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

Published on 03/24/2022

COVID-19 Genomics and Precision Public Health Weekly Update Content

Pathogen and Human Genomics Studies

- Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients (https://www.science.org/doi/10.1126/scitranslmed.abl6141)
  X Charmetant et al, Science, March 16, 2022

  This study compared the immune response elicited by SARS-CoV-2 infection and vaccination in kidney transplant recipients. Infection elicited a broader response to SARS-CoV-2 associated with fewer cases of reinfection. The authors also observed a subset of individuals that did not respond to two doses of mRNA vaccine, potentially due to exposure to the immunosuppressive drug, mycophenolate mofetil. A subset of nonresponders who received a third dose of mRNA vaccine developed antibodies comparable to responders to two doses, suggesting that populations with immunosuppression should be prioritized for booster vaccine doses.

- COVID-19 Prediction using Genomic Footprint of SARS-CoV-2 in Air, Surface Swab and Wastewater (https://www.medrxiv.org/content/10.1101/2022.03.14.22272314v1)
  HS Gabriele et al, MEDRXIV, March 17, 2022

  A total of 445 air, surface swab and wastewater samples were collected, and these data were aggregated by day. SARS-CoV-2 genomic footprints were detected in air, surface swab and wastewater samples on 52 (63.4%), 40 (50.0%) and 57 (68.6%) days, respectively, during the study period. On 19 (24%) of 78 days SARS-CoV-2 was detected in all three sample types. Clinically diagnosed COVID-19 cases were reported on 11 days during the study period and SARS-CoV-2 was also detected two days

before the case diagnosis on all 11 (100%), 9 (81.8%) and 8 (72.7%) days in air, surface swab and wastewater samples, respectively.

- SARS-CoV-2 variant Delta rapidly displaced variant Alpha in the United States and led to higher viral loads (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(22)00071-4)
  A Bolze et al, Cell Reports Medicine, March 15, 2022

  We report on the sequencing of 74,348 SARS-CoV-2 positive samples collected across the United States and show that the Delta variant, first detected in the United States in March 2021, made up the majority of SARS-CoV-2 infections by July 1, 2021 and accounted for >99.9% of the infections by September 2021. Not only did Delta displace variant Alpha, which was the dominant variant at the time, it also displaced the Gamma, Iota, and Mu variants. Through an analysis of quantification cycle (Cq) values, we demonstrate that Delta infections tend to have a 1.7× higher viral load compared to Alpha infections (a decrease of 0.8 Cq) on average.

- Effectiveness of mRNA Vaccination in Preventing COVID-19–Associated Invasive Mechanical Ventilation and Death — United States, March 2021–January 2022
  (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e1.htm)
  MW Tenforde et al, MMWR, March 18, 2022

  COVID-19 mRNA vaccines provide protection against COVID-19 hospitalization among adults. However, how well mRNA vaccines protect against the most severe outcomes of COVID-19–related illness, including use of invasive mechanical ventilation (IMV) or death, is uncertain. Receiving 2 or 3 doses of an mRNA COVID-19 vaccine was associated with a 90% reduction in risk for COVID-19–associated IMV or death. Protection of 3 mRNA vaccine doses during the period of Omicron predominance was 94%.

- Neutralizing immunity in vaccine breakthrough infections from the SARS-CoV-2 Omicron and Delta variants (https://www.cell.com/cell/fulltext/S0092-8674(22)00329-4)
  V Servelitta et al, Cell, March 17, 2022

  Virus-like particle (VLP) and live virus assays were used to investigate neutralizing immunity against Delta and Omicron SARS-CoV-2 variants in 259 samples from 128 vaccinated individuals. Following Delta breakthrough infection, titers against WT rose 57-fold and 3.1-fold compared to uninfected boosted and unboosted individuals, respectively, versus only a 5.8-fold increase and 3.1-fold decrease for Omicron breakthrough infection. Among immunocompetent, unboosted patients, Delta breakthrough infections induced 10.8-fold higher titers against WT compared to Omicron (p=0.037). Decreased antibody responses in Omicron breakthrough infections relative to Delta were potentially related to a higher proportion of asymptomatic or mild breakthrough infections (55.0% versus 28.6%, respectively).

- COVID-19–Associated Hospitalizations Among Adults During SARS-CoV-2 Delta and Omicron Variant Predominance, by Race/Ethnicity and Vaccination Status — COVID-NET, 14 States, July 2021–January

2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e2.htm?s_cid=mm7112e2_x)
CA Taylor et al, MMWR, March 18, 2022

> SARS-CoV-2 infections can result in COVID-19–associated hospitalizations, even among vaccinated persons. In January 2022, unvaccinated adults and those vaccinated with a primary series, but no booster or additional dose, were 12 and three times as likely to be hospitalized, respectively, as were adults who received booster or additional doses. Hospitalization rates among non-Hispanic Black adults increased more than rates in other racial/ethnic groups.

- Neutralisation sensitivity of the SARS-CoV-2 omicron (B.1.1.529) variant: a cross-sectional study (https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00129-3/fulltext)
  DJ Sheward et al, The Lancet, March 17, 2022

  > Neutralising antibody responses in reference sample pools sampled shortly after infection or vaccination were substantially less potent against the omicron variant than against wild-type SARS-CoV-2 (seven-fold to 42-fold reduction in ID50 titres). Similarly, for sera obtained before vaccination in 2020 from a cohort of convalescent hospital workers, neutralisation of the omicron variant was low to undetectable (all ID50 titres <20). However, in serum samples obtained in 2021 from two cohorts in Stockholm, substantial cross-neutralisation of the omicron variant was observed. These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that boosting with licensed vaccines might be sufficient to raise neutralising antibody titres to protective levels.

- Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/35302625)
  Chun June Young et al. JAMA network open 2022 3 (3) e223064

  > Among 106 866 confirmed COVID-19 infections (including 26 597 infections and 80 269 infections during the third and fourth waves of COVID-19 in Korea, respectively), a significant difference in age-specific susceptibility to the Delta vs pre-Delta variant was found in the younger age group. After adjustment for contact pattern and vaccination status, the increase in susceptibility to the Delta vs pre-Delta variant was estimated to be highest in the group aged 10 to 15 years, approximately doubling (1.92-fold increase [95% CI, 1.86-fold to 1.98-fold]), whereas in the group aged 50 years or more, susceptibility to the Delta vs pre-Delta variant remained stable at an approximately 1-fold change (eg, among individuals aged 50-55 years: 0.997-fold [95% CI, 0.989-fold to 1.001-fold). In this study, the Delta variant of SARS-CoV-2 was estimated to propagate more easily among children and adolescents than pre-Delta strains, even after adjusting for contact pattern and vaccination status.

