-19: An overview
8:50	Suellen Nicholson; VIDRL, Doherty Institute	Diagnostics for SARS-CoV-2 antibody detection
9:10	Bev Menner; COVID Vaccine Lead, CSL Limited	Making the AZ SARS-CoV-2 vaccine in Melbourne
9:30	Nik Petrovsky; Department of Diabetes and Endocrinology, Flinders Medical Centre	Covax-19/Spikogen: the first authorisation of an Australian-developed Covid vaccine
9:50	Raburn Mallory, Vice President Clinical Development Novavax, Gaithersburg, MD, USA	Safety and Immunogenicity of a Booster dose of the Novavax vaccine
10:10	Keith Chappell; School of Chemistry and Molecular Biosciences, University of Queensland	Creating Vaccines at Pandemic Speed
10:30	*Morning tea & time to look at the pre-recorded short talks*	

Plenary Session 5: Influenza and COVID-19 | Chair: Robert Booy, Adolescent Health, Sydney Medical School, The Children's Hospital at Westmead, Sydney, NSW

11:00	Bette Liu; School of Population Health, UNSW	Influenza vaccine coverage in culturally and linguistically diverse (CALD) adults and what we can learn for COVID-19 vaccine coverage
11:20	Martijn Kwaijtaal; Roche Products, Sydney	Casirivimab and imdevimab for COVID-19
11:40	Kristine Macartney; National Centre for Immunisation Research and Surveillance (NCIRS), Sydney	The AIR 2021; What have we learnt for COVID-19, influenza, and other vaccinations – update on its performance/acceptance
12:00	Randy Hyer, Moderna Cambridge, MA, USA and Jane Leong, Moderna, Sydney	Moderna mRNA platform and the future pipeline
12:20	Colin Pouton; Pharmacy & Pharmaceutical Sciences, Monash University	Development of second generation SARS-CoV-2 mRNA vaccines
12:45	*Lunch & time to look at the pre-recorded short talks*	

Plenary Session 6: RSV | Chair: Nigel Crawford, MCRI, Melbourne, VIC

13:15	John-Sebastian Eden; Centre for Virus Research, Westmead Institute for Medical Research, Sydney	Off season RSV epidemics in Australia after easing of COVID 19 restrictions
13:40	Gemma Saravanos; Children's Hospital at Westmead, The University of Sydney	The clinical epidemiology of RSV in children: subtypes, severity & syndromes
14:05	Ian Barr; WHO CC for Influenza, VIDRL, Doherty Institute	WHO RSV global surveillance program – Phase 2 – An update
14:30	Patricia Campbell; Department of Infectious Diseases, University of Melbourne, Doherty Institute	Modelling the household-level impact of a maternal respiratory syncytial virus (RSV) vaccine
14:55	Closing comments	
15:00	**Australian Influenza Symposium concludes or time to look at the pre-recorded short talks**	

Abstracts

Day 1	Plenary Session 1
9:15	**The Origins of SARS-CoV-2**
Speaker	Eddie Holmes; Marie Bashir Institute for Infectious Diseases & Biosecurity, University of Sydney, NSW

Edward C. Holmes

Sydney Institute for Infectious Disease, School of Life & Environmental Sciences and School of Medical Sciences, The University of Sydney, Sydney, New South Wales, 2006, Australia.

I will outline our current understanding of the key events in the origin and emergence of COVID-19 (SARS-CoV-2) at the end of 2019. Major topics of discussion will be possible zoonotic reservoirs for SARS-CoV-2, the diversity of SARS-CoV-2-like viruses in bats and other mammals, the signatures of origin written into genome sequences, and the possible role played by the Huanan seafood market in Wuhan in the initial animal-to-human cross-species transmission event. I will show that there is increasing evidence that the emergence of SARS-CoV-2 strongly resembles of that of SARS-CoV some 17 years earlier. I will also address whether it is possible that SARS-CoV-2 emerged as a result of 'lab leak' from the Wuhan Institute of Virology and show that there is currently no scientifically robust evidence in support of that theory. I will also briefly consider possible scenarios for the future evolution of SARS-CoV-2 and conclude by considering the steps that can be taken to stop such a catastrophic pandemic event ever happening again.

Day 1	Plenary Session 1
9:45	**Animal Models for COVID-19**
Speaker	Stanley Perlman; Department of Microbiology and Immunology, University of Iowa, USA

Stanley Perlman

Department of Microbiology and Immunology, University of Iowa, Iowa City, Iowa, USA

As the COVID-19 pandemic continues around the world, greater understanding of the immune response to the virus and pathogenesis are required. Experimentally infected animal models of COVID-19 are required for these purposes. Over the past few months, we have developed several mouse models for COVID-19. Mice are naturally resistant to the original strains of SARS-CoV-2, so either the mouse needs to be sensitized for SARS-CoV-2 infection or the virus needs to be modified to use the mouse host cell receptor. To obtain mice useful for studying COVID-19, we used several approaches. In a first approach, we sensitized mice for infection by transduction with an adenovirus vector expressing human ACE2, the virus receptor. We also used K18-hACE2 mice that we developed during the SARS epidemic. Most recently, we isolated a mouse-adapted SARS-CoV-2 that causes severe disease in young and old BALB/c mice, and in aged C57BL/6 mice. Disease is confined to the lungs but our preliminary results suggest that inflammatory changes are widespread, even in organs that are not infected. Mice infected with this virus are not only useful for studies of pathogenesis of COVID-19 in the lungs, but also for other manifestations, including anosmia and ageusia.

Day 1	Plenary Session 1
10:15	**Host immune responses to SARS-CoV-2**
Speaker	Jenifer Juno; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Jenifer A. Juno

Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia

Over the past 18 months, our understanding of the immune response to SARS-CoV-2 infection has rapidly evolved. In particular, it has become clear that the kinetics and magnitude of the adaptive immune response is critical to the outcome of infection and the establishment of long-term memory. Longitudinal study of COVID-19 convalescent individuals has shown that neutralising antibody titres, now understood to be a key correlate of protection, are elicited at highly variable levels following infection and decline in a bi-phasic pattern of decay. While both CD4 and CD8 T cell responses are elicited by SARS-CoV-2, CD4 Th1 and cTfh responses generally predominate, and appear to be critical for neutralising antibody generation. Recent development of HLA class I and II tetramer reagents has facilitated the precise characterisation of T cell recognition of the viral spike and nucleoprotein antigens in individuals with a range of clinical disease outcomes, providing the opportunity to understand how the interplay of humoral and cellular immunity can protect from severe disease. Overall, insights into host immunity to SARS-CoV-2 have supported the development of effective therapies and vaccines against this novel coronavirus.

Day 1	Plenary Session 2
11:15	**Epidemiology of COVID-19 in Australia**
Speaker	Freya Shearer; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, VIC

Freya Shearer[1], Nick Golding[2,3], David Price[1,4], Gerry Ryan[2,3], Jodie McVernon[1,4,5], James McCaw[1,4,6]

[1]School of Population and Global Health, University of Melbourne, Melbourne, Victoria, Australia; [2]Telethon Kids Institute, Nedlands, Western Australia, Australia; [3]Curtin University, Perth, Western Australia, Australia; [4] Victorian Infectious Diseases Reference Laboratory, The Royal Melbourne Hospital, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia; [5]Murdoch Children's Research Institute, Melbourne, Victoria, Australia; [6]School of Mathematics and Statistics, University of Melbourne, Parkville, Victoria, Australia

The epidemiology of COVID-19 in Australia has been strongly shaped by the responses of government and the public.

Across its eight states and territories, Australia has managed a number of distinct phases of the pandemic from an initial wave of importations, to sustained periods of zero local case incidence, to widespread community transmission. Like elsewhere in the world, key interventions have included: quarantine of overseas arrivals; restrictions on mobility and gathering sizes; advice on personal hygiene; case and contact management; and vaccination. The specific measures, and the level of control of SARS-CoV-2 transmission, has varied between states and over time, according to changing epidemiology and response objectives, among other factors.

In this talk, I will describe the epidemiology of SARS-CoV-2 in Australia since the onset of the pandemic in Australia in early 2020 through to the present day, drawing on outputs from quantitative and model-based epidemic assessment. Key analyses include estimates of the rate of virus spread among active cases (the effective reproduction number), trends in population behaviour, and the impact of behaviour, vaccination, and variants on the potential for virus spread. These analyses allow us to describe observed trends in COVID-19 epidemiology over time and space, and importantly, anticipate future possible trends.

Day 1	Plenary Session 2
11:35	**Epidemiological insights into the global COVID-19 pandemic**
Speaker	Sarah Cobey; Department of Ecology and Evolution, University of Chicago, USA

Sarah Cobey

Department of Ecology and Evolution, University of Chicago, Chicago, Illinois, USA

Nearly two years into the COVID-19 pandemic, despite unprecedented success with vaccines, most countries are still grappling with a poorly controlled virus. This is partly from direct and indirect choices. In this talk I explain what we knew in principle about SARS-CoV-2 in early 2020, what we have learned, and especially what we have failed to learn---all with consequences for control. Although predicting evolution is notoriously challenging, it is less understandable why we continue to know so little about populations' immune statuses and pandemic trajectories. This makes it difficult to measure the efficacies of different interventions and is a cause and consequence of persistent inequalities in public health. A silver lining of the pandemic is that it has shown that controlling other respiratory pathogens might be within reach, and that we might not need to live with them, if we choose.

Day 1	Plenary Session 2
11:55	**SARS-CoV-2 Vaccines and Antivirals**
Speaker	Kanta Subbarao; WHO CC, Department of Microbiology and Immunology, Doherty Institute, Melbourne, VIC

Kanta Subbarao

WHO Collaborating Centre for Reference and Research on Influenza and Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia

The development, manufacture and deployment of several effective SARS-CoV-2 vaccines using different platforms is a remarkable success story. Aside from issues related to global access to vaccines, we are now faced with a decline in immunity over time and the emergence of variant viruses against which vaccine effectiveness is reduced. The spread of variants with mutations in the S protein's receptor binding domain have raised concerns that COVID-19 vaccines may have to be updated because some mutations can render the variants less optimally targeted by current vaccines. The threshold for a strain change in COVID-19 vaccines is yet to be defined and time will tell whether SARS-CoV-2 vaccines will require occasional updates or annual updates, as are needed for influenza.

Antiviral drug treatment initially focused on re-purposing already licensed drugs. However, with the exception of Remdesivir, many compounds that showed promise in vitro were not found to be efficacious in clinical trials. Recent data suggest that an orally administered drug (Molnupiravir) will be an option for outpatient treatment. Attention has also focused on immunomodulatory drugs and monoclonal antibodies directed at the spike protein. Clinical management is tailored to the stage of disease.

Research on SARS-CoV-2 vaccines and antiviral drugs is an active and changing field. Pan-coronavirus vaccines and antiviral drugs will be important to prepare for future zoonotic spread of betacoronaviruses.

Day 1	Plenary Session 2
12:15	**SARS-CoV-2 Vaccine roll outs – the good the bad and the ugly**
Speaker	Peter McIntyre; Department of Women's and Children's Health, University of Otago, Dunedin, NZ

Peter B. McIntyre

Department of Women's and Children's Health, Dunedin School of Medicine University of Otago, Dunedin, Otago, New Zealand; National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead, The University of Sydney, Sydney, New South Wales, Australia

Almost all SARS-CoV-2 vaccines have a two-dose schedule. From the beginning of their availability and use, there was agreement that population groups most vulnerable to severe disease and death (the oldest and sickest) should be prioritised to receive vaccine, along with front-line workers. However, there was debate about how important it was to promptly deliver second doses. On the one hand, there was evidence from the first large clinical trials of significant protection from 12-14 days after the first dose particularly against severe disease and an imperative to provide protection to as many of the most vulnerable as quickly as possible. On the other, clinical trials were almost all conducted with a very short (21-28 day) interval between first and second doses and concerns about inadequate protection and that evolution of SARS-CoV-2 variants with resistance to vaccine immunity if large numbers of people received a single dose.

Subsequent experience in the UK and Canada has shown that rapid rollout of first doses to as many of the vulnerable population as possible, with a resultant longer gap to the second dose of 12 to 16 weeks was the preferable strategy. All SARS-CoV-2 variants of concern have arisen in contexts of high infection, not high vaccination and the delta variant is now dominant globally. In Australia, issues of vaccine preference further complicated rollout but during periods when vaccine supply was short, initially prioritising first doses was also more efficient. In late 2021, there is a need for approaches to vaccine rollout in settings where vaccine supply remains limited and high rates of infection to date have resulted in high population seroprevalence.

