

Archived Editions (COVID-19 Genomics and Precision Public Health Weekly Update)

Published on 02/10/2022

COVID-19 Genomics and Precision Public Health Weekly Update Content

- Pathogen and Human Genomics Studies
- Non-Genomics Precision Health Studies
- News, Reviews and Commentaries

Pathogen and Human Genomics Studies

Clinical Characteristics and Outcomes Among Adults Hospitalized with Laboratory-Confirmed SARS-CoV-2 Infection During Periods of B.1.617.2 (Delta) and B.1.1.529 (Omicron) Variant Predominance — One Hospital, California, July 15–September 23, 2021, and December 21, 2021–January 27, 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7106e2.htm?s_cid=mm7106e2_x)
ME Modes et al, MMWR< February 4, 2022

Among adults hospitalized with SARS-CoV-2 infection during Omicron predominance, COVID-19 vaccination, including with a booster dose, was associated with lower likelihood of intensive care unit admission. Compared with patients during the period of Delta predominance, Omicron-period patients had less severe illness, largely driven by an increased proportion who were fully vaccinated. Approximately 20% of early Omicron-period hospitalizations were for non-COVID-19 conditions, particularly among young and vaccinated adults.

 Delayed-interval BNT162b2 mRNA COVID-19 vaccination enhances humoral immunity and induces robust T cell responses. (https://pubmed.ncbi.nlm.nih.gov/35115679)
Hall Victoria G et al. Nature immunology 2022 2

Delayed dosing intervals are a strategy to immunize a greater proportion of the population. In an observational study, we compared humoral and cellular responses in health care workers receiving two doses of BNT162b2 (Pfizer-BioNTech) vaccine at standard (3- to 6-week) and delayed (8- to 16-week) intervals. In the delayed-interval group, anti-receptor-binding domain antibody titers were significantly enhanced compared to the standard-interval group. The 50% plaque reduction

neutralization test (PRNT50) and PRNT90 titers against wild-type (ancestral) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Alpha, Beta and Delta variants were higher in the delayed-interval group.

 Tracking cryptic SARS-CoV-2 lineages detected in NYC wastewater. (https://pubmed.ncbi.nlm.nih.gov/35115523)
Smyth Davida S et al. Nature communications 2022 2 (1) 635

We report detecting increasing frequencies of novel cryptic SARS-CoV-2 lineages not recognized in GISAID's EpiCoV database. These lineages contain mutations that had been rarely observed in clinical samples, including Q493K, Q498Y, E484A, and T572N and share many mutations with the Omicron variant of concern. Some of these mutations expand the tropism of SARS-CoV-2 pseudoviruses by allowing infection of cells expressing the human, mouse, or rat ACE2 receptor.

 Polymorphisms in ACE, ACE2, AGTR1 genes and severity of COVID-19 disease. (https://pubmed.ncbi.nlm.nih.gov/35120165)
Sabater Molina Maria et al. PloS one 2022 2 (2) e0263140

318 (aged 59.6 ± 17.3 years, males 62.6%) COVID-19 patients were grouped based on the severity of symptoms: Outpatients (n = 104, 32.7%), hospitalized on the wards (n = 73, 23.0%), Intensive Care Unit (ICU) (n = 84, 26.4%) and deceased (n = 57, 17.9%). Four SNPs in ACE2 were associated with the severity of disease. While rs2074192 andrs1978124showed a protector effectassuming an overdominant model of inheritance (G/A vs. GG-AA, OR = 0.32, 95%CI = 0.12-0.82; p = 0.016 and A/G vs. AA-GG, OR = 0.37, 95%CI: 0.14-0.96; p = 0.038, respectively); the SNPs rs2106809 and rs2285666were associated with an increased risk of being hospitalized and a severity course of the disease with recessive models of inheritance (C/C vs. T/C-T/T, OR = 11.41, 95% CI: 1.12-115.91; p = 0.012) and (A/A vs. GG-G/A, OR = 12.61, 95% CI: 1.26-125.87; p = 0.0081).

 Pyrimidine inhibitors synergize with nucleoside analogues to block SARS-CoV-2 (https://www.nature.com/articles/s41586-022-04482-x)
DC Schultz et al, Nature, February 7, 2022

The SARS-CoV-2 virus has infected more than 261 million people and led to more than 5 million deaths in the last year and a half1 (WHO.org). SARS-CoV-2-infected individuals typically develop mild to severe flu-like symptoms, while infection of a subset of individuals leads to severe to fatal clinical outcomes2. While vaccines have been rapidly developed to combat SARS-CoV-2, there has been a dearth of antiviral therapeutics. There is an urgent need for therapeutics which has been amplified by the emerging threats of variants that may evade vaccines.

