T-cell Immunity Against COVID-19 and UK Variant in Infected and Vaccinated Individuals

Stanley Jordan[1], Bong-Ha Shin[1], Terry-Ann Milfordgadsden[1], Maggie Chu[1], Anna Petrosyan[1], Catherine Le[1], Rachel Zabner[1], Jillian Oft[1], Isabel Pedraza[1], Norkio Ammerman[1], Susan Cheng[1], Ashley Vo[1], Jasmine Plummer[1], Anders Berg[1], Shili Ge[1], Mieko Toyoda[1], and Ruan Zhang[1]

[1]Cedars Sinai Med Ctr

April 05, 2024

Abstract

Understanding the composition of human immune responses to SARS-CoV-2 and vaccines is essential for predicting protection from infection and determining vaccine efficacy. Here, we explored T-cell immune responses to SARS-CoV-2 and the UK (B.1.1.7) variant of concern (VOC) in infected and vaccinated individuals. In infected patients, CD4+ T-cells demonstrated consistent, robust responses against Spike peptides, while CD8+ T-cells had heterogeneous responses to 5 SARS-CoV-2 proteins. We found 80% of infected and vaccinated individuals showed positive CD4+ T-cell immunity against SARS-CoV-2. Moreover, CD4+/CD8+ T-cell responses to SARS-CoV-2 and the United Kingdom (B.1.1.7) variant are robust and nearly identical in infected and vaccinated individuals. Thus, the UK variant did not interfere with T-cell recognition and elicited responses. These observations will be of critical importance in assessing human immune responses to emerging VOCs.

T-cell Immunity Against COVID-19 and UK Variant in Infected and Vaccinated Individuals

Stanley C Jordan, MD[1, f] Bong-Ha Shin,PhD[1,f] Terry-Ann M Gadsden,BS[1]Maggie Chu,BS[1] Anna Petrosyan,BS[1]Catherine N Le,MD[2] Rachel Zabner,MD[2]Jillian Oft,MD[2] Isabel Pedraza,MD[2]Susan Cheng,MD[3] Ashley Vo,PharmD[1]Noriko Ammerman,PharmD[1] Jasmine Plummer,PhD[4], Shili Ge[1], PhD, Anders Berg[5], PhD, Mieko Toyoda,PhD[1] and Ruan Zhang,PhD[1]. [1]Comprehensive Transplant Center, Transplant Immunology Laboratory,[2]Division of Infectious Diseases,[3]Cardiology, [4]Bioinformatics & Functional Genomics, and Department of Pathology & Laboratory Medicine[5] Cedars-Sinai Medical Center, Los Angeles, CA 90048.[f]Authors share first authorship.

Word Count Summary: 130

Word Count Text: 2015

Address Correspondence:

Stanley C. Jordan, MD, FASN, FAST

Director, Nephrology & Transplant Immunology

Cedars-Sinai Medical Center

8700 Beverly Blvd

Los Angeles, CA 90048

Phone: 3130-423-2641

Email: stan.jordan@cshs.org

Data Availability Statement:

Request for data relevant to the manuscript will be considered after assessment and review.

Competing Interest:

None of the authors report competing interest that are relevant to data presented in this manuscript.

Funding:

Funding of this study was entirely from internal resources at Cedars-Sinai Medical Center including funding from the Borstenin Family Foundation, Los Angeles.

Author Contributions:

Stanley C. Jordan,MD: Was involved in the design and execution of the research and was primarily responsible for writing and editing of the manuscript.

Bong-Ha Shin, PhD: Primarily involved in designing the T-cell assay and generating data for manuscript

Terry-Ann M Gadsden,BS: Involved in performance of the T-cell and antibody assays

Maggie Chu, BS: Involved in performance of the T-cell and antibody assays

Anna Petrosyan,BS: Involved in performance of the antibody assays

Catherine N Le,MD: Involved in gathering, analyzing data and writing the manuscript

Rachel Zabner,MD: Involved in gathering and analyzing data for the manuscript

Jillian Oft, MD: Involved in gathering and analyzing data for the manuscript

Isabel Pedraza, MD: Involved in gathering and analyzing data for the manuscript

Susan Cheng, MD: Provided technical and editing support for the project

Ashley Vo,PharmD: Provided support for developing protocol and regulatory documents

Noriko Ammerman,PharmD: Provided regulatory support for development of the project

Jasmine Plummer, PhD: Provided laboratory support and editing for project

Shili Ge, PhD: Helped in assay development and implementation

Anders Berg, PhD: Aided in development and implementation of antibody assays and interpretation.

