
Supplementary information

Prospects for durable immune control of SARS-CoV-2 and prevention of reinfection

In the format provided by the
authors and unedited

Supplementary Table 1 | **The decay of immune memory to coronavirus infections**

Data for Figure 1 in the main text were extracted from previously published studies on immune responses to SARS-CoV-2, SARS-CoV and human coronaviruses. The data for each reference are outlined below:

Reference	Reference number in main text	Virus species	Measure(s)	Information
Beaudoin-Bussi�res et al. (2020) ¹	17	SARS-CoV-2	Neutralizing antibody, IgG, IgA	Average values for area under the curve of anti-RBD IgG and IgA ELISAs were extracted from Figures 1A and 1C, respectively. We assumed maximal values at baseline (42 days) and calculated the drop one month later.
Beaudoin-Bussi�res et al. (2020) ¹	17	SARS-CoV-2	Neutralizing antibody	Neutralization half-maximal inhibitory plasma dilution values were extracted from Figure 3C. We assumed maximal values at baseline (42 days) and calculated the drop one month later.
Crawford et al. (2020) ²	15	SARS-CoV-2	Neutralizing antibody	Median fold decay in neutralising titre between days 30 and 90 was taken from the text.
Dan et al. (2021) ³	8	SARS-CoV-2	Neutralizing antibody, IgG, IgA	The half-lives for spike specific IgG and spike-specific IgA, as well as pseudovirus neutralising titre, were taken from the caption of Figure 1. Data from the longitudinal

				cohort was used. We assumed that the maximal response was at day 20 and that the measurement ended on day 240, as those are the limits of the data points.
Dan et al. (2021) ³	8	SARS-CoV-2	CD8 ⁺ T cells	Half-lives of spike-specific CD8 ⁺ T cells in the longitudinal cohort are taken from text.
Dan et al. (2021) ³	8	SARS-CoV-2	CD4 ⁺ T cells	Half-lives of spike-specific CD4 ⁺ T cells in the cross-sectional cohort are taken from text.
Dan et al. (2021) ³	8	SARS-CoV-2	Memory B cells	Percentage of spike-specific memory B cells present in the cross-sectional cohort is extracted from the red line in Figure 2l.
Ibarrondo et al. (2020) ⁴	14	SARS-CoV-2	IgG	Median starting day, and rate of decay of anti-SARS-CoV-2 IgG was taken from text.
Muecksch et al. (2021) ⁵	5	SARS-CoV-2	Neutralizing antibody	Average days of first and last measurements were taken from the text. A 45% reduction in neutralisation titre over the 4 weeks between visit 1 and visit 3 was also

				taken from the text.
Wajnberg et al. (2020) ⁶	7	SARS-CoV-2	Neutralizing antibody	Geometric mean neutralisation titres were read from Figure 3G and normalised to the value at day 30
Wajnberg et al. (2020) ⁶	7	SARS-CoV-2	IgG, IgA	Geometric mean antibody titres for spike-specific IgG and IgA were read from Figure 3A and 3D, respectively, and normalised to the value at day 30
Wu et al. (2020) ⁷	16	SARS-CoV-2	IgG	Curve fit to the IgG responses recognizing the RBD of spike detected by capture chemiluminescence immunoassays was extracted from Figure 1B
Yao et al. (2020) ⁸ (preprint)	18	SARS-CoV-2	Neutralizing antibody, IgG, IgA	The time of peak measurement concentration and half-lives for a pseudovirus-based neutralization assay, and RBD-specific IgG and IgA were taken from Table 2.
Gaebler et al. (2021) ⁹	2	SARS-CoV-2	IgG, IgA	Geometric mean area under the curve for ELISAs measuring plasma reactivity to RBD are extracted from the numbers in Figure 1e, showing the relative change in plasma antibody levels between 1.3

				and 6.2 months for anti-RBD IgG and IgA
Gaebler et al. (2021) ⁹	2	SARS-CoV-2	Memory B cells	Geometric mean of percentage of RBD-specific B cells was extracted from Figure 2B. We assumed that the maximum percent positive occurred at the final time point.
Sokal et al. (2021) ¹⁰	19	SARS-CoV-2	IgG	Linear regression of anti-SARS-Cov-2 spike protein serum IgG levels over time was taken from Figure 1C for both severe and mild infection groups.
Sokal et al. (2021) ¹⁰	19	SARS-CoV-2	Memory B cells	Linear regression of proportion of spike-specific memory B cells over time was taken from Figure 3E for both severe and mild infection groups.
Ellebedy et al. (2020) ¹¹ (preprint)	20	SARS-CoV-2	IgG	Half-lives of anti-spike IgG titres over two time intervals were taken from the first paragraph of the results section (lines 75-78).
Ellebedy et al. (2020) ¹¹ (preprint)	20	SARS-CoV-2	Memory B cells	Decay/increase of spike-specific memory B cells was estimated using pooled data (dots) extracted from Extended data Figure 1B.