 Multiplexed CRISPR-based microfluidic platform for clinical testing of respiratory viruses and identification of SARS-CoV-2 variants (https://www.nature.com/articles/s41591-022-01734-1)
NL Welch et al, Nature Medicine, February 7, 2022 We developed the mCARMEN respiratory virus panel (RVP) to test for up to 21 viruses, including SARS-CoV-2, other coronaviruses and both influenza strains, and demonstrated its diagnostic-grade performance on 525 patient specimens in an academic setting and 166 specimens in a clinical setting. We further developed an mCARMEN panel to enable identification of 6 SARS-CoV-2 variant lineages, including Delta and Omicron, and evaluated it on 2,088 patient specimens, with near-perfect concordance to sequencing-based variant classification.

 Comparative Analysis of the Risks of Hospitalisation and Death Associated with SARS-CoV-2 Omicron (B.1.1.529) and Delta (B.1.617.2) Variants in England (https://papers.ssrn.com/sol3/papers.cfm? abstract_id=4025932)

T Nyberg et al, SSRN, February 4, 2022

The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for Omicron compared with Delta cases, with higher reductions for more severe endpoints and significant variation with age. The (low) risk of hospital admission in children < 10 years of age did not differ significantly by variant, while 60-69 year-olds had an approximately 75% reduced risk of hospital admission with Omicron compared with Delta.

 Clinical Severity and mRNA Vaccine Effectiveness for Omicron, Delta, and Alpha SARS-CoV-2 Variants in the United States: A Prospective Observational Study (https://www.medrxiv.org/content/10.1101/2022.02.06.22270558v1)
AS Lauring et al, MEDRXIV, February 7, 2022

mRNA vaccines were highly effective in preventing COVID-19-associated hospitalizations from Alpha, Delta, and Omicron variants, but three vaccine doses were required to achieve protection against Omicron similar to the protection that two doses provided against Delta and Alpha. Among adults hospitalized with COVID-19, Omicron caused less severe disease than Delta, but still resulted in substantial morbidity and mortality. Vaccinated patients hospitalized with COVID-19 had significantly lower disease severity than unvaccinated patients for all the variants.

 Genomic epidemiology of SARS-CoV-2 under an elimination strategy in Hong Kong (https://www.nature.com/articles/s41467-022-28420-7)
H Gu et al, Nature Comms, February 8, 2022

Hong Kong employed a strategy of intermittent public health and social measures alongside increasingly stringent travel regulations to eliminate domestic SARS-CoV-2 transmission. By analyzing 1899 genome sequences (>18% of confirmed cases) from 23-January-2020 to 26-January-2021, we reveal the effects of fluctuating control measures on the evolution and epidemiology of SARS-CoV-2 lineages in Hong Kong. Despite numerous importations, only three introductions were responsible for 90% of locally-acquired cases.

Protection of COVID-19 vaccination and previous infection against Omicron BA.1 and Delta SARS-CoV-2 infections, the Netherlands, 22 November 2021- 19 January 2022

(https://www.medrxiv.org/content/10.1101/2022.02.06.22270457v1) SP Andeweg et al, MEDRXIV, February 7, 2022

Protection from primary vaccination was 25% (95% confidence interval (CI): 21-29) and from previous infection 33% (95% CI: 31-35) against Omicron BA.1 infection. Protection against Delta infection was higher with 76% (95% CI: 75-76) for primary vaccination and 78% (95% CI: 76-80) for previous infection. Higher protection was observed in individuals with both primary vaccination and earlier infection compared with either one. Waning of vaccine- or infection-induced protection over time was observed against both variants. Booster vaccination considerably increased vaccine effectiveness against Omicron BA.1 to 76% (95% CI: 72-79) and 68% (95% CI: 67-69) with and without previous infection, respectively.

 Rapid increase in Omicron infections in England during December 2021: REACT-1 study (https://www.science.org/doi/10.1126/science.abn8347)
P Elliott et al, Science, February 8, 2022

We analyzed prevalence of SARS-CoV-2 and its dynamics in England from end November to mid-December 2021 among almost 100,000 participants from the REACT-1 study. Prevalence was high with rapid growth nationally and particularly in London during December 2021, and an increasing proportion of infections due to Omicron. We observed large falls in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third (booster) vaccine dose vs. two doses.