Mieko Toyoda,PhD: Helped develop and implement the T-cell assay

Ruan Zhang, PhD: Primarily involved in the development of the assays and project. Contributed to writing and editing of the manuscript.

Summary

Understanding the composition of human immune responses to SARS-CoV-2 and vaccines is essential for predicting protection from infection and determining vaccine efficacy. Here, we explored T-cell immune responses to SARS-CoV-2 and the UK (B.1.1.7) variant of concern (VOC) in infected and vaccinated individuals. In infected patients, CD4+ T-cells demonstrated consistent, robust response against Spike peptides, while CD8+ T-cells had heterogeneous responses to 5 SARS-CoV-2 proteins. We found 80% of infected and vaccinated individuals showed positive CD4+ T-cell immunity against SARS-CoV-2. Moreover, CD4+/CD8+ T-cell responses to SARS-CoV-2 and the United Kingdom (B.1.1.7) variant are robust and nearly identical in infected and vaccinated individuals. Thus, the UK variant did not interfere with T-cell recognition and

elicited responses. These observations will be of critical importance in assessing human immune responses to emerging VOCs.

Introduction:

To date, there have been more than 200,757,931 COVID-19 cases and 4,266,367 deaths documented worldwide[1]. This has led to massive human suffering and disruption of global economies. The limited efficacy of most treatments and high death rates have focused on vaccines as the last best hope for stemming the pandemic. In general, this has been true[2]. However, the persistence of the SARS-CoV-2 epidemic, driven primarily by variants of concern (VOC), have raised concerns that this will pose potential challenges to our ability to provide effective sterilizing and durable immunity through vaccination[3]. This brings into question whether the composition of SARS-CoV-2 immunity garnered by previous infection or vaccination could respond effectively to emerging VOC or would require constant re-vaccination with an ever-changing composition of viral mRNAs or peptides to meet the potential pathogenic threat.

Since the advent of the epidemic, attempts to define the composition and duration of immune responses in infected and, more recently, vaccinated individuals have been ardently pursued[4,5]. Important early advances were achieved in describing antibody responses after infection, but concerns arose regarding the rapid and unpredictable dissipation of IgG responses to SARS-CoV-2 peptides and the potential effect on long-term immunity[5-7]. In addition, reports have shown that IgG spike protein immune responses to the BNT162b2 (Pfizer) vaccine may have reduced activity against the United Kingdom (UK, B.1.1.7) variant[8].

A better understanding of this important issue would benefit from analysis of CD4+/CD8+ T-cell responses to SARS-CoV-2 spike peptides and variants[9-11]. SARS-CoV-2-specific T-cell immunity was detected in COVID-19 patients as well as uninfected healthy controls[9,10]. Early and/or robust T-cell immunity has been associated with rapid viral clearance and mild symptoms in COVID-19 patients[11,12]. Thus, an analysis of T-cell reactivity to SARS-CoV-2 and VOC would aid in our understanding of the breadth and depth of human immune responses after infection and vaccination.

Here we report on the development of a sensitive whole blood assay to detect CD4+/CD8+ T-cell cytokine responses to SARS-CoV-2 and variant peptides. This information could be helpful in understanding the composition and durability of human immunity to SARS-CoV-2 and a VOC.

Patients & Methods

Participants and Sample Collection

Informed consent was obtained prior to study initiation. This study was approved by the institutional review board at Cedars-Sinai Medical Center (protocol IRB numbers: 000 42267 and 000 00621). The study was conducted in accordance with the ethical guideline based on federal regulations and the common rule. The study was composed and written entirely by the authors who vouch for the results presented here.

Nineteen healthy controls, 134 patients with confirmed COVID-19 infection (of which, 14 received vaccination), and 38 vaccinated healthy individuals without history of SARS-CoV-2 infection were enrolled in the study with similar age and gender composition. The demographics of 134 patients are shown in Table 1. The time of blood draw from previously infected patients ranged from day 16 to day 388 (Median = 102) after reported SARS-CoV-2 infection by viral PCR and/or antibody test. The blood from vaccinated individuals was drawn 1-month post 2nd dose of Pfizer BNT162b2 mRNA vaccine. Fresh whole blood was collected in sodium heparinized tubes and stimulated with SARS-CoV-2 peptides overnight. Plasma obtained was stored at -80°C for SARS-CoV-2 Spike IgG analysis.

