Supplementary Table 1: List of additional authors from the OCTAVE and OCTAVE-
DUO TMG consortium.

OCTAVE & OCTAVE DUO TMG Members		
Prof	Iain McInnes	Adult Rheumatology/Inflammatory diseases
Prof	Stefan Siebert	Adult Rheumatology/Inflammatory diseases
Prof	Pam Kearns	Adult Cancer (Solid Tumours)
Prof	Dan Rea	Adult Cancer (Solid Tumours)
Prof	Gordon Cook	Adult Cancer (Haematology Tumours)
Dr	Michelle Willicombe	Adult Chronic Renal Diseases
Prof	David Thomas	Adult Chronic Renal Diseases
Prof	Eleanor Barnes	Adult Chronic Liver Diseases
Prof	Thushan de Silva	Adult Haematopoietic Stem Cell Transplant
Prof	Lucy Wedderburn	Paediatric Rheumatology/Inflammatory diseases
Dr	Rossa Brugha	Paediatric Solid Organ Transplantation
Dr	Jessica Bate	Paediatric Cancer
Prof	Carl Goodyear	Laboratory Lead
Prof	Alex Richter	Primary Immunodeficiency
Prof	John Snowden	Adult Stem Cell Transplant
Prof	Jack Satsangi	CAR-T Cell Therapy
Prof	Sean Hua Lim	Lymphoid Malignancy
Miss	Amanda Kirkham	Lead Biostatistician
Dr	Sarah Bowden	CRCTU Director of Operations
Ms	Sophia Magwaro	Trial Management Team Leader
Mrs	Ana Hughes	Senior Trial Coordinator
Dr	Ann Pope	Trial Coordinator
Mrs	Elspeth Insch	Patient representative
Mrs	Vicky Churchill	Patient representative
Mrs	Richard Beesley	Patient representative
Miss	Eilean MacDonald	Patient representative

Supplementary Table 2: MesoScale Discovery (MSD) SARS-CoV-2 antigen information for ACE2 competition assays. Information supplied by MSD as reported in the product documentation "V-PLEX COVID-19 ACE2 Neutralization Assays insert".

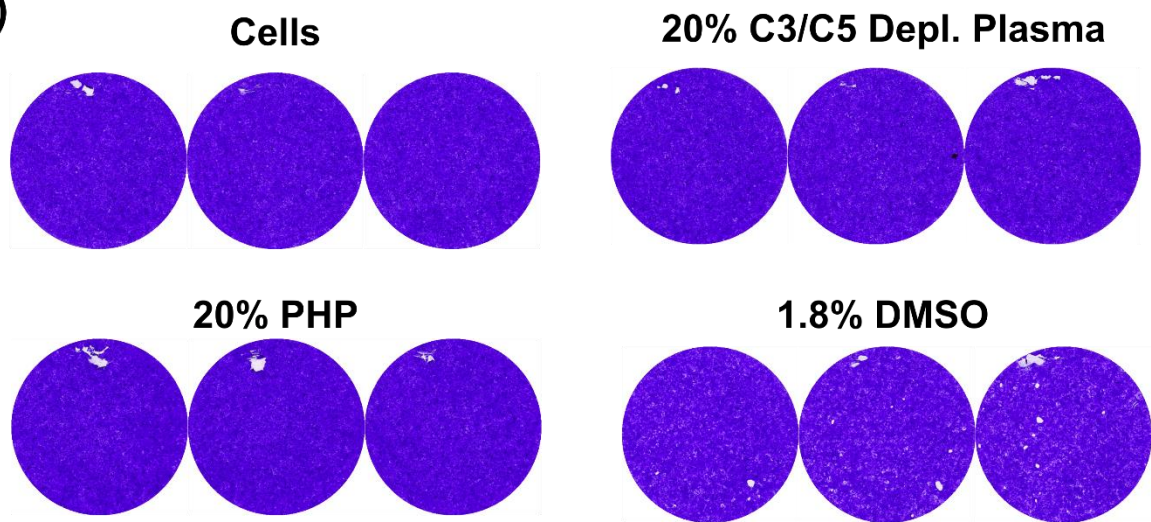| Spot	SARS-CoV-2 Antigen	Lineage	Amino Acid Modifications
1	Spike (Wuhan)	Wuhan	Not Applicable
2	Spike (BA.2.12.1)	Omicron	T19I, (L24-A27)toS, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452Q, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, S704LN764K, D796Y, Q954H, N969K
3	Nucleocapsid	Wuhan	Not Applicable
4	Spike (BA.2.75)	Omicron	T19I, L24-A27>S, G142D, K147E, W152R, F157L, I210V, V213G, G257S, G339H, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, G446S, N460K, S477N, T478K, E484A, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K
5	Spike (BA.2; BA.2.1; BA.2.2; BA.2.3; BA.2.5; BA.2.6; BA.2.7; BA.2.8; BA.2.10; BA.2.12)	Omicron	T19I, (L24-A27)toS, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K
6	Spike (B.1.1.529; BA.1; BA.1.15)	Omicron	A67V, ΔH69-V70, T95I, G142D, Δ143-145, Δ211/L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F
7	Spike (B.1.617.2; AY.4)	Delta	**(Alt Seq 2):** T19R, T95I, G142D, Δ156/157, R158G, L452R, T478K, D614G, P681R, D950N
8	Spike (B.1.1.7)	Alpha	ΔH69-V70, ΔY144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
9	Spike (B.1.351)	Beta	L18F, D80A, D215G, Δ242-244, R246I, K417N, E484K, N501Y, D614G, A701V
10	Spike (BA.5)	Omicron	T19I, (L24-A27)toS, del69/70, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K

