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

Published on 07/15/2021

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

- Mapping the human genetic architecture of COVID-19 (https://www.nature.com/articles/s41586-021-03767-x)
  COVID-19 Host Genetics Initiative, Nature, July 8, 2021

  > We describe the results of three genome-wide association meta-analyses comprised of up to 49,562 COVID-19 patients from 46 studies across 19 countries. We reported 13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19. Several of these loci correspond to previously documented associations to lung or autoimmune and inflammatory diseases3–7. They also represent potentially actionable mechanisms in response to infection. Mendelian Randomization analyses support a causal role for smoking and body mass index for severe COVID-19.

- Sequencing SARS-CoV-2 Genomes from Saliva. (https://pubmed.ncbi.nlm.nih.gov/34230934)
  Alpert Tara et al. medRxiv : the preprint server for health sciences 2021 7

  > Saliva has proven to be a safe and stable specimen for the detection of SARS-CoV-2 RNA via traditional diagnostic assays, however saliva is not commonly used for SARS-CoV-2 sequencing. Using the ARTIC Network amplicon-generation approach with sequencing on the Oxford Nanopore MinION, we demonstrate that sequencing SARS-CoV-2 from saliva produces genomes comparable to those from nasopharyngeal swabs.

- Genetic counselor experiences with telehealth before and after COVID-19. (https://pubmed.ncbi.nlm.nih.gov/34231953)
  Mills Rachel et al. Journal of genetic counseling 2021 7

  GCs reported an increase in the utilization of telehealth over time, with significant increases from pre-2017 (44%) to pre-COVID-19 (70%) and then to present (87%) (p<.001 and .02, respectively). There was no significant change in the total number of hours worked from pre-COVID-19 to the time of survey completion, nor were there significant changes in the amount of time spent on clinical responsibilities or interfacing with patients. However, the total number of hours worked in telehealth significantly increased (z = 5.05, p<.001) as did the percent of time spent interacting with patients via telehealth [t(72)=3.74, p<.001, d = 0.44]. Participants overwhelmingly preferred video (84%) over telephone.

- Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States (https://www.medrxiv.org/content/10.1101/2021.07.08.21259776v1)
  MW Tenford et al, MEDRXIV< July 8, 2021

  Overall vaccine effectiveness was 86.9% (95% CI: 80.4 to 91.2%). Vaccine effectiveness was similar for Pfizer-BioNTech and Moderna vaccines, and highest in adults aged 18-49 years (97.3%; 95% CI: 78.9 to 99.7%). Among 45 patients with vaccine-breakthrough Covid hospitalizations, 44 (97.8%) were at least 50 years old and 20 (44.4%) had immunosuppression. Vaccine effectiveness was lower among patients with immunosuppression (59.2%; 95% CI: 11.9 to 81.1%) than without immunosuppression (91.3%; 95% CI: 85.5 to 94.7%).

- Blood transcriptional biomarkers of acute viral infection for detection of pre-symptomatic SARS-CoV-2 infection: a nested, case-control diagnostic accuracy study (https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00146-4/fulltext)
  RK Gupta et al, The Lancet Microbe, July 2021

  We identified 20 candidate blood transcriptomic signatures of viral infection from 18 studies and evaluated their accuracy among 169 blood RNA samples from 96 participants over 24 weeks. Our findings support further urgent evaluation and development of blood IFI27 transcripts as a biomarker for early phase SARS-CoV-2 infection for screening individuals at high risk of infection

- Potent and protective IGHV3-53/3-66 public antibodies and their shared escape mutant on the spike of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/34244522)
  Zhang Qi et al. Nature communications 2021 7 (1) 4210

  Neutralizing antibodies (nAbs) to SARS-CoV-2 hold powerful potentials for clinical interventions against COVID-19 disease. However, their common genetic and biologic features remain elusive. Here we interrogate a total of 165 antibodies from eight COVID-19 patients, and find that potent nAbs from different patients have disproportionally high representation of IGHV3-53/3-66 usage, and therefore termed as public antibodies

- Updated SARS-CoV-2 Single Nucleotide Variants and Mortality Association. (https://pubmed.ncbi.nlm.nih.gov/34245452)
  Fang Shuyi et al. Journal of medical virology 2021 7

  > Our logistic regression model explored features contributing to mortality status, including 3 critical SNVs, G25088T(S:V1176F), T27484C (ORF7a:L31L), and T25A (upstream of ORF1ab), ages above 40 years old, and the gender of male. The protein structure analysis indicated that the emerging subgroups of non-synonymous SNVs and those mortality-related ones located on protein surface area.

