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References

Aktuell

Agarwal 2021

Ritu Agarwal, Michelle Dugas, Jui Ramaprasad, Junjie Luo, Gujie Li & Guodong (Gordon) Gao, *Socioeconomic privilege and political ideology are associated with racial disparity in COVID-19 vaccination*. PNAS **118** (2021), e2107873118. DOI:10.1073/pnas.2107873118.

Vaccine uptake is critical for mitigating the impact of COVID-19 in the United States, but structural inequities pose a serious threat to progress. Racial disparities in vaccination persist despite the increased availability of vaccines. We ask what factors are associated with such disparities. We combine data from state, federal, and other sources to estimate the relationship between social determinants of health and racial disparities in COVID-19 vaccinations at the county level. Analyzing vaccination data from 19 April 2021, when nearly half of the US adult population was at least partially vaccinated, we find associations between racial disparities in COVID-19 vaccination and median income (negative), disparity in high school education (positive), and vote share for the Republican party in the 2020 presidential election (negative), while vaccine hesitancy is not related to disparities. We examine differences in associations for COVID-19 vaccine uptake as compared with influenza vaccine. Key differences include an amplified role for socioeconomic privilege factors and political ideology, reflective of the unique societal context in which the pandemic has unfolded.

Keywords: racial disparity | COVID-19 | social determinants of health | vaccination

Arunachalam 2021

Prabhu S. Arunachalam et al., *Systems vaccinology of the BNT162b2 mRNA vaccine in humans*. nature **596** (2021), 410–416. DOI:10.1038/s41586-021-03791-x.

The emergency use authorization of two mRNA vaccines in less than a year from the emergence of SARS-CoV-2 represents a landmark in vaccinology1,2. Yet, how mRNA vaccines stimulate the immune system to elicit protective immune responses is unknown. Here we used a systems vaccinology approach to comprehensively profile the innate and adaptive immune responses of 56 healthy volunteers who were vaccinated with the Pfizer-BioNTech mRNA vaccine (BNT162b2). Vaccination resulted in the robust production of neutralizing antibodies against the wild-type SARS-CoV-2 (derived from 2019-nCOV/USA_WA1/2020) and, to a lesser extent, the B.1.351 strain, as well as significant increases in antigen-specific polyfunctional CD4 and CD8 T cells after the second dose. Booster vaccination stimulated a notably enhanced innate immune response as compared to primary vaccination, evidenced by (1) a greater frequency of CD14+CD16+ inflammatory monocytes; (2) a higher concentration of plasma IFNã; and (3) a transcriptional signature of innate antiviral immunity. Consistent with these observations, our single-cell transcriptomics analysis demonstrated an approximately 100-fold increase in the frequency of a myeloid cell cluster enriched in interferon-response transcription factors and reduced in AP-1 transcription factors, after secondary immunization. Finally, we identified distinct innate pathways associated with CD8

T cell and neutralizing antibody responses, and show that a monocyte-related signature correlates with the neutralizing antibody response against the B.1.351 variant. Collectively, these data provide insights into the immune responses induced by mRNA vaccination and demonstrate its capacity to prime the innate immune system to mount a more potent response after booster immunization.

Prabhu S. Arunachalam, Madeleine K. D. Scott, Thomas Hagan, Chunfeng Li, Yupeng Feng, Florian Wimmers, Lilit Grigoryan, Meera Trisal, Venkata Viswanadh Edara, Lilin Lai, Sarah Esther Chang, Allan Feng, Shaurya Dhingra, Mihir Shah, Alexandra S. Lee, Sharon Chinthrajah, Sayantani B. Sindher, Vamsee Mallajosyula, Fei Gao, Natalia Sigal, Sangeeta Kowli, Sheena Gupta, Kathryn Pellegrini, Gregory Tharp, Sofia Maysel-Auslender, Sydney Hamilton, Hadj Aoued, Kevin Hrusovsky, Mark Roskey, Steven E. Bosinger, Holden T. Maecker, Scott D. Boyd, Mark M. Davis, Paul J. Utz, Mehul S. Suthar, Purvesh Khatri, Kari C. Nadeau & Bali Pulendran

Collier 2021

Dami A. Collier et al., *Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2.* nature **596** (2021), 417–422. DOI:10.1038/s41586-021-03739-1.

