BIOENGINEERING

A multiplexed, next generation sequencing platform for high-throughput detection of SARS-CoV-2

Aynaud et al. describe the development of the platform “Systematic Parallel Analysis of RNA coupled to Sequencing for Covid-19 screening” (C19-SPAR-Seq), an automated and scalable detection method for SARS-CoV-2 utilizing next generation sequencing (NGS). NGS is a high-throughput technology (>10,000 samples per run) that recognizes known sequences within the genome using a system of multiplexed sequence-specific primers and barcoding. The group uses primers to identify two regions of the SARS-Cov-2 Spike (S) gene, including the receptor-binding domain (RBD) and the polybasic cleavage site (PBS), which is specific to a SARS-CoV-2 infection. To enable this technology for SARS-CoV-2 diagnosis, control-based Precision-Recall and Receiver Operator Characteristics (coPR) is employed in conjunction with NGS to establish viral thresholds and QC metrics for each run. When coupled together, the overall SPAR-Seq detection platform has a specificity of 100% and sensitivity of 91% for low viral loads and a sensitivity of >96% for high viral loads during disease onset. The C19-SPAR-Seq platform can be utilized to track emergent variants and adapted to other pathogens and host responses. It can also be coupled to saliva-based at-home tests to improve widespread SARS-CoV-2 detection.

Quantitative evaluation of SARS-CoV-2 inactivation using a deep ultraviolet light-emitting diode

Minamikawa et. al. performed a quantitative analysis of 265, 280, and 300 nm wavelength deep ultraviolet light-emitted diode (DUV-LED) on the inactivation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To quantify dose, or effective power density, of DUV irradiation, the group fabricated a DUV-LED irradiation apparatus which applied uniform irradiation in a 96-well plate containing virus inoculum. PBS or EMEM containing 2% FBS were selected as the viral culture media to minimize absorptivity. Viral inactivation was evaluated via plaque assay in Vero E6 cells. To achieve 99.9% inactivation of the virus, it was found that a power density of 1.8 mJ/cm² for 265 nm, 3.0 mJ/cm² for 280 nm, and 23 mJ/cm² for 300 nm is necessary—with 265 nm being the most effective. Radical species were produced at all three wavelengths; despite the possibility that these radical species would affect the inactivation of SARS-CoV-2, 300 nm showed the highest level of radical species, indicating radical species are unlikely to affect SARS-CoV-2 inactivation. The group discusses how this work could be improved by future studies investigating the precise mechanism by which viral inactivation occurs via DUV-LED irradiation.

* Please note all studies published in medRxiv and bioRxiv are preprints and have not yet undergone a rigorous peer review process.

Rapid Development of SARS-CoV-2 Spike Protein Receptor-Binding Domain Self-Assembled Nanoparticle Vaccine Candidates

Kang et. al describe the fabrication of three SARS-CoV-2 S RBD-conjugated nanoparticle vaccine candidates which target the RBD of a SARS-CoV-2 S glycoprotein. Conjugation to nanoparticles enables multivalent antigen presentation and the ability of the vaccine candidate to evoke an immune response, as well as rapid manufacturability. The three candidates developed are enabled by SpyTag-SpyCatcher bioconjugation technology and include RBD-Ferritin (24-mer), RBD-mi3 (60-mer) and RBD-I53-50 (120-mer). To first
confirm the production quality and structural stability of each candidate, SEC, SDS-PAGE analysis, and electron microscopy were performed. Nano differential scanning fluorimetry (nanoDSF) was performed on the RBD monomer and the RBD-conjugated NPs to evaluate thermostability. The antigenicity of RBD-conjugated NPs was characterized in vitro through binding affinity and kinetic studies between the RBD-conjugated NPs and RBD-specific antibodies. After performing an ELISA, the resulting profile showed that the RBD-conjugated NPs bound to the antibodies in a dose-dependent manner. In addition, in vivo, adjuvanted RBD-conjugated NPs elicited 71.8 to 168.4-fold higher antibody serum titers than those of the adjuvanted RBD monomer. Neutralizing assays of SARS-CoV-2 virus in immunized mice sera showed that the RBD-NPs outperformed the RBD monomer. The group highlights the universality of their nanoparticle-conjugation platform favored for future vaccine development, competitive efficiency, and rapid manufacturing.