Note: Alternative S-GENE mutations for Spike of B.1.617.2 is listed as "Alt Seq 2."

Supplementary Figure 1: Comparison of raw foci numbers as a measure of SARS-CoV-2 infection for microneutralisation assay controls in the absence of OPTIC immune sera. The addition of pooled human plasma (PHP) or heat-inactivated (HI)-FCS did not significantly reduce the level of infection in absence of immune sera. In some conditions, the level of infection was significantly higher than the conditions supplemented with media-only. Each spot indicates a single replicate from a total of 8 replicates per plate, with all plates tested. Significance with $P < 0.05$ was determined by Kruskal-Wallis test with Dunn's multiple comparisons test in GraphPad Prism (version 10).
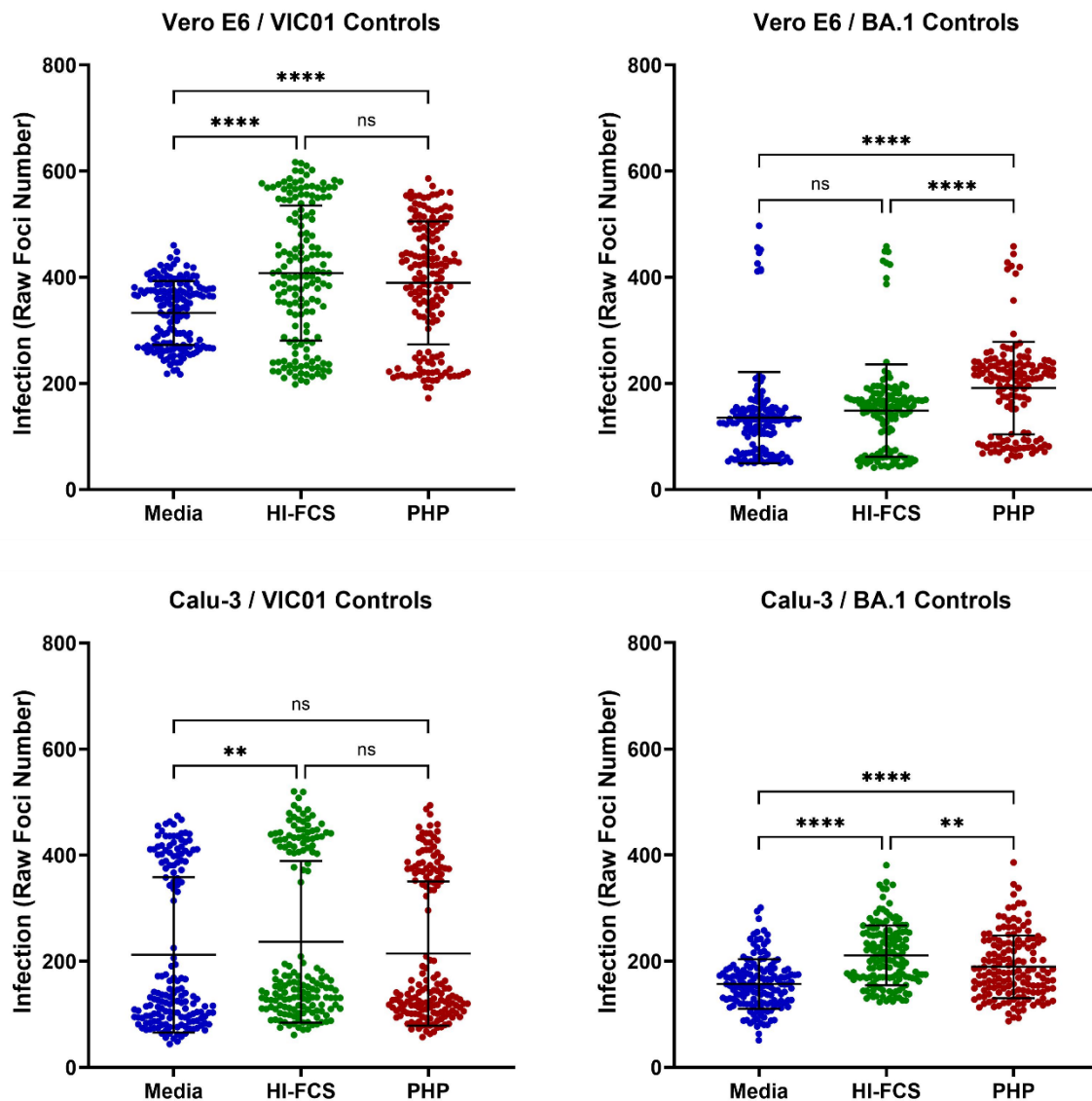
Supplementary Figure 2: (A) Cytotoxicity test using Calu-3 cells with media only, 20% pooled human plasma (PHP), 20% C3/C5 depleted plasma, or 1.8% DMSO as a positive control. Tearing from manual pipetting was evident in some conditions and cytotoxicity was evident only in the 1.8% DMSO condition. **(B)** Cytotoxicity test using Vero E6 cells with media only, 20% PHP, or 3% DMSO as a positive control. Conditions replicated the microneutralisation assay procedure and cells were stained with 0.2% crystal violet in 20% ethanol. Cytotoxicity was only evident in the 3% DMSO condition.