- SARS-CoV-2 host prediction based on virus-host genetic features. (https://pubmed.ncbi.nlm.nih.gov/35301337)
  Kawashima Irina Yuri et al. Scientific reports 2022 3 (1) 4576

  > Based on a previously computational tool, the Seq2Hosts, we developed a novel approach which uses new variables obtained from the frequency of spike-Coronaviruses codons, the Relative Synonymous

Codon Usage (RSCU) to shed new light on the molecular mechanisms involved in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) host specificity. By using the RSCU obtained from nucleotide sequences before the SARS-CoV-2 pandemic, we assessed the possibility of know the hosts capable to be infected by these new emerging species, which was first identified infecting humans during 2019 in Wuhan, China. According to the model trained and validated using sequences available before the pandemic, bats are the most likely the natural host to the SARS-CoV-2 infection, as previously suggested in other studies that searched for the host viral origin.

- End-point RT-PCR based on a conservation landscape for SARS-COV-2 detection (https://www.nature.com/articles/s41598-022-07756-6)
  AC Rangel et al, Scientific Reports, March 19, 2022

  End-point RT-PCR is a suitable alternative diagnostic technique since it is cheaper than RT-qPCR tests and can be implemented on a massive scale in low- and middle-income countries. In this work, a bioinformatic approach to guide the design of PCR primers was developed, and an alternative diagnostic test based on end-point PCR was designed. End-point PCR primers were designed through conservation analysis based on kmer frequency in SARS-CoV-2 and human respiratory pathogen genomes. Highly conserved regions were identified for primer design, and the resulting PCR primers were used to amplify 871 nasopharyngeal human samples with a previous RT-qPCR based SARS-CoV-2 diagnosis. The diagnostic test showed high accuracy in identifying SARS-CoV-2-positive samples including B.1.1.7, P.1, B.1.427/B.1.429 and B.1.617.2/ AY samples

- 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: a cohort study. (https://pubmed.ncbi.nlm.nih.gov/35305296)
  Nyberg Tommy et al. Lancet (London, England) 2022 3

  The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

- Comparative effectiveness of the BNT162b2 and ChAdOx1 vaccines against Covid-19 in people over 50 (https://www.nature.com/articles/s41467-022-29159-x)
  A Xie et al, Nature Communications, March 21, 2022

  We find that, compared with one dose of ChAdOx1, vaccination with BNT162b2 is associated with a 28% (95% CI, 12-42) decreased risk of SARS-CoV-2 infection. Also, two doses of BNT162b2 vs ChAdOx1 confers 30% (95% CI, 25-35) and 29% (95% CI, 10-45) lower risks of both infection and

hospitalization during the study period when the Delta variant is dominant. Furthermore, the comparative protection against the infection persists for at least six months among the fully vaccinated, suggesting no differential waning between the two vaccines.

- Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. (https://pubmed.ncbi.nlm.nih.gov/35296468)
  Li Xintong et al. BMJ (Clinical research ed.) 2022 3 e068373

  8?330?497 people who received at least one dose of covid-19 vaccines ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, or Ad.26.COV2.S between the rollout of the vaccination campaigns and end of data availability (UK: 9 May 2021; Spain: 30 June 2021). The study sample also comprised a cohort of 735?870 unvaccinated individuals with a first positive reverse transcription polymerase chain reaction test result for SARS-CoV-2 from 1 September 2020, and 14?330?080 participants from the general population. No safety signal was observed between covid-19 vaccines and the immune mediated neurological events of Bell's palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. An increased risk of Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome was, however, observed for people with SARS-CoV-2 infection.

- Whole-Genome Sequencing of SARS-CoV-2 Infection in a Cluster of Immunocompromised Children in Indonesia. (https://pubmed.ncbi.nlm.nih.gov/35308495)
  Putri Nina Dwi et al. Frontiers in medicine 2022 3 835998

  Real-time reverse-transcription polymerase chain reaction (RT-PCR) from nasopharyngeal (NP) swabs was used to diagnose the patients and also guardians and healthcare workers (HCWs) in the ward, followed by WGS of RT-PCR positive cases to establish their phylogenetic relationships. Using WGS, we showed that SARS-CoV-2 transmission in a cluster of children with underlying malignancy was characterized by high similarity of whole virus genome, which suggests nosocomial transmission.

- DNA methylation profiles in pneumonia patients reflect changes in cell types and pneumonia severity. (https://pubmed.ncbi.nlm.nih.gov/35311624)
  Morselli Marco et al. Epigenetics 2022 3 1-15

  Immune cell-type composition changes with age, potentially weakening the response to infectious diseases. Profiling epigenetics marks of immune cells can help us understand the relationship with disease severity. We therefore leveraged a targeted DNA methylation method to study the differences in a cohort of pneumonia patients (both COVID-19 positive and negative) and unaffected individuals from peripheral blood.This approach allowed us to predict the pneumonia diagnosis with high accuracy (AUC = 0.92), and the PCR positivity to the SARS-CoV-2 viral genome with moderate, albeit lower, accuracy (AUC = 0.77).

- Integrative transcriptomic, evolutionary, and causal inference framework for region-level analysis: Application to COVID-19 (https://www.nature.com/articles/s41525-022-00296-y)
  D Zhou et al, NPJ Genomic Medicine, March 22, 2022

We developed an integrative transcriptomic, evolutionary, and causal inference framework for a deep region-level analysis, which integrates several published approaches and a new summary-statistics-based methodology. To illustrate the framework, we applied it to understanding the host genetics of COVID-19 severity. We identified putative causal genes, including SLC6A20, CXCR6, CCR9, and CCR5 in the locus on 3p21.31, quantifying their effect on mediating expression and on severe COVID-19. We confirmed that individuals who carry the introgressed archaic segment in the locus have a substantially higher risk of developing the severe disease phenotype.

