

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

Published on 09/30/2021

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

• Multiple Transmission Chains within COVID-19 Cluster, Connecticut, USA, 2020. (https://pubmed.ncbi.nlm.nih.gov/34545794)

Bart Stephen M et al. Emerging infectious diseases 2021 9 (10) 2669-2672

In fall 2020, a coronavirus disease cluster comprising 16 cases occurred in Connecticut, USA. Epidemiologic and genomic evidence supported transmission among persons at a school and fitness center but not a workplace. The multiple transmission chains identified within this cluster highlight the necessity of a combined investigatory approach

 Protocol for safe, affordable, and reproducible isolation and quantitation of SARS-CoV-2 RNA from wastewater. (https://pubmed.ncbi.nlm.nih.gov/34555079) Trujillo Monica et al. PloS one 2021 9 (9) e0257454

Trujilio Monica et al. Plos one 2021 9 (9) e0257454

The following protocol describes our workflow for processing wastewater with the goal of detecting the genetic signal of SARS-CoV-2. The steps include pasteurization, virus concentration, RNA extraction, and quantification by RT-qPCR. We include auxiliary steps that provide new users with tools and strategies that will help troubleshoot key steps in the process. This protocol is one of the safest, cheapest, and most reproducible approaches for the detection of SARS-CoV-2 RNA in wastewater.

 The impact of real-time whole genome sequencing in controlling healthcare-associated SARS-CoV-2 outbreaks. (https://pubmed.ncbi.nlm.nih.gov/34555152) Francis Rodric V et al. The Journal of infectious diseases 2021 9

Nosocomial SARS-CoV-2 infections have severely affected bed capacity and patient flow. We utilised whole genome sequencing (WGS) to identify outbreaks and focus infection control resources and intervention during the UK's second pandemic wave in late 2020. Phylogenetic analysis of WGS and epidemiological data pinpointed an initial transmission event to an admission ward, with immediate prior community infection linkage documented. High incidence of asymptomatic staff infection with genetically identical viral sequences was also observed, which may have contributed to the propagation of the outbreak. WGS allowed timely nosocomial transmission intervention measures, including admissions ward point of care testing and introduction of portable HEPA14 filters.

Using genomic epidemiology of SARS-CoV-2 to support contact tracing and public health surveillance in rural Humboldt County, California. (https://www.medrxiv.org/content/10.1101/2021.09.21.21258385v1) G Stoddard et al, MEDRXIV, September 27, 2021

853 whole SARS-CoV-2 genomes were generated, representing ~58% of the 1,449 SARS-CoV-2positive cases detected in Humboldt County as of March 12, 2021. Phylogenetic analysis of these data was used to develop a comprehensive understanding of SARS-CoV-2 introductions to the county and to support contact tracing and epidemiologic investigations of all large outbreaks in the county. In the case of an outbreak on a commercial farm, viral genomic data were used to validate reported epidemiologic links and link additional cases within the community who did not report a farm exposure to the outbreak.

Modeling the transmission of the SARS-CoV-2 delta variant in a partially vaccinated population (https://www.medrxiv.org/content/10.1101/2021.09.23.21264032v1) U Avila et al, MEDRXIV, September 26, 2021

We developed a mathematical model that considers both subpopulations and immunity parameters including vaccination rates, vaccine effectiveness, and a gradual loss of protection. The model forecasted the spread of the SARS-CoV-2 delta variant in the US under varied transmission and vaccination rates. We further obtained the control reproduction number and conducted sensitivity analyses to determine how each parameter may affect virus transmission. Our results show that a combination of strengthening vaccine-induced immunity and preventative behavioral measures will likely be required to deaccelerate the rise of infectious SARS-CoV-2 variants.

 Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00283-4)
T Nakanayma et al, Cell Reports Medicine, September 27,2021

In this translational study, we discover key variabilities in the expression of ACE2 and TMPRSS2, essential SARS-CoV-2 entry factors, among the mucosal tissues of the human proximal airways. We show that SARS-CoV-2 infection is present in all examined head & neck tissues, with a notable tropism for the nasal cavity and tracheal mucosa. Finally, we uncover an association between smoking and

higher SARS-CoV-2 viral infection in the human proximal airway, which may explain the increased susceptibility of smokers to developing severe COVID-19.