Although two-dose mRNA vaccination provides excellent protection against SARS-CoV-2, there is little information about vaccine efficacy against variants of concern (VOC) in individuals above eighty years of age1. Here we analysed immune responses following vaccination with the BNT162b2 mRNA vaccine2 in elderly participants and younger healthcare workers. Serum neutralization and levels of binding IgG or IgA after the first vaccine dose were lower in older individuals, with a marked drop in participants over eighty years old. Sera from participants above eighty showed lower neutralization potency against the B.1.1.7 (Alpha), B.1.351 (Beta) and P.1. (Gamma) VOC than against the wild-type virus and were more likely to lack any neutralization against VOC following the first dose. However, following the second dose, neutralization against VOC was detectable regardless of age. The frequency of SARS-CoV-2 spike-specific memory B cells was higher in elderly responders (whose serum showed neutralization activity) than in non-responders after the first dose. Elderly participants showed a clear reduction in somatic hypermutation of class-switched cells. The production of interferon-ã and interleukin-2 by SARS-CoV-2 spike-specific T cells was lower in older participants, and both cytokines were secreted primarily by CD4 T cells. We conclude that the elderly are a high-risk population and that specific measures to boost vaccine responses in this population are warranted, particularly where variants of concern are circulating.

Dami A. Collier, Isabella A. T. M. Ferreira, Prasanti Kotagiri, Rawlings P. Datir, Eleanor Y. Lim, Emma Touizer, Bo Meng, Adam Abdullahi, The CITI-N. I. H. R. BioResource COV- Collaboratio, Anne Elmer, Nathalie Kingston, Barbara Graves, Emma Le Gresley, Daniela Caputo, Laura Bergamaschi, Kenneth G. C. Smith, John R. Bradley, Lourdes Ceron-Gutierrez, Paulina Cortes-Acevedo, Gabriela Barcenas-Morales, Michelle A. Linterman, Laura E. McCoy, Chris Davis, Emma Thomson, Paul A. Lyons, Eoin McKinney, Rainer Doffinger, Mark Wills & Ravindra K. Gupta

Föhse 2021

F. Konstantin Föhse et al., *The BNT162b2 mRNA vaccine against SARS-CoV-2 reprograms both adaptive and innate immune responses.* medRxiv **2021**, 21256520, 1–24. DOI:10.1101/2021.05.03.21256520.

medRxiv2021-a21256520-Supplement.pdf

The mRNA-based BNT162b2 vaccine from Pfizer/BioNTech was the first registered COVID-19 vaccine and has been shown to be up to 95 % effective in preventing SARS-CoV-2 infections. Little is known about the broad effects of the new class of mRNA vaccines, especially whether they have combined effects on innate and adaptive immune responses. Here we confirmed that BNT162b2 vaccination of healthy individuals induced effective humoral and cellular immunity against several SARS-CoV-2 variants. Interestingly, however, the BNT162b2 vaccine also modulated the production of inflammatory cytokines by innate immune cells upon stimulation with both specific (SARS-CoV-2) and non-specific (viral, fungal and bacterial) stimuli. The response of innate immune cells to TLR4 and TLR7/8 ligands was lower after BNT162b2 vaccination, while fungi-induced cytokine responses were stronger. In conclusion, the mRNA BNT162b2 vaccine induces complex functional reprogramming of innate immune responses, which should be considered in the development and use of this new class of vaccines.