- Systems vaccinology of the BNT162b2 mRNA vaccine in humans (https://www.nature.com/articles/s41586-021-03791-x)
  PA Arunachalam et al, Nature, July 12, 2021

  > We used a systems vaccinology approach to comprehensively profile the innate and adaptive immune responses of 56 healthy volunteers vaccinated with the Pfizer-BioNTech mRNA vaccine. Vaccination resulted in robust production of neutralizing antibodies (nAbs) against the parent Wuhan strain and, to a lesser extent, the B.1.351 strain, and significant increases in antigen-specific polyfunctional CD4 and CD8 T cells after the second dose.

- Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: an observational, genomic epidemiological study (https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00133-X/fulltext)
  The Lancet Public Health, July 9,2021

  > This study highlights how rapid escalation of clonal outbreaks can occur from a single incursion. However, strict quarantine measures and decisive public health responses to emergent cases are effective, even with high epidemic growth rates. Real-time genomic surveillance can alter the way in which public health agencies view and respond to COVID-19 outbreaks.

- Using genetic variants to evaluate the causal effect of serum vitamin D concentration on COVID-19 susceptibility, severity and hospitalization traits: a Mendelian randomization study. (https://pubmed.ncbi.nlm.nih.gov/34246301)
  Cui Zhiyong et al. Journal of translational medicine 2021 7 (1) 300

  > We performed a two-sample Mendelian randomization (MR) analysis to analyze the causal effect of the 25-hydroxyvitamin D [25(OH)D] concentration on COVID-19 susceptibility, severity and hospitalization traits by using summary-level GWAS data. We found no evidence to support the causal associations between the serum 25(OH)D concentration and the risk of COVID-19 susceptibility [IVW-fixed: odds ratio (OR) = 0.9049, 95% confidence interval (CI) 0.8197-0.9988, p = 0.0473], severity (IVW-fixed: OR = 1.0298, 95% CI 0.7699-1.3775, p = 0.8432) and hospitalized traits (IVW-fixed: OR = 1.0713, 95% CI 0.8819-1.3013, p = 0.4878).

- Viral infection and Transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant (https://www.medrxiv.org/content/10.1101/2021.07.07.21260122v1)

B Li et al, MEDRXIV, July 12, 2021

> We report the first local transmission of the Delta SARS-CoV-2 variant in mainland China. All 167 infections could be traced back to the first index case. The investigation on daily sequential PCR testing of the quarantined subjects indicated the viral load of the first positive test of Delta infections was ~1000 times higher than that of the 19A/19B strains infections back in the initial epidemic wave of 2020, suggesting the potential faster viral replication rate and more infectiousness of the Delta variant at the early stage of the infection.

- Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women (https://jamanetwork.com/journals/jama/fullarticle/2782047)
  I Goldstein et al, JAMA< July 12, 2021

  > In a retrospective cohort study that included 15?060 pregnant women in Israel, vaccination with BNT162b2 vs nonvaccination was associated with an adjusted hazard ratio for incident SARS-CoV-2 infection of 0.22. Among pregnant women, receipt of the BNT162b2 vaccine was associated with a lower risk of incident SARS-CoV-2 infection.

- Oral Microbiome Dysbiosis Is Associated With Symptoms Severity and Local Immune/Inflammatory Response in COVID-19 Patients: A Cross-Sectional Study. (https://pubmed.ncbi.nlm.nih.gov/34248910)
  Soffritti Irene et al. Frontiers in microbiology 2021 7 687513

  > The study showed the presence of oral dysbiosis in COVID-19 patients compared to matched controls, with significantly decreased alpha-diversity value and lower species richness in COVID-19 subjects. Notably, oral dysbiosis correlated with symptom severity ($p = 0.006$), and increased local inflammation ($p < 0.01$). In parallel, a decreased mucosal sIgA response was observed in more severely symptomatic patients ($p = 0.02$).

- Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination (https://www.nature.com/articles/s41591-021-01449-9)
  JB Martins et al, Nature Medicine, July 13, 2021

  > We used Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals to monitor ChAd-primed immune responses before and 3 weeks after booster with ChAd (n?=?32) or BioNTech/Pfizer's BNT162b2 (n?=?55). Although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern.

- Viral dynamics of acute SARS-CoV-2 infection and applications to diagnostic and public health strategies. (https://pubmed.ncbi.nlm.nih.gov/34252080)
  Kissler Stephen M et al. PLoS biology 2021 7 (7) e3001333

  > The dynamics of viral RNA concentration, particularly in the early stages of infection, can inform clinical measures and interventions such as test-based screening. We used prospective longitudinal quantitative reverse transcription PCR testing to measure the viral RNA trajectories for 68 individuals

during the resumption of the 2019-2020 National Basketball Association season....SARS-CoV-2 viral concentrations peak rapidly regardless of symptoms.

- Fecal SARS-CoV-2 RNA is associated with decreased COVID-19 survival. (https://pubmed.ncbi.nlm.nih.gov/34245255)
  Das Adhikari Upasana et al. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2021 7

  We found that extrapulmonary dissemination of infection to the gastrointestinal (GI) tract, assessed by the presence of SARS-CoV-2 RNA in stool, is associated with decreased COVID-19 survival. Measurement of SARS-CoV-2 RNA in stool may have utility for clinical risk assessment.

- Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. (https://pubmed.ncbi.nlm.nih.gov/34043894)
  Frenck Robert W et al. The New England journal of medicine 2021 5 (3) 239-250

  Overall, 2260 adolescents 12 to 15 years of age received injections; 1131 received BNT162b2, and 1129 received placebo. As has been found in other age groups, BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%], and headache [in 55 to 65%]); there were no vaccine-related serious adverse events and few overall severe adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion.

- Heterologous ChAdOx1 nCoV-19 and mRNA-1273 Vaccination. (https://pubmed.ncbi.nlm.nih.gov/34260850)
  Normark Johan et al. The New England journal of medicine 2021 7

  We conclude that the mRNA-1273 vaccine can efficiently stimulate the SARS-CoV-2–specific B-cell memory that has been generated by a prime dose of ChAdOx1 nCoV-19 vaccine 9 to 12 weeks earlier and that it may provide better protection against the B.1.351 variant than a ChAdOx1 nCoV-19 boost. These data also suggest that mRNA vaccines (here in the form of mRNA-1273) may be useful for vaccination strategies in which a third dose is to be administered to persons who have previously received two doses of ChAdOx1 nCoV-19.

Non-Genomics Precision Health Studies

- Mapping the human genetic architecture of COVID-19 (https://www.nature.com/articles/s41586-021-03767-x)
  COVID-19 Host Genetics Initiative, Nature, July 8, 2021

We describe the results of three genome-wide association meta-analyses comprised of up to 49,562 COVID-19 patients from 46 studies across 19 countries. We reported 13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19. Several of these loci correspond to previously documented associations to lung or autoimmune and inflammatory diseases3–7. They also represent potentially actionable mechanisms in response to infection. Mendelian Randomization analyses support a causal role for smoking and body mass index for severe COVID-19.

- Sequencing SARS-CoV-2 Genomes from Saliva. (https://pubmed.ncbi.nlm.nih.gov/34230934)
  Alpert Tara et al. medRxiv : the preprint server for health sciences 2021 7

  Saliva has proven to be a safe and stable specimen for the detection of SARS-CoV-2 RNA via traditional diagnostic assays, however saliva is not commonly used for SARS-CoV-2 sequencing. Using the ARTIC Network amplicon-generation approach with sequencing on the Oxford Nanopore MinION, we demonstrate that sequencing SARS-CoV-2 from saliva produces genomes comparable to those from nasopharyngeal swabs.