 A prenylated dsRNA sensor protects against severe COVID-19 (https://www.science.org/doi/10.1126/science.abj3624)
A Wickenhagen et al, Science, September 28, 2021

To better understand the antiviral defenses relevant to COVID-19, we used interferon-stimulated gene (ISG) expression screening to reveal that OAS1, through RNase L, potently inhibits SARS-CoV-2. We show that a common splice-acceptor SNP (Rs10774671) governs whether people express prenylated OAS1 isoforms that are membrane-associated and sense specific regions of SARS-CoV-2 RNAs, or only express cytosolic, nonprenylated OAS1 that does not efficiently detect SARS-CoV-2. Importantly, in hospitalized patients, expression of prenylated OAS1 was associated with protection from severe COVID-19, suggesting this antiviral defense is a major component of a protective antiviral response.

Large-scale analysis of SARS-CoV-2 spike-glycoprotein mutants demonstrates the need for continuous screening of virus isolates. (https://pubmed.ncbi.nlm.nih.gov/34570776)
Schrörs Barbara et al. PloS one 2021 9 (9) e0249254

We analyzed 1,036,030 SARS-CoV-2 genome assemblies and 30,806 NGS datasets from GISAID and European Nucleotide Archive (ENA) focusing on non-synonymous mutations in the spike protein. Only around 2.5% of the samples contained the wild-type spike protein with no variation from the reference. Among the spike protein mutants, we confirmed a low mutation rate exhibiting less than 10 non-synonymous mutations in 99.6% of the analyzed sequences, but the mean and median number of spike protein mutations per sample increased over time. 5,472 distinct variants were found in total. The majority of the observed variants were recurrent, but only 21 and 14 recurrent variants were found in at least 1% of the mutant genome assemblies and NGS samples.

 Effectiveness of BNT162b2 Vaccine in Adolescents during Outbreak of SARS-CoV-2 Delta Variant Infection, Israel, 2021. (https://pubmed.ncbi.nlm.nih.gov/34570694)
Glatman-Freedman Aharona et al. Emerging infectious diseases 2021 9 (11)

In Israel, the BNT162b2 vaccine against severe acute respiratory syndrome coronavirus 2 was approved for use in adolescents in June 2021, shortly before an outbreak of B.1.617.2 (Delta) variant-dominant infection. We evaluated short-term vaccine effectiveness and found the vaccine to be highly effective among this population in this setting.

 Modeling of COVID-19 Transmission Dynamics on US Population: Inter-transfer Infection in Age Groups, Mutant Variants, and Vaccination Strategies (https://www.medrxiv.org/content/10.1101/2021.09.25.21264118v1)
J Roy et al, MEDRXIV, September 28, 2021 We developed the SIRDV-Virulence epidemiological model based on a population balance equation to study the effect of mutants of the virus and the effect of vaccination strategies on mitigating the transmission among the population in the United States. Based on the available data from the Centers for Disease Control and Prevention (CDC), we obtain the key parameters governing the dynamic evolution of the spread of the COVID-19 pandemic.

No Significant Difference in Viral Load Between Vaccinated and Unvaccinated, Asymptomatic and Symptomatic Groups Infected with SARS-CoV-2 Delta Variant (https://www.medrxiv.org/content/10.1101/2021.09.28.21264262v1) CB Acharya et al, MEDRXIV, September 29, 2021

We found no significant difference in cycle threshold values between vaccinated and unvaccinated, asymptomatic and symptomatic groups infected with SARS-CoV-2 Delta. Given the substantial proportion of asymptomatic vaccine breakthrough cases with high viral levels, interventions, including masking and testing, should be considered for all in settings with elevated COVID-19 transmission.

Four SARS-CoV-2 vaccines induce quantitatively different antibody responses against SARS-CoV-2 variants (https://www.medrxiv.org/content/10.1101/2021.09.27.21264163v1)
MJ van Gils et al, MEDRXIV, September 28, 2021

e performed a head-to-head comparison of the ability of sera from individuals vaccinated with either one of four vaccines (BNT162b2, mRNA-1273, AZD1222 or Ad26.COV2.S) to recognize and neutralize the four SARS-CoV-2 variants of concern (VOCs; Alpha, Beta, Gamma and Delta). Four weeks after completing the vaccination series, SARS-CoV-2 wild-type neutralizing antibody titers were highest in recipients of BNT162b2 and mRNA-1273 (median titers of 1891 and 3061, respectively), and substantially lower in those vaccinated with the adenovirus vector-based vaccines AZD1222 and Ad26.COV2.S (median titers of 241 and 119, respectively). VOCs neutralization was reduced in all vaccine groups, with the largest (5.8-fold) reduction in neutralization being observed against the Beta variant. Overall, the mRNA vaccines appear superior to adenovirus vector-based vaccines in inducing neutralizing antibodies against VOCs four weeks after the final vaccination.

 Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce (https://www.nejm.org/doi/full/10.1056/NEJMc2112981?query=featured_home)
J Keehner et al, NEJM, September 30, 2021

The dramatic change in vaccine effectiveness from June to July is likely to be due to both the emergence of the delta variant and waning immunity over time, compounded by the end of masking requirements in California and the resulting greater risk of exposure in the community.

The Evolving Faces of the SARS-CoV-2 Genome. (https://pubmed.ncbi.nlm.nih.gov/34578345) Schmidt Maria et al. Viruses 2021 9 (9)

We applied molecular portrayal using self-organizing maps machine learning (SOM portrayal) to characterize the diversity of the virus genomes, their mutual relatedness and development since the

beginning of the pandemic. The genetic landscape obtained visualizes the relevant mutations in a lineage-specific fashion and provides developmental paths in genetic state space from early lineages towards the variants of concern alpha, beta, gamma and delta

Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort. (https://pubmed.ncbi.nlm.nih.gov/34580193) Clift Ashley K et al. Thorax 2021 9

Conflicting evidence has emerged regarding the relevance of smoking on risk of COVID-19 and its severity. We undertook large-scale observational and Mendelian randomisation (MR) analyses using UK Biobank. Genetically predicted higher number of cigarettes smoked per day was associated with higher risks of all outcomes (infection OR 2.51, 95% CI 1.20 to 5.24; hospitalization OR 5.08, 95% CI 2.04 to 12.66; and death OR 10.02, 95% CI 2.53 to 39.72). Congruent results from two analytical approaches support a causal effect of smoking on risk of severe COVID-19.

Impact of sickle cell trait on morbidity and mortality from SARS-CoV-2 infection.

(https://pubmed.ncbi.nlm.nih.gov/34581772)

Merz Lauren E et al. Blood advances 2021 9 (18) 3690-3693

Patients admitted for SARS-CoV-2 infection who identified as black or African American were included in the study (n = 166). Blood remnants were tested for SCT, and clinical data were abstracted from the chart. There was no difference in mortality between those with SCT and those without. There was no difference in respiratory complications between groups, but those without SCT had a much higher burden of chronic lung disease (P = .004). Those with SCT had higher creatinine on admission (P = .004), but no difference in in-hospital renal complications (P = .532).

Non-Genomics Precision Health Studies

Multiple Transmission Chains within COVID-19 Cluster, Connecticut, USA, 2020. (https://pubmed.ncbi.nlm.nih.gov/34545794) Bart Stephen M et al. Emerging infectious diseases 2021 9 (10) 2669-2672

In fall 2020, a coronavirus disease cluster comprising 16 cases occurred in Connecticut, USA. Epidemiologic and genomic evidence supported transmission among persons at a school and fitness center but not a workplace. The multiple transmission chains identified within this cluster highlight the necessity of a combined investigatory approach

Protocol for safe, affordable, and reproducible isolation and quantitation of SARS-CoV-2 RNA from wastewater. (https://pubmed.ncbi.nlm.nih.gov/34555079)

Trujillo Monica et al. PloS one 2021 9 (9) e0257454

The following protocol describes our workflow for processing wastewater with the goal of detecting the genetic signal of SARS-CoV-2. The steps include pasteurization, virus concentration, RNA

extraction, and quantification by RT-qPCR. We include auxiliary steps that provide new users with tools and strategies that will help troubleshoot key steps in the process. This protocol is one of the safest, cheapest, and most reproducible approaches for the detection of SARS-CoV-2 RNA in wastewater.