T-cell Stimulation with SARS-CoV-2 and VOC Peptides

Whole blood was incubated with 1 μg/mL SARS CoV-2 Spike glycoprotein (S), or variant B.1.1.7 Spike (B.1.1.7). For patients with previous infection, additional peptides were tested. These included virus membrane protein (VME), nucleoprotein (NCAP), protein 3A (AP3A), and non-structural protein 7A (NS7A) (JPT Peptide Technologies GmbH, Berlin, Germany). For all conditions, Brefeldin A and anti-CD28/CD49d

(BD Biosciences, San Jose, CA) were added and incubated for 9 hours at 37^{O}C. Negative and positive controls included cells not incubated with peptides and those stimulated with phytohemagglutinin (PHA).

Cytokine Flow Cytometry Analysis

Fresh whole blood was incubated with SARS-CoV-2-specific peptides for 9 hours and immune cells were stained for surface markers. Cells were stained with fluorochrome conjugated antibodies to CD3+ (FITC), CD4+ (PerCP Cy5.5), CD8+ (V450), CD45+ (V500) and CD56+ (PE-CF594) (BD Bioscience, CA). After erythrocytes were lysed by permeabilization, intracellular cytokines were stained with fluorochrome conjugated antibodies to IL-2 (APC), IFN-γ (PE), and TNF-α (PE-Cy7) (BD Bioscience, CA). The CD4+ $(\text{IL-2/TNF-}\alpha)^{+}$ cells and CD8+ $(\text{TNF-}\alpha/\text{IFN-}\gamma)^{+}$ stimulated with S, B.1.1.7 S, VME, NCAP, AP3A, NS7A were enumerated and defined as CoV-2-specific T-cells after deducting the background levels in blood only conditions. Dual cytokines % in CD4+ or CD8+ cells [?] 0.05% were considered positive.

Measurement of Nucleocapsid-Specific IgG Levels

Nucleocapsid-specific IgG titer in serum of patients was analyzed using SARS-CoV-2 IgG assay (Abbott Core Laboratory) on the Architect instrument according to the manufacturer instructions.

Measurement of SARS-CoV-2-Spike-specific IgG in Plasma

We next determined the levels of SARS-CoV-2 Spike IgG using CoVS1-RBD ELISA kit (Ray Biotech, GA) per the manufacture's manual. Briefly, the 96 well plates coated with the SARS-CoV-2 S1 RBD protein were incubated with plasma followed by biotinylated anti-human IgG. After washing, HRP-conjugated streptavidin was added, and spike-specific IgG was quantitated by OD450 nm reading.

Statistical analysis

Data were congregated in Excel and Graphpad Prism for statistical analysis. Student t-test was used for analyzing the statistical difference between two groups. Correlation between T-cell immune response and IgG titer was analyzed by Pearson's correlation coefficient test. P-value less than 0.05 was considered significant.

Results

SARS-CoV-2-specific T-cell Detection in Whole Blood

IL-2 is a key growth factor for activated T-cells, while TNF-α and IFN-γ are considered canonical inflammatory cytokines mediating effector/memory T-cell functions. Analysis of cytokine production in stimulated T-cells confirmed that IL-2 and TNF-α were consistent markers for activated CD4+ T-cells, while activated CD8+ T-cells mainly produced TNF-α and IFN-γ. After incubating whole blood with SARS-CoV-2 Spike peptide pool, we were able to discern Spike-reactive T-cells by dual cytokine gating (Figure 1). Here, healthy individuals without history of SARS-CoV-2 infection demonstrated no significant T-cell responses to SARS-CoV-2 spike peptide. However, T-cells from SARS-CoV-2-infected or vaccinated individuals showed substantial spike-specific CD4+ and CD8+ T-cells.