 Amplification Artifact in SARS-CoV-2 Omicron Sequences Carrying P681R Mutation, New York, USA. (https://pubmed.ncbi.nlm.nih.gov/35130474)
Heguy Adriana et al. Emerging infectious diseases 2022 2 (4)

Of 379 severe acute respiratory syndrome coronavirus 2 samples collected in New York, USA, we detected 86 Omicron variant sequences containing Delta variant mutation P681R. Probable explanations were co-infection with 2 viruses or contamination/amplification artifact. Repeated library preparation with fewer cycles showed the P681R calls were artifactual. Unusual mutations should be interpreted with caution.

Boosting of Serum Neutralizing Activity Against the Omicron Variant Among Recovered COVID-19
Patients by BNT162b2 and Coronavac Vaccines (https://papers.ssrn.com/sol3/papers.cfm?
abstract_id=4029746)

L Lu et al, SSRN, February 8, 2022

In this prospective cohort study with 135 recovered COVID-19 patients, we determined the serum NAb titers against ancestral virus or variants using a live virus NAb assay. We used the receiver operating characteristic analysis to determine the optimal cutoff for a commercially-available surrogate NAb assay. Among individuals with prior COVID-19, one dose of BNT162b2 and two doses of CoronaVac could induce detectable serum Omicron NAb. Our result would be particularly important for guiding vaccine policies in countries with COVID-19 vaccine shortage.

 SARS-CoV-2 Omicron Spike recognition by plasma from individuals receiving BNT162b2 mRNA vaccination with a 16-weeks interval between doses (https://www.cell.com/cell-reports/fulltext/S2211-1247(22)00153-X)

D Chatterjee et al, Cell Reports, February 2022

Here we evaluate the recognition of Omicron Spike by plasma from a cohort of SARS-CoV-2 naïve and previously infected individuals that received their BNT162b2 mRNA vaccine 16-weeks apart. Omicron Spike is recognized less efficiently than D614G, Alpha, Beta, Gamma and Delta Spikes. We compare to plasma activity from participants receiving a short (4-weeks) interval regimen. Plasma from individuals of the long interval cohort recognize and neutralize better the Omicron Spike compared to those that received a short interval.

 Development of a T cell-based immunodiagnostic system to effectively distinguish SARS-CoV-2 infection and COVID-19 vaccination status (https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(22)00089-0)

ED Yu et al, Cell, February 9, 2022

We report the development of two pools of experimentally-defined SARS-CoV-2 T cell epitopes, that in combination with spike, were used to discriminate four groups of subjects with different SARS-CoV-2 infection and COVID-19 vaccine status. The overall T cell-based classification accuracy was 89.2% and 88.5% in the experimental and validation cohorts. This scheme was applicable to different mRNA vaccines, different lengths of time post-infection/post-vaccination, and yielded increased accuracy when compared to serological readouts.

Non-Genomics Precision Health Studies

Clinical Characteristics and Outcomes Among Adults Hospitalized with Laboratory-Confirmed SARS-CoV-2 Infection During Periods of B.1.617.2 (Delta) and B.1.1.529 (Omicron) Variant Predominance — One Hospital, California, July 15-September 23, 2021, and December 21, 2021-January 27, 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7106e2.htm?s_cid=mm7106e2_x)
ME Modes et al, MMWR< February 4, 2022

Among adults hospitalized with SARS-CoV-2 infection during Omicron predominance, COVID-19 vaccination, including with a booster dose, was associated with lower likelihood of intensive care unit admission. Compared with patients during the period of Delta predominance, Omicron-period patients had less severe illness, largely driven by an increased proportion who were fully vaccinated. Approximately 20% of early Omicron-period hospitalizations were for non–COVID-19 conditions, particularly among young and vaccinated adults.

 Delayed-interval BNT162b2 mRNA COVID-19 vaccination enhances humoral immunity and induces robust T cell responses. (https://pubmed.ncbi.nlm.nih.gov/35115679)
Hall Victoria G et al. Nature immunology 2022 2 Delayed dosing intervals are a strategy to immunize a greater proportion of the population. In an observational study, we compared humoral and cellular responses in health care workers receiving two doses of BNT162b2 (Pfizer-BioNTech) vaccine at standard (3- to 6-week) and delayed (8- to 16-week) intervals. In the delayed-interval group, anti-receptor-binding domain antibody titers were significantly enhanced compared to the standard-interval group. The 50% plaque reduction neutralization test (PRNT50) and PRNT90 titers against wild-type (ancestral) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Alpha, Beta and Delta variants were higher in the delayed-interval group.