- Venous Thromboembolism in Ambulatory Covid-19 patients: Clinical and Genetic Determinants (https://www.medrxiv.org/content/10.1101/2022.03.22.22272748v1)
  J Xie et al, MEDRXIV, March 22, 2022
- Effect of prior infection, vaccination, and hybrid immunity against symptomatic BA.1 and BA.2 Omicron infections and severe COVID-19 in Qatar (https://www.medrxiv.org/content/10.1101/2022.03.22.22272745v1)
  HN Altarawneh et al, MEDRXIV, March 22, 2022

  Protection offered by five different forms of immunity, combining natural and vaccine immunity, was investigated against SARS-CoV-2 Omicron symptomatic BA.1 infection, symptomatic BA.2 infection, BA.1 hospitalization and death, and BA.2 hospitalization and death, in Qatar, between December 23, 2021 and February 21, 2022. We found no discernable differences in the effects of prior infection, vaccination, and hybrid immunity against BA.1 versus BA.2. Hybrid immunity resulting from prior infection and recent booster vaccination confers the strongest protection against either subvariant. Vaccination enhances protection of those with a prior infection.
- Early detection of SARS-CoV-2 variants using traveler-based genomic surveillance at four US airports, September 2021- January 2022 (https://www.medrxiv.org/content/10.1101/2022.03.21.22272490v1)
  RD Wegrzyn et al, MEDRXIV, March 22, 2022

  We enrolled arriving international air travelers in SARS-CoV-2 genomic surveillance, using molecular testing of pooled nasal swabs, and sequencing positive samples for viral lineage. Traveler-based genomic surveillance provided early warning variant detection; we reported the first U.S. Omicron BA.2 and first BA.3 in North America, weeks before next reported detection.
- Detecting SARS-CoV-2 Variants in Wastewater and Their Correlation With Circulating Variants in the Communities. (https://pubmed.ncbi.nlm.nih.gov/35313589)
  Li Lin et al. Research square 2022 3

  Detection of SARS-CoV-2 viral load in wastewater has been highly informative in estimating the approximate number of infected individuals in the surrounding communities. Recent developments in wastewater monitoring to determine community prevalence of COVID-19 further extends into identifying SARS-CoV-2 variants, including those being monitored for having enhanced transmissibility. We sequenced genomic RNA derived from wastewater to determine the variants of coronaviruses circulating in the communities.

- Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine. (https://pubmed.ncbi.nlm.nih.gov/35320659)
  Moreira Edson D et al. The New England journal of medicine 2022 3

  In this ongoing, placebo-controlled, randomized, phase 3 trial, we assigned participants who had received two 30-μg doses of the BNT162b2 vaccine at least 6 months earlier to be injected with a third dose of the BNT162b2 vaccine or with placebo. We assessed vaccine safety and efficacy against Covid-19 starting 7 days after the third dose. A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months.

- Waning effectiveness of BNT162b2 and ChAdOx1 COVID-19 vaccines over six months since second dose: a cohort study using linked electronic health records (https://www.medrxiv.org/content/10.1101/2022.03.23.22272804v1)
  EMF Horne et al, MEDRXIV, March 23, 2022

  The BNT162b2, ChAdOx1 and unvaccinated groups comprised 1,773,970, 2,961,011 and 2,433,988 individuals, respectively. Waning of vaccine effectiveness was similar across outcomes and vaccine brands: e.g. in the 65+ years subgroup ratios of aHRs versus unvaccinated for COVID-19 hospitalisation, COVID-19 death and positive SARS-CoV-2 test ranged from 1.23 (95% CI 1.15-1.32) to 1.27 (1.20-1.34) for BNT162b2 and 1.16 (0.98-1.37) to 1.20 (1.14-1.27) for ChAdOx1. Despite waning, rates of COVID-19 hospitalisation and COVID-19 death were substantially lower among vaccinated individuals compared to unvaccinated individuals up to 26 weeks after second dose, with estimated aHRs <0.20 (>80% vaccine effectiveness) for BNT162b2, and <0.26 (>74%) for ChAdOx1. By weeks 23-26, rates of SARS-CoV-2 infection in fully vaccinated individuals were similar to or higher than those in unvaccinated individuals

Non-Genomics Precision Health Studies

- Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients (https://www.science.org/doi/10.1126/scitranslmed.abl6141)
  X Charmetant et al, Science, March 16, 2022

  This study compared the immune response elicited by SARS-CoV-2 infection and vaccination in kidney transplant recipients. Infection elicited a broader response to SARS-CoV-2 associated with fewer cases of reinfection. The authors also observed a subset of individuals that did not respond to two doses of mRNA vaccine, potentially due to exposure to the immunosuppressive drug, mycophenolate mofetil. A subset of nonresponders who received a third dose of mRNA vaccine developed antibodies comparable to responders to two doses, suggesting that populations with immunosuppression should be prioritized for booster vaccine doses.

- COVID-19 Prediction using Genomic Footprint of SARS-CoV-2 in Air, Surface Swab and Wastewater (https://www.medrxiv.org/content/10.1101/2022.03.14.22272314v1)
  HS Gabriele et al, MEDRXIV, March 17, 2022

  A total of 445 air, surface swab and wastewater samples were collected, and these data were aggregated by day. SARS-CoV-2 genomic footprints were detected in air, surface swab and wastewater samples on 52 (63.4%), 40 (50.0%) and 57 (68.6%) days, respectively, during the study period. On 19 (24%) of 78 days SARS-CoV-2 was detected in all three sample types. Clinically diagnosed COVID-19 cases were reported on 11 days during the study period and SARS-CoV-2 was also detected two days before the case diagnosis on all 11 (100%), 9 (81.8%) and 8 (72.7%) days in air, surface swab and wastewater samples, respectively.

- SARS-CoV-2 variant Delta rapidly displaced variant Alpha in the United States and led to higher viral loads (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(22)00071-4)
  A Bolze et al, Cell Reports Medicine, March 15, 2022

  We report on the sequencing of 74,348 SARS-CoV-2 positive samples collected across the United States and show that the Delta variant, first detected in the United States in March 2021, made up the majority of SARS-CoV-2 infections by July 1, 2021 and accounted for >99.9% of the infections by September 2021. Not only did Delta displace variant Alpha, which was the dominant variant at the time, it also displaced the Gamma, Iota, and Mu variants. Through an analysis of quantification cycle (Cq) values, we demonstrate that Delta infections tend to have a 1.7× higher viral load compared to Alpha infections (a decrease of 0.8 Cq) on average.