Day 1	Plenary Session 2
12:35	**Tracking COVID-19 in New Zealand using genomics**
Speaker	Jemma Geoghegan; Department of Microbiology and Immunology, University of Otago, Dunedin, NZ

Jemma L. Geoghegan

Department of Microbiology and Immunology, University of Otago, Dunedin, New Zealand; The Institute of Environmental Science and Research, Wellington, New Zealand

Viral genomics continues to be critical to New Zealand's successful public health response with genomic sequencing being used as a key tool for understanding and limiting the spread of COVID-19. By integrating genomics with epidemiological data, local transmission chains and regional spread were able to be tracked and audited in real-time. This information, provided to public health, helped to prevent multiple regional lockdowns of New Zealand's cities, avoiding significant economic costs. In addition, ongoing genomic surveillance of COVID-19 cases at the border has provided the world's first genomic evidence of in-flight transmission, as well as highlighting the role of aerosol transmission in managed quarantine and isolation (MIQ) facilities, prompting investigations of MIQ ventilation systems and testing practices both in New Zealand and overseas.

Day 1	Plenary Session 3
13:30	**The 2020/2021 influenza seasons in Australia and what to expect in 2022**
Speaker	Sheena Sullivan, WHO CC, Doherty Institute, Melbourne, VIC

Sheena G. Sullivan

WHO Collaborating Centre for Reference and Research on Influenza, The Royal Melbourne Hospital, and Department of Infectious Diseases, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia

When the WHO declared a pandemic in March 2020, it came with fears that in the southern hemisphere we would be faced with co-circulation of both SARS-CoV-2 and influenza, which could put significant strain on healthcare systems. In Australia, these fears were not borne out. In stark contrast to expectations, influenza activity has been at an all-time low in 2020 and 2021. Australia's pandemic mitigation strategies have effectively prevented continued circulation of influenza, and mandatory quarantine policies for returned travellers have effectively prevented the re-introduction of influenza and, to a large extent, SARS-CoV-2. Influenza is now in a bottleneck, with few countries reporting cases. Nevertheless, sporadic outbreaks have continued to occur, mainly in tropical and sub-tropical regions, and cases of influenza have been detected among returned travellers in hotel quarantine. Experience with delayed rhinovirus and respiratory syncytial virus outbreaks in 2020 and 2021 suggest that the initial suppression of a virus may be followed by a rebound in activity that could place significant strain on our healthcare system. Some of this may be attributable to the increased pool of susceptible children who avoided infection during the usual winter respiratory virus season. Australia's children have now been unexposed to influenza for 2 seasons and the roughly 600,000 children aged <2 years—who have the highest influenza-associated hospitalisation rates—have never been exposed. As pandemic restrictions relax, including the reopening of the borders, there is increased opportunity for influenza to be re-introduced into Australia. Not every introduction will result in an outbreak and the time by which any outbreaks of significance occur is impossible to predict. Initial epidemics may occur outside the usual seasonal period and it may be some time before influenza circulation returns to a seasonal pattern. Coupled with a highly susceptible population of children such unpredictable seasonality of influenza could place a significant strain on our health care system.

Day 1	Plenary Session 3
13:50	**Influenza A virus infection during pregnancy induces severe maternal vascular dysfunction and fetal growth restriction in mice**
Speaker	Stella Liong; School of Health and Biomedical Sciences, STEM College, RMIT University, Melbourne, VIC

Stella Liong[1], Osezua Oseghale[1], Eunice To[1], Kurt Brassington[1], Jonathan Erlich[1], Raymond Luong[1], Felicia Liong[1], Robert Brooks[2], Cara Martin[3], Sharon O'Toole[3], Antony Vinh[4], Steven Bozinovski[1], Ross Vlahos[1], Paris C. Papagianis[1], John J. O'Leary[3], Doug A. Brooks[4], Stavros Selemidis[1]

[1]School of Health and Biomedical Sciences, RMIT University, Melbourne, Victoria, Australia; [2]School of Pharmacy and Medical Sciences, University of South Australia Cancer Research Institute, Adelaide, South Australia, Australia; [3]Histopathology, School of Medicine, Trinity College Dublin, Dublin, Ireland; [4]Department of Physiology, Anatomy and Microbiology, School of Life Sciences, La Trobe University, Bundoora, Victoria, Australia

Introduction: Influenza A virus (IAV) infection during pregnancy can be life-threatening to both mother and child. IAV-infected pregnant women have a higher incidence of acute respiratory distress syndrome, pneumonia and heart failure. Although IAV is not vertically transmitted to the fetus, the risks to the offspring include preterm birth, congenital malformations, growth restriction, and long-term chronic immune and cognitive diseases later in life. How IAV infection in pregnancy causes these adverse fetal effects *in utero* is unknown.

Aims: To characterise the lung, systemic, placental and vascular inflammation following IAV-infection in pregnancy.

Methods: Eight-to-twelve-week old time-mated pregnant (E12 gestation) and non-pregnant C57BL/6 female mice were intranasally infected with the H3N2 IAV strain (HKx31; 10^4 PFU) or PBS for tissue analysis 3 days post-infection. Maternal and pup weights were recorded. Inflammation and viral mRNA expression in lungs, aorta and placenta were determined by qPCR or flow cytometry. Thoracic aorta reactivity was assessed with myography and endothelium-dependent and independent smooth muscle relaxation determined using Ach and sodium nitroprusside, respectively.

Results: IAV infection during pregnancy resulted in exacerbated systemic inflammation characterised by a significant increase in blood neutrophils and circulating cell-free fetal DNA compared to non-pregnant IAV-infected mice. Pup weights were significantly reduced with IAV-infection, however, there was no evidence of pro-inflammatory cytokine expression in the placentas. IAV infection during pregnancy caused a significant ~60-70% impairment in maximal relaxation of the thoracic aorta. This was associated with significantly elevated levels of pro-inflammatory cytokines and influenza viral mRNA. No impairment in vascular function was observed in non-pregnant IAV-infected mice.

Discussion: This study is the first to demonstrate that IAV infection disseminates into the maternal aorta causing severe impairment of vascular function that occurs selectively in pregnancy. This impairment in vascular function is likely to reduce the blood flow to the placenta and offspring resulting in fetal growth restriction. Therapies restoring vascular function are an exciting and novel strategy for the management of IAV infection during pregnancy.

Day 1	Plenary Session 3
14:10	**Influenza & COVID-19 digital surveillance in 2020-2021**
Speaker	Sandra Carlson, Hunter New England Population Health, Newcastle, New South Wales, Australia

Sandra Carlson[1], Craig Dalton[1,2,3]

[1]Population Health, Hunter New England Health, Newcastle, New South Wales, Australia; [2]School of Public Health and Medicine, University of Newcastle, Newcastle, New South Wales, Australia; [3]Hunter Medical Research Institute, Newcastle, New South Wales, Australia

Background: Flutracking is an online community based public health surveillance system, with historical data on influenza-like illness (ILI) in Australia since 2006, and receiving over 70,000 weekly surveys during the 2020-21 COVID-19 pandemic across Australia. The expanded COVID-19 survey takes approximately 30 seconds to complete, and asks questions on seven respiratory symptoms, severity of illness, health care seeking behaviour, and COVID-19 and influenza vaccination status. We describe the contribution FluTracking has made to COVID-19 surveillance in Australia over the 2020-21 period.

Respiratory symptom rates: ILI was historically low, at or below 0.5% across most of 2020 and below 1.0% during 2021(figure). Changes in weekly ILI rates aligned with the timing of public health restrictions/international border closures in Australia, and a similar pattern was observed in the FluTracking New Zealand data. Children younger than five years continued to have the highest weekly incidence of ILI, peaking at 6.4% over the 2020-21 period, compared to 7.6% in 2019.

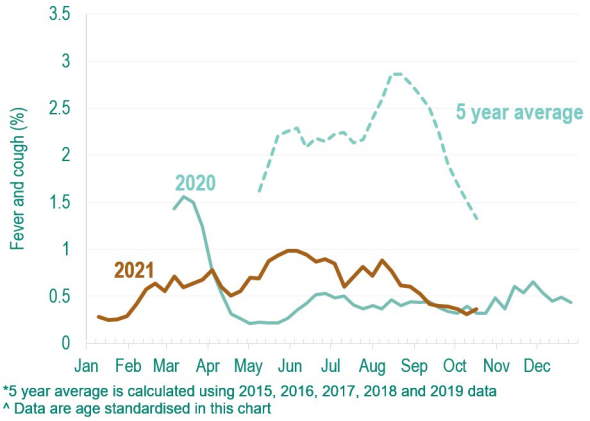

Figure. FluTracking weekly percentage of participants with fever and cough, 2015-21, Australia.

COVID-19 testing rates: On average 49.6% of participants with new fever and cough symptoms and 27.3% of participants with new sore throat and runny nose symptoms reported being tested each week during 2020-21 for COVID-19. Increases in COVID-19 case counts aligned with increased COVID-19 self-reported testing in communities, and decreased ILI activity.

Vaccination Rates: Flutracking participants have higher levels of vaccination than the general Australian population, however, comparisons within the cohort over time are useful. Influenza vaccination decreased substantially from 2020 to 2021, particularly in children: from 78.5% to 57.5% of children under 5 years and 62.7% to 39.0% of children 5 – 17 years.

Participation: FluTracking underwent substantial growth in participation in 2020 due to public interest in the COVID-19 pandemic. However, we have seen a gradual decline in participation in 2021, possibly due to sustained low ILI activity, participant fatigue, and additional COVID-19 questions added to the survey.

Challenges and Lessons: It has been an art to balance additional questions of relevance to COVID-19 and surveillance all year round, with maintaining high levels of participation from the Australian community.

Communicating levels of COVID-19 testing among symptomatic participants has required care to not imply judgement, and future plans to explore why participants are not getting tested will need to be managed sensitively.

Day 1	Plenary Session 3
14:30	**Evolutionary ecology of avian influenza A virus in Australia**
Speaker	Michelle Wille; Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, NSW

Michelle Wille[1,2,3], National Avian Influenza Wild Bird Program[#], Edward Holmes[1], Frank Wong[4], Marcel Klaassen[5]

[1]Marie Bashir Institute for Infectious Diseases and Biosecurity, School of Life and Environmental Sciences and School of Medical Sciences, The University of Sydney, Sydney, New South Wales, Australia; [2]WHO Collaborating Centre for Reference and Research on Influenza, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia; [3]Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia; [4]Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australian Centre for Disease Preparedness, Geelong, Victoria, Australia; [5]Centre for Integrative Ecology, Deakin University, Geelong, Victoria, Australia; Victorian Wader Study Group, Australia; Australasian Wader Studies Group, Australia; [#]Wildlife Health Australia; Agriculture Victoria, Victoria; Department of Primary Industries, Water and Environment, Tasmania; Department of Primary Industries and Regional Development, Western Australia; James Cook University, Queensland; North Australia Quarantine Strategy Northern Territory, Queensland and Western Australia; New South Wales Department of Primary Industries, University of Newcastle, University of Technology Sydney, Centenary Institute; Department of Primary Industries and Regions, South Australia; Department of Agriculture and Fisheries, Queensland; Australian Government Department of Agriculture, Water and Environment; WHO Collaborating Centre for Reference and Research on Influenza

Although research on Australian wild birds pioneered the view that low pathogenic avian influenza A virus (LPAIV) can be commonly found in wild birds and is not limited to outbreaks in poultry, little is known about the ecology and evolution of LPAIV in Australia and how Australia fits into global LPAIV dynamics. Herein we present the results of two studies. First, using paired virology and serology data collected between 2010-2021 from wild birds in Australia, we reveal the key roles of host phylogeny, age and year in modulating LPAIV ecology. While age and season are key factors in temperate northern hemisphere datasets, this is the first study to firmly reveal the role of host phylogeny and to confirm the crucial role of long-term climate on the Australian continent. Second, utilizing the long-term viral genome repository comprising 303 unique LPAIV genome sequences generated by the National Avian Influenza Wild Bird (NAIWB) program, we reveal that Australia is a sink for global AIV diversity. Further, unlike data from North America, there are no consistent viral migration patterns across the Australian continent, however virus migration was most frequent between adjacent states. Taken together, we provide new insights into host-LPAIV evolutionary ecology, not only defining distinctive processes within Australia but expanding our understanding of LPAIV global dynamics.