 Tracking cryptic SARS-CoV-2 lineages detected in NYC wastewater. (https://pubmed.ncbi.nlm.nih.gov/35115523)
Smyth Davida S et al. Nature communications 2022 2 (1) 635

We report detecting increasing frequencies of novel cryptic SARS-CoV-2 lineages not recognized in GISAID's EpiCoV database. These lineages contain mutations that had been rarely observed in clinical samples, including Q493K, Q498Y, E484A, and T572N and share many mutations with the Omicron variant of concern. Some of these mutations expand the tropism of SARS-CoV-2 pseudoviruses by allowing infection of cells expressing the human, mouse, or rat ACE2 receptor.

 Polymorphisms in ACE, ACE2, AGTR1 genes and severity of COVID-19 disease. (https://pubmed.ncbi.nlm.nih.gov/35120165)
Sabater Molina Maria et al. PloS one 2022 2 (2) e0263140

318 (aged 59.6 ± 17.3 years, males 62.6%) COVID-19 patients were grouped based on the severity of symptoms: Outpatients (n = 104, 32.7%), hospitalized on the wards (n = 73, 23.0%), Intensive Care Unit (ICU) (n = 84, 26.4%) and deceased (n = 57, 17.9%). Four SNPs in ACE2 were associated with the severity of disease. While rs2074192 andrs1978124showed a protector effectassuming an overdominant model of inheritance (G/A vs. GG-AA, OR = 0.32, 95%CI = 0.12-0.82; p = 0.016 and A/G vs. AA-GG, OR = 0.37, 95%CI: 0.14-0.96; p = 0.038, respectively); the SNPs rs2106809 and rs2285666were associated with an increased risk of being hospitalized and a severity course of the disease with recessive models of inheritance (C/C vs. T/C-T/T, OR = 11.41, 95% CI: 1.12-115.91; p = 0.012) and (A/A vs. GG-G/A, OR = 12.61, 95% CI: 1.26-125.87; p = 0.0081).

 Pyrimidine inhibitors synergize with nucleoside analogues to block SARS-CoV-2 (https://www.nature.com/articles/s41586-022-04482-x)
DC Schultz et al, Nature, February 7, 2022

The SARS-CoV-2 virus has infected more than 261 million people and led to more than 5 million deaths in the last year and a half1 (WHO.org). SARS-CoV-2-infected individuals typically develop mild to severe flu-like symptoms, while infection of a subset of individuals leads to severe to fatal clinical outcomes2. While vaccines have been rapidly developed to combat SARS-CoV-2, there has been a dearth of antiviral therapeutics. There is an urgent need for therapeutics which has been amplified by the emerging threats of variants that may evade vaccines.

 Multiplexed CRISPR-based microfluidic platform for clinical testing of respiratory viruses and identification of SARS-CoV-2 variants (https://www.nature.com/articles/s41591-022-01734-1)
NL Welch et al, Nature Medicine, February 7, 2022

We developed the mCARMEN respiratory virus panel (RVP) to test for up to 21 viruses, including SARS-CoV-2, other coronaviruses and both influenza strains, and demonstrated its diagnostic-grade performance on 525 patient specimens in an academic setting and 166 specimens in a clinical setting. We further developed an mCARMEN panel to enable identification of 6 SARS-CoV-2 variant lineages, including Delta and Omicron, and evaluated it on 2,088 patient specimens, with near-perfect concordance to sequencing-based variant classification.

 Comparative Analysis of the Risks of Hospitalisation and Death Associated with SARS-CoV-2 Omicron (B.1.1.529) and Delta (B.1.617.2) Variants in England (https://papers.ssrn.com/sol3/papers.cfm? abstract_id=4025932)

T Nyberg et al, SSRN, February 4, 2022

The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for Omicron compared with Delta cases, with higher reductions for more severe endpoints and significant variation with age. The (low) risk of hospital admission in children <10 years of age did not differ significantly by variant, while 60-69 year-olds had an approximately 75% reduced risk of hospital admission with Omicron compared with Delta.