T-cell Immunity in Infected Individuals

To explore the breadth and depth of memory T-cell immunity against SARS-CoV-2, we examined responses in 34 selected patients with documented SARS-CoV-2 infection (Figure 2A). T-cell immune responses to peptide pools of 5 major SARS-CoV-2 proteins (Spike, VME, NCAP, AP3A, and NS7A) were analyzed. In healthy control individuals, no significant CD4+ T-cell responses to the 5 SARS-CoV2 proteins were seen (Figure 2B, IL-2+TNF-α+(%) in CD4+ <0.05%, mean = 0.01%). However, 20% of healthy individuals showed heterogenous TNF-α+/IFN-γ+ CD8+ T-cell (>0.05%) responses to the 5 SARS-CoV-2 proteins, which could represent cross-reaction of CD8+ T-cells generated from previous endemic coronavirus infection (Figure 2B)[9,10]. Based on the background level of CD4+ T-cell response in healthy controls, we set 0.05% of dual-positive CD4+ and CD8+ T-cells as the cutoff level determining positive T-cell immunity against SARS-CoV-2. Overall, we observed 88% (30 of 34) infected patients had either positive CD4+ or CD8+ T-cell immunity to one or more of 5 CoV-2 peptides. Most patients showed positive CD4+ T-cell immunity

(85%, 29 of 34), and CD4+ T-cells demonstrated immunodominant responses to Spike peptides as previously described[11,12] (Figure 2A). CD8+ T-cells showed similar responses to the 5 proteins; 68% (23 of 34) had positive CoV-2 specific CD8+ T-cells to one or more of 5 CoV-2 proteins.

T-cell Immunity in Vaccinated Individuals

Next, we analyzed Spike-specific CD4+/CD8+ immune responses to the Pfizer BNT162b2 vaccine. We compared Spike-specific T-cell immunity to 19 healthy controls, 38 infected patients, and 38 vaccinated individuals 1 month after the 2nd vaccine dose (Figure 2B). No healthy unvaccinated individuals showed positive CD4+ T-cells against SARS-CoV-2, but infected patients and vaccinated individuals demonstrated substantial spike-specific CD4+ T-cell immunity: 87% (33 of 38) and 89% (34 of 38) respectively. CD8+ T-cells from healthy controls, infected patients, and vaccinated individuals showed 21% (4 of 19), 34% (13 of 38), and 58% (22 of 38) positive immune responses against SARS-CoV-2 spike peptides, respectively. Therefore, the Pfizer BNT162b2 vaccine induced T-cell reactivity to Spike-specific peptides that was equivalent to that seen in infected patients after recovery.

Association of T-cell Immunity with IgG Serology

T-cell immunity to SARS-CoV-2 was generally associated with Spike-specific IgG responses[11,12]. Serum from SARS-CoV-2 patients were submitted for clinical nucleoprotein IgG titer. In 25 patients with nucleocapsid IgG positivity, we analyzed the association with CD4+ T-cell immunity to the 5 SARS-CoV-2 peptides (the highest response was compared). Although the T-cell immunity was not nucleocapsid-specific, there was a significant association between CD4+ T-cell immunity and nucleocapsid IgG titers (p=0.022; R= 0.457; Figure 2C).

We then examined Spike-specific IgG levels in 80 SARS-CoV2 infected patients and compared them to Spike-specific T-cell immunity. Here, 72.58% of patients with positive Spike-specific CD4+ T-cells had positive Spike-specific IgG levels. For patients with negative Spike-specific T-cell immunity, 61.11% also showed negative Spike-specific IgG levels. In 13 patients with high Spike-specific CD4+ T-cell immunity (IL-2+TNF-α+(%) in CD4+ $>$ 0.3%), we also observed a correlation between T-cell immunity and level of Spike-specific IgG (p=0.0316; R=0.5288; Figure 2D). Therefore, T-cell immunity in SARS-CoV-2 patients, in general, was associated with positive IgG levels. However, 39% of previously infected patients with positive Spike-IgG antibodies did not demonstrate T-cell immunity. This may represent variability in the composition of immune responses from one individual to another as has been reported[4-6].

UK Variant and Immune Evasion

The B.1.1.7 variant contains the E484K mutation which renders resistance to serologic responses in infected individuals[8].To determine if this VOC evaded T-cell immunity, we analyzed 19 infected/recovered patients and 18 vaccinated individuals for CD4+/CD8+ T-cell responses against B.1.1.7 variant Spike protein. As shown in Figure 3, there is no significant reduction in CD4+/CD8+ T-cell responses to the variant B.1.1.7 Spike peptides as compared to the original Wuhan Spike peptides (mean of infected patients: 0.23% original to 0.18% variant; mean of vaccinated individuals: 0.16% original to 0.14% variant). Five of 20 infected patients and 6 of 18 vaccinated individuals had no detectable CD8+ T-cells against the original or variant Spike peptides (data not shown). The other 15 infected and 12 vaccinated individuals demonstrated nearly identical CD8+ responses to the original Wuhan Spike and variant Spike (Figure 3B). When the individual T-cell responses to the original and variant spikes were compared, those with higher CD4+ T-cell immunity tend to lose some reactivity to the variant peptide, but not at a significant level (Figure 3C and 3D). In summary, T-cell memory induced by SARS-CoV-2 infection or vaccination establishes effective immune response against the B.1.1.7 variant. This would suggest protective immunity against B.1.1.7 infection and possibly other VOC[13].