Day 1	Roundtable discussion
1505	**Measures to mitigate airborne virus transmission**
Panel	• Kirsty Buising • Simon Joosten • Jason Monty • Lidia Morawska • Robyn Schofield
Moderator	Kanta Subbarao, WHO CC Melbourne

Day 2	Plenary Session 4
8:30	**Rapid antigen testing for COVID-19: An overview**
Speaker	Deb Williamson; Royal Melbourne Hospital, Victorian Infectious Diseases Reference Laboratory, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC

Deborah A. Williamson

Victorian Infectious Diseases Reference Laboratory, The Royal Melbourne Hospital, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia; Department of Infectious Diseases, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia

To complement laboratory-based RT-PCR testing, many countries are assessing and implementing rapid point-of-care test (PoCT) modalities. In particular, point-of-care lateral flow rapid antigen tests (LFDs) have been used to complement laboratory-based PCR testing and have been widely publicised as a potential means of upscaling population-level testing to facilitate the safe re-opening of societies, and to enable access to COVID-19 testing in resource-poor settings. In theory, large-scale testing of asymptomatic populations using LFDs (in conjunction with other public health measures) could detect infectious individuals with pre-symptomatic or asymptomatic COVID-19 and rapidly interrupt transmission networks and is a conceptually attractive option for facilitating a 'COVID Normal' return to daily activities. This talk will provide an overview of the performance, use and implementation of antigen tests, both in Australia and globally.

Day 2	Plenary Session 4
8:50	**Diagnostics for SARS-CoV-2 antibody detection**
Speaker	Suellen Nicholson; VIDRL, Doherty Institute, Melbourne, VIC

Suellen Nicholson[1], Theo Karapanagiotidis[1], Deborah A. Williamson[1]

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As we move into the post vaccination phase of the coronavirus disease 2019 (COVID-19) pandemic our understanding of the immune response for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is constantly evolving. This presentation will provide an overview of some aspects of SARS-CoV-2 serological testing.

Serology assay performance: It is important to understand the reliability of assays with different antigen or antibody targets to detect humoral immunity after SARS-CoV-2 infection or vaccination, how antibody binding assays compare to those detecting neutralising antibody and how these compare to the gold standard cell-culture based microneutralisation assay.

Binding vs neutralising antibodies: Binding antibodies attach to various parts of the virus but do not block its entry into the host cell in contrast to neutralising antibodies which block virus entry into the host cell and are used to measure vaccine efficacy. More recent evidence has shown a strong correlation between IgG anti-spike and neutralising antibodies and protective efficacy in clinical trials.

Detection of natural immunity post vaccination: The ability to determine if an immune response is due to natural infection with SARS-CoV-2 or as a result of vaccination is playing an increasingly important role for public health decision-making. Immunisation using spike protein based vaccines, such as those used in Australia, enables the use of serology tests that detect anti-SARS-CoV-2 nucleocapsid (NCP) antibody to discriminate an immune response due to vaccination or infection.

Vaccine Efficacy: Vaccine efficacy studies have shown the waning of SARS-CoV-2 antibodies post-vaccination however there appears to be greater vaccine efficacy against severe disease than against any infection regardless of vaccine type.

The immune system produces a spectrum of immune responses, both antibody and cellular. Currently the correlates of protection and the potential for a protective antibody threshold for prevention of infection or disease are yet to be elucidated.

Day 2	Plenary Session 4
9:10	**Making the AZ SARS-CoV-2 vaccine in Melbourne**
Speaker	Bev Menner; CSL Limited, Melbourne, VIC

Bev Menner

CSL Limited, Parkville, Victoria, Australia

CSL has a longstanding biosecurity partnership with the Australian government and is the largest private investor of translational research in Australia. CSL engaged with the Federal Government in early 2020 to determine how it might contribute to the Australian response to the COVID-19 pandemic and has been working closely with them ever since.

Following the cessation of initial work with the University of Queensland to advance their spike protein candidate, CSL agreed to act as a contract manufacturer for the AstraZeneca vaccine (Vaxzevria) for supply to the Australian population. To facilitate this work, CSL entered into contracts with the Department of Health and AstraZeneca (AZ) to manufacture Vaxzevria, following a technology transfer of AZ's manufacturing process to CSL. CSL will be manufacturing 50 million doses of the vaccine.

CSL has proudly been able to respond to this humanitarian crisis with the production of more than 24 million doses of Vaxzevria to date, protecting Australians and those in the Asia Pacific region. It is expected that the remaining production will be completed in the first half of next year.

Day 2	Plenary Session 4
9:30	**Covax-19/Spikogen: the first authorisation of an Australian-developed Covid vaccine**
Speaker	Nik Petrovsky; Department of Diabetes and Endocrinology, Flinders Medical Centre, Adelaide, SA

Nikolai Petrovsky

Vaxine Pty Ltd, Adelaide, South Australia, Australia

The development of safe and effective vaccines is a key requirement to conquering the COVID-19 pandemic. Recombinant proteins represent arguably the most reliable and safe approach but face challenges in design, manufacture, structural characterisation and delivery. We used the SARS-CoV-2 genomic sequence and *in silico* structural modelling to design a recombinant protein vaccine based on a stabilised spike extracellular domain (ECD). The codon optimised sequenced was inserted into a baculovirus backbone to allow the protein to be expressed in insect cell cultures. The spike ECD was formulated with our proprietary Advax-CpG55.2 adjuvant and tested for immunogenicity in C57BL/6 and BALB/c mice. The Advax-SM adjuvanted vaccine induced high titers of binding antibody against spike protein that were able to neutralise the original wildtype virus on which the vaccine was based as well as the variant B.1.1.7 lineage virus. The Covax-19 vaccine also induced potent spike-specific $CD4^+$ and $CD8^+$ memory T-cells with a dominant Th1 phenotype, and this was shown to be associated with cytotoxic T lymphocyte killing of spike labelled target cells *in vivo*. Ferrets or aged monkeys immunised with Covax-19 vaccine twice 2 weeks apart were protected against SARS-CoV-2 infection with no detectable virus in their lungs in nasal washes, post-challenge. Covax-19 vaccine was also able to block virus transmission in the hamster model. Following a successful human Phase 1, 2 and 3 clinical trial program in which it demonstrated high tolerability and safety and met its prespecified primary efficacy endpoint of >60% protection against symptomatic disease with the delta variant, it has now received its first emergency use authorisation, the only Australian-developed Covid-19 vaccine to reach this critical milestone. The current focus is in extending the clinical data to paediatric populations and exploring its use as a booster dose to counter waning immunity in individuals previously immunised with adenovirus vector or mRNA. We continue to closely monitor new SARS-CoV-2 variants, but with our vaccine's broad-based immunity have not yet seen the need to modify the antigen in our vaccine.

Day 2	Plenary Session 4
9:50	**Safety and Immunogenicity of a Booster dose of the Novavax vaccine**
Speaker	Raburn Mallory, Novavax, Gaithersburg, MD, USA

Raburn Mallory, Neil Formica, Susan Pfeiffer, Bethanie Wilkinson, Alex Marcheschi, Gary Albert, Heather McFall, Michelle Robinson, Joyce S. Plested, Iksung Cho, Andreana Robertson, Sonia Maciejewski, Gale Smith, Nita Patel, Gregory M. Glenn, Filip Dubovsky for the 2019nCoV-101 Study Group

All listed authors are employees of, or consultants for, Novavax.

Introduction: Emerging SARS CoV-2 variants and evidence of waning vaccine efficacy present significant obstacles toward controlling the COVID-19 pandemic. Booster doses of SARS-CoV-2 vaccines may address these concerns by both amplifying and broadening the immune responses seen with initial vaccination regimens.

Methods: In a phase 2 study, a single booster dose of NVX-CoV2373 was administered to healthy adult participants 18 to 84 years of age approximately 6 months following their primary 2-dose series. Safety and immunogenicity parameters were assessed, including assays for IgG, MN_{50}, and hACE2 inhibition against the original SARS-CoV-2 strain and select variants (B.1.351 [Beta], B.1.1.7 [Alpha], and B.1.617.2 [Delta]).

Results: An incremental increase in the incidence of solicited local and systemic reactogenicity events was observed with subsequent vaccinations. Following the boost, incidence rates of local and systemic reactions were 76.2% (12.4% ≥ Grade 3) and 71.4% (14.3% ≥ Grade 3), respectively, compared to 70.5% (3.8% ≥ Grade 3) and 53.3% (3.8% ≥ Grade 3), respectively, following the primary vaccination series. Events were primarily mild or moderate in severity and transient in nature, with a median duration of 1.0 to 2.5 days. Immune responses observed 4 weeks following the boost were compared with those seen 2 weeks following the primary series. For the ancestral SARS-CoV-2 strain, GMT anti-spike IgG titers increased ~4.6-fold from 43,749 EU to 200,408 EU following the boost. GMT MN_{50} assay titers showed a similar increase of ~4.3-fold from 1,433 to 6,231. A functional hACE2 inhibition assay analyzing activity against the original, Delta, Beta, and Alpha variant strains of SARS-CoV-2 found 6-fold, 6.6-fold, 10.8-fold, and 8.1-fold increases in titers, respectively.

Conclusions: Administration of a booster dose of NVX-CoV2373 approximately 6 months following the primary series resulted in an incremental increase in reactogenicity along with enhanced immune responses. Immune responses following the boost were notably higher than those associated with high levels of efficacy in Phase 3 studies of the vaccine.

Day 2	Plenary Session 4
10:10	**Creating Vaccines at Pandemic Speed**
Speaker	Keith Chappell; School of Chemistry and Molecular Biosciences, University of Queensland, St Lucia, QLD

Keith Chappell[1,2,3], Daniel Watterson[1,2,3,], Danushka K. Wijesundara[1,2], Naphak Modhiran[1,2], Francesca L. Mordant[4], Zheyi Li[5], Michael S. Avumegah[1,2], Christopher McMillan[1,2], Julia Lackenby[1,2], Kate Guilfoyle[6], Geert van Amerongen[6], Koert Stittelaar[6], Stacey Cheung[1], Summa Bibby[1], Mallory Daleris[2], Kym Hoger[2], Marianne Gillard[2], Eve Radunz[2], Martina L. Jones[2], Karen Hughes[2], Ben Hughes[2], Justin Goh[2], David Edwards[2], Judith Scoble[7], Lesley Pearce[7], Lukasz Kowalczyk[7], Tram Phan[7], Mylinh La[7], Louis Lu[7], Tam Pham[7], Qi Zhou[7], David A. Brockman[8], Sherry J. Morgan[9], Cora Lau[10], Mai H. Tran[8], Peter Tapley[8], Fernando Villalón-Letelier[4], James Barnes[11], Andrew Young[1,2], Noushin Jaberolansar[1,2], Connor A.P. Scott[1], Ariel Isaacs[1], Alberto A. Amarilla[1], Alexander A. Khromykh[1,3], Judith M.A. van den Brand[12], Paula Ellenberg[4], Christina L. Henderson[1,2], Kym Hoger[2], Paul Griffin[13,14,15], Jillian Bennet[16], Luca Hensen[4], Wuji Zhang[4], Thi H.O. Nguyen[4], Sara Marrero-Hernandez[4], Kevin J. Selva[4], Amy W. Chung[4], Suellen Nicholson[17], Stavroula Corby[17], Thomas Holgate[17], Bruce D. Wines[18], P. Mark Hogarth[18,19,20], Katherine Kedzierska[4], Damian Purcell[4], Kanta Subbarao[4,11], Patrick Reading[4,11], Charani Ranasinghe[5], Paul R. Young[1,2,3], and Trent P. Munro[1,2]

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The last 22 months has been a wild ride for the Rapid Response Vaccine Team at UQ. The University of Queensland and partner organisations, including CSL have developed a SARS-CoV-2 subunit vaccine that completed pre-clinical development and entered phase I human trials within 6 months of the sequence information on SARS-CoV-2 being released. This vaccine consisted of the spike protein held in its pre-fusion conformation by UQ's rapid response molecular clamp platform. The structure of the purified spike protein has been resolved to 5Å resolution and shown to adopt a conformation equivalent to that on the surface of the virus. When formulated with MF59 adjuvant (Seqirus), this vaccine was shown to be safe and to elicit a strong neutralizing immune response at a similar magnitude to those currently in use. Unfortunately, however, due to the molecular clamp containing short peptide sequences from a HIV-1 protein, this vaccine elicited an immune response that interfered with some HIV diagnostic tests and so was not progressed beyond phase I. This year the Rapid Response Vaccine Team have been focusing on re-engineering a molecular clamp2.0 that does not include HIV sequences, validating this new vaccine platform and developing a new purification method.

