

New Research

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COVID-19 related publications by Providence caregivers – see [Digital Commons](#)

Basic Science / Virology / Pre-clinical

1. **HLA-A*02:01 restricted T cell receptors against the highly conserved SARS-CoV-2 polymerase cross-react with human coronaviruses.** Su Yapeng, Ng Rachel H, Chour William, Xie Jingyi, Heath James R, et al [**Providence authors**] *Cell Rep.* 2021 Dec 10:110167. doi: 10.1016/j.celrep.2021.110167. <https://doi.org/10.1016/j.celrep.2021.110167>
Cross-reactivity and direct killing of target cells remain underexplored for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-specific CD8+ T cells. Isolation of T cell receptors (TCRs) and overexpression in allogeneic cells allows for extensive T cell reactivity profiling. We identify SARS-CoV-2 RNA-dependent RNA polymerase (RdRp/NSP12) as highly conserved, likely due to its critical role in the virus life cycle. We perform single-cell TCR $\alpha\beta$ sequencing in human leukocyte antigen (HLA)-A*02:01-restricted, RdRp-specific T cells from SARS-CoV-2-unexposed individuals. Human T cells expressing these TCR $\alpha\beta$ constructs kill target cell lines engineered to express full-length RdRp. Three TCR constructs recognize homologous epitopes from common cold coronaviruses, indicating CD8+ T cells can recognize evolutionarily diverse coronaviruses. Analysis of individual TCR clones may help define vaccine epitopes that can induce long-term immunity against SARS-CoV-2 and other coronaviruses.

Epidemiology & Public Health

2. **Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa.** Viana R, et al. *Nature.* January 6, 2022. <https://www.nature.com/articles/d41586-021-03832-5>
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic in southern Africa has been characterised by three distinct waves. The first was associated with a mix of SARS-CoV-2 lineages, whilst the second and third waves were driven by the Beta and Delta variants, respectively^{1–3}. In November 2021, genomic surveillance teams in South Africa and Botswana detected a new SARS-CoV-2 variant associated with a rapid resurgence of infections in Gauteng Province, South Africa. Within three days of the first genome being uploaded, it was designated a variant of concern (Omicron) by the World Health Organization and, within three weeks, had been identified in 87 countries. The Omicron variant is exceptional for carrying over 30 mutations in the spike glycoprotein, predicted to influence antibody neutralization and spike

function⁴. Here, we describe the genomic profile and early transmission dynamics of Omicron, highlighting the rapid spread in regions with high levels of population immunity.

3. **Characteristics and Factors Associated with Coronavirus Disease 2019 Infection, Hospitalization, and Mortality Across Race and Ethnicity.** Dai Chengzhen L, Kornilov Sergey A, Roper Ryan T, Cohen-Cline Hannah, Jade Kathleen, Smith Brett, Heath James R, Diaz George, Goldman Jason D, Magis Andrew T, Hadlock Jennifer J. **[Providence authors]** *Clin Infect Dis.* 2021 Dec 16;73(12):2193-2204. doi: 10.1093/cid/ciab154. <https://doi.org/10.1093/cid/ciab154>
A total of 570 298 patients with known race/ethnicity were tested for SARS-CoV-2, of whom 27.8% were non-White minorities: 54 645 individuals tested positive, with minorities representing 50.1%. Hispanics represented 34.3% of infections but only 13.4% of tests. Although generally younger than White patients, Hispanics had higher rates of diabetes but fewer other comorbidities. A total of 8536 patients were hospitalized and 1246 died, of whom 56.1% and 54.4% were non-White, respectively. Major healthcare disparities were evident, especially among Hispanics who tested positive at a higher rate, required excess hospitalization and mechanical ventilation, and had higher odds of in-hospital mortality despite younger age.
4. **Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in tshwane, South Africa.** Abdullah F et al. *Int J Infect Dis.* 2021 Dec 28:S1201-9712(21)01256-X. doi: 10.1016/j.ijid.2021.12.357. [https://www.ijidonline.com/article/S1201-9712\(21\)01256-X/fulltext](https://www.ijidonline.com/article/S1201-9712(21)01256-X/fulltext)
Deaths and ICU admissions were 4.5% vs 21.3% ($p < 0.00001$), and 1% vs 4.3% ($p < 0.00001$); length of stay was 4.0 days vs 8.8 days; and mean age was 39 years vs 49 years for the Omicron and previous waves respectively. Admissions peaked and declined rapidly with peak bed occupancy at 51% of highest previous peak. Sixty two (63%) patients in COVID-19 wards had incidental COVID-19 following a positive SARS-CoV-2 PCR test. Only one third (36) had COVID-19 pneumonia, of which 72% had mild to moderate disease. The remaining 38% required high care or ICU admission. Fewer than half (45%) of patients in COVID-19 wards compared to 99.5% in the first wave required oxygen supplementation. City and provincial rates show decoupling of cases, hospitalisations and deaths compared to previous waves, corroborating the clinical findings of milder omicron disease in the hospital. There was decreased severity of disease in the Omicron driven fourth wave in the City of Tshwane, its first global epicentre.
5. **Notes from the Field: COVID-19-Associated Mucormycosis - Arkansas, July-September 2021.** Dulski TM et al. *MMWR Morb Mortal Wkly Rep.* 2021 Dec 17;70(50):1750-1751. doi: 10.15585/mmwr.mm7050a3. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7050a3.htm>
Ten COVID-19-associated mucormycosis cases that occurred during July 12–September 28, 2021, were reported to ADH by six hospitals. Nine patients lived in Arkansas, with patients representing each of the state’s five public health unit regions; one patient lived in a bordering state. Among all 10 patients, the median age was 57 years (range = 17–78 years), all patients were non-Hispanic White persons, seven were male, one had a history of solid organ transplantation, and one had a history of recent traumatic injury at the body site where mucormycosis later developed. Eight patients had diabetes; among these, the median hemoglobin A1c was 8.6% (range = 6.0%–14.3% [normal <5.7%]). During hospitalization, three

