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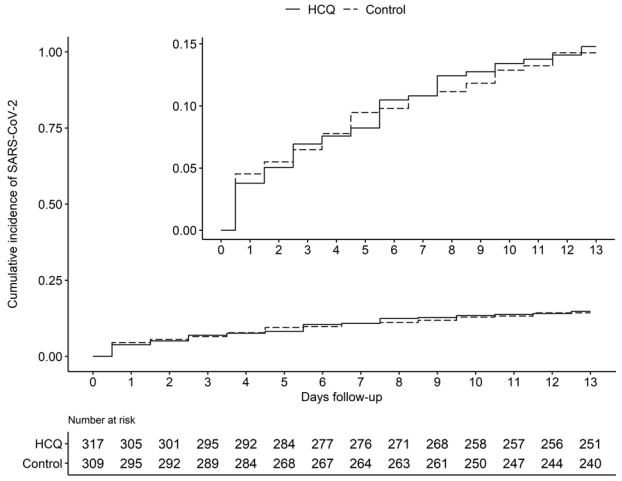
Background. Prevention interventions for coronavirus disease (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), are currently limited to non-pharmaceutical strategies. Observational and laboratory data suggested that hydroxychloroquine (HCQ) had biologic activity against SARS-CoV-2. A blinded trial of HCQ in persons with confirmed exposure and virologic and clinical endpoints is needed.

Methods. We conducted a national, householdrandomized, double-blind, controlled trial of HCQ post-exposure prophylaxis, with entirely remote study procedures. We enrolled close contacts exposed to persons with SARS-CoV-2 infection in the past 96 hours. Participants were randomized to either HCQ (400 mg daily for three days followed by 200 mg daily for eleven days) or ascorbic acid (500 mg followed by 250 mg daily), as a placebo-equivalent control. Participants self-collected mid-turbinate swabs daily (days 1–14) for SARS-CoV-2 PCR testing. The primary outcome was PCR-confirmed, incident SARS-CoV-2 infection among persons SARS-CoV-2 negative at enrollment. Symptoms were assessed using criteria from the US CDC.

Results. From March-August 2020, 623 households were randomized; 311 households (381 participants) to the HCQ group and 312 households (400 participants) to the control group. Ninety- one percent of participants were retained up to day 14 and 9,595 of 10,588 (91%) of swabs were tested. Among participants who were SARS-CoV-2 negative at baseline (n=626/781, 80%), the cumulative incidence of SARS-CoV-2 was 14.5% (95% CI: 11.6–17.4) and the cumulative incidence of COVID-19 symptoms was 11.6% (95% CI: 8.9–14.2) at day 14. By day 14, there was no difference between the HCQ group and control group in SARS-CoV-2 acquisition (46 vs. 43 events, aHR= 0.99, 95% CI 0.64–1.52, p=0.95) or symptomatic disease (40 vs. 32 events, aHR= 1.23, 95% CI: 0.76–1.99, p=0.40). The adverse event frequency was similar between groups (59 [15.5%] participants in the HCQ and 45 [11.3%] in the control group, p=0.092).

Cumulative incidence of RT-PCR-confirmed SARS-CoV-2 infection among close contacts of diagnosed cases, by study group



Conclusion. This randomized, double-blind, controlled trial among persons with recent exposure and high incidence of SAR-CoV2 provides strong evidence that HCQ post-exposure prophylaxis did not prevent SARS-CoV-2 infection or modify clinical disease.

Disclosures. **Anna Bershteyn, PhD**, **Bill and Melinda Gates Foundation** (Grant/Research Support)**Gates Ventures** (Consultant)**National Institutes of Health** (Grant/Research Support) **Kristopher M. Paolino, MD, MTM&H**, Nothing to disclose **Raphael J. Landovitz, MD, MSc**, **Gilead** (Advisor or Review Panel member)**Merck** (Advisor or Review Panel member)**Roche** (Other Financial or Material Support, Speaker Honoraria) **Anna Wald, MD, MPH**, Aicuris (Individual(s) Involved: Self): Consultant; Gilead (Individual(s) Involved: Self): Consultant; GlaxoSmithKline (Individual(s) Involved: Self): Scientific Research Study Investigator; Merck (Individual(s) Involved: Self): DSMB participation; provision of vaccine for a study, Other Financial or Material Support; Sanofi (Individual(s) Involved: Self): Scientific Research Study Investigator; X-Vax (Individual(s) Involved: Self): Consultant **Helen Y. Chu, MD MPH**, **Cepheid** (Grant/Research Support)**Ellume** (Grant/Research Support)**Glaxo Smith Kline** (Consultant)**Merck** (Consultant)**Sanofi-Pasteur** (Grant/Research Support)

LB-18. Broad and Prevalent SARS-CoV-2 CD8+ T Cell Response in Recovered COVID-19 Individuals Demonstrates Kinetics of Early Differentiation