Discussion

Assessing the composition, scope, and durability of protective immunity generated after SARS-CoV-2 infection or vaccination are critical for control of the pandemic and future vaccination strategies. It is likely that

analyzing immune responses to SARS-CoV-2 has garnered more attention and information than any other human infection in history. Traditional assessments have included antibody responses which are often transient or rapidly declining in patients with moderate infections. However, we now know that T-cell immunity against SARS-CoV-2 is more diverse and cross-reactive with peptides expressed on other Coronaviruses[9,11-12]. These observations suggest that robust T-cell responses are an important and essential element of long-term immunity to SARS-CoV-2. However, assessments of T-cell immunity to SARS-CoV-2 are not readily available. In this regard, we present data from a flow cytometry-based assay detecting dual cytokine-producing, SARS-CoV-2-antigen-specific memory T-cells which demonstrates specificity and accuracy for detection of CD4+/CD8+ T-cell responses to SARS-CoV-2 peptides and differentiates infected and vaccinated individuals from those not exposed to SARS-CoV-2.

Finally, analysis of T-cell responses to an important VOC (B.1.1.7) showed that exposure to SARS-CoV-2 infection or BNT162b2 vaccine elicited nearly equivalent T-cell responses. Recent observations suggest that IgG responses to SARS-CoV-2 infection did not reduce viremia in patients infected with the B.1.1.7 variant[8] however, SARS-CoV-2 T-cell responses were not explored in that study. Long term analysis of immune responses will be important since memory responses differ greatly from acute responses, especially at the antibody level[7,14-15]. Here, dormancy of memory T-cells, B-cells, and plasma cells that can rapidly be activated upon re-exposure to SARS-CoV-2 exposure are likely to have an important role in preventing SARS-CoV-2 infection and possibly infection from current and emerging VOC[13].

Acknowledgements :

We wish to thank the members of the Transplant Immunology Laboratory and Division of Infectious Diseases at Cedars-Sinai Medical Center for their hard work and dedication to this project. We also want to express our gratitude to the patients with COVID-19 and vaccine participants for donating their time and blood for this study.

Figure Legends :

Figure 1. Detection of SARS-CoV-2-specific T-cells in whole blood. Fresh whole blood from participants was stimulated by SARS-CoV-2 Spike peptides. Activated CD4+ T-cells were identified as CD45+CD3+CD4+IL-2+/TNF-α+ cells while activated CD8+ T-cell were CD45+CD3+CD8+TNF-α+/IFN-γ+ cells. Also shown is Blood + PHA which is positive control and Blood only which is negative control.

Figure 2. T cell immune response in SARS-CoV-2 infected patients and vaccinated individuals. A.CD4+ and CD8+ T-cell immune responses to SARS-CoV-2 peptides from 134 patients with confirmed SARS-CoV-2 infection. T-cells were stimulated separately using 5 major CoV-2 peptides: Spike, VME, NCAP, AP3A, NS7A. Activated CD4+ and CD8+ T cells were enumerated in Figure 1. Each dot represents one individual reading. B. CD4+ and CD8+ T-cell immune responses to SARS-CoV-2 Spike peptides in healthy, infected and vaccinated individuals. C. The correlation of Nucleocapsid-specific IgG levels with CD4+ T-cell immune responses to one or more of 5 major SARS-CoV-2 peptides in 25 patients. D. The correlation between Spike-specific CD4+ T-cell immune responses and Spike-specific IgG levels in 13 patients with elevated CD4+ Spike-specific T-cell immune responses (IL-2+/TNF-α+ cell% in CD4+ $> 0.3\%$).