- Genetic counselor experiences with telehealth before and after COVID-19.
  (https://pubmed.ncbi.nlm.nih.gov/34231953)
  Mills Rachel et al. Journal of genetic counseling 2021 7

  GCs reported an increase in the utilization of telehealth over time, with significant increases from pre-2017 (44%) to pre-COVID-19 (70%) and then to present (87%) ($p<.001$ and .02, respectively). There was no significant change in the total number of hours worked from pre-COVID-19 to the time of survey completion, nor were there significant changes in the amount of time spent on clinical responsibilities or interfacing with patients. However, the total number of hours worked in telehealth significantly increased ($z = 5.05$, $p<.001$) as did the percent of time spent interacting with patients via telehealth [$t(72)=3.74$, $p<.001$, $d = 0.44$]. Participants overwhelmingly preferred video (84%) over telephone.

- Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States (https://www.medrxiv.org/content/10.1101/2021.07.08.21259776v1)
  MW Tenford et al, MEDRXIV< July 8, 2021

  Overall vaccine effectiveness was 86.9% (95% CI: 80.4 to 91.2%). Vaccine effectiveness was similar for Pfizer-BioNTech and Moderna vaccines, and highest in adults aged 18-49 years (97.3%; 95% CI: 78.9 to 99.7%). Among 45 patients with vaccine-breakthrough Covid hospitalizations, 44 (97.8%) were at least 50 years old and 20 (44.4%) had immunosuppression. Vaccine effectiveness was lower among patients with immunosuppression (59.2%; 95% CI: 11.9 to 81.1%) than without immunosuppression (91.3%; 95% CI: 85.5 to 94.7%).

- Blood transcriptional biomarkers of acute viral infection for detection of pre-symptomatic SARS-CoV-2 infection: a nested, case-control diagnostic accuracy study

(https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00146-4/fulltext)
RK Gupta et al, The Lancet Microbe, July 2021

> We identified 20 candidate blood transcriptomic signatures of viral infection from 18 studies and evaluated their accuracy among 169 blood RNA samples from 96 participants over 24 weeks. Our findings support further urgent evaluation and development of blood IFI27 transcripts as a biomarker for early phase SARS-CoV-2 infection for screening individuals at high risk of infection

- Potent and protective IGHV3-53/3-66 public antibodies and their shared escape mutant on the spike of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/34244522)
  Zhang Qi et al. Nature communications 2021 7 (1) 4210

  > Neutralizing antibodies (nAbs) to SARS-CoV-2 hold powerful potentials for clinical interventions against COVID-19 disease. However, their common genetic and biologic features remain elusive. Here we interrogate a total of 165 antibodies from eight COVID-19 patients, and find that potent nAbs from different patients have disproportionally high representation of IGHV3-53/3-66 usage, and therefore termed as public antibodies

- Updated SARS-CoV-2 Single Nucleotide Variants and Mortality Association.
  (https://pubmed.ncbi.nlm.nih.gov/34245452)
  Fang Shuyi et al. Journal of medical virology 2021 7

  > Our logistic regression model explored features contributing to mortality status, including 3 critical SNVs, G25088T(S:V1176F), T27484C (ORF7a:L31L), and T25A (upstream of ORF1ab), ages above 40 years old, and the gender of male. The protein structure analysis indicated that the emerging subgroups of non-synonymous SNVs and those mortality-related ones located on protein surface area.

- Systems vaccinology of the BNT162b2 mRNA vaccine in humans
  (https://www.nature.com/articles/s41586-021-03791-x)
  PA Arunachalam et al, Nature, July 12, 2021

  > We used a systems vaccinology approach to comprehensively profile the innate and adaptive immune responses of 56 healthy volunteers vaccinated with the Pfizer-BioNTech mRNA vaccine. Vaccination resulted in robust production of neutralizing antibodies (nAbs) against the parent Wuhan strain and, to a lesser extent, the B.1.351 strain, and significant increases in antigen-specific polyfunctional CD4 and CD8 T cells after the second dose.

- Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: an observational, genomic epidemiological study (https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00133-X/fulltext)
  The Lancet Public Health, July 9,2021

  > This study highlights how rapid escalation of clonal outbreaks can occur from a single incursion. However, strict quarantine measures and decisive public health responses to emergent cases are

effective, even with high epidemic growth rates. Real-time genomic surveillance can alter the way in which public health agencies view and respond to COVID-19 outbreaks.