The impact of real-time whole genome sequencing in controlling healthcare-associated SARS-CoV-2 outbreaks. (https://pubmed.ncbi.nlm.nih.gov/34555152)

Francis Rodric V et al. The Journal of infectious diseases 2021 9

Nosocomial SARS-CoV-2 infections have severely affected bed capacity and patient flow. We utilised whole genome sequencing (WGS) to identify outbreaks and focus infection control resources and intervention during the UK's second pandemic wave in late 2020. Phylogenetic analysis of WGS and epidemiological data pinpointed an initial transmission event to an admission ward, with immediate prior community infection linkage documented. High incidence of asymptomatic staff infection with genetically identical viral sequences was also observed, which may have contributed to the propagation of the outbreak. WGS allowed timely nosocomial transmission intervention measures, including admissions ward point of care testing and introduction of portable HEPA14 filters.

 Using genomic epidemiology of SARS-CoV-2 to support contact tracing and public health surveillance in rural Humboldt County, California. (https://www.medrxiv.org/content/10.1101/2021.09.21.21258385v1) G Stoddard et al, MEDRXIV, September 27, 2021

853 whole SARS-CoV-2 genomes were generated, representing ~58% of the 1,449 SARS-CoV-2positive cases detected in Humboldt County as of March 12, 2021. Phylogenetic analysis of these data was used to develop a comprehensive understanding of SARS-CoV-2 introductions to the county and to support contact tracing and epidemiologic investigations of all large outbreaks in the county. In the case of an outbreak on a commercial farm, viral genomic data were used to validate reported epidemiologic links and link additional cases within the community who did not report a farm exposure to the outbreak.

 Modeling the transmission of the SARS-CoV-2 delta variant in a partially vaccinated population (https://www.medrxiv.org/content/10.1101/2021.09.23.21264032v1)
U Avila et al, MEDRXIV, September 26, 2021

We developed a mathematical model that considers both subpopulations and immunity parameters including vaccination rates, vaccine effectiveness, and a gradual loss of protection. The model forecasted the spread of the SARS-CoV-2 delta variant in the US under varied transmission and vaccination rates. We further obtained the control reproduction number and conducted sensitivity analyses to determine how each parameter may affect virus transmission. Our results show that a combination of strengthening vaccine-induced immunity and preventative behavioral measures will likely be required to deaccelerate the rise of infectious SARS-CoV-2 variants.

 Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00283-4) T Nakanayma et al, Cell Reports Medicine, September 27,2021

In this translational study, we discover key variabilities in the expression of ACE2 and TMPRSS2, essential SARS-CoV-2 entry factors, among the mucosal tissues of the human proximal airways. We show that SARS-CoV-2 infection is present in all examined head & neck tissues, with a notable tropism for the nasal cavity and tracheal mucosa. Finally, we uncover an association between smoking and higher SARS-CoV-2 viral infection in the human proximal airway, which may explain the increased susceptibility of smokers to developing severe COVID-19.

 A prenylated dsRNA sensor protects against severe COVID-19 (https://www.science.org/doi/10.1126/science.abj3624)
A Wickenhagen et al, Science, September 28, 2021

To better understand the antiviral defenses relevant to COVID-19, we used interferon-stimulated gene (ISG) expression screening to reveal that OAS1, through RNase L, potently inhibits SARS-CoV-2. We show that a common splice-acceptor SNP (Rs10774671) governs whether people express prenylated OAS1 isoforms that are membrane-associated and sense specific regions of SARS-CoV-2 RNAs, or only express cytosolic, nonprenylated OAS1 that does not efficiently detect SARS-CoV-2. Importantly, in hospitalized patients, expression of prenylated OAS1 was associated with protection from severe COVID-19, suggesting this antiviral defense is a major component of a protective antiviral response.

 Large-scale analysis of SARS-CoV-2 spike-glycoprotein mutants demonstrates the need for continuous screening of virus isolates. (https://pubmed.ncbi.nlm.nih.gov/34570776)
Schrörs Barbara et al. PloS one 2021 9 (9) e0249254

We analyzed 1,036,030 SARS-CoV-2 genome assemblies and 30,806 NGS datasets from GISAID and European Nucleotide Archive (ENA) focusing on non-synonymous mutations in the spike protein. Only around 2.5% of the samples contained the wild-type spike protein with no variation from the reference. Among the spike protein mutants, we confirmed a low mutation rate exhibiting less than 10 non-synonymous mutations in 99.6% of the analyzed sequences, but the mean and median number of spike protein mutations per sample increased over time. 5,472 distinct variants were found in total. The majority of the observed variants were recurrent, but only 21 and 14 recurrent variants were found in at least 1% of the mutant genome assemblies and NGS samples.