 Clinical Severity and mRNA Vaccine Effectiveness for Omicron, Delta, and Alpha SARS-CoV-2 Variants in the United States: A Prospective Observational Study (https://www.medrxiv.org/content/10.1101/2022.02.06.22270558v1)
AS Lauring et al, MEDRXIV, February 7, 2022

mRNA vaccines were highly effective in preventing COVID-19-associated hospitalizations from Alpha, Delta, and Omicron variants, but three vaccine doses were required to achieve protection against Omicron similar to the protection that two doses provided against Delta and Alpha. Among adults hospitalized with COVID-19, Omicron caused less severe disease than Delta, but still resulted in substantial morbidity and mortality. Vaccinated patients hospitalized with COVID-19 had significantly lower disease severity than unvaccinated patients for all the variants.

 Genomic epidemiology of SARS-CoV-2 under an elimination strategy in Hong Kong (https://www.nature.com/articles/s41467-022-28420-7)
H Gu et al, Nature Comms, February 8, 2022

Hong Kong employed a strategy of intermittent public health and social measures alongside increasingly stringent travel regulations to eliminate domestic SARS-CoV-2 transmission. By analyzing 1899 genome sequences (>18% of confirmed cases) from 23-January-2020 to 26-January-2021, we reveal the effects of fluctuating control measures on the evolution and epidemiology of SARS-CoV-2 lineages in Hong Kong. Despite numerous importations, only three introductions were responsible for 90% of locally-acquired cases.

Protection of COVID-19 vaccination and previous infection against Omicron BA.1 and Delta SARS-CoV-2 infections, the Netherlands, 22 November 2021- 19 January 2022
 (https://www.medrxiv.org/content/10.1101/2022.02.06.22270457v1)

SP Andeweg et al, MEDRXIV, February 7, 2022

Protection from primary vaccination was 25% (95% confidence interval (CI): 21-29) and from previous infection 33% (95% CI: 31-35) against Omicron BA.1 infection. Protection against Delta infection was higher with 76% (95% CI: 75-76) for primary vaccination and 78% (95% CI: 76-80) for previous infection. Higher protection was observed in individuals with both primary vaccination and earlier infection compared with either one. Waning of vaccine- or infection-induced protection over time was observed against both variants. Booster vaccination considerably increased vaccine effectiveness against Omicron BA.1 to 76% (95% CI: 72-79) and 68% (95% CI: 67-69) with and without previous infection, respectively.

 Rapid increase in Omicron infections in England during December 2021: REACT-1 study (https://www.science.org/doi/10.1126/science.abn8347)
P Elliott et al, Science, February 8, 2022

We analyzed prevalence of SARS-CoV-2 and its dynamics in England from end November to mid-December 2021 among almost 100,000 participants from the REACT-1 study. Prevalence was high with rapid growth nationally and particularly in London during December 2021, and an increasing proportion of infections due to Omicron. We observed large falls in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third (booster) vaccine dose vs. two doses.

 Amplification Artifact in SARS-CoV-2 Omicron Sequences Carrying P681R Mutation, New York, USA. (https://pubmed.ncbi.nlm.nih.gov/35130474)
Heguy Adriana et al. Emerging infectious diseases 2022 2 (4)

Of 379 severe acute respiratory syndrome coronavirus 2 samples collected in New York, USA, we detected 86 Omicron variant sequences containing Delta variant mutation P681R. Probable explanations were co-infection with 2 viruses or contamination/amplification artifact. Repeated library preparation with fewer cycles showed the P681R calls were artifactual. Unusual mutations should be interpreted with caution.

Boosting of Serum Neutralizing Activity Against the Omicron Variant Among Recovered COVID-19
Patients by BNT162b2 and Coronavac Vaccines (https://papers.ssrn.com/sol3/papers.cfm?
abstract_id=4029746)

L Lu et al, SSRN, February 8, 2022

In this prospective cohort study with 135 recovered COVID-19 patients, we determined the serum NAb titers against ancestral virus or variants using a live virus NAb assay. We used the receiver operating characteristic analysis to determine the optimal cutoff for a commercially-available surrogate NAb assay. Among individuals with prior COVID-19, one dose of BNT162b2 and two doses

of CoronaVac could induce detectable serum Omicron NAb. Our result would be particularly important for guiding vaccine policies in countries with COVID-19 vaccine shortage.

 SARS-CoV-2 Omicron Spike recognition by plasma from individuals receiving BNT162b2 mRNA vaccination with a 16-weeks interval between doses (https://www.cell.com/cell-reports/fulltext/S2211-1247(22)00153-X)

D Chatterjee et al, Cell Reports, February 2022

Here we evaluate the recognition of Omicron Spike by plasma from a cohort of SARS-CoV-2 naïve and previously infected individuals that received their BNT162b2 mRNA vaccine 16-weeks apart. Omicron Spike is recognized less efficiently than D614G, Alpha, Beta, Gamma and Delta Spikes. We compare to plasma activity from participants receiving a short (4-weeks) interval regimen. Plasma from individuals of the long interval cohort recognize and neutralize better the Omicron Spike compared to those that received a short interval.