Figure 3. Immunogenicity of variant B.1.1.7 spike peptides. A&B. CD4+ & CD8+ T-cell immune responses to Spike-specific peptides are shown in infected/recovered and vaccinated patients. T cells were stimulated by the original SARS-CoV-2 Spike (Wuhan) or variant B.1.1.7 Spike peptides. Activated CD4+ (A) and CD8+ T- cell (B) in 19 infected patients and 18 vaccinated individuals are shown. C&D.The paired data for immune responses to SARS-CoV-2 Spike peptides and UK (B.1.1.7)Spike peptides for each individual.

References :

1. https://www.worldometers.info/coronavirus/ July 3, 2021
2. Thompson MG, Burgess JL, Naleway AL, et al. Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines. N Engl J Med. 2021 Jun 30. Doi: 10.1056/NEJMoa2107058.

Epub ahead of print.
3. Krause PR, Fleming TR, Longini IM,et al. SARS-CoV-2 Variants and Vaccines. N Engl J Med. 2021 Jun 23. Doi: 10.1056/NEJMsr2105280. Epub ahead of print.
4. Dan JM, Mateus J, Kato Y, et al Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science. 2021 Feb 5;371(6529):eabf4063. Doi: 10.1126/science.abf4063. Epub 2021 Jan 6. PMID: 33408181; PMCID: PMC7919858.
5. Jordan SC. Innate and adaptive immune responses to SARS-CoV-2 in humans: relevance to acquired immunity and vaccine responses. Clin Exp Immunol. 2021 Jun;204(3):310-320. Doi: 10.1111/cei.13582. Epub 2021 Mar 4. PMID: 33534923
6. Anand SP, Prévost J, Nayrac M, et al Longitudinal analysis of humoral immunity against SARS-CoV-2 Spike in convalescent individuals up to 8 months post-symptom onset. Cell Rep Med. 2021 Jun 15;2(6):100290. Doi: 10.1016/j.xcrm.2021.100290. Epub 2021 May 5. PMID: 33969322; PMCID: PMC8097665.
7. Radbruch A, Chang HD. A long-term perspective on immunity to COVID. Nature. 2021 Jun 14. Doi: 10.1038/d41586-021-01557-z. Epub ahead of print
8. Ratcliff J, Nguyen D, Fish M, et al. Virological and serological characterization of critically ill patients with COVID-19 in the UK: Interactions of viral load, antibody status and B.1.1.7 variant infection. J Infect Dis. 2021 May 24:jiab283. doi: 10.1093/infdis/jiab283. Epub ahead of print. PMID: 34031695; PMCID:
9. Braun J, Loyal L, Frentsch M et al. SARS-CoV-2-reactive T-cells in healthy donors and patients with COVID-19. Nature 2020; 587:270–274.
10. Mateus J, Grifoni A, Tarke A et al. Selective and cross-reactive SARS-CoV-2 T-Cell epitopes in unexposed humans. Science 2020; 370:89–94.
11. Peng Y, Mentzer A, Liu G et al. Broad and strong memory CD4+ and CD8+ T cells induced by SARS-CoV-2 in UK convalescent individuals following COVID-19. Nat Immunol 2020; 21:1336–1345.
12. Swadling L, Maini M. T-cells in COVID-19 – united in diversity. Nat Immunol 2020; 21:1307–1308.
13. Tarke A, Sidney J, Methot N, Negligible impact of SARS-CoV-2 variants on CD4 + and CD8 + T-cell reactivity in COVID-19 exposed donors and vaccinees. bioRxiv [Preprint]. 2021 Mar 1:2021.02.27.433180. doi: 10.1101/2021.02.27.433180. PMID: 33688655;
14. Turner JS, Kim W, Kalaidina E, Goss CW, Rauseo AM, Schmitz AJ, Hansen L, Haile A, Klebert MK, Pusic I, O'Halloran JA, Presti RM, Ellebedy AH. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. Nature. 2021 May 24. doi: 10.1038/s41586-021-03647-4. Epub ahead of print.
15. Wang, Z., Muecksch, F., Schaefer-Babajew, D. et al. Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection. Nature (2021). https://doi.org/10.1038/s41586-021-03696-9

Hosted file

`Table 1 COVID-Tc.docx` available at https://authorea.com/users/380273/articles/711317-t-cell-immunity-against-covid-19-and-uk-variant-in-infected-and-vaccinated-individuals

Hosted file

`COVID Tc Figures 07-28-2021 - Read-Only.pptx` available at https://authorea.com/users/380273/articles/711317-t-cell-immunity-against-covid-19-and-uk-variant-in-infected-and-vaccinated-individuals