**CLINICAL PRESENTATION AND MANAGEMENT**

**Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK**

Bloom et al analyzed data from the International Severe Acute Respiratory and emerging Infection Consortium WHO Clinical Characterization Protocol UK study to examine underlying respiratory health issues of COVID-19 patients, as well as the level of care they received, in-hospital mortality, and the effects of corticosteroid use. Analysis of data from 75,463 patients found that patients age 16-49 with asthma had a higher odds of receiving critical care than those without asthma (OR 1.20, 95% CI 1.05–1.37). COPD patients 50 or older had a lower odds of receiving critical care compared to those without a respiratory condition (OR 0.66, 95% CI 0.60–0.2 for those without asthma; OR 0.74, 95% CI 0.62–0.87 for those with asthma). The researchers examined outcomes across different age groups and mortality risks and found that no matter how severe the symptoms of COVID-19 or the comorbidity, asthma patients were more likely, and COPD patients were less likely, to receive critical care. Patients who were 50 or older who also suffered from severe asthma, had an increased mortality compared to those who did not (HR 1.24 95% CI 1.04–1.49). Inhaled corticosteroids among patients 50 years or older with asthma improves survival rates. In patients 16 and older, severe asthma was associated with higher mortality risk. The authors suggest that patients with respiratory comorbidities are high-risk patients and should engage in behaviors to reduce exposure to COVID-19.

**NON-CLINICAL TRENDS**

**Impact of COVID-19 on vegetable supply chain and food security: Empirical evidence from Bangladesh**

This study from Bangladesh aimed to discover the impact of the COVID-19 pandemic on vegetable supply chain, farmers’ gross margin and plans for the future. From June 8th to July 14, 2020, mobile devices were used to contact and interview 100 vegetable farmers about current prices, marketing, future plans for production, and food security. Results reveal that the pandemic caused an abrupt stop in the supply chain of food. Findings show that 53% of the farmer’s income came from produce sales which decreased during the pandemic and left farmers concerned about food security. Many families reduced their meals per day and consumed fewer healthy foods to compensate for their lower income. Authors support the need for additional financial support for smallholder farmers to keep them in the farming business and support them throughout the pandemic.
Global effect of the COVID-19 pandemic on paediatric cancer care: a cross-sectional study

Graetz et al. conducted a cross-sectional study of 311 pediatric oncology providers from 213 institutions worldwide to assess the effects of the pandemic on healthcare delivery for children with cancer. The survey was conducted June 22 to August 21, 2020. The authors found that 7% of centers had closed their pediatric hematology-oncology services, 43% saw a decrease in reported pediatric cancer cases, and 34% of centers saw more treatments abandoned during the pandemic. There was also a reduction in surgical care, modifications to chemotherapy, blood shortages in clinics, and increased interruptions to radiotherapy. It is important to note that the sample primarily included centers in low- and middle-income countries, where treatment abandonment, inconsistent radiotherapy, and lack of chemotherapeutics were statistically significant. The researchers conclude the pandemic has negatively affected the delivery of care to children with cancer and suggest there needs to be a global response to help increase the standard of care for pediatric oncology.

NON-PHARMACUETICAL/PUBLIC HEALTH INTERVENTIONS

Impact of contact tracing on COVID-19 mortality: An impact evaluation using surveillance data from Colombia

Vecino-Ortiz et al. assessed the impact of contact tracing, as a public health surveillance toolkit, on COVID-19 mortality in Colombia. In the primary sample, publicly available data were obtained for 54,931 cases in the Colombian National Institute of Health “Open Data” portal. To assess the proportion of cases identified through contact tracing on daily COVID-19 mortality, a sequential log-log fixed-effects model was used. Results show a 10% increase in cases identified through contact training was related to a reduction of morality between 0.8% and 3.4%. Contact tracing can be an impactful surveillance tool for containing COVID-19 while also limiting the economic impact of the pandemic in LMICs. Ideally, it will be used as part of an integrated approach utilizing testing, isolation, and economic and social support for identified contacts.