- Effectiveness of mRNA Vaccination in Preventing COVID-19–Associated Invasive Mechanical Ventilation and Death — United States, March 2021–January 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e1.htm)
  MW Tenforde et al, MMWR, March 18, 2022

  COVID-19 mRNA vaccines provide protection against COVID-19 hospitalization among adults. However, how well mRNA vaccines protect against the most severe outcomes of COVID-19–related illness, including use of invasive mechanical ventilation (IMV) or death, is uncertain. Receiving 2 or 3 doses of an mRNA COVID-19 vaccine was associated with a 90% reduction in risk for COVID-19–associated IMV or death. Protection of 3 mRNA vaccine doses during the period of Omicron predominance was 94%.

- Neutralizing immunity in vaccine breakthrough infections from the SARS-CoV-2 Omicron and Delta variants (https://www.cell.com/cell/fulltext/S0092-8674(22)00329-4)
  V Servelitta et al, Cell, March 17, 2022

  Virus-like particle (VLP) and live virus assays were used to investigate neutralizing immunity against Delta and Omicron SARS-CoV-2 variants in 259 samples from 128 vaccinated individuals. Following Delta breakthrough infection, titers against WT rose 57-fold and 3.1-fold compared to uninfected boosted and unboosted individuals, respectively, versus only a 5.8-fold increase and 3.1-fold decrease

for Omicron breakthrough infection. Among immunocompetent, unboosted patients, Delta breakthrough infections induced 10.8-fold higher titers against WT compared to Omicron (p=0.037). Decreased antibody responses in Omicron breakthrough infections relative to Delta were potentially related to a higher proportion of asymptomatic or mild breakthrough infections (55.0% versus 28.6%, respectively).

- COVID-19–Associated Hospitalizations Among Adults During SARS-CoV-2 Delta and Omicron Variant Predominance, by Race/Ethnicity and Vaccination Status — COVID-NET, 14 States, July 2021–January 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e2.htm?s_cid=mm7112e2_x)
  CA Taylor et al, MMWR, March 18, 2022

  SARS-CoV-2 infections can result in COVID-19–associated hospitalizations, even among vaccinated persons. In January 2022, unvaccinated adults and those vaccinated with a primary series, but no booster or additional dose, were 12 and three times as likely to be hospitalized, respectively, as were adults who received booster or additional doses. Hospitalization rates among non-Hispanic Black adults increased more than rates in other racial/ethnic groups.

- Neutralisation sensitivity of the SARS-CoV-2 omicron (B.1.1.529) variant: a cross-sectional study (https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00129-3/fulltext)
  DJ Sheward et al, The Lancet, March 17, 2022

  Neutralising antibody responses in reference sample pools sampled shortly after infection or vaccination were substantially less potent against the omicron variant than against wild-type SARS-CoV-2 (seven-fold to 42-fold reduction in ID50 titres). Similarly, for sera obtained before vaccination in 2020 from a cohort of convalescent hospital workers, neutralisation of the omicron variant was low to undetectable (all ID50 titres <20). However, in serum samples obtained in 2021 from two cohorts in Stockholm, substantial cross-neutralisation of the omicron variant was observed. These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that boosting with licensed vaccines might be sufficient to raise neutralising antibody titres to protective levels.

- Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/35302625)
  Chun June Young et al. JAMA network open 2022 3 (3) e223064

  Among 106 866 confirmed COVID-19 infections (including 26 597 infections and 80 269 infections during the third and fourth waves of COVID-19 in Korea, respectively), a significant difference in age-specific susceptibility to the Delta vs pre-Delta variant was found in the younger age group. After adjustment for contact pattern and vaccination status, the increase in susceptibility to the Delta vs pre-Delta variant was estimated to be highest in the group aged 10 to 15 years, approximately doubling (1.92-fold increase [95% CI, 1.86-fold to 1.98-fold]), whereas in the group aged 50 years or more, susceptibility to the Delta vs pre-Delta variant remained stable at an approximately 1-fold change (eg, among individuals aged 50-55 years: 0.997-fold [95% CI, 0.989-fold to 1.001-fold). In this

study, the Delta variant of SARS-CoV-2 was estimated to propagate more easily among children and adolescents than pre-Delta strains, even after adjusting for contact pattern and vaccination status.

- SARS-CoV-2 host prediction based on virus-host genetic features.
  (https://pubmed.ncbi.nlm.nih.gov/35301337)
  Kawashima Irina Yuri et al. Scientific reports 2022 3 (1) 4576

  Based on a previously computational tool, the Seq2Hosts, we developed a novel approach which uses new variables obtained from the frequency of spike-Coronaviruses codons, the Relative Synonymous Codon Usage (RSCU) to shed new light on the molecular mechanisms involved in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) host specificity. By using the RSCU obtained from nucleotide sequences before the SARS-CoV-2 pandemic, we assessed the possibility of know the hosts capable to be infected by these new emerging species, which was first identified infecting humans during 2019 in Wuhan, China. According to the model trained and validated using sequences available before the pandemic, bats are the most likely the natural host to the SARS-CoV-2 infection, as previously suggested in other studies that searched for the host viral origin.

- End-point RT-PCR based on a conservation landscape for SARS-COV-2 detection
  (https://www.nature.com/articles/s41598-022-07756-6)
  AC Rangel et al, Scientific Reports, March 19, 2022

  End-point RT-PCR is a suitable alternative diagnostic technique since it is cheaper than RT-qPCR tests and can be implemented on a massive scale in low- and middle-income countries. In this work, a bioinformatic approach to guide the design of PCR primers was developed, and an alternative diagnostic test based on end-point PCR was designed. End-point PCR primers were designed through conservation analysis based on kmer frequency in SARS-CoV-2 and human respiratory pathogen genomes. Highly conserved regions were identified for primer design, and the resulting PCR primers were used to amplify 871 nasopharyngeal human samples with a previous RT-qPCR based SARS-CoV-2 diagnosis. The diagnostic test showed high accuracy in identifying SARS-CoV-2-positive samples including B.1.1.7, P.1, B.1.427/B.1.429 and B.1.617.2/ AY samples

- 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: a cohort study.
  (https://pubmed.ncbi.nlm.nih.gov/35305296)
  Nyberg Tommy et al. Lancet (London, England) 2022 3

  The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint.

Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

- Comparative effectiveness of the BNT162b2 and ChAdOx1 vaccines against Covid-19 in people over 50 (https://www.nature.com/articles/s41467-022-29159-x)
  A Xie et al, Nature Communications, March 21, 2022

  We find that, compared with one dose of ChAdOx1, vaccination with BNT162b2 is associated with a 28% (95% CI, 12-42) decreased risk of SARS-CoV-2 infection. Also, two doses of BNT162b2 vs ChAdOx1 confers 30% (95% CI, 25-35) and 29% (95% CI, 10-45) lower risks of both infection and hospitalization during the study period when the Delta variant is dominant. Furthermore, the comparative protection against the infection persists for at least six months among the fully vaccinated, suggesting no differential waning between the two vaccines.
- Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. (https://pubmed.ncbi.nlm.nih.gov/35296468)
  Li Xintong et al. BMJ (Clinical research ed.) 2022 3 e068373

  8?330?497 people who received at least one dose of covid-19 vaccines ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, or Ad.26.COV2.S between the rollout of the vaccination campaigns and end of data availability (UK: 9 May 2021; Spain: 30 June 2021). The study sample also comprised a cohort of 735?870 unvaccinated individuals with a first positive reverse transcription polymerase chain reaction test result for SARS-CoV-2 from 1 September 2020, and 14?330?080 participants from the general population. No safety signal was observed between covid-19 vaccines and the immune mediated neurological events of Bell's palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. An increased risk of Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome was, however, observed for people with SARS-CoV-2 infection.
- Whole-Genome Sequencing of SARS-CoV-2 Infection in a Cluster of Immunocompromised Children in Indonesia. (https://pubmed.ncbi.nlm.nih.gov/35308495)
  Putri Nina Dwi et al. Frontiers in medicine 2022 3 835998

  Real-time reverse-transcription polymerase chain reaction (RT-PCR) from nasopharyngeal (NP) swabs was used to diagnose the patients and also guardians and healthcare workers (HCWs) in the ward, followed by WGS of RT-PCR positive cases to establish their phylogenetic relationships. Using WGS, we showed that SARS-CoV-2 transmission in a cluster of children with underlying malignancy was characterized by high similarity of whole virus genome, which suggests nosocomial transmission.
- DNA methylation profiles in pneumonia patients reflect changes in cell types and pneumonia severity. (https://pubmed.ncbi.nlm.nih.gov/35311624)
  Morselli Marco et al. Epigenetics 2022 3 1-15

Immune cell-type composition changes with age, potentially weakening the response to infectious diseases. Profiling epigenetics marks of immune cells can help us understand the relationship with disease severity. We therefore leveraged a targeted DNA methylation method to study the differences in a cohort of pneumonia patients (both COVID-19 positive and negative) and unaffected individuals from peripheral blood.This approach allowed us to predict the pneumonia diagnosis with high accuracy (AUC = 0.92), and the PCR positivity to the SARS-CoV-2 viral genome with moderate, albeit lower, accuracy (AUC = 0.77).

- Integrative transcriptomic, evolutionary, and causal inference framework for region-level analysis: Application to COVID-19 (https://www.nature.com/articles/s41525-022-00296-y)
  D Zhou et al, NPJ Genomic Medicine, March 22, 2022

  We developed an integrative transcriptomic, evolutionary, and causal inference framework for a deep region-level analysis, which integrates several published approaches and a new summary-statistics-based methodology. To illustrate the framework, we applied it to understanding the host genetics of COVID-19 severity. We identified putative causal genes, including SLC6A20, CXCR6, CCR9, and CCR5 in the locus on 3p21.31, quantifying their effect on mediating expression and on severe COVID-19. We confirmed that individuals who carry the introgressed archaic segment in the locus have a substantially higher risk of developing the severe disease phenotype.
- Venous Thromboembolism in Ambulatory Covid-19 patients: Clinical and Genetic Determinants (https://www.medrxiv.org/content/10.1101/2022.03.22.22272748v1)
  J Xie et al, MEDRXIV, March 22, 2022
- Effect of prior infection, vaccination, and hybrid immunity against symptomatic BA.1 and BA.2 Omicron infections and severe COVID-19 in Qatar (https://www.medrxiv.org/content/10.1101/2022.03.22.22272745v1)
  HN Altarawneh et al, MEDRXIV, March 22, 2022

  Protection offered by five different forms of immunity, combining natural and vaccine immunity, was investigated against SARS-CoV-2 Omicron symptomatic BA.1 infection, symptomatic BA.2 infection, BA.1 hospitalization and death, and BA.2 hospitalization and death, in Qatar, between December 23, 2021 and February 21, 2022. We found no discernable differences in the effects of prior infection, vaccination, and hybrid immunity against BA.1 versus BA.2. Hybrid immunity resulting from prior infection and recent booster vaccination confers the strongest protection against either subvariant. Vaccination enhances protection of those with a prior infection.
- Early detection of SARS-CoV-2 variants using traveler-based genomic surveillance at four US airports, September 2021- January 2022 (https://www.medrxiv.org/content/10.1101/2022.03.21.22272490v1)
  RD Wegrzyn et al, MEDRXIV, March 22, 2022

  We enrolled arriving international air travelers in SARS-CoV-2 genomic surveillance, using molecular testing of pooled nasal swabs, and sequencing positive samples for viral lineage. Traveler-based

genomic surveillance provided early warning variant detection; we reported the first U.S. Omicron BA.2 and first BA.3 in North America, weeks before next reported detection.

- Detecting SARS-CoV-2 Variants in Wastewater and Their Correlation With Circulating Variants in the Communities. (https://pubmed.ncbi.nlm.nih.gov/35313589)
  Li Lin et al. Research square 2022 3

  Detection of SARS-CoV-2 viral load in wastewater has been highly informative in estimating the approximate number of infected individuals in the surrounding communities. Recent developments in wastewater monitoring to determine community prevalence of COVID-19 further extends into identifying SARS-CoV-2 variants, including those being monitored for having enhanced transmissibility. We sequenced genomic RNA derived from wastewater to determine the variants of coronaviruses circulating in the communities.

- Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine. (https://pubmed.ncbi.nlm.nih.gov/35320659)
  Moreira Edson D et al. The New England journal of medicine 2022 3

  In this ongoing, placebo-controlled, randomized, phase 3 trial, we assigned participants who had received two 30-μg doses of the BNT162b2 vaccine at least 6 months earlier to be injected with a third dose of the BNT162b2 vaccine or with placebo. We assessed vaccine safety and efficacy against Covid-19 starting 7 days after the third dose. A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months.

- Waning effectiveness of BNT162b2 and ChAdOx1 COVID-19 vaccines over six months since second dose: a cohort study using linked electronic health records (https://www.medrxiv.org/content/10.1101/2022.03.23.22272804v1)
  EMF Horne et al, MEDRXIV, March 23, 2022

  The BNT162b2, ChAdOx1 and unvaccinated groups comprised 1,773,970, 2,961,011 and 2,433,988 individuals, respectively. Waning of vaccine effectiveness was similar across outcomes and vaccine brands: e.g. in the 65+ years subgroup ratios of aHRs versus unvaccinated for COVID-19 hospitalisation, COVID-19 death and positive SARS-CoV-2 test ranged from 1.23 (95% CI 1.15-1.32) to 1.27 (1.20-1.34) for BNT162b2 and 1.16 (0.98-1.37) to 1.20 (1.14-1.27) for ChAdOx1. Despite waning, rates of COVID-19 hospitalisation and COVID-19 death were substantially lower among vaccinated individuals compared to unvaccinated individuals up to 26 weeks after second dose, with estimated aHRs <0.20 (>80% vaccine effectiveness) for BNT162b2, and <0.26 (>74%) for ChAdOx1. By weeks 23-26, rates of SARS-CoV-2 infection in fully vaccinated individuals were similar to or higher than those in unvaccinated individuals

News, Reviews and Commentaries

- Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients (https://www.science.org/doi/10.1126/scitranslmed.abl6141)
  X Charmetant et al, Science, March 16, 2022

  This study compared the immune response elicited by SARS-CoV-2 infection and vaccination in kidney transplant recipients. Infection elicited a broader response to SARS-CoV-2 associated with fewer cases of reinfection. The authors also observed a subset of individuals that did not respond to two doses of mRNA vaccine, potentially due to exposure to the immunosuppressive drug, mycophenolate mofetil. A subset of nonresponders who received a third dose of mRNA vaccine developed antibodies comparable to responders to two doses, suggesting that populations with immunosuppression should be prioritized for booster vaccine doses.
- COVID-19 Prediction using Genomic Footprint of SARS-CoV-2 in Air, Surface Swab and Wastewater (https://www.medrxiv.org/content/10.1101/2022.03.14.22272314v1)
  HS Gabriele et al, MEDRXIV, March 17, 2022

  A total of 445 air, surface swab and wastewater samples were collected, and these data were aggregated by day. SARS-CoV-2 genomic footprints were detected in air, surface swab and wastewater samples on 52 (63.4%), 40 (50.0%) and 57 (68.6%) days, respectively, during the study period. On 19 (24%) of 78 days SARS-CoV-2 was detected in all three sample types. Clinically diagnosed COVID-19 cases were reported on 11 days during the study period and SARS-CoV-2 was also detected two days before the case diagnosis on all 11 (100%), 9 (81.8%) and 8 (72.7%) days in air, surface swab and wastewater samples, respectively.
- SARS-CoV-2 variant Delta rapidly displaced variant Alpha in the United States and led to higher viral loads (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(22)00071-4)
  A Bolze et al, Cell Reports Medicine, March 15, 2022

  We report on the sequencing of 74,348 SARS-CoV-2 positive samples collected across the United States and show that the Delta variant, first detected in the United States in March 2021, made up the majority of SARS-CoV-2 infections by July 1, 2021 and accounted for >99.9% of the infections by September 2021. Not only did Delta displace variant Alpha, which was the dominant variant at the time, it also displaced the Gamma, Iota, and Mu variants. Through an analysis of quantification cycle (Cq) values, we demonstrate that Delta infections tend to have a 1.7× higher viral load compared to Alpha infections (a decrease of 0.8 Cq) on average.
- Effectiveness of mRNA Vaccination in Preventing COVID-19–Associated Invasive Mechanical Ventilation and Death — United States, March 2021–January 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e1.htm)
  MW Tenforde et al, MMWR, March 18, 2022

  COVID-19 mRNA vaccines provide protection against COVID-19 hospitalization among adults. However, how well mRNA vaccines protect against the most severe outcomes of COVID-19–related illness, including use of invasive mechanical ventilation (IMV) or death, is uncertain. Receiving 2 or 3

doses of an mRNA COVID-19 vaccine was associated with a 90% reduction in risk for COVID-19–associated IMV or death. Protection of 3 mRNA vaccine doses during the period of Omicron predominance was 94%.

- Neutralizing immunity in vaccine breakthrough infections from the SARS-CoV-2 Omicron and Delta variants (https://www.cell.com/cell/fulltext/S0092-8674(22)00329-4)
  V Servelitta et al, Cell, March 17, 2022

  Virus-like particle (VLP) and live virus assays were used to investigate neutralizing immunity against Delta and Omicron SARS-CoV-2 variants in 259 samples from 128 vaccinated individuals. Following Delta breakthrough infection, titers against WT rose 57-fold and 3.1-fold compared to uninfected boosted and unboosted individuals, respectively, versus only a 5.8-fold increase and 3.1-fold decrease for Omicron breakthrough infection. Among immunocompetent, unboosted patients, Delta breakthrough infections induced 10.8-fold higher titers against WT compared to Omicron (p=0.037). Decreased antibody responses in Omicron breakthrough infections relative to Delta were potentially related to a higher proportion of asymptomatic or mild breakthrough infections (55.0% versus 28.6%, respectively).