 Development of a T cell-based immunodiagnostic system to effectively distinguish SARS-CoV-2 infection and COVID-19 vaccination status (https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(22)00089-0)

ED Yu et al, Cell, February 9, 2022

We report the development of two pools of experimentally-defined SARS-CoV-2 T cell epitopes, that in combination with spike, were used to discriminate four groups of subjects with different SARS-CoV-2 infection and COVID-19 vaccine status. The overall T cell-based classification accuracy was 89.2% and 88.5% in the experimental and validation cohorts. This scheme was applicable to different mRNA vaccines, different lengths of time post-infection/post-vaccination, and yielded increased accuracy when compared to serological readouts.

News, Reviews and Commentaries

Clinical Characteristics and Outcomes Among Adults Hospitalized with Laboratory-Confirmed SARS-CoV-2 Infection During Periods of B.1.617.2 (Delta) and B.1.1.529 (Omicron) Variant Predominance — One Hospital, California, July 15-September 23, 2021, and December 21, 2021-January 27, 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7106e2.htm?s_cid=mm7106e2_x)
ME Modes et al, MMWR< February 4, 2022

Among adults hospitalized with SARS-CoV-2 infection during Omicron predominance, COVID-19 vaccination, including with a booster dose, was associated with lower likelihood of intensive care unit admission. Compared with patients during the period of Delta predominance, Omicron-period patients had less severe illness, largely driven by an increased proportion who were fully vaccinated. Approximately 20% of early Omicron-period hospitalizations were for non-COVID-19 conditions, particularly among young and vaccinated adults.

 Delayed-interval BNT162b2 mRNA COVID-19 vaccination enhances humoral immunity and induces robust T cell responses. (https://pubmed.ncbi.nlm.nih.gov/35115679)
Hall Victoria G et al. Nature immunology 2022 2

Delayed dosing intervals are a strategy to immunize a greater proportion of the population. In an observational study, we compared humoral and cellular responses in health care workers receiving two doses of BNT162b2 (Pfizer-BioNTech) vaccine at standard (3- to 6-week) and delayed (8- to 16-week) intervals. In the delayed-interval group, anti-receptor-binding domain antibody titers were significantly enhanced compared to the standard-interval group. The 50% plaque reduction neutralization test (PRNT50) and PRNT90 titers against wild-type (ancestral) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Alpha, Beta and Delta variants were higher in the delayed-interval group.

 Tracking cryptic SARS-CoV-2 lineages detected in NYC wastewater. (https://pubmed.ncbi.nlm.nih.gov/35115523)
Smyth Davida S et al. Nature communications 2022 2 (1) 635

We report detecting increasing frequencies of novel cryptic SARS-CoV-2 lineages not recognized in GISAID's EpiCoV database. These lineages contain mutations that had been rarely observed in clinical samples, including Q493K, Q498Y, E484A, and T572N and share many mutations with the Omicron variant of concern. Some of these mutations expand the tropism of SARS-CoV-2 pseudoviruses by allowing infection of cells expressing the human, mouse, or rat ACE2 receptor.

 Polymorphisms in ACE, ACE2, AGTR1 genes and severity of COVID-19 disease. (https://pubmed.ncbi.nlm.nih.gov/35120165)
Sabater Molina Maria et al. PloS one 2022 2 (2) e0263140

318 (aged 59.6 ± 17.3 years, males 62.6%) COVID-19 patients were grouped based on the severity of symptoms: Outpatients (n = 104, 32.7%), hospitalized on the wards (n = 73, 23.0%), Intensive Care Unit (ICU) (n = 84, 26.4%) and deceased (n = 57, 17.9%). Four SNPs in ACE2 were associated with the severity of disease. While rs2074192 andrs1978124showed a protector effectassuming an overdominant model of inheritance (G/A vs. GG-AA, OR = 0.32, 95%CI = 0.12-0.82; p = 0.016 and A/G vs. AA-GG, OR = 0.37, 95%CI: 0.14-0.96; p = 0.038, respectively); the SNPs rs2106809 and rs2285666were associated with an increased risk of being hospitalized and a severity course of the disease with recessive models of inheritance (C/C vs. T/C-T/T, OR = 11.41, 95% CI: 1.12-115.91; p = 0.012) and (A/A vs. GG-G/A, OR = 12.61, 95% CI: 1.26-125.87; p = 0.0081).