- Using genetic variants to evaluate the causal effect of serum vitamin D concentration on COVID-19 susceptibility, severity and hospitalization traits: a Mendelian randomization study. (https://pubmed.ncbi.nlm.nih.gov/34246301)
  Cui Zhiyong et al. Journal of translational medicine 2021 7 (1) 300

  We performed a two-sample Mendelian randomization (MR) analysis to analyze the causal effect of the 25-hydroxyvitamin D [25(OH)D] concentration on COVID-19 susceptibility, severity and hospitalization traits by using summary-level GWAS data. We found no evidence to support the causal associations between the serum 25(OH)D concentration and the risk of COVID-19 susceptibility [IVW-fixed: odds ratio (OR) = 0.9049, 95% confidence interval (CI) 0.8197-0.9988, p = 0.0473], severity (IVW-fixed: OR = 1.0298, 95% CI 0.7699-1.3775, p = 0.8432) and hospitalized traits (IVW-fixed: OR = 1.0713, 95% CI 0.8819-1.3013, p = 0.4878).

- Viral infection and Transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant (https://www.medrxiv.org/content/10.1101/2021.07.07.21260122v1)
  B Li et al, MEDRXIV, July 12, 2021

  We report the first local transmission of the Delta SARS-CoV-2 variant in mainland China. All 167 infections could be traced back to the first index case. The investigation on daily sequential PCR testing of the quarantined subjects indicated the viral load of the first positive test of Delta infections was ~1000 times higher than that of the 19A/19B strains infections back in the initial epidemic wave of 2020, suggesting the potential faster viral replication rate and more infectiousness of the Delta variant at the early stage of the infection.

- Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women (https://jamanetwork.com/journals/jama/fullarticle/2782047)
  I Goldstein et al, JAMA< July 12, 2021

  In a retrospective cohort study that included 15?060 pregnant women in Israel, vaccination with BNT162b2 vs nonvaccination was associated with an adjusted hazard ratio for incident SARS-CoV-2 infection of 0.22. Among pregnant women, receipt of the BNT162b2 vaccine was associated with a lower risk of incident SARS-CoV-2 infection.

- Oral Microbiome Dysbiosis Is Associated With Symptoms Severity and Local Immune/Inflammatory Response in COVID-19 Patients: A Cross-Sectional Study. (https://pubmed.ncbi.nlm.nih.gov/34248910)
  Soffritti Irene et al. Frontiers in microbiology 2021 7 687513

  The study showed the presence of oral dysbiosis in COVID-19 patients compared to matched controls, with significantly decreased alpha-diversity value and lower species richness in COVID-19 subjects. Notably, oral dysbiosis correlated with symptom severity (p = 0.006), and increased local inflammation

($p < 0.01$). In parallel, a decreased mucosal sIgA response was observed in more severely symptomatic patients ($p = 0.02$).

- Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination (https://www.nature.com/articles/s41591-021-01449-9)
  JB Martins et al, Nature Medicine, July 13, 2021

  We used Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals to monitor ChAd-primed immune responses before and 3 weeks after booster with ChAd (n?=?32) or BioNTech/Pfizer's BNT162b2 (n?=?55). Although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern.

- Viral dynamics of acute SARS-CoV-2 infection and applications to diagnostic and public health strategies. (https://pubmed.ncbi.nlm.nih.gov/34252080)
  Kissler Stephen M et al. PLoS biology 2021 7 (7) e3001333

  The dynamics of viral RNA concentration, particularly in the early stages of infection, can inform clinical measures and interventions such as test-based screening. We used prospective longitudinal quantitative reverse transcription PCR testing to measure the viral RNA trajectories for 68 individuals during the resumption of the 2019-2020 National Basketball Association season....SARS-CoV-2 viral concentrations peak rapidly regardless of symptoms.

- Fecal SARS-CoV-2 RNA is associated with decreased COVID-19 survival. (https://pubmed.ncbi.nlm.nih.gov/34245255)
  Das Adhikari Upasana et al. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2021 7

  We found that extrapulmonary dissemination of infection to the gastrointestinal (GI) tract, assessed by the presence of SARS-CoV-2 RNA in stool, is associated with decreased COVID-19 survival. Measurement of SARS-CoV-2 RNA in stool may have utility for clinical risk assessment.

- Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. (https://pubmed.ncbi.nlm.nih.gov/34043894)
  Frenck Robert W et al. The New England journal of medicine 2021 5 (3) 239-250

  Overall, 2260 adolescents 12 to 15 years of age received injections; 1131 received BNT162b2, and 1129 received placebo. As has been found in other age groups, BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%], and headache [in 55 to 65%]); there were no vaccine-related serious adverse events and few overall severe adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion.

- Heterologous ChAdOx1 nCoV-19 and mRNA-1273 Vaccination. (https://pubmed.ncbi.nlm.nih.gov/34260850)
  Normark Johan et al. The New England journal of medicine 2021 7

  > We conclude that the mRNA-1273 vaccine can efficiently stimulate the SARS-CoV-2–specific B-cell memory that has been generated by a prime dose of ChAdOx1 nCoV-19 vaccine 9 to 12 weeks earlier and that it may provide better protection against the B.1.351 variant than a ChAdOx1 nCoV-19 boost. These data also suggest that mRNA vaccines (here in the form of mRNA-1273) may be useful for vaccination strategies in which a third dose is to be administered to persons who have previously received two doses of ChAdOx1 nCoV-19.

News, Reviews and Commentaries

- Mapping the human genetic architecture of COVID-19 (https://www.nature.com/articles/s41586-021-03767-x)
  COVID-19 Host Genetics Initiative, Nature, July 8, 2021

  > We describe the results of three genome-wide association meta-analyses comprised of up to 49,562 COVID-19 patients from 46 studies across 19 countries. We reported 13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19. Several of these loci correspond to previously documented associations to lung or autoimmune and inflammatory diseases3–7. They also represent potentially actionable mechanisms in response to infection. Mendelian Randomization analyses support a causal role for smoking and body mass index for severe COVID-19.

- Sequencing SARS-CoV-2 Genomes from Saliva. (https://pubmed.ncbi.nlm.nih.gov/34230934)
  Alpert Tara et al. medRxiv : the preprint server for health sciences 2021 7

  > Saliva has proven to be a safe and stable specimen for the detection of SARS-CoV-2 RNA via traditional diagnostic assays, however saliva is not commonly used for SARS-CoV-2 sequencing. Using the ARTIC Network amplicon-generation approach with sequencing on the Oxford Nanopore MinION, we demonstrate that sequencing SARS-CoV-2 from saliva produces genomes comparable to those from nasopharyngeal swabs.

- Genetic counselor experiences with telehealth before and after COVID-19. (https://pubmed.ncbi.nlm.nih.gov/34231953)
  Mills Rachel et al. Journal of genetic counseling 2021 7

  > GCs reported an increase in the utilization of telehealth over time, with significant increases from pre-2017 (44%) to pre-COVID-19 (70%) and then to present (87%) ($p<.001$ and .02, respectively). There was no significant change in the total number of hours worked from pre-COVID-19 to the time of survey completion, nor were there significant changes in the amount of time spent on clinical responsibilities or interfacing with patients. However, the total number of hours worked in telehealth

significantly increased (z = 5.05, p<.001) as did the percent of time spent interacting with patients via telehealth [t(72)=3.74, p<.001, d = 0.44]. Participants overwhelmingly preferred video (84%) over telephone.

- Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States (https://www.medrxiv.org/content/10.1101/2021.07.08.21259776v1)
  MW Tenford et al, MEDRXIV< July 8, 2021

  Overall vaccine effectiveness was 86.9% (95% CI: 80.4 to 91.2%). Vaccine effectiveness was similar for Pfizer-BioNTech and Moderna vaccines, and highest in adults aged 18-49 years (97.3%; 95% CI: 78.9 to 99.7%). Among 45 patients with vaccine-breakthrough Covid hospitalizations, 44 (97.8%) were at least 50 years old and 20 (44.4%) had immunosuppression. Vaccine effectiveness was lower among patients with immunosuppression (59.2%; 95% CI: 11.9 to 81.1%) than without immunosuppression (91.3%; 95% CI: 85.5 to 94.7%).