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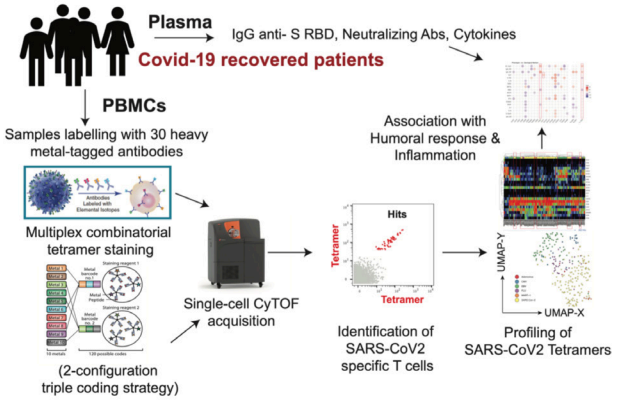
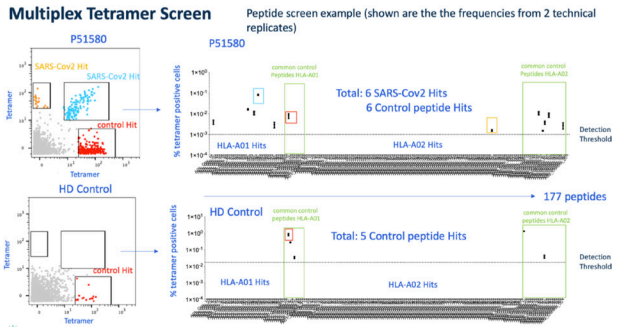
Background. Understanding the diversity, breadth, magnitude, and functional profile of the T cell response against SARS-CoV-2 in recovered COVID-19 individuals is critical to evaluate the contribution of T cells to produce a potentially protective immune response.

Methods. We used a multiplexed peptide-MHC tetramer approach to screen a total of 408 SARS-CoV-2 candidate peptide epitopes for CD8+ T cell recognition in a cohort of 30 individuals recovered from COVID-19. The peptides spanned the whole viral genome and were restricted to six prevalent HLA alleles; T cells were simultaneously characterized by a 28-marker phenotypic panel. The evolution of the SARS-CoV-2 T cell responses was then statistically modeled against time from diagnosis, and in relation to humoral and inflammatory response.

Workflow for Study. A multiplexed peptide-MHC tetramer approach was used to screen SARS-CoV-2 candidate peptide epitopes in a cohort of 30 COVID-19 recovered patients across 6 prevalent HLA alleles, and T cells profiled with a 28-marker phenotypic panel.

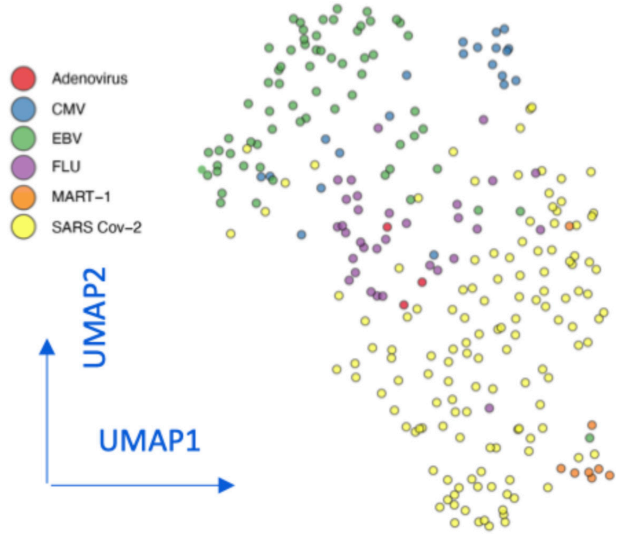


Multiplex tetramer screen. One representative COVID-19 recovered patient and one healthy donor were screened for HLA- relevant SARS-CoV-2 epitopes, as well as epitopes for CMV, EBV, Influenza, Adenovirus and MART-1. Shown are the frequencies of tetramer-positive CD8 T cells from 2 technical replicates per subject.

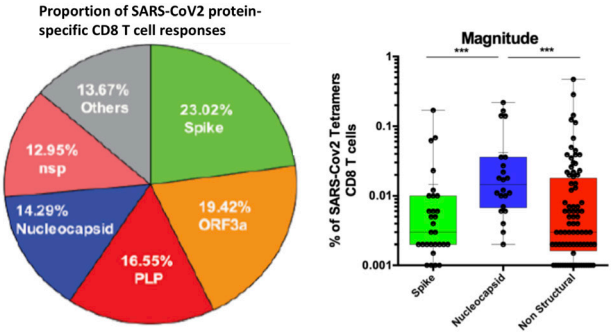


Results. Almost all individuals screened showed a T cell response against SARS-CoV-2 (29/30): 132 SARS-CoV-2-specific CD8+ T cells hits were detected, corresponding to 52 unique reactive epitopes. Twelve of the 52 unique SARS-CoV-2-specific epitopes were recognized by more than 40% of the individuals screened, indicating high prevalence in the subjects. Importantly, these CD8+ T cell responses were directed against both structural and non-structural viral proteins, with the highest magnitude against nucleocapsid derived peptides, but without any antigen-driven bias in the phenotype of specific T cells. Overall, SARS-CoV-2 T cells showed specific states of differentiation (stem-cell memory and transitional memory), which differed from those of MART-1, influenza, CMV and EBV-specific T cells.