patients with diabetes experienced diabetic ketoacidosis. Mucormycosis clinical signs and symptoms included those that were rhino-orbital (four patients, including three with cerebral involvement), pulmonary (three), disseminated (two), and gastrointestinal (one).

Prognosis

6. **Coronavirus Disease 2019 in Solid Organ Transplant: A Multicenter Cohort Study.** Goldman Jason D, et al [Providence author]; UW COVID-19 SOT Study Team. *Clin Infect Dis.* 2021 Dec 6;73(11):e4090-e4099. doi: 10.1093/cid/ciaa1097. <https://doi.org/10.1093/cid/ciaa1097> Mortality among SOT recipients hospitalized for COVID-19 was 20.5%. Age and underlying comorbidities rather than immunosuppression intensity-related measures were major drivers of mortality.
7. **Relationship between Myocardial Injury during Index Hospitalization for SARS-CoV-2 Infection and Longer-Term Outcomes.** Weber B et al. *J Am Heart Assoc.* 2021 Dec 31:e022010. doi: 10.1161/JAHA.121.022010. <https://www.ahajournals.org/doi/10.1161/JAHA.121.022010> Conclusions Myocardial injury during index hospitalization for COVID-19 was associated with increased mortality and may predict who are more likely to have postacute sequelae of COVID-19. Among patients who survived their index hospitalization, the incremental mortality through 12 months was low, even among troponin-positive patients.
8. **Risk for Newly Diagnosed Diabetes >30 Days after SARS-CoV-2 Infection among Persons Aged <18 years — United States, March 1, 2020–June 28, 2021.** Barrett CE, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 7 January 2022. DOI: <http://dx.doi.org/10.15585/mmwr.mm7102e2> SARS-CoV-2 infection is associated with worsening of diabetes symptoms, and persons with diabetes are at increased risk for severe COVID-19. SARS-CoV-2 infection might also induce newly diagnosed diabetes. Persons aged <18 years with COVID-19 were more likely to receive a new diabetes diagnosis >30 days after infection than were those without COVID-19 and those with prepandemic acute respiratory infections. Non-SARS-CoV-2 respiratory infection was not associated with an increased risk for diabetes. The increased diabetes risk among persons aged <18 years following COVID-19 highlights the importance of COVID-19 prevention strategies in this age group, including vaccination for all eligible persons and chronic disease prevention and treatment.

Therapeutics

9. **Compassionate Use of REGEN-COV[®] in Patients with COVID-19 and Immunodeficiency-Associated Antibody Disorders.** Stein D et al. *Clin Infect Dis.* 2021 Dec 31:ciab1059. doi: 10.1093/cid/ciab1059. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab1059/6491226> In this retrospective analysis of immunodeficient patients granted REGEN-COV under the compassionate use program, REGEN-COV treatment was associated with rapid viral clearance and clinical improvement in patients with long-standing COVID-19. Adverse events were

consistent with COVID-19 and its associated complications, and due to patients' concurrent medical conditions.

10. Predictors for extubation failure in COVID-19 patients using a machine learning approach.

Dutch ICU Data Sharing Against Covid-19 Collaborators. *Crit Care*. 2021 Dec 27;25(1):448. doi: 10.1186/s13054-021-03864-3. <https://doi.org/10.1186/s13054-021-03864-3>

Determining the optimal timing for extubation can be challenging in the intensive care. Determining the optimal timing for extubation can be challenging in the intensive care.

Vaccines / Immunology

11. Risk Factors for Severe COVID-19 Outcomes Among Persons Aged ≥ 18 Years Who Completed a Primary COVID-19 Vaccination Series — 465 Health Care Facilities, United States, December 2020–October 2021.