Day 2	Plenary Session 5
11:00	**Influenza vaccine coverage in culturally and linguistically diverse (CALD) adults and what we can learn for COVID-19 vaccine coverage**
Speaker	Bette Liu; School of Population Health, University of New South Wales, Sydney, NSW

Bette Liu

School of Population Health, University of New South Wales, Sydney, New South Wales, Australia; National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead, The University of Sydney, Sydney, New South Wales, Australia

High population vaccine coverage to protect against influenza and SARS-CoV-2 are key to ensuring disease control. While it is known that coverage varies by individual characteristics and in different sub-populations, there is limited information on uptake, particularly in migrants and culturally and linguistically diverse adult groups.
Internationally, Australia has a high proportion of migrants from diverse cultural backgrounds with census data showing that close to a third of the population are migrants. Therefore, understanding and addressing disparities in vaccine uptake in culturally and linguistically diverse groups is important for the success of our vaccine programs.
This presentation will outline research related to influenza vaccine uptake in migrant and culturally and linguistically diverse adults in Australia and suggest some areas for future research and action.

Day 2	Plenary Session 5
11:20	**Casirivimab and imdevimab for COVID-19**
Presenter	Martijn Kwaijtaal; Roche Products, Sydney, NSW

Martijn Kwaijtaal

Roche Products Australia, Sydney, New South Wales, Australia

Casirivimab and imdevimab (cas/imd) are two neutralising antibodies in development for the treatment and prophylaxis for COVID-19. Cas/imd binds to distinct, non-overlapping epitopes on the spike protein and prevents the virus from entering the cell. Three phase 3 studies investigated the use of cas/imd in different settings. A study (NCT04425629) in high-risk ambulatory patients observed a relative reduction of risk to hospitalisation or death by 70.4% (p=0.0024) in those treated with 1200 mg (n=736) and by 71.3% (p<0.0001) in those treated with 2400 mg (n=1355) of cas/imd vs placebo (n=2089)[1]. A study (NCT04452318) in household contacts of a positive SARS-CoV-2 case showed a relative reduction of risk for symptomatic infection by 81.4% (p<0.001) in those treated with 1200 mg (n=752) of cas/imd vs placebo (n=753)[2]. The RECOVERY trial (NCT04381936) showed in severe hospitalised seronegative COVID-19 patients a reduced mortality of 20% (RR 0.80, 0.70-0.91, p=0.001) in patients treated with 8000 mg (n=1633) of cas/imd compared to usual care (n=1520)[3]. In all studies, the safety profile was similar for the treatment and placebo or usual care arms.

To date, loss of susceptibility has been detected in vitro to the individual components of cas/imd however the combination has remained effective against all current variants of concerns and variants of interest of SARS-CoV-2 both in vitro and in vivo. Based on current trial data there is no evidence for treatment emergent loss of susceptibility or resistance for cas/imd.

References:

1 Weinreich DM, et. al. NEJM 2021

2 O'Brien MP, et. al. NEJM 2021

3 Horby PW, et. al. medRxiv 2021

Day 2	Plenary Session 5
11:40	**The AIR 2021; What have we learnt for COVID-19, influenza, and other vaccinations – update on its performance/acceptance**
Presenter	Kristine Macartney; National Centre for Immunisation Research and Surveillance, Sydney, NSW

Kristine Macartney

National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead, The University of Sydney, Sydney, New South Wales, Australia

The Australian Immunisation Register is to celebrate its 25th anniversary in 2022. The Register began by recording childhood vaccines up to age 7 years; in late 2016 it was expanded to include all vaccines across the lifespan. Incomplete reporting of adult vaccines has been addressed by introduction of mandatory reporting requirements for COVID-19, influenza and all NIP-funded vaccines in 2021. Efforts to increase data submission by newer vaccine provider types, such as pharmacists, hospital and work-place clinics and others should see reporting more accurately reflect true coverage levels. Data on COVID-19 vaccination has been generated and analysed on daily basis, using different population denominators. New linkages to other Commonwealth, as well as state and territory databases are being pursued in order to explore coverage in specific subpopulations recommended vaccines (eg by occupation, medical risk factors, culturally and linguistically diverse groups and others). New COVID-19 vaccine mandates underpin the need to for the highest possible accuracy; challenges incorporating vaccine doses and algorithms, for examples on mixed schedules and for vaccines administered overseas, exist. Potential remains to further leverage use of the AIR to improve equity, effectiveness and efficiency of immunisation program delivery.

Day 2	Plenary Session 5
12:00	**Moderna mRNA platform and the future pipeline**
Presenter	Randy Hyer, Moderna Cambridge, MA, USA and Jane Leong, Moderna, Sydney

Randall Hyer[1], Jane Leong[2], Lynn Sartori[2]

[1]Moderna, Cambridge, Massachusetts, USA; [2]Moderna Australia, Sydney, New South Wales, Australia

Background: Every cell in living organisms uses messenger RNA (mRNA) to provide real-time instructions to make the proteins necessary to drive all aspects of biology, including in human health and disease. Given its essential role, the potential for mRNA as a drug or vaccine is far-reaching and could meaningfully change how medicines are discovered, developed and manufactured. Moderna is working to pioneer a new class of medicines based on mRNA. The company's scientific platform focuses on advancing the frontier of mRNA science and technology, trying to take advantage of the intrinsic pharmacological advantages of mRNA to advance mRNA-based medicines.

Modalities: Since its founding in 2010, Moderna has advanced 6 different modalities within its scientific platform: prophylactic vaccines, cancer vaccines, intratumoural immune-oncology, localised regenerative therapeutics, system secreted & cell surface therapeutics and systemic intracellular therapeutics. Whilst the programmes within a modality may target diverse diseases, they share similar mRNA technologies, delivery technologies and manufacturing processes. The programmes within a modality will also generally share similar pharmacology profiles, including the desired dose response, the expected dosing regimen, the target tissue for protein expression, safety and tolerability goals, as well as pharmaceutical properties. Programmes within a modality often have correlated technology risk but, because they pursue diverse diseases, they often have uncorrelated biology risk.

Programmes: The mRNA prophylactic vaccine modality currently includes nine programmes, all of which mimic the process by which natural viral infections occur. Multiple mRNAs encoding for multiple viral proteins can be included in a single vaccine. Moderna's cancer vaccines modality includes the creation of individualised, mRNA-based personalised cancer vaccines through neoepitopes. Intratumoural immune-oncology efforts focus on driving robust, specific anti-cancer T cell responses. The localised regenerative therapeutics modality is developing mRNA medicines to address injured or diseased tissues, allowing for the local production of proteins that provide a therapeutic benefit in the targeted tissue. The systemic secreted & cell surface therapeutics modality has been designed to increase levels of desired secreted proteins across a wide range of diseases and will initially focus on rare genetic diseases. Finally, the systemic intracellular therapeutics modality is designed to increase levels of intracellular proteins to achieve a therapeutic effect in one or more tissues or cell types.

Day 2	Plenary Session 5
12:20	**Development of second generation SARS-CoV-2 mRNA vaccines**
Presenter	Colin Pouton; Pharmacy & Pharmaceutical Sciences, Monash University, Parkville, VIC

Harry Al-Wassiti[1], Stewart Fabb[1], Ruby Kochappan[1], Asuka Takanashi[1], Tom Payne[1], Samantha Grimley[2], Paula Ellenberg[2], Chinn Yi Wong[2], Georgia Delyannis[2], Damian Purcell[2] and Colin Pouton[1]

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mRNA vaccines have been in development for various infections for over ten years but came of age in 2020 as a rapid means to respond to the threat of SARS-CoV-2. Crucial to their deployment is the lipid nanoparticle (LNP) delivery technology, which emerged initially as a means to deliver siRNA to the liver by intravenous injection. LNPs were repurposed, with limited modification, for delivery of COVID-19 mRNA vaccines by intramuscular injection. The LNP-mRNA particles do not require an additional adjuvant, and the precise mechanism by which innate immune responses are induced is not clear. The crucial mechanisms that drive adaptive immunity are also not in the public domain. There is much to learn about mRNA vaccination and plenty of scope for development of new delivery technologies.

We embarked on a strategy to address the need to boost immunity against SARS-CoV-2 variants, by vaccinating with the receptor-binding domain (RBD) rather than the whole spike protein. Initially we developed vaccines against the Wuhan RBD, which proved to be functional. We then optimised the mRNA using 1) codon-optimisation, 2) efficient RNA 5' capping and 3) use of the modified nucleotide N-methyl-pseudoUTP. After purification and encapsulation in LNPs, the vaccine was effective in mice over a dose range of 1-5ug mRNA, similar to the dose of *Comirnaty* required to induce a strong antibody response in mice. Doses in this range protected mice from challenge with a N501Y strain of SARS-CoV-2 that was isolated in Melbourne.

As the pandemic progressed we focussed on development of an RBD vaccine against the Beta strain of SARS-CoV-2, which at present is one of the strains that evades protection afforded by the existing commercial mRNA vaccines. We are working towards a Phase I clinical study of this vaccine in the near future.

Day 2	Plenary Session 6
13:15	**Off-season RSV epidemics in Australia after easing of COVID-19 restrictions**
Speaker	John-Sebastian Eden; Centre for Virus Research, Westmead Institute for Medical Research, Sydney, NSW

John-Sebastian Eden[1,2], Chisha Sikazwe[3,4], Ruopeng Xie[5,6], Yi-Mo Deng[7,8], Sheena G. Sullivan[7,9], Alice Michie[4], Avram Levy[3], Elena Cutmore[1,2], Christopher C. Blyth[3,10-12], Philip N. Britton[2,13], Nigel Crawford[14-16], Xiaomin Dong[7,8], Dominic E. Dwyer[2,17], Kimberly M. Edwards[5,6], Bethany A. Horsburgh[1,2], David Foley[3], Karina Kennedy[18], Cara Minney-Smith[3], David Speers[3,10], Rachel L. Tulloch[1,2], Edward C. Holmes[2], Vijaykrishna Dhanasekaran[5,6#], David W. Smith[3,10#], Jen Kok[17#] & Ian G. Barr[7,8#] and the Australian RSV study group

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Human respiratory syncytial virus (RSV) is an important cause of acute respiratory infection (ARI) with the most severe disease in the young and elderly. Non-pharmaceutical interventions (NPIs) and travel restrictions for controlling COVID-19 have impacted the circulation of most respiratory viruses including RSV globally, particularly in Australia, where during 2020 the normal winter epidemics were notably absent. However, in late 2020, unprecedented widespread RSV outbreaks occurred, beginning in spring, and extending into summer across two widely separated states of Australia, Western Australia (WA) and New South Wales (NSW) including the Australian Capital Territory (ACT). Genome sequencing revealed a significant reduction in RSV genetic diversity following COVID-19 emergence except for two genetically distinct RSV-A clades. These clades circulated cryptically, likely localized for several months prior to an epidemic surge in cases upon relaxation of COVID-19 control measures. The NSW/ACT clade subsequently spread to the neighbouring state of Victoria (VIC) and caused extensive outbreaks and hospitalisations in early 2021. These findings highlight the need for continued surveillance and sequencing of RSV and other respiratory viruses during and after the COVID-19 pandemic as mitigation measures introduced may result in unusual seasonality, along with larger or more severe outbreaks in the future.