 Pyrimidine inhibitors synergize with nucleoside analogues to block SARS-CoV-2 (https://www.nature.com/articles/s41586-022-04482-x)
DC Schultz et al, Nature, February 7, 2022

The SARS-CoV-2 virus has infected more than 261 million people and led to more than 5 million deaths in the last year and a half1 (WHO.org). SARS-CoV-2-infected individuals typically develop mild to severe flu-like symptoms, while infection of a subset of individuals leads to severe to fatal clinical

outcomes 2. While vaccines have been rapidly developed to combat SARS-CoV-2, there has been a dearth of antiviral therapeutics. There is an urgent need for therapeutics which has been amplified by the emerging threats of variants that may evade vaccines.

 Multiplexed CRISPR-based microfluidic platform for clinical testing of respiratory viruses and identification of SARS-CoV-2 variants (https://www.nature.com/articles/s41591-022-01734-1)
NL Welch et al, Nature Medicine, February 7, 2022

We developed the mCARMEN respiratory virus panel (RVP) to test for up to 21 viruses, including SARS-CoV-2, other coronaviruses and both influenza strains, and demonstrated its diagnostic-grade performance on 525 patient specimens in an academic setting and 166 specimens in a clinical setting. We further developed an mCARMEN panel to enable identification of 6 SARS-CoV-2 variant lineages, including Delta and Omicron, and evaluated it on 2,088 patient specimens, with near-perfect concordance to sequencing-based variant classification.

 Comparative Analysis of the Risks of Hospitalisation and Death Associated with SARS-CoV-2 Omicron (B.1.1.529) and Delta (B.1.617.2) Variants in England (https://papers.ssrn.com/sol3/papers.cfm? abstract_id=4025932)

T Nyberg et al, SSRN, February 4, 2022

The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for Omicron compared with Delta cases, with higher reductions for more severe endpoints and significant variation with age. The (low) risk of hospital admission in children <10 years of age did not differ significantly by variant, while 60-69 year-olds had an approximately 75% reduced risk of hospital admission with Omicron compared with Delta.

 Clinical Severity and mRNA Vaccine Effectiveness for Omicron, Delta, and Alpha SARS-CoV-2 Variants in the United States: A Prospective Observational Study (https://www.medrxiv.org/content/10.1101/2022.02.06.22270558v1)
AS Lauring et al, MEDRXIV, February 7, 2022

mRNA vaccines were highly effective in preventing COVID-19-associated hospitalizations from Alpha, Delta, and Omicron variants, but three vaccine doses were required to achieve protection against Omicron similar to the protection that two doses provided against Delta and Alpha. Among adults hospitalized with COVID-19, Omicron caused less severe disease than Delta, but still resulted in substantial morbidity and mortality. Vaccinated patients hospitalized with COVID-19 had significantly lower disease severity than unvaccinated patients for all the variants.

 Genomic epidemiology of SARS-CoV-2 under an elimination strategy in Hong Kong (https://www.nature.com/articles/s41467-022-28420-7)
H Gu et al, Nature Comms, February 8, 2022

Hong Kong employed a strategy of intermittent public health and social measures alongside increasingly stringent travel regulations to eliminate domestic SARS-CoV-2 transmission. By analyzing

1899 genome sequences (>18% of confirmed cases) from 23-January-2020 to 26-January-2021, we reveal the effects of fluctuating control measures on the evolution and epidemiology of SARS-CoV-2 lineages in Hong Kong. Despite numerous importations, only three introductions were responsible for 90% of locally-acquired cases.

Protection of COVID-19 vaccination and previous infection against Omicron BA.1 and Delta SARS-CoV-2 infections, the Netherlands, 22 November 2021- 19 January 2022
 (https://www.medrxiv.org/content/10.1101/2022.02.06.22270457v1)

SP Andeweg et al, MEDRXIV, February 7, 2022

Protection from primary vaccination was 25% (95% confidence interval (CI): 21-29) and from previous infection 33% (95% CI: 31-35) against Omicron BA.1 infection. Protection against Delta infection was higher with 76% (95% CI: 75-76) for primary vaccination and 78% (95% CI: 76-80) for previous infection. Higher protection was observed in individuals with both primary vaccination and earlier infection compared with either one. Waning of vaccine- or infection-induced protection over time was observed against both variants. Booster vaccination considerably increased vaccine effectiveness against Omicron BA.1 to 76% (95% CI: 72-79) and 68% (95% CI: 67-69) with and without previous infection, respectively.