Keywords: COVID-19 | coronaviruses | mRNA vaccines | trained immunity | innate immune tolerance

F. Konstantin Föhse, Büsranur Geckin, Gijs J. Overheul, Josephine van de Maat, Gizem Kilic, Ozlem Bulut, Helga Dijkstra, Heidi Lemmers, S. Andrei Sarlea, Maartje Reijnders, Jacobien Hoogerwerf, Jaap ten Oever, Elles Simonetti, Frank L. van de Veerdonk, Leo A. B. Joosten, Bart L. Haagmans, Reinout van Crevel, Yang Li, Ronald P. van Rij, Corine GeurtsvanKessel, Marien I. de Jonge, Jorge Domínguez-Andrés & Mihai G. Netea

Kraemer 2021

Moritz U. G. Kraemer et al., *Spatiotemporal invasion dynamics of SARS-CoV-2 lineage B.1.1.7 emergence*. science **373** (2021), 889–895. DOI:10.1126/science.abj0113.

s373-0889-Supplement.pdf

Understanding the causes and consequences of the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern is crucial to pandemic control yet difficult to achieve because they arise in the context of variable human behavior and immunity. We investigated the spatial invasion dynamics of lineage B.1.1.7 by jointly analyzing UK human mobility, virus genomes, and community-based polymerase chain reaction data. We identified a multistage spatial invasion process in which early B.1.1.7 growth rates were associated with mobility and asymmetric lineage export from a dominant source location, enhancing the effects of B.1.1.7's increased intrinsic transmissibility. We further explored how B.1.1.7 spread was shaped by nonpharmaceutical interventions and spatial variation in previous attack rates. Our findings show that careful accounting of the behavioral and epidemiological context within which variants of concern emerge is necessary to interpret correctly their observed relative growth rates.

Moritz U. G. Kraemer, Verity Hill, Christopher Ruis, Simon Dellicour, Sumali Bajaj, John T. McCrone, Guy Baele, Kris V. Parag, Anya Lindström Battle, Bernardo Gutierrez, Ben Jackson, Rachel Colquhoun, Áine O'Toole, Brennan Klein, Alessandro Vespignani, COVID-19 Genomics UK (COG-UK) Consortium, Erik Volz, Nuno R. Faria, David M. Aanensen, Nicholas J. Loman, Louis du Plessis, Simon Cauchemez, Andrew Rambaut, Samuel V. Scarpino & Oliver G. Pybus

Kupferschmidt 2021

Kai Kupferschmidt, *Evolving Threat*. science **373** (2021), 844–849. DOI:10.1126/science.373.6557.844.

New variants have changed the face of the pandemic. What will the virus do next?

Pouwels 2021

Koen B. Pouwels et al., *Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK*. unknown (2021), preprint, 1–39.

The effectiveness of BNT162b2, ChAdOx1, and mRNA-1273 vaccines against new SARS-CoV-2 infections requires continuous re-evaluation, given the increasingly dominant Delta variant. We investigated the effectiveness of the vaccines in a large community-based survey of randomly selected households across the UK. We found that the effectiveness of BNT162b2 and ChAd0x1 against any infections (new PCR positives) and infections with symptoms or high viral burden is reduced with the Delta variant. A single dose of the mRNA-1273 vaccine had similar or greater effectiveness compared to a single dose of BNT162b2 or ChAdOx1. Effectiveness of two doses remains at least as great as protection afforded by prior natural infection. The dynamics of immunity following second doses differed significantly between BNT162b2 and ChAdOx1, with greater initial effectiveness against new PCR-positives but faster declines in protection against high viral burden and symptomatic infection with BNT162b2. There was no evidence that effectiveness varied by dosing interval, but protection was higher among those vaccinated following a prior infection and younger adults. With Delta, infections occurring following two vaccinations had similar peak viral burden to those in unvaccinated individuals. SARS-CoV-2 vaccination still reduces new infections, but effectiveness and attenuation of peak viral burden are reduced with Delta.