Day 2	Plenary Session 6
13:40	**The clinical epidemiology of RSV in children: subtypes, severity & syndromes**
Speaker	Gemma Saravanos; The Children's Hospital at Westmead, The University of Sydney, NSW

Gemma L. Saravanos

National Centre for Immunisation Research & Surveillance and The University of Sydney, Children's Hospital at Westmead Clinical School, Sydney, New South Wales, Australia; Susan Wakil School of Nursing & Midwifery, The University of Sydney, Sydney, New South Wales, Australia

Background: Respiratory syncytial virus (RSV) is a leading cause of acute lower respiratory infection and the development of effective and affordable RSV-specific prevention, including vaccines and immunoprophylaxis, is a global priority. Understanding the clinical epidemiology of RSV will inform the implementation of RSV-specific prevention. Our research aimed to understand 1) the circulation and disease severity associated with RSV subtypes, 2) if there were age or severity specific differences between the unseasonal 2020 RSV epidemic compared to previous years, and 3) to what extent RSV infection is associated with severe acute neurological disease.

Methods: This research encompassed a variety of studies and methods including: a comparison of the circulation and severity of RSV-A and RSV-B infections (2014-2018); a time series analysis of routinely collected clinical datasets to examine the 'shifted' 2020 RSV season (2014-2020); and a systematic literature review to understand the association of RSV infection with severe acute neurological disease. Clinical cohorts were sampled from the Sydney Children's Hospital Network in New South Wales (NSW), Australia.

Results: During a five-year-period, we identified 3,591 RSV infections and found that RSV-A (1,585, 44.1%) and RSV-B (2,006, 55.9%) co-circulated with alternating predominance each season. A random sample of 200 cases did not demonstrate a difference between indicators of disease severity for the two subtypes. In 2020, we observed a shift in the peak of RSV-related disease from autumn-winter to early summer. Compared to previous years, there was an increase in the frequency of RSV infections in children aged 2 to 4 years (83.91%, 95% CI 34.21 to 192.07%, $p<0.01$) but an overall reduction of RSV-coded hospitalisations (-31.80%, 95% CI -41.13% to -18.96%, $p<0.01$). From the global published literature, we identified 87 unique studies from 26 countries describing a spectrum of RSV-associated severe acute neurologic syndromes including proven encephalitis, acute encephalopathy, and complex seizures.

Conclusions: RSV-A and RSV-B co-circulate in NSW children and both contribute to severe RSV disease thus RSV-specific interventions will need to be equally effective against both subtypes to have the greatest impact. The shifted 2020 RSV season appeared no more severe than previous years. Increased RSV infections in children aged 2 to 4 years may be explained by a build-up in population susceptibility and increased testing in older children. RSV-associated severe acute neurologic complications have been widely reported but there is substantial heterogeneity in existing studies. The establishment of robust RSV surveillance that captures demographic, clinical and virological features is needed to inform existing and future RSV prevention efforts.

Day 2	Plenary Session 6
14:05	**WHO RSV global surveillance program – Phase 2 – An update**
Speaker	Ian Barr, WHO CC, Doherty Institute, Melbourne, VIC

Ian G. Barr[1,2], Nigel Crawford[3], Annette Alafaci[3], The Australian WHO RSV Study Group and The WHO Global RSV Surveillance Participants

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Human Respiratory syncytial virus (RSV) is one of the most common childhood respiratory infections, especially in very young children, but also causes repeated infections throughout life. In 2017, the World Health Organisation (WHO) launched a 2-year global RSV surveillance pilot to test the feasibility of leveraging the Global Influenza Surveillance and Response System (GISRS) platform to assist in determining the burden of RSV in 15 countries globally. An additional role of this pilot was to develop a global evidence base on RSV to inform health policy on the potential benefits of the introduction of an RSV vaccine. Following the success of the pilot program in collecting data on the incidence of RSV in participating countries without disrupting influenza surveillance, a second phase of RSV surveillance was instigated in April 2019, to run for a further 3 years. Phase 2 saw an expansion to 24 countries with more LMIC recruited along with the original 15 countries that participated in Phase 1. Changes were also made in the case enrolment eligibility, from a focus on children <5 years of age in Phase 1 to hospitalized children <2 years of age in Phase 2. Despite interruptions caused by the COVID-19 pandemic, a number of countries have still managed to screen patients for RSV as well as SARS-CoV-2.

Australia had provided data for Phase 1 from a single site (Royal Children's Hospital (RCH) Melbourne) but this was expanded to include 3 other sites (Perth Children's Hospital, Queensland's Children's Hospital, Royal Darwin Hospital) for 2021 and 2022 with the support of the Australian Government Department of Health. Australia's participation in the Phase 2 program will contribute to determining the burden of RSV globally, as well as provide background information for assessing the potential future utility of an RSV vaccine or expanded use of anti-RSV monoclonal antibody prophylaxis in the Australian context, in the near future.

More information is available at: https://www.who.int/teams/global-influenza-programme/global-respiratory-syncytial-virus-surveillance

Day 2	Plenary Session 6
14:30	**Modelling the household-level impact of a maternal respiratory syncytial virus (RSV) vaccine**
Speaker	Patricia Campbell; Department of Infectious Diseases, University of Melbourne, Doherty Institute, Melbourne, VIC

Patricia T. Campbell[1,2], Nicholas Geard[3], Alexandra B. Hogan[4]

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Respiratory syncytial virus (RSV) is a ubiquitous infection that is a major cause of respiratory morbidity in young children, with the risk of hospitalization highest in the first six months of life. There is no approved vaccine for RSV, however, a recent phase 3 clinical trial of maternal vaccination estimated efficacy of around 40% for the first 90 days of life. Households play a key role in RSV transmission, however, few estimates of population-level RSV vaccine impact account for household structure. We simulated RSV transmission within a stochastic, individual-based model structured by household using an existing demographic model parameterized with Australian data. Our model simulated pregnancy, with RSV vaccination given from 6 weeks to 3 months before the scheduled date of birth. In our model, maternal vaccination produced the greatest reduction in RSV infection incidence among infants younger than 3 months, with around 17% reduction at 70% coverage. A more modest decrease of around 5% was observed in infants aged 3–6 months. The incidence rate for infants born to unvaccinated mothers was 1.26 times that of infants born to vaccinated mothers. The incidence of RSV infection increased in children aged 1–2 years, with evidence of infections being delayed to the second year of life. Overall, population-level reductions in RSV infection incidence obtained from imperfect, short-lived maternal vaccines are anticipated to be modest, while the benefit to infants born to vaccinated mothers is likely to be more substantial, particularly if severity is reduced by delaying an infant's first infection to their second year of life.

	Pre-recorded short talks
	Relative Vaccine Effectiveness of Cell-Based Quadrivalent Influenza Vaccine vs Egg-Based Quadrivalent Influenza Vaccine in Children and Adults During the 2017-2018, 2018-2019, and 2019-2020 US Influenza Seasons
Speaker	Julianne Bayliss, Seqirus Australia, Parkville, VIC

Julianne Bayliss[1], Constantina Boikos[2], Ian McGovern[3], Deborah Molrine[3], Justin R. Ortiz[4], Joan Puig-Barbara[5], Chris Clarke[1], Mendel Haag[6]

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Background: During traditional influenza vaccine production in fertilized hen's eggs, vaccine-strain viruses sometimes adapt to avian receptors in a process known as egg adaptation. These changes may lead to antigenic mismatch and, potentially, reduced vaccine effectiveness. There is no possibility of egg adaptation when influenza vaccines are produced using mammalian cell lines. To determine whether the cell-based quadrivalent inactivated influenza vaccine (IIV4c) provides improved protection relative to egg-based vaccines, we estimated the relative vaccine effectiveness (rVE) of IIV4c versus egg-derived quadrivalent influenza vaccines (IIV4e) in preventing influenza-related medical encounters (IRMEs) in children and adults for three consecutive U.S. influenza seasons.

Methods: Three retrospective, observational cohort studies were conducted during the 2017-2018, 2018-2019, or 2019-2020 influenza seasons in the U.S. Data from 18.4 million persons ≥4 years of age who were vaccinated with IIV4c or IIV4e were included in integrated datasets compiled for each season from electronic medical records linked to pharmacy and medical claims data, where available. The outcome of interest was influenza-related medical encounters (IRME) identified from patient records using codes specific to influenza disease diagnosis (ICD J09*-J11*). Propensity score methods that adjusted for prespecified confounders (age, sex, race, ethnicity, geographic location, week of vaccination, health status) were used to estimate rVE in the overall population and age-specific and high-risk subgroups.

Results: Over three consecutive seasons, IIV4c provided greater protection from IRMEs than IIV4e in the overall population and paediatric and adult subgroups, except for ages 4-17 years in 2017-2018 and ≥65 years in all seasons (Figure). This benefit was consistent in the high-risk cohort evaluated in 2018-2019. The rVE was greatest during the 2017-2018 season, during which A/H3N2 viruses predominated and egg-adaptation was documented in the A/H3N2 strains of IIV4e vaccines.

Conclusions: Findings from three retrospective cohort studies conducted in the 2017-2018, 2018-2019, and 2019-2020 influenza seasons using an integrated dataset support the use of cell-derived influenza viruses as a more effective approach than vaccines containing influenza viruses propagated in eggs, which are subject to egg-adaptive antigenic mutations.

	Pre-recorded short talks
	Different TCR repertoire and transcriptome between optimal HLA-A*02:01- and high-risk HLA-A*24:02-restricted CD8$^+$ T cell immunity against influenza A virus
Speaker	So Young Chang; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

So Young Chang[1], Oanh Nguyen[1], Marios Koutsakos[1], Luca Hensen[1], Brendon Chua[1], Carolien van de Sandt[1], Simone Rizzetto[2], Fabio Luciani[2], and Katherine Kedzierska[1]

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Influenza viruses circulate annually and cause significant morbidity and mortality during seasonal epidemics. CD8$^+$ T cells provide broad protective immunity against influenza viruses. The quality of CD8$^+$ T cell response against viral infections and its protective capacity can be influenced by Major histocompatibility complex (MHC)/Human leukocyte antigen (HLA) class I polymorphisms, binding affinity of T cell receptor (TCR)/peptide-HLA-I complex, functional avidity, and the nature of the TCRαβ repertoire. HLA-A*24:02 is frequently found in Indigenous Australians and associated with severe influenza disease during the pH1N1 outbreak. Here, we assessed at the single cell level, the TCRαβ repertoire and transcriptome of CD8$^+$ T cells against an influenza-specific HLA-A*24:02-PB1$_{498\text{-}505}$ (A24/PB1$_{498}$) epitope. Using ex-vivo peptide-HLA tetramer-associated magnetic enrichment (TAME), single-cell multiplex-nested RT-PCR for paired TCRαβ repertoires, and TCRdist analysis of PBMCs from HLA-A*24:02 healthy donors, we assessed the quality of A24/PB1$_{498}^+$CD8$^+$ T cells compared to the HLA-*02:01-M1$_{58\text{-}66}$ (A2/M1$_{58}$) epitope, which is the most well-defined and immunodominant human influenza epitope restricted to the most common HLA-allele in Caucasians. We found that the TCRαβ repertoire of A24/PB1$_{498}^+$CD8$^+$ T cells was biased in usage of TRBV9 (42.5%) with variable TRAV segment usage and highly diverse TCRαβ clonotypes. To further understand global qualitative differences between optimal A2/M1$_{58}$ and high-risk A24/PB1$_{498}$ epitopes, we performed single-cell RNA sequencing of A24/PB1$_{498}$ and A2/M1$_{58}$ tetramer-specific CD8$^+$ T cells *ex vivo* and demonstrated that gene expression levels of cytotoxic molecules such as granzyme A, granzyme B and CCL5 were lower in A24/PB1$_{498}^+$CD8$^+$ T cells than in A2/M1$_{58}^+$CD8$^+$ T cells. Overall, our findings provide new insights into the mortality-associated HLA-A*24:02 allomorph and suggest strategies to develop universal T cell-mediated vaccines and immunotherapies.