Liu et al. (2006) ¹²	89	SARS-CoV	IgG	SARS-CoV IgG geometric mean reciprocal titres were extracted from Figure 1.
Liu et al. (2006) ¹²	89	SARS-CoV	Neutralizing antibody	Neutralizing antibody geometric mean reciprocal titres were extracted from Figure 1.
Tang et al. (2011) ¹³	90	SARS-CoV	IgG	Anti SARS-CoV IgG antibody titres were extracted from Figure 1.
Callow et al. (1990) ¹⁴	76	Human coronavirus	Neutralizing antibody, IgG, IgA	Serum specific IgG and IgA responses, as well as neutralisation titres, were extracted from data extracted from Figures 1A, 1B, 2B and 2C.
Widge et al. (2021) ¹⁵	69	SARS-CoV-2 vaccination	Neutralizing antibody, total immunoglobulin	Data on total RBD-specific immunoglobulin responses and neutralisation for three different assays on days 43 and 119 (pseudovirus, PRNT and FRNT) were extracted from Figure 1.
Wang et al. (2021) ¹⁶	91	SARS-CoV-2 vaccination	IgG	Anti-spike IgG responses over time since first and second dose were extracted from Figure 1F and Extended Data Figure 2H, respectively, for both Moderna and Pfizer vaccines. The

				pooled decay rate was calculated (F-test showed rates were not significantly different between groups).
Wang et al. (2021) ¹⁶	91	SARS-CoV-2 vaccination	Neutralizing antibody	Half-maximal neutralizing titres over time since first and second dose of vaccine for were extracted from Figure 1G and Extended Data Figure 2F, respectively, for both Moderna and Pfizer vaccines. The pooled decay rate was calculated (F-test showed rates were not significantly different between groups).

ELISA, enzyme-linked immunosorbent assay; FRNT, focus reduction neutralization test; PRNT, plaque reduction neutralization test; RBD, receptor binding domain of viral spike protein.

Supplementary Table 2 | Well documented cases of SARS-CoV-2 reinfection

Age, gender	Interval between infections (days)	Severity of infection (PCR Ct, where reported)		Sequence differences	Ref
		Primary infection	Secondary infection		
33, male	142	Mild	Asymptomatic	N.D.	17
25, male	48	Mild (35)	Severe (35)	N.D.	18
51, female	93	Mild (26–27)	Mild (33)	N.D.	19
46, male	62	Mild	Moderate	Clade 20A versus Clade 19B	20
89, female (immunocompromised)	59	5-day hospitalisation (26)	Severe (death) (25)	10 SNPs	21
39, female	185	Mild	Mild	Clade G versus Clade V, 17 SNPs	22
25, male	108	Asymptomatic (36)	Asymptomatic (17)	9 SNPs	23
28, female	111	Asymptomatic (28)	Asymptomatic (17)	10 SNPs	23
42, male	51	Mild	Severe	Unclear	24
Age of 60–69, gender not reported	140	Severe (23)	Moderate (43)	Clade 19B versus Clade 20A (10 SNPs)	25 (preprint)
27, male	66	Mild (32)	Mild (25)	8 SNPs	26 (preprint)
31, male	65	Asymptomatic (33)	Mild (36)	9 SNPs	26
27, male	19	Asymptomatic (36)	Mild (21)	9 SNPs	26
24, female	55	Mild (32)	Mild (17)	12 SNPs	26
36, female	204	Asymptomatic (29)	Mild (21)	Distinct nosocomial clusters	27
45, female	153	Mild (27)	Mild (more severe than primary infection) (17)	Lineage B.1.1.33 versus B.1.1.28.2	28

78, male	250	Mild (27)	Severe (27)	Lineage B.2 versus B.1.1.7	²⁹
----------	-----	--------------	----------------	----------------------------------	---------------

N.D., not determined; PCR Ct, polymerase chain reaction cycle threshold; SNP, single nucleotide polymorphism.