 Effectiveness of BNT162b2 Vaccine in Adolescents during Outbreak of SARS-CoV-2 Delta Variant Infection, Israel, 2021. (https://pubmed.ncbi.nlm.nih.gov/34570694)
Glatman-Freedman Aharona et al. Emerging infectious diseases 2021 9 (11)

In Israel, the BNT162b2 vaccine against severe acute respiratory syndrome coronavirus 2 was approved for use in adolescents in June 2021, shortly before an outbreak of B.1.617.2 (Delta) variant-dominant infection. We evaluated short-term vaccine effectiveness and found the vaccine to be highly effective among this population in this setting.

 Modeling of COVID-19 Transmission Dynamics on US Population: Inter-transfer Infection in Age Groups, Mutant Variants, and Vaccination Strategies
(https://www.medrxiv.org/content/10.1101/2021.09.25.21264118v1)
J Roy et al, MEDRXIV, September 28, 2021

We developed the SIRDV-Virulence epidemiological model based on a population balance equation to study the effect of mutants of the virus and the effect of vaccination strategies on mitigating the transmission among the population in the United States. Based on the available data from the Centers for Disease Control and Prevention (CDC), we obtain the key parameters governing the dynamic evolution of the spread of the COVID-19 pandemic.

No Significant Difference in Viral Load Between Vaccinated and Unvaccinated, Asymptomatic and

Symptomatic Groups Infected with SARS-CoV-2 Delta Variant (https://www.medrxiv.org/content/10.1101/2021.09.28.21264262v1) CB Acharya et al, MEDRXIV, September 29, 2021

We found no significant difference in cycle threshold values between vaccinated and unvaccinated, asymptomatic and symptomatic groups infected with SARS-CoV-2 Delta. Given the substantial proportion of asymptomatic vaccine breakthrough cases with high viral levels, interventions, including masking and testing, should be considered for all in settings with elevated COVID-19 transmission.

Four SARS-CoV-2 vaccines induce quantitatively different antibody responses against SARS-CoV-2 variants (https://www.medrxiv.org/content/10.1101/2021.09.27.21264163v1)
MJ van Gils et al, MEDRXIV, September 28, 2021

e performed a head-to-head comparison of the ability of sera from individuals vaccinated with either one of four vaccines (BNT162b2, mRNA-1273, AZD1222 or Ad26.COV2.S) to recognize and neutralize the four SARS-CoV-2 variants of concern (VOCs; Alpha, Beta, Gamma and Delta). Four weeks after completing the vaccination series, SARS-CoV-2 wild-type neutralizing antibody titers were highest in recipients of BNT162b2 and mRNA-1273 (median titers of 1891 and 3061, respectively), and substantially lower in those vaccinated with the adenovirus vector-based vaccines AZD1222 and Ad26.COV2.S (median titers of 241 and 119, respectively). VOCs neutralization was reduced in all vaccine groups, with the largest (5.8-fold) reduction in neutralization being observed against the Beta variant. Overall, the mRNA vaccines appear superior to adenovirus vector-based vaccines in inducing neutralizing antibodies against VOCs four weeks after the final vaccination.

Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce (https://www.nejm.org/doi/full/10.1056/NEJMc2112981?query=featured_home) J Keehner et al, NEJM, September 30, 2021

The dramatic change in vaccine effectiveness from June to July is likely to be due to both the emergence of the delta variant and waning immunity over time, compounded by the end of masking requirements in California and the resulting greater risk of exposure in the community.

The Evolving Faces of the SARS-CoV-2 Genome. (https://pubmed.ncbi.nlm.nih.gov/34578345)
Schmidt Maria et al. Viruses 2021 9 (9)

We applied molecular portrayal using self-organizing maps machine learning (SOM portrayal) to characterize the diversity of the virus genomes, their mutual relatedness and development since the beginning of the pandemic. The genetic landscape obtained visualizes the relevant mutations in a lineage-specific fashion and provides developmental paths in genetic state space from early lineages towards the variants of concern alpha, beta, gamma and delta

 Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort. (https://pubmed.ncbi.nlm.nih.gov/34580193)
Clift Ashley K et al. Thorax 2021 9

Conflicting evidence has emerged regarding the relevance of smoking on risk of COVID-19 and its severity. We undertook large-scale observational and Mendelian randomisation (MR) analyses using UK Biobank. Genetically predicted higher number of cigarettes smoked per day was associated with higher risks of all outcomes (infection OR 2.51, 95% CI 1.20 to 5.24; hospitalization OR 5.08, 95% CI 2.04 to 12.66; and death OR 10.02, 95% CI 2.53 to 39.72). Congruent results from two analytical approaches support a causal effect of smoking on risk of severe COVID-19.