Koen B. Pouwels, Emma Pritchard, Philippa C. Matthews, Nicole Stoesser, David W. Eyre, Karina-Doris Vihta, Thomas House, Jodie Hay, John I. Bell, John N. Newton, Jeremy Farrar, Derrick Crook, Duncan Cook, Emma Rourke, Ruth Studley, Tim Peto, Ian Diamond, A. Sarah Walker & the COVID-19 Infection Survey Team

Seneff 2021

Stephanie Seneff & Greg Nigh, *Worse Than the Disease? Reviewing Some Possible Unintended Consequences of the mRNA Vaccines Against COVID-19*. IJVTPR **2** (2021), 38–79.

Operation Warp Speed brought to market in the United States two mRNA vaccines, produced by Pfizer and Moderna. Interim data suggested high efficacy for both of these vaccines, which helped legitimize Emergency Use Authorization (EUA) by the FDA. However, the exceptionally rapid movement of these vaccines through controlled trials and into mass deployment raises multiple safety concerns. In this review we first describe the technology underlying these vaccines in detail. We then review both components of and the intended biological response to these vaccines, including production of the spike protein itself, and their potential relationship to a wide range of both acute and long-term induced pathologies, such as blood disorders, neurodegenerative diseases and autoimmune diseases. Among these potential induced pathologies, we discuss the relevance of prion-protein-related amino acid sequences within the spike protein. We also present a brief review of studies supporting the potential for spike protein "shedding", transmission of the protein from a vaccinated to an unvaccinated person, resulting in symptoms induced in the latter. We finish by addressing a common point of debate, namely, whether or not these vaccines could modify the DNA of those receiving the vaccination. While there are no studies demonstrating definitively that this is happening, we provide a plausible scenario, supported by previously established pathways for transformation and transport of genetic material, whereby injected mRNA could ultimately be incorporated into germ cell DNA for transgenerational transmission. We conclude with our recommendations regarding surveillance that will help to

clarify the long-term effects of these experimental drugs and allow us to better assess the true risk/benefit ratio of these novel technologies.

Keywords: antibody dependent enhancement | autoimmune diseases | gene editing | lipid nanoparticles | messenger RNA | prion diseases | reverse transcription | SARS-CoV-2 vaccines

Subbaraman 2021

Nidhi Subbaraman, *How do vaccinated people spread Delta? What the science says.* nature **596** (2021), 327–328. .

Delta spreads more readily than other coronavirus variants among vaccinated people, data suggest.

Wadman 2021

Meredith Wadman, *Israel's grim warning, Delta can overwhelm shots.* science **373** (2021), 838–839. DOI:10.1126/science.373.6557.838.

With early vaccination and outstanding data, country is the world's real-life COVID-19 lab.

Yu 2021

Jingyou Yu et al., *Protective efficacy of Ad26.COV2.S against SARS-CoV-2 B.1.351 in macaques.* nature **596** (2021), 423–427. DOI:10.1038/s41586-021-03732-8.

The emergence of SARS-CoV-2 variants that partially evade neutralizing antibodies poses a threat to the efficacy of current COVID-19 vaccines1,2. The Ad26.COV2.S vaccine expresses a stabilized spike protein from the WA1/2020 strain of SARS-CoV-2, and has recently demonstrated protective efficacy against symptomatic COVID-19 in humans in several geographical regions—including in South Africa, where 95 % of sequenced viruses in cases of COVID-19 were the B.1.351 variant3. Here we show that Ad26.COV2.S elicits humoral and cellular immune responses that cross-react with the B.1.351 variant and protects against B.1.351 challenge in rhesus macaques. Ad26.COV2.S induced lower binding and neutralizing antibodies against B.1.351 as compared to WA1/2020, but elicited comparable CD8 and CD4 T cell responses against the WA1/2020, B.1.351, B.1.1.7, P.1 and CAL.20C variants. B.1.351 infection of control rhesus macaques resulted in higher levels of virus replication in bronchoalveolar lavage and nasal swabs than did WA1/2020 infection. Ad26.COV2.S provided robust protection against both WA1/2020 and B.1.351, although we observed higher levels of virus in vaccinated macaques after B.1.351 challenge. These data demonstrate that Ad26.COV2.S provided robust protection against B.1.351 challenge in rhesus macaques. Our findings have important implications for vaccine control of SARS-CoV-2 variants of concern.