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PEDIATRIC PRESENTATION

Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome

Using the Overcoming COVID-19 network, this study identified and included 1659 children and adolescents (age <21) from 61 hospitals across 31 US states with acute illness hospitalization related to SARS-CoV-2, with the aim of investigating the extent of neurologic involvement in this population. Results showed documented neurologic involvement in 22% of patients in 52 sites across 29 states; these patients were more likely to have underlying neurologic conditions compared to others (p<0.001). Proportion of patients meeting multisystem inflammatory syndrome in children (MIS-C) criteria and previously healthy patients were similar in frequency in both groups. Four percent of patients who experienced neurological involvement died, while 5% was discharged with a new neurological deficit. This research will support future efforts to better understand the
pathogenesis of neurologic diseases related to COVID-19 and MIS-C and its implications on children and adolescents.

**PHARMACEUTICAL INTERVENTIONS**

**Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19**

This double-blind randomized clinical trial conducted in Colombia between July 15 – December 21, 2020, aimed to determine the efficacy of ivermectin when treating for mild COVID-19. Participants with mild disease, symptoms lasting 7 days or less, and who did not receive mechanical ventilation or high-flow nasal oxygen were included in the study. Of the 398 patients included in the analysis, 200 received ivermectin and 198 received placebo. The median age was 37 years and the majority of participants were women (58%). Across groups, the time for resolution of symptoms was not significantly different (placebo group 79% and ivermectin group 82%). Results do not support the use of ivermectin for this study population as no significant differences were found.

**SCREENING AND TESTING**

**SARS-CoV-2 on Ocular Surfaces in a Cohort of Patients with COVID-19 From the Lombardy Region, Italy**

This cross-sectional study examined the presence of SARS-CoV-2 on ocular surfaces of patients hospitalized with COVID-19 in intensive care units at Sette-Laghi Hospital in Lombardy, Italy, between April 9 and May 5, 2020. A conjunctival swab was performed on 176 eyes of 91 COVID-19 patients, as well as 17 patients in a healthy control group. Specimens were examined by rRT-PCR to detect the presence of SARS-CoV-2. The mean age of participants was 58.7 years and 51% of participants were female. The study found that SARS-CoV-2 was present on the ocular surface in 52 of 91 patients with COVID-19 (57.1%) compared to none of the healthy patients. The virus was present in both eyes in 31 of 52 patients. Several patients (22 of 31 [71%]) had a slight difference in viral load values between the two eyes. The authors found 10 individuals with positive conjunctival swabs who had negative nasopharyngeal swabs, suggesting the conjunctival swab may be considered as a supplementary and less invasive sampling method for diagnostic testing. The authors caution while this study detected the presence of SARS-CoV-2 on ocular surfaces, this study does not suggest anything about the infectivity of ocular material.

**TRANSMISSION PATTERNS**

**Characteristics associated with household transmission of SARS-CoV-2 in Ontario, Canada: A cohort study**

This retrospective analyzed 7,993 confirmed cases of COVID-19 within private households in Ontario, Canada between January and July 2020 to understand secondary transmission, defined as cases occurring 1-14 days after the index case occurred within the household. The study found that longer COVID-19 testing delays, male gender, neighborhoods with larger average family size and a higher proportion of households with multiple persons per room, were all associated with greater odds of household secondary transmission. There was also increased odds for secondary transmission in neighborhoods with a higher proportion of multi-family households, which was a strong predictor of transmission to older adults. Adults 20-59 years of age were both the most frequent transmitters and acquirers of COVID-19 within households. Where the index
case was a healthcare worker, the odds of any household transmission decreased. The median serial interval from index case to secondary case was four days. The study reinforced the importance testing for COVID-19 as soon as symptoms appear. The authors call for further study of transmission involving children and youth as lockdown restrictions are eased.

ADDITIONAL RESOURCES
UCSF Library COVID-19 Research and Information Resources
UCSF Institute for Global Health Sciences COVID-19 Resources
UC Davis One Health Institute COVID-19 FAQs
Harvard Viswanath Lab Myths vs Facts
Accesocovid.com

Note on this Document: This document was assembled by undergraduate attending the University of California, San Francisco with the intent of facilitating the rapid dissemination of information to the global community. Graham Hinchcliffe, Maya Ganeshan, Micaela Reyna, Lina Salam, Emily Ng, Jiho Kim, Kaylie Bair, and Brooke Jackson contributed to these summaries. This work is volunteer based.

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