 Impact of sickle cell trait on morbidity and mortality from SARS-CoV-2 infection. (https://pubmed.ncbi.nlm.nih.gov/34581772)

Merz Lauren E et al. Blood advances 2021 9 (18) 3690-3693

Patients admitted for SARS-CoV-2 infection who identified as black or African American were included in the study (n = 166). Blood remnants were tested for SCT, and clinical data were abstracted from the chart. There was no difference in mortality between those with SCT and those without. There was no difference in respiratory complications between groups, but those without SCT had a much higher burden of chronic lung disease (P = .004). Those with SCT had higher creatinine on admission (P = .004), but no difference in in-hospital renal complications (P = .532).

News, Reviews and Commentaries

 Multiple Transmission Chains within COVID-19 Cluster, Connecticut, USA, 2020. (https://pubmed.ncbi.nlm.nih.gov/34545794)
Bart Stephen M et al. Emerging infectious diseases 2021 9 (10) 2669-2672
In fall 2020, a coronavirus disease cluster comprising 16 cases occurred in Connecticut, USA. Epidemiologic and genomic evidence supported transmission among persons at a school and fitness center but not a workplace. The multiple transmission chains identified within this cluster highlight the necessity of a combined investigatory approach Protocol for safe, affordable, and reproducible isolation and quantitation of SARS-CoV-2 RNA from wastewater. (https://pubmed.ncbi.nlm.nih.gov/34555079)
Truiillo Monica et al. PloS one 2021 9 (9) e0257454

Trujillo Monica et al. PloS one 2021 9 (9) e0257454

The following protocol describes our workflow for processing wastewater with the goal of detecting the genetic signal of SARS-CoV-2. The steps include pasteurization, virus concentration, RNA extraction, and quantification by RT-qPCR. We include auxiliary steps that provide new users with tools and strategies that will help troubleshoot key steps in the process. This protocol is one of the safest, cheapest, and most reproducible approaches for the detection of SARS-CoV-2 RNA in wastewater.

The impact of real-time whole genome sequencing in controlling healthcare-associated SARS-CoV-2 outbreaks. (https://pubmed.ncbi.nlm.nih.gov/34555152) Francis Rodric V et al. The Journal of infectious diseases 2021 9

Nosocomial SARS-CoV-2 infections have severely affected bed capacity and patient flow. We utilised whole genome sequencing (WGS) to identify outbreaks and focus infection control resources and intervention during the UK's second pandemic wave in late 2020. Phylogenetic analysis of WGS and epidemiological data pinpointed an initial transmission event to an admission ward, with immediate prior community infection linkage documented. High incidence of asymptomatic staff infection with genetically identical viral sequences was also observed, which may have contributed to the propagation of the outbreak. WGS allowed timely nosocomial transmission intervention measures, including admissions ward point of care testing and introduction of portable HEPA14 filters.

 Using genomic epidemiology of SARS-CoV-2 to support contact tracing and public health surveillance in rural Humboldt County, California. (https://www.medrxiv.org/content/10.1101/2021.09.21.21258385v1)
G Stoddard et al, MEDRXIV, September 27, 2021

853 whole SARS-CoV-2 genomes were generated, representing ~58% of the 1,449 SARS-CoV-2positive cases detected in Humboldt County as of March 12, 2021. Phylogenetic analysis of these data was used to develop a comprehensive understanding of SARS-CoV-2 introductions to the county and to support contact tracing and epidemiologic investigations of all large outbreaks in the county. In the case of an outbreak on a commercial farm, viral genomic data were used to validate reported epidemiologic links and link additional cases within the community who did not report a farm exposure to the outbreak.