 Rapid increase in Omicron infections in England during December 2021: REACT-1 study (https://www.science.org/doi/10.1126/science.abn8347)
P Elliott et al, Science, February 8, 2022

We analyzed prevalence of SARS-CoV-2 and its dynamics in England from end November to mid-December 2021 among almost 100,000 participants from the REACT-1 study. Prevalence was high with rapid growth nationally and particularly in London during December 2021, and an increasing proportion of infections due to Omicron. We observed large falls in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third (booster) vaccine dose vs. two doses.

 Amplification Artifact in SARS-CoV-2 Omicron Sequences Carrying P681R Mutation, New York, USA. (https://pubmed.ncbi.nlm.nih.gov/35130474)
Heguy Adriana et al. Emerging infectious diseases 2022 2 (4)

Of 379 severe acute respiratory syndrome coronavirus 2 samples collected in New York, USA, we detected 86 Omicron variant sequences containing Delta variant mutation P681R. Probable explanations were co-infection with 2 viruses or contamination/amplification artifact. Repeated library preparation with fewer cycles showed the P681R calls were artifactual. Unusual mutations should be interpreted with caution.

Boosting of Serum Neutralizing Activity Against the Omicron Variant Among Recovered COVID-19
Patients by BNT162b2 and Coronavac Vaccines (https://papers.ssrn.com/sol3/papers.cfm?
abstract_id=4029746)

L Lu et al, SSRN, February 8, 2022

In this prospective cohort study with 135 recovered COVID-19 patients, we determined the serum NAb titers against ancestral virus or variants using a live virus NAb assay. We used the receiver operating characteristic analysis to determine the optimal cutoff for a commercially-available surrogate NAb assay. Among individuals with prior COVID-19, one dose of BNT162b2 and two doses of CoronaVac could induce detectable serum Omicron NAb. Our result would be particularly important for guiding vaccine policies in countries with COVID-19 vaccine shortage.

 SARS-CoV-2 Omicron Spike recognition by plasma from individuals receiving BNT162b2 mRNA vaccination with a 16-weeks interval between doses (https://www.cell.com/cell-reports/fulltext/S2211-1247(22)00153-X)

D Chatterjee et al, Cell Reports, February 2022

Here we evaluate the recognition of Omicron Spike by plasma from a cohort of SARS-CoV-2 naïve and previously infected individuals that received their BNT162b2 mRNA vaccine 16-weeks apart. Omicron Spike is recognized less efficiently than D614G, Alpha, Beta, Gamma and Delta Spikes. We compare to plasma activity from participants receiving a short (4-weeks) interval regimen. Plasma from individuals of the long interval cohort recognize and neutralize better the Omicron Spike compared to those that received a short interval.

 Development of a T cell-based immunodiagnostic system to effectively distinguish SARS-CoV-2 infection and COVID-19 vaccination status (https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(22)00089-0)

ED Yu et al, Cell, February 9, 2022

We report the development of two pools of experimentally-defined SARS-CoV-2 T cell epitopes, that in combination with spike, were used to discriminate four groups of subjects with different SARS-CoV-2 infection and COVID-19 vaccine status. The overall T cell-based classification accuracy was 89.2% and 88.5% in the experimental and validation cohorts. This scheme was applicable to different mRNA vaccines, different lengths of time post-infection/post-vaccination, and yielded increased accuracy when compared to serological readouts.

Disclaimer: Articles listed in COVID-19 Genomics and Precision Public Health Weekly Update are selected by the CDC Office of Public Health Genomics to provide current awareness of the scientific literature and news. Inclusion in the update does not necessarily represent the views of the Centers for Disease Control and Prevention nor does it imply endorsement of the article's methods or findings. CDC and DHHS assume no responsibility for the factual accuracy of the items presented. The selection, omission, or content of items does not imply any endorsement or other position taken by CDC or DHHS. Opinion, findings and conclusions expressed by the original authors of items included in the Clips, or persons quoted therein, are strictly their own and are in no way meant to represent the opinion or views of CDC or DHHS. References to publications, news sources, and non-CDC Websites are provided solely for informational purposes and do not imply endorsement by CDC or DHHS.

Page last reviewed: Oct 1, 2021 Page last updated: Feb 11, 2022

Content source: Office of Genomics and Precision Public Health (http://www.cdc.gov/genomics/), CDC Office of Science (https://www.cdc.gov/od/science/index.htm)