- COVID-19–Associated Hospitalizations Among Adults During SARS-CoV-2 Delta and Omicron Variant Predominance, by Race/Ethnicity and Vaccination Status — COVID-NET, 14 States, July 2021–January 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7112e2.htm?s_cid=mm7112e2_x)
  CA Taylor et al, MMWR, March 18, 2022

  SARS-CoV-2 infections can result in COVID-19–associated hospitalizations, even among vaccinated persons. In January 2022, unvaccinated adults and those vaccinated with a primary series, but no booster or additional dose, were 12 and three times as likely to be hospitalized, respectively, as were adults who received booster or additional doses. Hospitalization rates among non-Hispanic Black adults increased more than rates in other racial/ethnic groups.

- Neutralisation sensitivity of the SARS-CoV-2 omicron (B.1.1.529) variant: a cross-sectional study (https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00129-3/fulltext)
  DJ Sheward et al, The Lancet, March 17, 2022

  Neutralising antibody responses in reference sample pools sampled shortly after infection or vaccination were substantially less potent against the omicron variant than against wild-type SARS-CoV-2 (seven-fold to 42-fold reduction in ID50 titres). Similarly, for sera obtained before vaccination in 2020 from a cohort of convalescent hospital workers, neutralisation of the omicron variant was low to undetectable (all ID50 titres <20). However, in serum samples obtained in 2021 from two cohorts in Stockholm, substantial cross-neutralisation of the omicron variant was observed. These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that boosting with licensed vaccines might be sufficient to raise neutralising antibody titres to protective levels.

- Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/35302625)
  Chun June Young et al. JAMA network open 2022 3 (3) e223064

  > Among 106 866 confirmed COVID-19 infections (including 26 597 infections and 80 269 infections during the third and fourth waves of COVID-19 in Korea, respectively), a significant difference in age-specific susceptibility to the Delta vs pre-Delta variant was found in the younger age group. After adjustment for contact pattern and vaccination status, the increase in susceptibility to the Delta vs pre-Delta variant was estimated to be highest in the group aged 10 to 15 years, approximately doubling (1.92-fold increase [95% CI, 1.86-fold to 1.98-fold]), whereas in the group aged 50 years or more, susceptibility to the Delta vs pre-Delta variant remained stable at an approximately 1-fold change (eg, among individuals aged 50-55 years: 0.997-fold [95% CI, 0.989-fold to 1.001-fold). In this study, the Delta variant of SARS-CoV-2 was estimated to propagate more easily among children and adolescents than pre-Delta strains, even after adjusting for contact pattern and vaccination status.

- SARS-CoV-2 host prediction based on virus-host genetic features. (https://pubmed.ncbi.nlm.nih.gov/35301337)
  Kawashima Irina Yuri et al. Scientific reports 2022 3 (1) 4576

  > Based on a previously computational tool, the Seq2Hosts, we developed a novel approach which uses new variables obtained from the frequency of spike-Coronaviruses codons, the Relative Synonymous Codon Usage (RSCU) to shed new light on the molecular mechanisms involved in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) host specificity. By using the RSCU obtained from nucleotide sequences before the SARS-CoV-2 pandemic, we assessed the possibility of know the hosts capable to be infected by these new emerging species, which was first identified infecting humans during 2019 in Wuhan, China. According to the model trained and validated using sequences available before the pandemic, bats are the most likely the natural host to the SARS-CoV-2 infection, as previously suggested in other studies that searched for the host viral origin.

- End-point RT-PCR based on a conservation landscape for SARS-COV-2 detection (https://www.nature.com/articles/s41598-022-07756-6)
  AC Rangel et al, Scientific Reports, March 19, 2022

  > End-point RT-PCR is a suitable alternative diagnostic technique since it is cheaper than RT-qPCR tests and can be implemented on a massive scale in low- and middle-income countries. In this work, a bioinformatic approach to guide the design of PCR primers was developed, and an alternative diagnostic test based on end-point PCR was designed. End-point PCR primers were designed through conservation analysis based on kmer frequency in SARS-CoV-2 and human respiratory pathogen genomes. Highly conserved regions were identified for primer design, and the resulting PCR primers were used to amplify 871 nasopharyngeal human samples with a previous RT-qPCR based SARS-CoV-2 diagnosis. The diagnostic test showed high accuracy in identifying SARS-CoV-2-positive samples including B.1.1.7, P.1, B.1.427/B.1.429 and B.1.617.2/ AY samples

- 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: a cohort study. (https://pubmed.ncbi.nlm.nih.gov/35305296)
  Nyberg Tommy et al. Lancet (London, England) 2022 3

  > The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

- Comparative effectiveness of the BNT162b2 and ChAdOx1 vaccines against Covid-19 in people over 50 (https://www.nature.com/articles/s41467-022-29159-x)
  A Xie et al, Nature Communications, March 21, 2022

  > We find that, compared with one dose of ChAdOx1, vaccination with BNT162b2 is associated with a 28% (95% CI, 12-42) decreased risk of SARS-CoV-2 infection. Also, two doses of BNT162b2 vs ChAdOx1 confers 30% (95% CI, 25-35) and 29% (95% CI, 10-45) lower risks of both infection and hospitalization during the study period when the Delta variant is dominant. Furthermore, the comparative protection against the infection persists for at least six months among the fully vaccinated, suggesting no differential waning between the two vaccines.

- Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. (https://pubmed.ncbi.nlm.nih.gov/35296468)
  Li Xintong et al. BMJ (Clinical research ed.) 2022 3 e068373

  > 8?330?497 people who received at least one dose of covid-19 vaccines ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, or Ad.26.COV2.S between the rollout of the vaccination campaigns and end of data availability (UK: 9 May 2021; Spain: 30 June 2021). The study sample also comprised a cohort of 735?870 unvaccinated individuals with a first positive reverse transcription polymerase chain reaction test result for SARS-CoV-2 from 1 September 2020, and 14?330?080 participants from the general population. No safety signal was observed between covid-19 vaccines and the immune mediated neurological events of Bell's palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. An increased risk of Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome was, however, observed for people with SARS-CoV-2 infection.