Jingyou Yu, Lisa H. Tostanoski, Noe B. Mercado, Katherine McMahan, Jinyan Liu, Catherine Jacob-Dolan, Abishek Chandrashekar, Caroline Atyeo, David R. Martinez, Tochi Anioke, Esther A. Bondzie, Aiquan Chang, Sarah Gardner, Victoria M. Giffin, David L. Hope, Felix Nampanya, Joseph Nkolola, Shivani Patel, Owen Sanborn, Daniel Sellers, Huahua Wan, Tammy Hayes, Katherine Bauer, Laurent Pessaint, Daniel Valentin, Zack Flinchbaugh, Renita Brown, Anthony Cook, Deandre Bueno-Wilkerson, Elyse Teow, Hanne Andersen, Mark G. Lewis, Amanda J. Martinot, Ralph S. Baric, Galit Alter, Frank Wegmann, Roland Zahn, Hanneke Schuitemaker & Dan H. Barouch

Mittelpaläolithikum

Martí 2021

Africa Pitarch Martí et al., *The symbolic role of the underground world among Middle Paleolithic Neanderthals*. PNAS **118** (2021), e2021495118.

pnas118-e2021495118-Supplement.pdf

Cueva de Ardales in Málaga, Spain, is one of the richest and bestpreserved Paleolithic painted caves of southwestern Europe, containing over a thousand graphic representations. Here, we study the red pigment in panel II.A.3 of "Sala de las Estrellas," dated by U-Th to the Middle Paleolithic, to determine its composition, verify its anthropogenic nature, infer the associated behaviors, and discuss their implications. Using optical microscopy, scanning electron microscopy coupled with energy dispersive X-ray spectroscopy, micro-Raman spectroscopy, and X-ray diffraction, we analyzed a set of samples from the panel and compared them to natural coloring materials collected from the floor and walls of the cave. The conspicuously different texture and composition of the geological samples indicates that the pigments used in the paintings do not come from the outcrops of colorant material known in the cave. We confirm that the paintings are not the result of natural processes and show that the composition of the paint is consistent with the artistic activity being recurrent. Our Results strengthen the hypothesis that Neanderthals symbolically used these paintings and the large stalagmitic dome harboring them over an extended time span.

Keywords: cave art | symbolism | pigment | spectroscopic analyses | Iberian Peninsula

Africa Pitarch Martí, João Zilhão, Francesco d'Errico, Pedro Cantalejo-Duarte, Salvador Domínguez-Bella, Josep M. Fullola, Gerd C. Weniger & José Ramos-Muñoz

Significance: The emergence of symbolic behavior in our genus is a controversial issue. The dating of paintings in three caves from the Iberian Peninsula supports the view that Neanderthals developed a form of cave art more than 20,000 years before the emergence of anatomical modernity in Europe. In this study, we confirm that the paintings on a large speleothem from one of these sites, Cueva de Ardales, were human made, and we show that the pigments do not come from the outcrops of colorant material known inside the cave. Variations in the composition of the paint correspond to differences in the age of the paintings, supporting the hypothesis that Neanderthals used the speleothems symbolically over an extended time span.

Story or Book

Mitton 2021

Simon Mitton, *Before the Big Bang became scientific dogma*. science **373** (2021), 861.

A dual biography traces the entangled efforts of a pair of contentious cosmologists.

Flashes of Creation: George Gamow, Fred Hoyle, and the Great Big Bang Debate. Paul Halpern. Basic Books, 2021. 304 pp.

The Gamowian school had considered the role of neutrinos in core collapse, but Hoyle's powerful rebuttal of their model in 1946 was vastly more efficient at building heavy elements. By 1957, Hoyle's team had completed its brilliant synthesis of element building via neutron capture reactions.