Modeling the transmission of the SARS-CoV-2 delta variant in a partially vaccinated population (https://www.medrxiv.org/content/10.1101/2021.09.23.21264032v1) U Avila et al, MEDRXIV, September 26, 2021

We developed a mathematical model that considers both subpopulations and immunity parameters including vaccination rates, vaccine effectiveness, and a gradual loss of protection. The model forecasted the spread of the SARS-CoV-2 delta variant in the US under varied transmission and vaccination rates. We further obtained the control reproduction number and conducted sensitivity

analyses to determine how each parameter may affect virus transmission. Our results show that a combination of strengthening vaccine-induced immunity and preventative behavioral measures will likely be required to deaccelerate the rise of infectious SARS-CoV-2 variants.

Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers (https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00283-4) T Nakanayma et al, Cell Reports Medicine, September 27,2021

I Nakanayma et al, Cell Reports Medicine, September 27,202

In this translational study, we discover key variabilities in the expression of ACE2 and TMPRSS2, essential SARS-CoV-2 entry factors, among the mucosal tissues of the human proximal airways. We show that SARS-CoV-2 infection is present in all examined head & neck tissues, with a notable tropism for the nasal cavity and tracheal mucosa. Finally, we uncover an association between smoking and higher SARS-CoV-2 viral infection in the human proximal airway, which may explain the increased susceptibility of smokers to developing severe COVID-19.

• A prenylated dsRNA sensor protects against severe COVID-19

(https://www.science.org/doi/10.1126/science.abj3624)

A Wickenhagen et al, Science, September 28, 2021

To better understand the antiviral defenses relevant to COVID-19, we used interferon-stimulated gene (ISG) expression screening to reveal that OAS1, through RNase L, potently inhibits SARS-CoV-2. We show that a common splice-acceptor SNP (Rs10774671) governs whether people express prenylated OAS1 isoforms that are membrane-associated and sense specific regions of SARS-CoV-2 RNAs, or only express cytosolic, nonprenylated OAS1 that does not efficiently detect SARS-CoV-2. Importantly, in hospitalized patients, expression of prenylated OAS1 was associated with protection from severe COVID-19, suggesting this antiviral defense is a major component of a protective antiviral response.

Large-scale analysis of SARS-CoV-2 spike-glycoprotein mutants demonstrates the need for continuous screening of virus isolates. (https://pubmed.ncbi.nlm.nih.gov/34570776) Schrörs Barbara et al. PloS one 2021 9 (9) e0249254

We analyzed 1,036,030 SARS-CoV-2 genome assemblies and 30,806 NGS datasets from GISAID and European Nucleotide Archive (ENA) focusing on non-synonymous mutations in the spike protein. Only around 2.5% of the samples contained the wild-type spike protein with no variation from the reference. Among the spike protein mutants, we confirmed a low mutation rate exhibiting less than 10 non-synonymous mutations in 99.6% of the analyzed sequences, but the mean and median number of spike protein mutations per sample increased over time. 5,472 distinct variants were found in total. The majority of the observed variants were recurrent, but only 21 and 14 recurrent variants were found in at least 1% of the mutant genome assemblies and NGS samples.

Effectiveness of BNT162b2 Vaccine in Adolescents during Outbreak of SARS-CoV-2 Delta Variant Infection, Israel, 2021. (https://pubmed.ncbi.nlm.nih.gov/34570694) Glatman-Freedman Aharona et al. Emerging infectious diseases 2021 9 (11) In Israel, the BNT162b2 vaccine against severe acute respiratory syndrome coronavirus 2 was approved for use in adolescents in June 2021, shortly before an outbreak of B.1.617.2 (Delta) variant-dominant infection. We evaluated short-term vaccine effectiveness and found the vaccine to be highly effective among this population in this setting.

Modeling of COVID-19 Transmission Dynamics on US Population: Inter-transfer Infection in Age Groups, Mutant Variants, and Vaccination Strategies (https://www.medrxiv.org/content/10.1101/2021.09.25.21264118v1) J Roy et al, MEDRXIV, September 28, 2021

We developed the SIRDV-Virulence epidemiological model based on a population balance equation to study the effect of mutants of the virus and the effect of vaccination strategies on mitigating the

transmission among the population in the United States. Based on the available data from the Centers for Disease Control and Prevention (CDC), we obtain the key parameters governing the dynamic evolution of the spread of the COVID-19 pandemic.