Yek C, et al. *MMWR Morb Mortal Wkly Rep* 2022;71:19–25. DOI: <http://dx.doi.org/10.15585/mmwr.mm7101a4>

Among 1,228,664 persons who completed primary vaccination during December 2020–October 2021, severe COVID-19–associated outcomes (0.015%) or death (0.0033%) were rare. Risk factors for severe outcomes included age ≥ 65 years, immunosuppressed, and six other underlying conditions. All persons with severe outcomes had at least one risk factor; 78% of persons who died had at least four. Vaccinated persons who are older, immunosuppressed, or have other underlying conditions should receive targeted interventions including chronic disease management, precautions to reduce exposure, additional primary and booster vaccine doses, and effective pharmaceutical therapy to mitigate risk for severe outcomes. Increasing vaccination coverage is a critical public health priority.

12. Severe breakthrough COVID-19 with a heavily mutated variant in a multiple myeloma patient 10 weeks after vaccination.

Feinstein Aaron J, et al [Providence author], *Clin Infect Pract*. 2022 Jan;13:100130. doi: 10.1016/j.clinpr.2021.100130. Epub 2021 Dec 9.

<https://doi.org/10.1016/j.clinpr.2021.100130>

A multiple myeloma patient developed protective anti-spike antibodies after vaccination (608 IU/mL), but nonetheless developed severe breakthrough COVID-19 just 10 weeks following his second vaccination with mRNA-1273. Sequencing of the viral isolate revealed an extensively mutated variant with 10 spike protein mutations, including E484Q and N440K. Serology testing showed a dramatic decline in anti-spike antibodies immediately prior to virus exposure.

Multiple myeloma patients who do develop detectable antibody responses to vaccination may be at increased risk for breakthrough infections due to rapid decline in antibody levels. Viral variants with immune escape mutations such as N440K, also seen independently in the SARS-CoV-2 Omicron variant (B.1.1.529) and in viral passaging experiments, likely require a higher level of anti-spike antibodies to prevent severe COVID-19.

13. Safety of vaccination against SARS-CoV-2 in people with rheumatic and musculoskeletal diseases: results from the EULAR Coronavirus Vaccine (COVAX) physician-reported registry.

Machado PM et al. *Ann Rheum Dis*. 2021 Dec 31;annrheumdis-2021-221490. doi:

10.1136/annrheumdis-2021-221490.

<https://ard.bmj.com/content/early/2021/12/30/annrheumdis-2021-221490>

The safety profiles of SARS-CoV-2 vaccines in patients with I-RMD was reassuring and comparable with patients with NI-RMDs. The majority of patients tolerated their vaccination well with rare reports of I-RMD flare and very rare reports of serious AEs. These findings should provide reassurance to rheumatologists and vaccine recipients and promote confidence in SARS-CoV-2 vaccine safety in I-RMD patients.

14. Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021. Zambrano LD, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 7 January 2022.

DOI: <http://dx.doi.org/10.15585/mmwr.mm7102e1>

The Pfizer-BioNTech vaccine, currently authorized for persons aged ≥ 5 years, provides a high level of protection against severe COVID-19 in persons aged 12–18 years. Vaccine effectiveness against multisystem inflammatory syndrome in children (MIS-C), which can occur 2–6 weeks after SARS-CoV-2 infection, has remained uncharacterized. Estimated effectiveness of 2 doses of Pfizer-BioNTech vaccine against MIS-C was 91% (95% CI = 78%–97%). Among critically ill MIS-C case-patients requiring life support, all were unvaccinated. Receipt of 2 doses of Pfizer-BioNTech vaccine is highly effective in preventing MIS-C in persons aged 12–18 years. These findings further reinforce the COVID-19 vaccination recommendation for eligible children.

15. Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth — Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021. Lipkind HS, et al. *MMWR Morb Mortal Wkly Rep* 2022;71:26–30. DOI:

<http://dx.doi.org/10.15585/mmwr.mm7101e1>

In a retrospective cohort of >40,000 pregnant women, COVID-19 vaccination during pregnancy was not associated with preterm birth or small-for-gestational-age at birth overall, stratified by trimester of vaccination, or number of vaccine doses received during pregnancy, compared with unvaccinated pregnant women. These data support the safety of COVID-19 vaccination during pregnancy. CDC recommends COVID-19 vaccination for women who are pregnant, recently pregnant, who are trying to become pregnant now, or who might become pregnant in the future.

FDA / CDC / NIH / WHO Updates

CDC - [Expands Booster Shot Eligibility and Strengthens Recommendations for 12-17 Year Olds](#)

FDA - [amended the EUA](#) for the Pfizer-BioNTech COVID-19 Vaccine to: expand the use of a single booster dose to include use in individuals 12 through 15 years of age, shorten the time between the completion of primary vaccination of the Pfizer-BioNTech COVID-19 Vaccine and a booster dose to at least five months, allow for a third primary series dose for certain immunocompromised children 5 through 11 years of age.

NIH – [The COVID-19 Treatment Guidelines Panel’s Statement on Tixagevimab Plus Cilgavimab \(Evusheld\) for Pre-Exposure Prophylaxis for SARS-CoV-2 Infection](#), Jan 5, 2022

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