	Pre-recorded short talks
	TLR2-mediated activation of innate responses in the upper airways confers anti-viral protection of the lungs
Speaker	Brendon Chua; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Georgia Deliyannis[1], Chinn Yi Wong[1], Hayley A. McQuilten[1], Annabell Bachem[1], Michele Clarke[1], Xiaoxiao Jia[1], Kylie Horrocks[1], Weiguang Zeng[1], Jason Girkin[2,4], Nichollas Scott[1], Sarah Londrigan[1], Patrick Reading[1,3], Nathan W. Bartlett[2,4], Katherine Kedzierska[1], Lorena Brown[1], Francesca Mercuri[5], Christophe Demaison[5], David Jackson[1], Brendon Chua[1]

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The impact of respiratory virus infections on global health is felt not just during a pandemic but for many, endemic seasonal infections pose an equal and ongoing risk of severe disease. Moreover, vaccines and antiviral drugs are not always effective or available for many respiratory viruses. We investigated how induction of effective and appropriate antigen independent innate immunity in the upper airways can prevent spread of respiratory virus infection to the vulnerable lower airways. Activation of toll-like receptor-2 (TLR2), when restricted to the nasal turbinates results in prompt induction of innate immune-driven anti-viral responses through action of cytokines, chemokines and cellular activity in the upper but not the lower airways. We define how nasal epithelial cells and recruitment of macrophages work in concert and play pivotal roles to limit progression of influenza virus to the lungs and sustain protection for up to seven days. We also present findings to show that protection can be extended to rhinovirus infection as well as reduce virus infection in the throat and nasal passages of ferrets following exposure to SARS-CoV-2. These results reveal underlying mechanisms of how control of viral infection in the upper airways can occur and also support the implementation of strategies that can activate TLR2 in nasal passages to provide rapid protection, especially for at-risk populations, against severe respiratory infection when vaccines and antiviral drugs are not always effective or available.

	Pre-recorded short talks
	Increased immunopathology and perturbed immune dynamics during influenza virus and arbovirus co-infection.
Speaker	Isabelle Foo; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Isabelle J. Foo[1,2], Brendon Y. Chua[1], So Young Chang[1], Xiaoxiao Jia[1], Katherine Kedzierska[1], John K. Fazakerley[1,2], Lukasz Kedzierski[1,2]

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Infection with more than one pathogen, in sequence or concurrently, occurs commonly in nature and can substantially affect immune responses. Reports on co-infections often note poorer health outcomes and increased pathogen burdens compared to single infections. Viral co-infections can affect individual antiviral responses, reduce protection, and enhance immunopathology. Limited information exists on the outcome of co-infection with influenza and non-respiratory viruses. As influenza is prevalent worldwide, its geographical distribution overlaps with that of many arboviruses. To explore the interaction between these two types of virus infection, we established a C57BL/6 mouse model of co-infection using Semliki Forest Virus (SFV), a neurotropic arbovirus, and Influenza A virus (IAV). Adult C57BL/6 mice were infected with IAV only (respiratory infection); SFV only (systemic infection followed by encephalitis); or sequentially co-infected on day 8 post-primary infection (either SFV→IAV or IAV→SFV). Viral, inflammatory and immunological analyses were performed on day 7 following either single infection (IAV; SFV) or co-infection (SFV→IAV; IAV→SFV). In the SFV→IAV co-infection group, we observed more severe disease. This was linked to an exacerbated lung cytokine storm and delayed viral clearance in co-infected animals, resulting in more severe lung pathology. Moreover, we found altered trafficking of immune responses, particularly IAV-specific $CD8^+$ T cells being redirected to the brain in SFV→IAV co-infection. These data provide new insights into how co-infection with viruses which cause predominantly either lung or brain disease each alter the immune response and disease outcome of the other. Improved fundamental knowledge on how viral infections interact to affect the course of immune responses, could be of a direct relevance to improved disease management programs, specialist treatments and optimisation of vaccination strategies.

	Pre-recorded short talks
	Integrated immune networks in SARS-CoV-2 infected pregnant women reveal differential NK cell and unconventional T cell activation
Speaker	Jennifer Habel, Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, VIC

Jennifer R. Habel[1¶], Brendon Y. Chua[1,2], Lukasz Kedzierski[1,3], Kevin J. Selva[1], Timon Damelang[1], Ebene R. Haycroft[1], Thi H.O. Nguyen[1], Hui-Fern Koay[1], Suellen Nicholson[4], Hayley McQuilten[1], Xiaoxiao Jia[1], Lilith F. Allen[1], Luca Hensen[1], Wuji Zhang[1], Carolien E. van de Sandt[1], Jessica A. Neil[1], Fatima Amanat[5,6], Florian Krammer[5], Kathleen Wragg[1], Jenifer A. Juno[1], Adam K. Wheatley[1, 7], Hyon-Xhi Tan[1], Gabrielle Pell[8], Jennifer Audsley[9], Irani Thevarajan[9, 10], Justin Denholm[9,10], Kanta Subbarao[1, 11], Dale I. Godfrey[1], Allen C. Cheng[12,13], Steven Y.C. Tong[10, 14], Katherine Bond[1,15], Deborah A. Williamson[1,15], Fiona James[16], Natasha E. Holmes[16-19], Olivia C. Smibert[16,20,21], Jason A. Trubiano[19-22], Claire L. Gordon[1,16], Amy W. Chung[1], Clare L. Whitehead[23,24], Stephen J. Kent[1,7,25], Martha Lappas[8,26], Louise C. Rowntree[1#], Katherine Kedzierska[1,2#]

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Although pregnancy poses a greater risk for severe COVID-19, the underlying immunological changes associated with SARS-CoV-2 infection during pregnancy are poorly understood. We defined immune responses to SARS-CoV-2 in pregnant and non-pregnant women during acute and convalescent COVID-19 up to 258 days post symptom onset, quantifying 217 immunological parameters. Additionally, matched maternal and cord blood were collected from COVID-19 convalescent pregnancies. Although serological responses to SARS-CoV-2 were similar in pregnant and non-pregnant women, cellular immune analyses revealed marked differences in key NK cell and unconventional T cell responses during COVID-19 in pregnant women. While NK cells, γδ T cells and MAIT cells displayed pre-activated phenotypes in healthy pregnant women when compared to non-pregnant age-matched women, activation profiles of these pre-activated NK and unconventional T cells remained unchanged at acute and convalescent COVID-19 in pregnancy. Conversely, activation dynamics of NK and unconventional T cells were prototypical in non-pregnant women in COVID-19. In contrast, activation of αβ $CD4^+$ and $CD8^+$ T cells, T follicular helper cells and antibody-secreting cells was similar in pregnant and non-pregnant women with COVID-19. Elevated levels of IL-1β, IFN-γ, IL-8, IL-18 and IL-33 were also found in pregnant women in their healthy state, and these cytokine levels remained elevated during acute and convalescent COVID-19. Collectively, our study provides the first comprehensive map of longitudinal immune responses to SARS-CoV-2 infection in pregnant women, providing insights into patient management and education for COVID-19 during pregnancy.

	Pre-recorded short talks
	A history of obesity reduces the immune response to influenza virus in a canonical NLRP3 inflammasome-dependent manner
Speaker	Katina Hulme, School of Chemistry and Molecular Biosciences, University of Queensland, St Lucia, QLD

Katina D. Hulme[1], Ellesandra C. Noye[1], Conor J. Bloxham[2], Nathalie A.J. Verzele[1], Marcus Z.W. Tong[1], Larisa L. Labzin[3], Keng Yih Chew[1], Helle Bielefeldt-Ohmann[1,4], Kate Schroder[3], Kirsty R. Short[1,4]

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Background: Obesity significantly increases the risk of death following an influenza virus infection. Consistent with these clinical observations, we and others have shown that mice with diet-induced obesity develop much more severe influenza than their lean-fed counterparts. Traditionally, it has been assumed that this increased susceptibility can be reversed by weight loss. However, this remains to be tested experimentally.

Methods: Here, a novel mouse model was developed to study the long-term effects of obesity on anti-viral immunity. Four-weeks old C57BL/6 mice were fed a high fat or lean diet for 10 weeks. After 10 weeks, mice fed a high-fat diet had a significantly higher total body weight and percentage body fat compared to mice fed the lean diet. Obese mice were then swapped to a lean diet for 10 weeks.

Results: After 10 weeks on the lean diet, mice that were previously obese (PO) had an equivalent body weight and percentage body fat to mice that received the lean diet for the entirety of the 20-week treatment period. However, upon infection with influenza virus (A/Auckland/09(H1N1)), PO mice displayed increased viral replication, lung inflammation, body weight loss and pulmonary dysfunction compared to lean-fed mice. Alveolar cells of PO mice also had an altered metabolic state compared to those of lean fed mice. Importantly, deficiency in NLRP3 blocked the long-term effect of murine obesity on susceptibility to severe influenza virus infection.

Conclusions: We propose that obesity can have long-term, canonical NLRP3 dependent, effects on the metabolism of innate inflammatory cells rendering their anti-viral responses impaired. Understanding the long-term effects that obesity has on anti-viral immunity will help pave the way for development of novel therapeutics to improve the health of the billions of people who are, or previously have been, obese.

	Pre-recorded short talks
	Influenza vaccination after myocardial infarction: A randomised, double-blind, placebo-controlled, multicentre trial
Speaker	Raina MacIntyre, The Kirby Institute, University of New South Wales, Kensington, NSW

Ole Fröbert[1], Matthias Götberg[2], David Erlinge[2], Zubair Akhtar[3], Evald H. Christiansen[4], Chandini R. MacIntyre[5], Keith G. Oldroyd[6], Zuzana Motovska[7], Andrejs Erglis[8], Rasmus Moer[9], Ota Hlinomaz[10], Lars Jakobsen[4], Thomas Engstrøm[11], Lisette O. Jensen[12], Christian O. Fallesen[12], Svend E. Jensen[13], Oskar Angerås[14], Fredrik Calais[1], Amra Kåregren[15], Jörg Lauermann[16], Arash Mokhtari[2], Johan Nilsson[17], Jonas Persson[18], Per Stalby[19], Abu K.M.M. Islam[20], Afzalur Rahman[20], Fazila Malik[21], Sohel Choudhury[21], Timothy Collier[22], Stuart J. Pocock[22], John Pernow[23]

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Background: Observational and small randomized studies suggest that influenza vaccine may reduce future cardiovascular events in patients with cardiovascular disease.

Methods: We conducted an investigator-initiated, randomized, double-blind trial to compare inactivated influenza vaccine with saline placebo administered shortly after myocardial infarction (MI) (99.7% of patients) or high-risk stable coronary heart disease (0.3%). The primary endpoint was the composite of all-cause death, MI, or stent thrombosis at 12 months. A hierarchical testing strategy was used for the key secondary endpoints: all-cause death, cardiovascular death, MI, and stent thrombosis.

Results: Due to the Covid-19 pandemic, the data safety and monitoring board decided to halt the trial before attaining the prespecified sample size. Between October 1, 2016, and March 1, 2020, 2571 participants were randomized at 30 centers across eight countries; 1290 assigned to influenza vaccine and 1281 to placebo. Over the 12-month follow-up, the primary outcome occurred in 67 participants (5.3%) assigned influenza vaccine and 91 participants (7.2%) assigned placebo (hazard ratio, 0.72; 95% confidence interval, 0.52 to 0.99; P=0.040). Rates of all-cause death were 2.9% and 4.9% (hazard ratio, 0.59; 0.39 to 0.89; P=0.010), of cardiovascular death 2.7% and 4.5%, (hazard ratio, 0.59; 0.39 to 0.90; P=0.014), and of MI 2.0% and 2.4% (hazard ratio, 0.86; 0.50 to 1.46, P=0.57) in the influenza vaccine and placebo groups, respectively.

Conclusions: Influenza vaccination early after an MI or in high-risk coronary heart disease resulted in a lower risk of a composite of all-cause death, MI, or stent thrombosis, as well as a lower risk of all-cause death and cardiovascular death at 12 months compared with placebo.

	Pre-recorded short talks
	Silencing Pulmonary Sensory Neurons Increases Influenza Disease Severity
Speaker	Alice McGovern; Department of Anatomy and Physiology, University of Melbourne, Parkville, VIC

Nathalie A.J. Verzele[1,2], Matthew W. Trewella[1], Eloise M. Whitehead, Stuart B. Mazzone[1], Kirsty R. Short[2], Alice E. McGovern[1]

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Introduction: The respiratory tract has a rich supply of sensory nerves that are critical for protecting the lungs against harmful or potentially threatening stimuli such as pathogens. We recently showed that during a respiratory viral infection with influenza, the pulmonary sensory nerves change their genetic makeup and take on a neuroinflammatory phenotype. However, the role they play in maintaining airway immunity during influenza infection remains elusive.

Methods: Using a murine model (C57Bl6/J mice, 8-10 weeks age) of influenza respiratory infection (Auckland/1/09 H1N1), pulmonary sensory nerve activity was blocked by daily inhaled treatment with the drug QX-314 (a charged sodium channel inhibitor). Disease severity was measured using whole body plethysmography, pulse oximetry, clinical scoring, gene expression and cytokine levels.