References

1. Beaudoin-Bussieres, G., *et al.* Decline of Humoral Responses against SARS-CoV-2 Spike in Convalescent Individuals. *mBio* **11**, e02590-02520 (2020).
2. Crawford, K.H.D., *et al.* Dynamics of neutralizing antibody titers in the months after SARS-CoV-2 infection. *J Infect Dis* **223**, 197-205 (2020).
3. Dan, J.M., *et al.* Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Science* **371**, eabf4063 (2021).
4. Ibarrondo, F.J., *et al.* Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19. *N Engl J Med* **383**, 1085-1087 (2020).
5. Muecksch, F., *et al.* Longitudinal Serological Analysis and Neutralizing Antibody Levels in Coronavirus Disease 2019 Convalescent Patients. *J Infect Dis* **223**, 389-398 (2021).
6. Wajnberg, A., *et al.* Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. *Science* **370**, 1227-1230 (2020).
7. Wu, J., *et al.* SARS-CoV-2 infection induces sustained humoral immune responses in convalescent patients following symptomatic COVID-19. *Nat Commun* **12**, 1813 (2021).
8. Yao, X.-Y., *et al.* Neutralizing and binding antibody kinetics of COVID-19 patients during hospital and convalescent phases. Preprint at *medRxiv* <https://doi.org/10.1101/2020.07.18.20156810> (2020).
9. Gaebler, C., *et al.* Evolution of antibody immunity to SARS-CoV-2. *Nature* **591**, 639-644 (2021).
10. Sokal, A., *et al.* Maturation and persistence of the anti-SARS-CoV-2 memory B cell response. *Cell* **184**, 1201-1213 e1214 (2021).
11. Ellebedy, A., *et al.* SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. Preprint at *Research Square* <https://doi.org/10.21203/rs.3.rs-132821/v1> (2020).
12. Liu, W., *et al.* Two-year prospective study of the humoral immune response of patients with severe acute respiratory syndrome. *J Infect Dis* **193**, 792-795 (2006).
13. Tang, F., *et al.* Lack of peripheral memory B cell responses in recovered patients with severe acute respiratory syndrome: a six-year follow-up study. *J Immunol* **186**, 7264-7268 (2011).
14. Callow, K.A., Parry, H.F., Sergeant, M. & Tyrrell, D.A. The time course of the immune response to experimental coronavirus infection of man. *Epidemiol Infect* **105**, 435-446 (1990).
15. Widge, A.T., *et al.* Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination. *N Engl J Med* **384**, 80-82 (2021).
16. Wang, Z., *et al.* mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. *Nature* <https://doi.org/10.1038/s41586-021-03324-6> (2021).
17. To, K.K., *et al.* COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1275> (2020).
18. Tillett, R.L., *et al.* Genomic evidence for reinfection with SARS-CoV-2: a case study. *The Lancet Infectious Diseases* **21**, 52-58 (2021).
19. Van Elslande, J., *et al.* Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1330> (2020).

20. Prado-Vivar, B., *et al.* A case of SARS-CoV-2 reinfection in Ecuador. *The Lancet Infectious Diseases* [https://doi.org/10.1016/S1473-3099\(20\)30910-5](https://doi.org/10.1016/S1473-3099(20)30910-5) (2020).
21. Mulder, M., *et al.* Reinfection of SARS-CoV-2 in an immunocompromised patient: a case report. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1538> (2020).
22. Selhorst, P., *et al.* Symptomatic SARS-CoV-2 reinfection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1850> (2020).
23. Gupta, V., *et al.* Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1451> (2020).
24. Larson, D., *et al.* A Case of Early Re-infection with SARS-CoV-2. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciaa1436> (2020).
25. Goldman, J.D., *et al.* Reinfection with SARS-CoV-2 and Failure of Humoral Immunity: a case report. Preprint at *medRxiv* <https://doi.org/10.1101/2020.09.22.20192443> (2020).
26. Shastri, J., *et al.* Whole Genome Sequencing Confirmed SARS-CoV-2 Reinfections Among Healthcare Workers in India with Increased Severity in the Second Episode. Preprint at *SSRN* <https://dx.doi.org/10.2139/ssrn.3688220> (2021).
27. Vetter, P., *et al.* Clinical, virological and immunological features of a mild case of SARS-CoV-2 re-infection. *Clin Microbiol Infect* <https://doi.org/10.1016/j.cmi.2021.02.010> (2021).
28. Nonaka, C.K.V., *et al.* Genomic Evidence of SARS-CoV-2 Reinfection Involving E484K Spike Mutation, Brazil. *Emerg Infect Dis* <https://doi.org/10.3201/eid2705.210191> (2021).
29. Harrington, D., *et al.* Confirmed Reinfection with SARS-CoV-2 Variant VOC-202012/01. *Clin Infect Dis* <https://doi.org/10.1093/cid/ciab014> (2021).