UMAP visualization revealed a phenotypic profile of SARS-CoV-2-specific CD8 T cells in COVID-19 convalescent donors that is distinct from other viral specificities, such as influenza, CMV, EBV and Adenovirus.



SARS-CoV-2 epitope screening revealed CD8+ T cell responses directed against both structural and non-structural viral proteins, with the highest magnitude response against nucleocapsid derived peptides



Conclusion. The kinetics modeling demonstrates a dynamic, evolving immune response characterized by a time-dependent decrease in overall inflammation, increase in neutralizing antibody titer, and progressive differentiation of a broad SARS-CoV-2 CD8 T cell response. It could be desirable to aim at recapitulating the hallmarks of this robust CD8 T cell response in the design of protective COVID-19 vaccines.

Disclosures. **Hassen Kared, PhD**, **ImmunoScape** (Shareholder) **Alessandra Nardin, DvM**, **ImmunoScape** (Shareholder) **Hermi Sumatoh, BSc, Dip MTech**, **ImmunoScape** (Shareholder) **Faris Kairi, BSc**, **ImmunoScape** (Shareholder) **Daniel Carbajo, PhD**, **ImmunoScape** (Shareholder) **Brian Abel, PhD, MBA**, **ImmunoScape** (Shareholder) **Evan Newell, PhD**, **ImmunoScape** (Shareholder)

LB-19. Association between contract staffing and reported outbreaks of SARS-CoV-2 in a cluster-randomized trial of 965 U.S. nursing homes.

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Background. Nursing home residents account for 45% SARS-CoV-2 related deaths in the U.S. but only 0.6% of the population. Our research group conducted a large pragmatic cluster randomized influenza vaccine trial in 965 nursing homes (NCT03965195). Due to the pandemic and its impact after the influenza season, we prospectively collected reports of SARS-CoV-2 outbreaks and performed a prospective study on the association between contract staffing and reported outbreaks of SARS-CoV-2. We hypothesized those using more contract nursing care would have higher risk of an outbreak.

Methods. From February through April, we collected monthly facility-level, self-reported data on SARS-CoV-2 outbreaks. Facility characteristics were taken from public data from Centers for Medicaid and Medicare services. Predictors of SARS-CoV-2 outbreaks were identified using a LASSO variable selection procedure, with a generalized linear, Poisson family model. Facility characteristics evaluated include demographics (e.g. number of residents), influenza vaccination rates, quality measures (e.g. % with UTI), and functional status (e.g. % with tube feedings). Facilities with contract staffing hours in the upper 25% quantile of direct care (RN, LPN, CNA) were considered 'heavy use'.

Results. Of 965 randomized NHs, 663/965 (69%) reported data on SARS-CoV-2 outbreaks. On average, 13% of facilities had at least one outbreak, with 5/842 (0.5%) outbreaks in February, 91/835 (10.8%) in March and 217/686 (30%) in April. SARS-CoV-2 (+) facilities were larger (average total beds, 151 vs. 117), but were mostly similar by functional and cognitive status. Occupancy rate, total residents, Influenza vaccination rate, % with UTI, receiving respiratory treatments, tube feedings, and Medicaid payers were adjusted for in the analysis. The 'heavy use' of contract staffing included those with >223 hours per quarter. A multivariable regression found the relative risk SARS-CoV-2 outbreak was 1.56 (95% Confidence Interval: 1.22, 1.99) with heavy use of contract staffing.

Conclusion. The participating nursing homes in our vaccine trial with SARS-CoV-2 outbreaks were larger. Our study highlights that heavy use of contract staffing was associated with 56% increased risk of an outbreak.

Disclosures. **Kevin McConeghy, Pharm.D.**, **Pfizer** (Grant/Research Support)**Sanofi-Pasteur** (Grant/Research Support)**Seqirus Pharmaceuticals** (Grant/Research Support) **H. Edward Davidson, PharmD, MPH**, **Sanofi pasteur** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support)**Seqirus** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support) **Lisa Han, MPH**, **Sanofi Pasteur** (Grant/Research Support)**Seqirus** (Grant/Research Support) **David Canaday, M.D.**, **Pfizer** (Research Grant or Support)**Sanofi Pasteur** (Research Grant or Support)**Seqirus** (Advisor or Review Panel member, Research Grant or Support) **Vincent Mor, Ph.D.**, **naviHealth** (Consultant)