Results: Silencing the activity of pulmonary sensory neurons in mice with QX-314 during influenza infection resulted in more severe weight loss (% body weight from original - vehicle treated, 81.2 ± 1.2%; QX-314 treated, 76.2 ± 0.6%; p=0.003) and increased severity of clinical symptoms compared to vehicle treated influenza-infected mice. This was accompanied by an increase in pulmonary concentrations of cytokines IFN-γ (vehicle treated, 58.4 ± 4.4; QX-314 treated, 161.6 ± 27.4 pg/ ml; p=0.013) and IL-6 (vehicle treated, 257.3 ± 57.2; QX-314 treated, 468.9 ± 39.7 pg/ ml; p=0.016) and an increased number of immune cells in the lungs (vehicle treated, $4.5x10^7 \pm 1.7x10^6$; QX-314 treated, $5.5x10^7 \pm 1.6x10^6$ cells/ ml; p=0.0002). Interestingly, QX-314 treatment resulted in a significant decrease of genes initially found to be upregulated as a result of influenza infection, in the pulmonary sensory neurons (neuropeptides - *Calca, Tac1;* interferon-related genes - *Irf9, Ifit1, Il1b, Isg15*).

Conclusions: Our results indicate that pulmonary sensory neurons play a major role in airway immunity by potentially limiting influenza-induced disease progression. The exact mechanism by which this occurs remains uncertain but may likely provide potential future therapeutic avenues for treating respiratory viral infections.

	Pre-recorded short talks
	Complete protection by a single dose skin patch delivered SARS-CoV-2 spike vaccine in mice
Speaker	David Muller, School of Chemistry and Molecular Biosciences, University of Queensland, St Lucia, QLD

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SARS-CoV-2 has infected over 242 million people and resulted in more than 4.9 million deaths, and we still face many challenges in the rollout of vaccines. Here, we use the high-density microarray patch to deliver a SARS-CoV-2 spike subunit vaccine directly to the skin. We show the vaccine, dry-coated on the patch is thermostable, and delivery of spike via HD-MAP induced greater cellular and antibody immune responses, with serum able to potently neutralize clinically relevant isolates including those from the B.1.1.7 and B.1.351 lineages. Finally, a single dose of HD-MAP-delivered spike provided complete protection from a lethal virus challenge, demonstrating that HD-MAP delivery of a SARS-CoV-2 vaccine is superior to traditional needle-and-syringe vaccination and has the potential to greatly impact the ongoing COVID-19 pandemic.

	Pre-recorded short talks
	In-concert immune dynamics during natural influenza virus infection and recovery in acute hospitalized patients
Speaker	Oanh Nguyen, Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Thi H.O. Nguyen[1], Marios Koutsakos[1], Carolien E. van de Sandt[1,2], Jeremy Chase Crawford[3], Liyen Loh[1], Sneha Sant[1], Ludivine Grzelak[4], Emma K. Allen[3], Tim Brahm[3], E. Bridie Clemens[1], Maria Auladell[1], Luca Hensen[1], Zhongfang Wang[1], Simone Nüssing[1], Xiaoxiao Jia[1], Patrick Günther[1], Adam K. Wheatley[1], Stephen J. Kent[1,5,6], Malet Aban[7], Yi-Mo Deng[7], Karen L. Laurie[7], Aeron C. Hurt[7], Stephanie Gras[8,9], Jamie Rossjohn[8-10], Jane Crowe[11], Jianqing Xu[12], David Jackson[1], Lorena E. Brown[1], Nicole L. La Gruta[8], Weisan Chen[13], Peter C. Doherty[1], Stephen J. Turner[14], Tom C. Kotsimbos[15,16], Paul G. Thomas[3], Allen C. Cheng[17,18*], Katherine Kedzierska[1*]

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Background: How innate and adaptive immune responses work in concert to resolve influenza disease is yet to be fully investigated in one single study. Here, we utilised longitudinal samples from patients hospitalized with acute influenza to understand these immune responses. We recruited 64 patients admitted to the Alfred Hospital (Prahran, Australia) between 2014-2017, including 44 influenza-infected patients and 20 control patients with other respiratory viral infections.

Methods: The dynamics of 18 important immune parameters, related to clinical, genetic and virological factors, were examined in influenza patients across different severity levels. These included antiviral/inflammatory cytokines and chemokines, haemagglutinin (HA)-directed antibodies, HA-specific B cells, antibody-secreting cells (ASCs), circulatory $CD4^+$ T follicular helper (cTfh) cells, influenza peptide/MHC-specific $CD8^+/CD4^+$ T cells, IFN-γ-producing $CD8^+/CD4^+$ T cells, IFN-γ-producing innate lymphocytes (NK, MAIT and γδ T cells) and the expression of cytotoxic molecules (granzyme A, B, K, M and perforin).

Results: Influenza disease correlated with increases in IL-6/IL-8/MIP-1α/β cytokines and lower antibody responses. Robust activation of circulating cTfh cells correlated with peak ASCs and influenza HA-specific memory B-cell numbers, which differed phenotypically from vaccination-induced B-cell responses. Numbers of influenza-specific $CD8^+$ or $CD4^+$ T cells increased early in disease and retained an activated phenotype during patient recovery.

Conclusions: We report the characterization of immune cellular networks activated during influenza infection to promote recovery. Our study suggests that a rational design of universal influenza vaccines needs to consider circulating Tfh cells, pre-existing serological memory, and effective B cell and T cell immunity that provide broad protection against distinct influenza virus strains and subtypes. We provide the broadest to-date description of immune cellular networks underlying recovery from influenza infection, in humans or mice, and suggest these findings are highly relevant to other viral diseases.

	Pre-recorded short talks
	Detection of influenza infection through supervised hotel quarantine in Australia
Speaker	Heidi Peck, WHO CC, Doherty Institute, Melbourne, VIC

Heidi Peck[1], Kimberley McMahon[2], Kevin Freeman[3], Leah Gillespie[1], Ian Barr[1,4], Sheena Sullivan[1,5,6]

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Introduction: In March 2020, the Australian Federal Government announced the suspension of incoming international air travel to Australia, due to the emerging threat of the SARS-CoV-2 virus. Returning Australian citizens were required to complete 14 days of quarantine in managed hotels. In tandem with other non-pharmaceutical interventions (NPIs), such as social distancing, this policy has had a dramatic impact on the transmission and detection of influenza in Australia. Notifications of influenza to the National Notifiable Disease Surveillance System (NNDSS) are at historical lows, with little to no community circulation of influenza since April 2020.

Methods: The Australian Federal Government in partnership with QANTAS, has operated repatriation flights from major international destinations such as London, Los Angeles and New Delhi in 2020-21. A large number of these flights arrived in Darwin where there is a large open air quarantine facility located at Howard Springs. Nasal and throat samples were taken at three time points during quarantine – upon arrival, and 7 and 12 days after arrival. Samples were tested at the Royal Darwin Hospital Pathology laboratory for Influenza A, Influenza B, SARS-CoV-2 and Respiratory Syncytial Virus (RSV). Samples positive for Influenza A or B were sent to the WHO Collaborating Centre for Reference and Research on Influenza (WHO CC) in Melbourne for further characterisation.

Results: A total of 58 influenza positive clinical samples were sent to the WHO CC from the quarantine sampling in 2021. A majority (n=54, 93%) were taken from travellers returning from the Indian subcontinent, while the remaining 4 (7%) were from Timor-Leste. After duplicate swabs from different sampling time-points were removed, there were 46 influenza-positive clinical samples from individuals available for analysis. 36 (78%) were influenza A(H3N2) and all were in the genetic clade 3C.2a1b.2a.2, which represents the dominant genetic clade for A(H3N2) viruses over the SARS-CoV-2 pandemic period. 10 (22%) were influenza B (B/Victoria lineage) viruses and all were in the V1A.3a.2 genetic clade, which has increased significantly in proportion in 2021. These A(H3N2) and B/Victoria viruses were antigenically distinct from their respective 2021 Southern Hemisphere vaccine viruses. One of the A(H3N2) viruses recovered has been used as a candidate vaccine virus for the 2022 Southern Hemisphere influenza vaccine.

Conclusions: Although circulating influenza has been undetectable in Australia since April 2020, viruses have continued to circulate in isolated pockets and in some countries, including India. Detection of influenza in repatriated travellers has provided a source of viruses for development of A(H3N2) vaccine seed viruses. It also presents as a warning for the re-introduction of influenza to Australia, the risk for which may increase as quarantine arrangements are relaxed.

	Pre-recorded short talks
	SARS-CoV-2 infection in children does not necessitate establishment of adaptive SARS-CoV-2-specific immunological memory
Speaker	Louise Rowntree; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Louise Rowntree[1]*, Oanh Nguyen[1]*, Lukasz Kedzierski[1,2]*, Melanie Neeland[3,4], Jan Petersen[5,6], Jeremy Crawford[7], Lilith Allen[1], Anastasia Minervina[7], Mikhail Pogorelyy[7], Priyanka Chaurasia[5], Hyon-Xhi Tan[1], Adam Wheatley[1,8], Hayley McQuilten[1], Bridie Clemens[1], Fatima Amanat[9], Florian Krammer[9], Sabrina Sonda[10], Katie Flanagan[10-13], Paul Licciardi[3,4], Stephen Kent[1,8,14], Jamie Rossjohn[5,6,15], Paul Thomas[7], Shidan Tosif[3,4,16], Nigel Crawford[3,17], Carolien van de Sandt[1] and Katherine Kedzierska[1]

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Children are at lower risk of developing severe COVID-19, yet the underlying immune mechanisms are understudied. While children's innate immunity can drive rapid resolution of SARS-CoV-2 infection, the establishment of SARS-CoV-2-specific T-cell and B-cell memory in mild COVID-19 in children remains unexplored. We recruited a household cohort to understand SARS-CoV-2-specific $CD4^+$ and $CD8^+$ T-cell immune responses at one month after mild SARS-CoV-2 infection in PCR-positive children, in comparison to their mothers. We analysed SARS-CoV-2-specific T-cell responses, together with B-cells, directly *ex vivo* using six SARS-CoV-2 T-cell HLA class-I tetramers (A1/ORF1a$_{1637}$, A2/S$_{269}$, A3/N$_{361}$, A24/S$_{1208}$, B7/N$_{105}$, B40/N$_{322}$), one class-II tetramer (DPB4/S$_{167}$), and Spike- and Receptor Binding Domain (RBD)-specific B-cell probes. Our in-depth profiling of epitope-specific T-cell responses at quantitative, phenotypic and clonal levels found that only children who seroconverted had prominent memory T-cell and B-cell profiles. These children had a high magnitude of SARS-CoV-2-specific T-cells displaying memory phenotypes and prevalent T cell receptor motifs, which were not observed in RBD IgG^- but PCR^+ children. This suggests that seroconversion but not PCR-positivity defines establishment of adaptive SARS-CoV-2-specific immunological memory in children, which is in contrast to adults with a mild SARS-CoV-2 infection. SARS-CoV-2-specific $CD8^+$ and $CD4^+$ T-cell responses in RBD IgG^+ children were comparable to those of their mothers, with more prominent tetramer-specific T-cell responses associated with seropositivity rather than PCR status alone. Our study suggests that COVID-19 vaccination of children with mRNA vaccines could be a major advantage in terms of establishing T-cell and B-cell immunological memory.

	Pre-recorded short talks
	A universal diagnostic platform technology for influenza and coronaviruses
Speaker	Patrick Schaeffer, College of Public Health, Medical and Veterinary Sciences, James Cook University, QLD

Patrick Schaeffer[1]

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The detection of viral antigens generally relies on traditional immunoassays and, more recently, on immuno-PCR assays and their derivatives. Viral RNA-binding nucleo(capsid)proteins (NP) are validated targets of a number of influenza A and B viruses (IAV and IBV) as well as novel coronavirus (SARS-CoV-2) rapid antigen tests. It is clear that antigen detection is here to stay. However, do we really need the old antibody-antigen sandwich? Here I will discuss from the point of view of a protein chemist some of the major limitations of current rapid antigen tests and the possible alternatives such as aptamers and their challenges. I will then provide a perspective on our new diagnostic platform technology for the universal detection of influenza and coronaviruses.

