**Supplementary methods**

SARS-CoV-2 PCR and isolation in sputum and faeces

SARS CoV-2 PCR and virus isolation were performed as previously described [1]. In brief, Real time reverse transcription (RT) PCR testing for RdRP gene of SARS-CoV-2 was performed on material from a nasopharyngeal swabs in 200 μL of viral transport medium, and separately for sputum and faeces... Material from RT-PCR positive nasopharyngeal swab and sputum were used to inoculate a Vero/hSLAM cell line monolayer (European Collection of Authenticated Cell Cultures [ECACC] #04091501) and flasks were monitored for the development of viral cytopathic effect (CPE). On observation of CPE, aliquots were removed to assess virus burden by real time RT-PCR. Additionally, for faecal isolation, faeces was processed as a 10% suspension in viral transport medium (VTM), centrifuged at 3000 rpm for 5 minutes, and 100-500uL of supernatant applied to cells in a T25 flask. Medium was changed at 24 hours and replaced with fresh medium so that inoculum input was not a significant read burden by RT-PCR measurement. Medium was collected at day 7 at which time CPE was 100% (representing infection of 100% of cells).

Antibody responses to SARS-CoV-2

Microneutralisation assays were performed as previously described [2]. In brief, the ability of serial 2-fold dilutions of samples to neutralise the infectivity of 100 median tissue culture infectious doses of SARS-CoV-2 was assessed by inhibition of viral cytopathic effect in Vero cells. The neutralizing antibody titre was calculated using the Reed/Muench method.

Serological testing by Enzyme Linked Immunosorbent assay (ELISA) was performed in accordance to manufacturers’ Instructions For Use (IFU) with results reported semi-quantitatively as either a signal/cut-off ratio (for Euroimmun and Wantai assays) or percentage inhibition (for surrogate virus neutralization assay).

Euroimmun anti-SARS-CoV-2 Spike IgG, Spike IgA and Nucleocapsid IgG (Euroimmun Medizinische Labordiagnostika, Lubeck, Germany). These are indirect ELISAs for detection of immunoglobulin (Ig) class IgG or IgA against SARS-CoV-2 antigens. Microtitre plate wells are coated with either (i) spike (S) protein S1-domain or (ii) modified nucleocapsid protein (NCP). SARS-CoV-2 binding antibodies are detected using enzyme-labelled anti-human-IgG or anti-human-IgA conjugates; and a colourimetric substrate; the results are read spectrophotometrically.

Wantai IgM (Beijing Wantai Biological Pharmacy Enterprise, Beijing China).Wantai SARS-CoV-2 IgM is a capture ELISA for detection of IgM-class antibodies to SARS-CoV-2 virus. Anti-µ chain antibodies on the microtitre plate capture any patient IgM-class antibodies, and detection is by recombinant SARS-CoV-2-antigen-horseradish peroxidase (HRP) conjugate followed by a colourimetric substrate; and the results are read spectrophotometrically.

GenScript SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT). (GenScript USA, Inc. 860 Centennial Ave, Piscataway, NJ 08854). The sVNT is a blocking ELISA which mimics the virus neutralization process, detecting circulating neutralizing SARS-CoV-2 antibodies that block the interaction between the viral spike Receptor Binding Domain (RBD) and angiotensin converting enzyme 2 (ACE2) cell surface receptor of the host. The test is species and isotype independent. HRP conjugated recombinant SARS-CoV-2 RBD fragment binds to any circulating neutralizing antibodies to RBD preventing capture by the hACE2protein on the well which is subsequently removed in the following wash step. Substrate reaction incubation time is determined by temperature; the IFU indicating that the ideal reaction temperature and time are 25°C for 15 minutes. For temperatures lower than 25°C, the time can be extended. At 15 minutes our control values did not meet the assay validity criteria, but at 20 minutes they fell within the acceptable ranges. Therefore a 20 minute substrate incubation time was used and results read spectrophotometrically. Colour intensity is inversely dependent on the titer of anti-SARS-CoV-2 neutralizing antibodies. Surrogate virus neutralization (Genscript), Spike IgA (Euroimmun), Spike IgG (Euroimmun), NCP IgG (Euroimmun), IgM (Wantai) were performed in accordance with the manufacturer’s instructions.

Immune activation to SARS-CoV-2

Immune cell populations were measured by staining fresh whole blood as described previously [3]. In brief, aliquots of 200 ul whole blood were stained for immune cell activation (monocytes and T/B/NK/γδ T cells), TFH and ASC cell activation, and cytotoxicity profiles of T cell’s expressing intracellular granzymes (A, B, K and M) and perforin using 3 staining panels before undergoing RBC lysis, then fixation in 1% PFA or intracellularly staining using the eBioscienceTM Foxp3/Transcription Factor Staining Buffer Set (Thermo Fisher Scientific, Carlsbad, CA, USA). Samples were acquired on a BD LSRII Fortessa and analysed using FlowJo software v10 (FlowJo LLC, Ashland, OR, USA.

Viral genomics

Genomic sequencing and bioinformatic analysis were performed as previously described [4]. In brief, extracted RNA from SARS-CoV2 RT-PCR-positives samples underwent tiled amplicon PCR using both ARTIC version 1 and version 3 primers using published protocols, and Illumina sequencing. Reads were aligned to the reference genome (Wuhan-Hu-1; GenBank MN908947.3) and consensus sequences generated. We applied quality control checks on consensus sequences, requiring ≥80% genome recovered, ≤25 SNPs from the reference genome, and ≤300 ambiguous or missing bases for sequences to “pass” QC. Variants were identified from the consensus VCF file using bcftools query (v1.11) to create a matrix with positions of alternate alleles.

1. Caly L, Druce J, Roberts J, et al. Isolation and rapid sharing of the 2019 novel coronavirus (SARS-CoV-2) from the first patient diagnosed with COVID-19 in Australia. The Medical journal of Australia **2020**; 212:459-62.

2. Bond K, Nicholson S, Lim SM, et al. Evaluation of Serological Tests for SARS-CoV-2: Implications for Serology Testing in a Low-Prevalence Setting. The Journal of infectious diseases **2020**; 222:1280-8.

3. Thevarajan I, Nguyen THO, Koutsakos M, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nature medicine **2020**; 26:453-5.

4. Seemann T, Lane CR, Sherry NL, et al. Tracking the COVID-19 pandemic in Australia using genomics. Nature communications **2020**; 11:4376.