35 **Supplementary Figure 3:** Transmission electron microscopy images of SARS-CoV-
36 2 in the presence of OPTIC serum sample 10 and pooled human plasma (PHP). No
37 clear difference was observed between the virus-only condition and the addition of
38 immune sera with PHP or heat-inactivated PHP (HI-PHP). The black arrows indicate
39 examples of SARS-CoV-2 particles.

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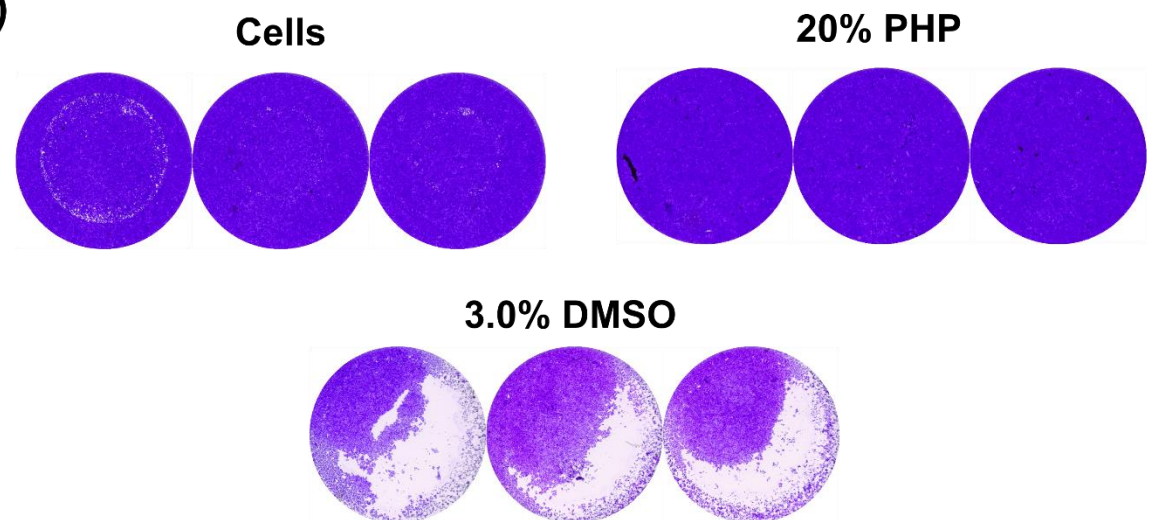
43 **Supplementary Figure 4:** Correlations with IgM and IgG binding to Coronavirus spike
44 proteins determined via MesoScale Discovery (MSD) against SARS-CoV-2 (VIC01
45 strain) neutralisation titres for the OCTAVE (n = 21) and OPTIC (n = 10) cohorts.
46 Corrected for multiple comparisons using Benjamini-Hochberg test (false discovery