	Pre-recorded short talks
	Largest recorded avian influenza outbreak event in Australian poultry, July-August 2020 Victoria
Speaker	Angela Scott, Australian Centre for Disease Preparedness, CSIRO, Geelong, VIC

Angela Scott, Jeff Butler, John Bingham, Honglei Chen, Kelly Davies, Gemma Harvey, Patrick Mileto, Matthew Neave, Tristan Reid, Vicky Stevens, William Suen, Som Walker, Jianning Wang, David Williams, Mark Ford, Frank Wong

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Background: Avian influenza viruses (AIVs) have caused extensive losses in poultry industries globally and have zoonotic potential. Australian-lineage low pathogenic avian influenza (LPAI) viruses naturally circulate in Australian wild water birds. When AIV are introduced from wild birds into poultry populations, AIV of subtypes H5 and H7 have the potential to mutate to high pathogenic avian influenza (HPAI) virus. In July to August 2020 in Victoria, HPAI H7N7 and LPAI H7N6 were detected in 3 commercial egg-laying chicken farms and an emu farm respectively.

Methods: Molecular AIV characterisation included real-time PCR, HA and NA gene sequencing, and next generation sequencing (NGS). Full necropsy, including histopathology and immunohistochemistry, was also performed on infected chicken carcasses. AIV pathogenicity was determine in vivo by intravenous inoculation of virus isolate into susceptible chickens.

Results: Sequence analysis of the HA cleavage sites of chicken/Lethbridge/2020(H7N7) and emu/Kerang/2020(H7N6) AIVs revealed high pathogenicity PEIPGKREKR*GLF and low pathogenicity PEIPRKR*GLF motifs, respectively. Virus genomes revealed that both viruses belonged to Australian lineage H7 AIVs and contained genes related to those previously detected in wild birds in Australia. Virus characterisation also indicated that both H7 AI outbreaks were independent and unrelated events. Necropsy of chicken carcasses revealed consistent necrotising salpingitis with abundant antigen. The chicken H7N7 HPAIV caused rapid mortality or severe illness requiring euthanasia in 100% of intravenously infected chickens within 48 hours; whilst the emu H7N6 LPAIV was confirmed to be low pathogenic in chickens with an intravenous pathogenic index (IVPI) of 0.02.

Conclusions: The detection of Australian-lineage AIVs in poultry related to viruses circulating in Australian wild birds has previously occurred in Australia. The 2020 H7N7 HPAI outbreak in Victoria was the eighth and largest ever reported HPAI event in commercial poultry in Australia. To contain the outbreak, approximately half a million birds were destroyed, causing significant impacts in poultry production and trade. The LPAI infection in emus also jeopardised Australia's largest commercial emu genetic stock. Assessment of the genetic characteristics of both H7 AIVs indicated typical avian-adapted viruses of likely low zoonotic risk. Continued AIV surveillance in wildlife and livestock is important to improve future outbreak preparedness and response.

	Pre-recorded short talks
	IL-6, IL-8 and IFN-β are elevated in individuals with long COVID
Speaker	Jane Sinclair, School of Chemistry and Molecular Biosciences, University of Queensland, St Lucia, QLD

Jane Sinclair[1], Zhen Wei Marcus Tong[1], Ellesandra C. Noye[1], Keng Yih Chew[1], Matthew Trau[2], Alain Wuethrich[2], Corey Smith[3,4], Kirsty Short[1]

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Background: Long COVID patients may experience a range of persistent, *de novo* and recurring symptoms affecting the respiratory, cardiovascular, musculoskeletal, and neurological systems >4 weeks post-infection. Emerging literature indicates that chronic inflammation drives long COVID in a subpopulation of recovered COVID-19 patients, while for others, disease symptoms are instead linked to SARS-CoV-2 induced organ damage, the nonspecific effects of hospitalisation and/or the adverse effects of medication/interventions applied during acute infection. This heterogenous pathophysiology highlights the importance of determining in which patients anti-inflammatory therapies would be of clinical benefit.

Methods: Serum was donated from Australians who have recovered from COVID-19, 2-4 months post-COVID-19 diagnosis. Long COVID was defined as the presence of persisting, recurring or *de novo* symptoms that could not be attributable to another diagnosis at the time of sera donation. BioLegend LEGENDplex Human Anti-Virus Response Panel (13-plex) was used to measure serum levels of IL-1β, IL-6, TNF-α, IP-10, IFN-λ1, IL-8, IL-12p70, IFN-α2, IFN-λ2/3, GM-CSF, IFN-β, IL-10, and IFN-γ.

Results: Upon blood donation, 19/68 (27.9%) of patients who had recovered from COVID-19 reported persistent COVID-19 symptoms. Of the patients suffering from long COVID, 6 (31.6%) reported experiencing lethargy and fatigue, 4 (21.1%) cardiovascular problems, 4 (21.1%) respiratory problems, 3 (15.8%) altered sense of smell, 2 (10.5%) kidney problems, 1 (5.3%) elevated C-reactive protein, 1 (5.3%) brain fog, and 1 (5.3%) body ache, while 3 (15.8%) reported undisclosed persistent symptoms. Patients suffering from long COVID experienced significant elevations in serum IL-6 (p=0.0271), IL-8 (p=0.0441), and IFN-β (p=0.0005).

Conclusions: Cytokines IL-6, IL-8 and IFN-β were significantly increased in Australian patients suffering from long COVID in comparison to patients who had fully recovered from COVID-19. Characterising inflammation in long COVID patients is a vital step in aiding identification of those that would benefit from anti-inflammatory therapy.

	Pre-recorded short talks
	Repeated and enhanced influenza vaccine responses in mouse models for protective immunity
Speaker	Sophie Valkenburg, HKU Pasteur Research Pole, School of Public Health, University of Hong Kong, Hong Kong SAR, China

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Current seasonal inactivated influenza vaccines (S-IIV) provide suboptimal protection against antigenic drift, and repeated annual vaccinations are recommended to sustain antibody levels whilst more immunogenic enhanced inactivated influenza vaccines (eIIV) may increase the durability of responses. We assessed protection from influenza challenge in a mouse model of repeated S-IIV and eIIV in parallel to a human randomized control trial of vaccine immunogenicity. In a mouse model, FluAd elicited an earlier and larger induction of HA-stem antibodies with increased germinal center responses and upregulation and long-term expression of B cell switch transcription factors. Long-term cross-reactive memory responses were sustained by FluAd following lethal heterosubtypic influenza challenge, with reduced lung damage and viral loads, coinciding with increased T and B cell recall. Furthermore, we found that the timing of vaccination and antigenic change impacted the quality of immune responses for S-IIV. When mice received two different H3N2 strains (A/Hong Kong/4801/2014 and A/Singapore/INFIMH-16-0019/2016) by staggered timing of vaccination, there was a higher H3-HA antibody and B-cell memory responses than four cumulative vaccinations or when two vaccinations were successive. Interestingly, after challenge with a lethal drifted H3N2 virus (A/Hong Kong/1/1968), mice with staggered vaccination were unable to produce high titers of antibodies specific to the challenge strain compared to other vaccination regimens due to high levels of vaccine specific cross-reactive antibodies. All S-IIV vaccination regimens resulted in protection, in terms of viral loads and survival, from lethal challenge, whilst lung IL-6 and inflammation was lowest in staggered or cumulative vaccination groups, indicating further advantage. Therefore, repeated vaccination may result in higher titer antibody response that can reduce recognition of new viruses, but this could possibly be countered by FluAd, which can increase the longevity of responses and stimulate cross-reactive antibodies.

	Pre-recorded short talks
	Molecular and functional mechanisms underlying age-related changes in influenza virus-specific CD8⁺ T-cells across human lifespan
Speaker	Carolien van de Sandt; Department of Microbiology and Immunology, University of Melbourne, Doherty Institute, Melbourne, VIC

Carolien E. van de Sandt[1,2], Thi H.O. Nguyen [1], Nicholas A. Gherardin[1], Simone Rizzetto[3], Christopher Szeto[4,10], Sneha Sant[1], Jeremy C. Crawford[5], Xiaoxiao Jia[1], Jasveen Kaur[6], Nicole Ranson[6], Samuel J. Redmond[1], Ratana Lim[7,8], Sophie A. Valkenburg[9], Emma J. Grant[4,10], E. Bridie Clemens[1], Jessica Chadderton[1], Nicole L. La Gruta[10], Jane Crowe[11], Martha Lappas[7,8], Katie L. Flanagan[6], Paul G. Thomas[5], Jamie Rossjohn[10,12,13], Dale I. Godfrey[1], Stephanie Gras[4,10], Fabio Luciani[3], Katherine Kedzierska[1]

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Background: Influenza viruses remain a constant global threat, causing significant morbidity and mortality. Although age is the major factor in determining disease duration and outcome during seasonal epidemic and pandemic outbreaks, the underlying mechanisms that drive age-related changes and disease severity are not well understood. A robust CD8⁺ T-cell response plays a key role in protection against novel influenza virus strains and subtypes. CD8⁺ T-cell receptors (TCRs) can recognize conserved influenza proteins, resulting in broad cross-reactivity across distinct influenza viruses. This makes them an attractive target for universal influenza vaccine strategies. As memory CD8⁺ T-cells gradually change throughout human lifetime, we investigated how TCR composition and diversity relate to CD8⁺ T-cell responses across immunologically-distinct phases of human life.

Methods: We combined ex vivo detection of influenza-specific CD8₊ T cells using peptide-HLA tetramers with single-cell multiplex-nested RT-PCR to analyse paired TCRαβ clonotypes directed against the most prominent human influenza epitope, HLA-A*02:01-$M1_{58\text{-}66}$ ($A2^+M1_{58}$) in cord blood, children, adults and elderly individuals. We linked the TCR clonotype dynamics across different ages to the magnitude and phenotype of the $A2^+M1_{58}$-specific CD8⁺ T-cells.

Results: Our data show that frequency and phenotype of the $A2^+M1_{58}^+$-specific CD8⁺ T-cells changes across human lifetime. Furthermore, the $A2^+M1_{58}$-specific TCRαβ clonotypes in children and adults differ to those in cord blood and elderly. The optimal TCRαβ repertoire found in children and adults is dominated by the public TRAV27-TRBV19 clonotype, which is absent in cord blood and is replaced by a private TCRαβ signature which is clonally expanded and include broader usage of TRAV-TRBV gene segments with shorter and/or longer CDR3-loops in the elderly.

Conclusions: Overall, our study indicates that the changes in frequency and phenotype of the influenza virus-specific CD8⁺ T-cells go hand-in-hand with changes in the TCRαβ clonal composition, which together affect the overall strength of the virus-specific CD8⁺ T-cells. These findings suggest that priming T-cell compartments at different stages of life may influence the clonal composition and diversity of responding TCR repertoires against viral infections.

	Pre-recorded short talks
	Immune responses in the respiratory tract and blood of COVID-19 patients reveal mechanisms of disease severity
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Background: Although the respiratory tract is the primary site of SARS-CoV-2 infection and the ensuing immunopathology, respiratory immune responses are understudied and urgently needed to understand mechanisms underlying COVID-19 disease pathogenesis.

Methods: We collected paired longitudinal blood and respiratory tract samples (endotracheal aspirate, sputum, or pleural fluid) from hospitalized COVID-19 patients and non-COVID-19 controls. Cellular, humoral and cytokine responses were analysed and correlated with clinical data.

Results: SARS-CoV-2-specific IgM, IgG and IgA antibodies were detected using ELISA and multiplex assay in both the respiratory tract and blood of COVID-19 patients, although a higher receptor binding domain (RBD)-specific IgM and IgG seroconversion level was found in respiratory specimens. SARS-CoV-2 neutralization activity in respiratory samples was detected only when high levels of RBD-specific antibodies were present. Strikingly, cytokine/chemokine levels and profiles greatly differed between respiratory samples and plasma, indicating that inflammation needs to be assessed in respiratory specimens for the accurate assessment of SARS-CoV-2 immunopathology. Diverse immune cell subsets were detected in respiratory samples, albeit dominated by neutrophils. Importantly, we also showed that dexamethasone with/without remdesivir treatment did not affect humoral responses in blood of COVID-19 patients.

Conclusion: Overall, our study unveils stark differences in innate and adaptive immune responses between respiratory samples and blood and provides important insights into effect of drug therapy on immune responses in COVID-19 patients.

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