- Whole-Genome Sequencing of SARS-CoV-2 Infection in a Cluster of Immunocompromised Children in Indonesia. (https://pubmed.ncbi.nlm.nih.gov/35308495)
  Putri Nina Dwi et al. Frontiers in medicine 2022 3 835998

Real-time reverse-transcription polymerase chain reaction (RT-PCR) from nasopharyngeal (NP) swabs was used to diagnose the patients and also guardians and healthcare workers (HCWs) in the ward, followed by WGS of RT-PCR positive cases to establish their phylogenetic relationships. Using WGS, we showed that SARS-CoV-2 transmission in a cluster of children with underlying malignancy was characterized by high similarity of whole virus genome, which suggests nosocomial transmission.

- DNA methylation profiles in pneumonia patients reflect changes in cell types and pneumonia severity. (https://pubmed.ncbi.nlm.nih.gov/35311624)
  Morselli Marco et al. Epigenetics 2022 3 1-15

  Immune cell-type composition changes with age, potentially weakening the response to infectious diseases. Profiling epigenetics marks of immune cells can help us understand the relationship with disease severity. We therefore leveraged a targeted DNA methylation method to study the differences in a cohort of pneumonia patients (both COVID-19 positive and negative) and unaffected individuals from peripheral blood.This approach allowed us to predict the pneumonia diagnosis with high accuracy (AUC = 0.92), and the PCR positivity to the SARS-CoV-2 viral genome with moderate, albeit lower, accuracy (AUC = 0.77).

- Integrative transcriptomic, evolutionary, and causal inference framework for region-level analysis: Application to COVID-19 (https://www.nature.com/articles/s41525-022-00296-y)
  D Zhou et al, NPJ Genomic Medicine, March 22, 2022

  We developed an integrative transcriptomic, evolutionary, and causal inference framework for a deep region-level analysis, which integrates several published approaches and a new summary-statistics-based methodology. To illustrate the framework, we applied it to understanding the host genetics of COVID-19 severity. We identified putative causal genes, including SLC6A20, CXCR6, CCR9, and CCR5 in the locus on 3p21.31, quantifying their effect on mediating expression and on severe COVID-19. We confirmed that individuals who carry the introgressed archaic segment in the locus have a substantially higher risk of developing the severe disease phenotype.

- Venous Thromboembolism in Ambulatory Covid-19 patients: Clinical and Genetic Determinants (https://www.medrxiv.org/content/10.1101/2022.03.22.22272748v1)
  J Xie et al, MEDRXIV, March 22, 2022

- Effect of prior infection, vaccination, and hybrid immunity against symptomatic BA.1 and BA.2 Omicron infections and severe COVID-19 in Qatar (https://www.medrxiv.org/content/10.1101/2022.03.22.22272745v1)
  HN Altarawneh et al, MEDRXIV, March 22, 2022

  Protection offered by five different forms of immunity, combining natural and vaccine immunity, was investigated against SARS-CoV-2 Omicron symptomatic BA.1 infection, symptomatic BA.2 infection, BA.1 hospitalization and death, and BA.2 hospitalization and death, in Qatar, between December 23, 2021 and February 21, 2022. We found no discernable differences in the effects of prior infection,

vaccination, and hybrid immunity against BA.1 versus BA.2. Hybrid immunity resulting from prior infection and recent booster vaccination confers the strongest protection against either subvariant. Vaccination enhances protection of those with a prior infection.

- Early detection of SARS-CoV-2 variants using traveler-based genomic surveillance at four US airports, September 2021- January 2022 (https://www.medrxiv.org/content/10.1101/2022.03.21.22272490v1)
  RD Wegrzyn et al, MEDRXIV, March 22, 2022

  We enrolled arriving international air travelers in SARS-CoV-2 genomic surveillance, using molecular testing of pooled nasal swabs, and sequencing positive samples for viral lineage. Traveler-based genomic surveillance provided early warning variant detection; we reported the first U.S. Omicron BA.2 and first BA.3 in North America, weeks before next reported detection.

- Detecting SARS-CoV-2 Variants in Wastewater and Their Correlation With Circulating Variants in the Communities. (https://pubmed.ncbi.nlm.nih.gov/35313589)
  Li Lin et al. Research square 2022 3

  Detection of SARS-CoV-2 viral load in wastewater has been highly informative in estimating the approximate number of infected individuals in the surrounding communities. Recent developments in wastewater monitoring to determine community prevalence of COVID-19 further extends into identifying SARS-CoV-2 variants, including those being monitored for having enhanced transmissibility. We sequenced genomic RNA derived from wastewater to determine the variants of coronaviruses circulating in the communities.

- Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine. (https://pubmed.ncbi.nlm.nih.gov/35320659)
  Moreira Edson D et al. The New England journal of medicine 2022 3

  In this ongoing, placebo-controlled, randomized, phase 3 trial, we assigned participants who had received two 30-μg doses of the BNT162b2 vaccine at least 6 months earlier to be injected with a third dose of the BNT162b2 vaccine or with placebo. We assessed vaccine safety and efficacy against Covid-19 starting 7 days after the third dose. A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months.

- Waning effectiveness of BNT162b2 and ChAdOx1 COVID-19 vaccines over six months since second dose: a cohort study using linked electronic health records (https://www.medrxiv.org/content/10.1101/2022.03.23.22272804v1)
  EMF Horne et al, MEDRXIV, March 23, 2022

  The BNT162b2, ChAdOx1 and unvaccinated groups comprised 1,773,970, 2,961,011 and 2,433,988 individuals, respectively. Waning of vaccine effectiveness was similar across outcomes and vaccine brands: e.g. in the 65+ years subgroup ratios of aHRs versus unvaccinated for COVID-19 hospitalisation, COVID-19 death and positive SARS-CoV-2 test ranged from 1.23 (95% CI 1.15-1.32)

to 1.27 (1.20-1.34) for BNT162b2 and 1.16 (0.98-1.37) to 1.20 (1.14-1.27) for ChAdOx1. Despite waning, rates of COVID-19 hospitalisation and COVID-19 death were substantially lower among vaccinated individuals compared to unvaccinated individuals up to 26 weeks after second dose, with estimated aHRs <0.20 (>80% vaccine effectiveness) for BNT162b2, and <0.26 (>74%) for ChAdOx1. By weeks 23-26, rates of SARS-CoV-2 infection in fully vaccinated individuals were similar to or higher than those in unvaccinated individuals

Page last reviewed: Oct 1, 2021

Page last updated: Mar 25, 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)