 No Significant Difference in Viral Load Between Vaccinated and Unvaccinated, Asymptomatic and Symptomatic Groups Infected with SARS-CoV-2 Delta Variant (https://www.medrxiv.org/content/10.1101/2021.09.28.21264262v1)
CB Acharya et al, MEDRXIV, September 29, 2021

We found no significant difference in cycle threshold values between vaccinated and unvaccinated, asymptomatic and symptomatic groups infected with SARS-CoV-2 Delta. Given the substantial proportion of asymptomatic vaccine breakthrough cases with high viral levels, interventions, including masking and testing, should be considered for all in settings with elevated COVID-19 transmission.

Four SARS-CoV-2 vaccines induce quantitatively different antibody responses against SARS-CoV-2 variants (https://www.medrxiv.org/content/10.1101/2021.09.27.21264163v1)
MJ van Gils et al, MEDRXIV, September 28, 2021

e performed a head-to-head comparison of the ability of sera from individuals vaccinated with either one of four vaccines (BNT162b2, mRNA-1273, AZD1222 or Ad26.COV2.S) to recognize and neutralize the four SARS-CoV-2 variants of concern (VOCs; Alpha, Beta, Gamma and Delta). Four weeks after completing the vaccination series, SARS-CoV-2 wild-type neutralizing antibody titers were highest in recipients of BNT162b2 and mRNA-1273 (median titers of 1891 and 3061, respectively), and substantially lower in those vaccinated with the adenovirus vector-based vaccines AZD1222 and Ad26.COV2.S (median titers of 241 and 119, respectively). VOCs neutralization was reduced in all vaccine groups, with the largest (5.8-fold) reduction in neutralization being observed against the Beta variant. Overall, the mRNA vaccines appear superior to adenovirus vector-based vaccines in inducing neutralizing antibodies against VOCs four weeks after the final vaccination.

Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce (https://www.nejm.org/doi/full/10.1056/NEJMc2112981?query=featured_home)

J Keehner et al, NEJM, September 30, 2021

The dramatic change in vaccine effectiveness from June to July is likely to be due to both the emergence of the delta variant and waning immunity over time, compounded by the end of masking requirements in California and the resulting greater risk of exposure in the community.

The Evolving Faces of the SARS-CoV-2 Genome. (https://pubmed.ncbi.nlm.nih.gov/34578345) Schmidt Maria et al. Viruses 2021 9 (9)

We applied molecular portrayal using self-organizing maps machine learning (SOM portrayal) to characterize the diversity of the virus genomes, their mutual relatedness and development since the beginning of the pandemic. The genetic landscape obtained visualizes the relevant mutations in a lineage-specific fashion and provides developmental paths in genetic state space from early lineages towards the variants of concern alpha, beta, gamma and delta

 Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort. (https://pubmed.ncbi.nlm.nih.gov/34580193)

Clift Ashley K et al. Thorax 2021 9

Conflicting evidence has emerged regarding the relevance of smoking on risk of COVID-19 and its severity. We undertook large-scale observational and Mendelian randomisation (MR) analyses using UK Biobank. Genetically predicted higher number of cigarettes smoked per day was associated with higher risks of all outcomes (infection OR 2.51, 95% CI 1.20 to 5.24; hospitalization OR 5.08, 95% CI 2.04 to 12.66; and death OR 10.02, 95% CI 2.53 to 39.72). Congruent results from two analytical approaches support a causal effect of smoking on risk of severe COVID-19.

 Impact of sickle cell trait on morbidity and mortality from SARS-CoV-2 infection. (https://pubmed.ncbi.nlm.nih.gov/34581772)
Merz Lauren E et al. Blood advances 2021 9 (18) 3690-3693

Patients admitted for SARS-CoV-2 infection who identified as black or African American were included in the study (n = 166). Blood remnants were tested for SCT, and clinical data were abstracted from the chart. There was no difference in mortality between those with SCT and those without. There was no difference in respiratory complications between groups, but those without SCT had a much higher burden of chronic lung disease (P = .004). Those with SCT had higher creatinine on admission (P = .004), but no difference in in-hospital renal complications (P = .532).

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

sources, and non-CDC Websites are provided solely for informational purposes and do not imply endorsement by CDC or DHHS.

Page last reviewed: Oct 1, 2020

Page last updated: Oct 01, 2021

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

(https://www.cdc.gov/od/science/index.htm)