47 rate < 0.05) in GraphPad Prism (version 10). * P <0.05, ** P <0.01, *** P < 0.001, ****
48 P <0.0001.
49
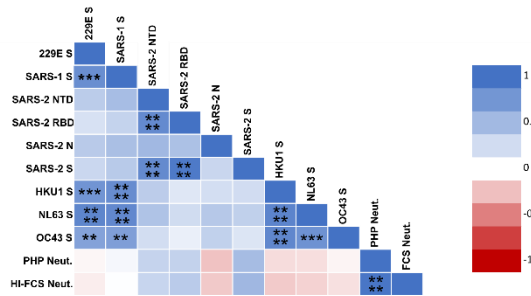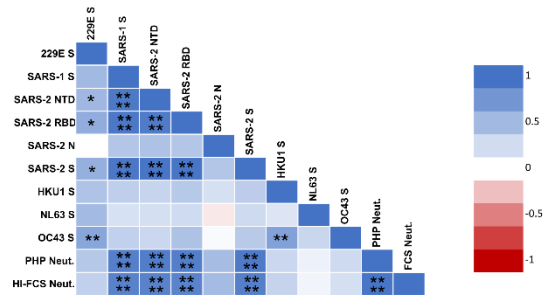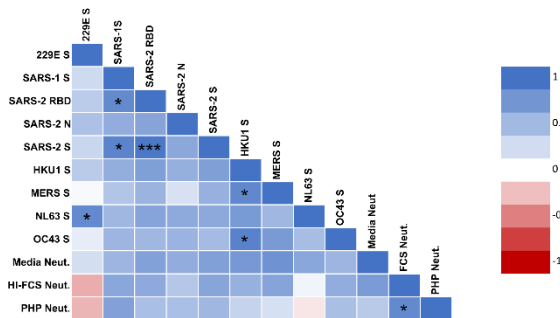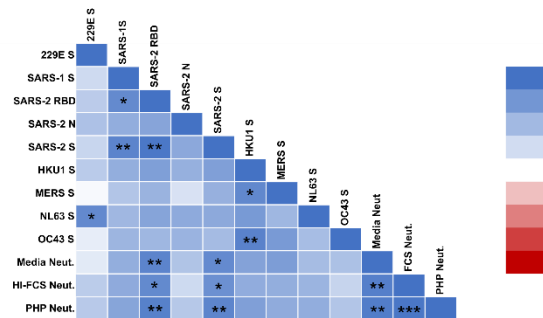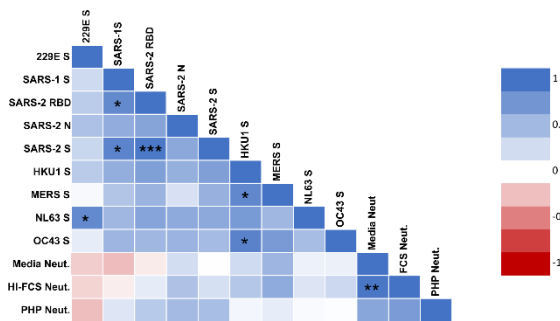
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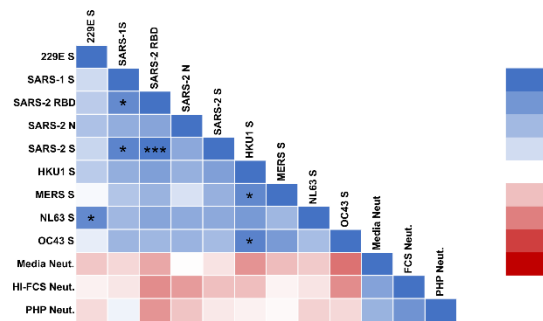
Supplementary Figure 5: Comparison of wild-type SARS-CoV-2 spike IgG titres between the OPTIC (n = 10) and OCTAVE (n = 21) cohorts as determined via MesoScale Discovery (MSD). Each spot represents the mean value of each sample tested in duplicate. Error bars show the mean and standard error. Significance was determined via an unpaired t test with Welch's correction. **** P <0.0001.