- Blood transcriptional biomarkers of acute viral infection for detection of pre-symptomatic SARS-CoV-2 infection: a nested, case-control diagnostic accuracy study (https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00146-4/fulltext)
  RK Gupta et al, The Lancet Microbe, July 2021

  We identified 20 candidate blood transcriptomic signatures of viral infection from 18 studies and evaluated their accuracy among 169 blood RNA samples from 96 participants over 24 weeks. Our findings support further urgent evaluation and development of blood IFI27 transcripts as a biomarker for early phase SARS-CoV-2 infection for screening individuals at high risk of infection

- Potent and protective IGHV3-53/3-66 public antibodies and their shared escape mutant on the spike of SARS-CoV-2. (https://pubmed.ncbi.nlm.nih.gov/34244522)
  Zhang Qi et al. Nature communications 2021 7 (1) 4210

  Neutralizing antibodies (nAbs) to SARS-CoV-2 hold powerful potentials for clinical interventions against COVID-19 disease. However, their common genetic and biologic features remain elusive. Here we interrogate a total of 165 antibodies from eight COVID-19 patients, and find that potent nAbs from different patients have disproportionally high representation of IGHV3-53/3-66 usage, and therefore termed as public antibodies

- Updated SARS-CoV-2 Single Nucleotide Variants and Mortality Association. (https://pubmed.ncbi.nlm.nih.gov/34245452)
  Fang Shuyi et al. Journal of medical virology 2021 7

  Our logistic regression model explored features contributing to mortality status, including 3 critical SNVs, G25088T(S:V1176F), T27484C (ORF7a:L31L), and T25A (upstream of ORF1ab), ages above 40 years old, and the gender of male. The protein structure analysis indicated that the emerging subgroups of non-synonymous SNVs and those mortality-related ones located on protein surface area.

- Systems vaccinology of the BNT162b2 mRNA vaccine in humans (https://www.nature.com/articles/s41586-021-03791-x)
  PA Arunachalam et al, Nature, July 12, 2021

  > We used a systems vaccinology approach to comprehensively profile the innate and adaptive immune responses of 56 healthy volunteers vaccinated with the Pfizer-BioNTech mRNA vaccine. Vaccination resulted in robust production of neutralizing antibodies (nAbs) against the parent Wuhan strain and, to a lesser extent, the B.1.351 strain, and significant increases in antigen-specific polyfunctional CD4 and CD8 T cells after the second dose.

- Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: an observational, genomic epidemiological study (https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00133-X/fulltext)
  The Lancet Public Health, July 9,2021

  > This study highlights how rapid escalation of clonal outbreaks can occur from a single incursion. However, strict quarantine measures and decisive public health responses to emergent cases are effective, even with high epidemic growth rates. Real-time genomic surveillance can alter the way in which public health agencies view and respond to COVID-19 outbreaks.

- Using genetic variants to evaluate the causal effect of serum vitamin D concentration on COVID-19 susceptibility, severity and hospitalization traits: a Mendelian randomization study. (https://pubmed.ncbi.nlm.nih.gov/34246301)
  Cui Zhiyong et al. Journal of translational medicine 2021 7 (1) 300

  > We performed a two-sample Mendelian randomization (MR) analysis to analyze the causal effect of the 25-hydroxyvitamin D [25(OH)D] concentration on COVID-19 susceptibility, severity and hospitalization traits by using summary-level GWAS data. We found no evidence to support the causal associations between the serum 25(OH)D concentration and the risk of COVID-19 susceptibility [IVW-fixed: odds ratio (OR) = 0.9049, 95% confidence interval (CI) 0.8197-0.9988, p = 0.0473], severity (IVW-fixed: OR = 1.0298, 95% CI 0.7699-1.3775, p = 0.8432) and hospitalized traits (IVW-fixed: OR = 1.0713, 95% CI 0.8819-1.3013, p = 0.4878).

- Viral infection and Transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant (https://www.medrxiv.org/content/10.1101/2021.07.07.21260122v1)
  B Li et al, MEDRXIV, July 12, 2021

  > We report the first local transmission of the Delta SARS-CoV-2 variant in mainland China. All 167 infections could be traced back to the first index case. The investigation on daily sequential PCR testing of the quarantined subjects indicated the viral load of the first positive test of Delta infections was ~1000 times higher than that of the 19A/19B strains infections back in the initial epidemic wave of 2020, suggesting the potential faster viral replication rate and more infectiousness of the Delta variant at the early stage of the infection.

- Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women (https://jamanetwork.com/journals/jama/fullarticle/2782047)
  I Goldstein et al, JAMA< July 12, 2021

  > In a retrospective cohort study that included 15?060 pregnant women in Israel, vaccination with BNT162b2 vs nonvaccination was associated with an adjusted hazard ratio for incident SARS-CoV-2 infection of 0.22. Among pregnant women, receipt of the BNT162b2 vaccine was associated with a lower risk of incident SARS-CoV-2 infection.

- Oral Microbiome Dysbiosis Is Associated With Symptoms Severity and Local Immune/Inflammatory Response in COVID-19 Patients: A Cross-Sectional Study. (https://pubmed.ncbi.nlm.nih.gov/34248910)
  Soffritti Irene et al. Frontiers in microbiology 2021 7 687513

  > The study showed the presence of oral dysbiosis in COVID-19 patients compared to matched controls, with significantly decreased alpha-diversity value and lower species richness in COVID-19 subjects. Notably, oral dysbiosis correlated with symptom severity ($p = 0.006$), and increased local inflammation ($p < 0.01$). In parallel, a decreased mucosal sIgA response was observed in more severely symptomatic patients ($p = 0.02$).

- Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination (https://www.nature.com/articles/s41591-021-01449-9)
  JB Martins et al, Nature Medicine, July 13, 2021

  > We used Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals to monitor ChAd-primed immune responses before and 3 weeks after booster with ChAd (n?=?32) or BioNTech/Pfizer's BNT162b2 (n?=?55). Although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern.

- Viral dynamics of acute SARS-CoV-2 infection and applications to diagnostic and public health strategies. (https://pubmed.ncbi.nlm.nih.gov/34252080)
  Kissler Stephen M et al. PLoS biology 2021 7 (7) e3001333

  > The dynamics of viral RNA concentration, particularly in the early stages of infection, can inform clinical measures and interventions such as test-based screening. We used prospective longitudinal quantitative reverse transcription PCR testing to measure the viral RNA trajectories for 68 individuals during the resumption of the 2019-2020 National Basketball Association season....SARS-CoV-2 viral concentrations peak rapidly regardless of symptoms.

- Fecal SARS-CoV-2 RNA is associated with decreased COVID-19 survival. (https://pubmed.ncbi.nlm.nih.gov/34245255)
  Das Adhikari Upasana et al. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2021 7

We found that extrapulmonary dissemination of infection to the gastrointestinal (GI) tract, assessed by the presence of SARS-CoV-2 RNA in stool, is associated with decreased COVID-19 survival. Measurement of SARS-CoV-2 RNA in stool may have utility for clinical risk assessment.

- Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. (https://pubmed.ncbi.nlm.nih.gov/34043894)
  Frenck Robert W et al. The New England journal of medicine 2021 5 (3) 239-250

  Overall, 2260 adolescents 12 to 15 years of age received injections; 1131 received BNT162b2, and 1129 received placebo. As has been found in other age groups, BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%], and headache [in 55 to 65%]); there were no vaccine-related serious adverse events and few overall severe adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion.

- Heterologous ChAdOx1 nCoV-19 and mRNA-1273 Vaccination. (https://pubmed.ncbi.nlm.nih.gov/34260850)
  Normark Johan et al. The New England journal of medicine 2021 7

  We conclude that the mRNA-1273 vaccine can efficiently stimulate the SARS-CoV-2–specific B-cell memory that has been generated by a prime dose of ChAdOx1 nCoV-19 vaccine 9 to 12 weeks earlier and that it may provide better protection against the B.1.351 variant than a ChAdOx1 nCoV-19 boost. These data also suggest that mRNA vaccines (here in the form of mRNA-1273) may be useful for vaccination strategies in which a third dose is to be administered to persons who have previously received two doses of ChAdOx1 nCoV-19.

Page last reviewed: Oct 1, 2020

Page last updated: Jul 20, 2021

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)