

IgA dominates the early neutralizing antibody response to SARS-CoV-2

[Delphine Sterlin](#)^{1,2,3}, [Alexis Mathian](#)^{1,4}, [Makoto Miyara](#)^{1,2}, [Audrey Mohr](#)¹, [François Anna](#)^{5,6}, [Laetitia Claër](#)¹, [Paul Quentric](#)¹, [Jehane Fadlallah](#)^{1,4}, [Hervé Devilliers](#)⁷, [Pascale Ghillani](#)², [Cary Gunn](#)⁸, [Rick Hockett](#)⁸, [Sasi Mudumba](#)⁸, [Amélie Guihot](#)^{1,2}, [Charles-Edouard Luyt](#)^{9,10}, [Julien Mayaux](#)¹¹, [Alexandra Beurton](#)^{11,12}, [Salma Fourati](#)^{13,14}, [Timothée Bruel](#)^{15,16,17}, [Olivier Schwartz](#)^{15,16,17}, [Jean-Marc Lacorte](#)^{10,13}, [Hans Yssel](#)¹, [Christophe Parizot](#)^{1,2}, [Karim Dorgham](#)¹, [Pierre Charneau](#)^{5,6}, [Zahir Amoura](#)^{1,4}, [Guy Gorochov](#)^{18,2}

Affiliations [expand](#)

- PMID: 33288662
- PMCID: [PMC7857408](#)
- DOI: [10.1126/scitranslmed.abd2223](#)

[Free PMC article](#)

Abstract

Humoral immune responses are typically characterized by primary IgM antibody responses followed by secondary antibody responses associated with immune memory and composed of IgG, IgA, and IgE. Here, we measured acute humoral responses to SARS-CoV-2, including the frequency of antibody-secreting cells and the presence of SARS-CoV-2-specific neutralizing antibodies in the serum, saliva, and bronchoalveolar fluid of 159 patients with COVID-19. Early SARS-CoV-2-specific humoral responses were dominated by IgA antibodies. Peripheral expansion of IgA plasmablasts with mucosal homing potential was detected shortly after the onset of symptoms and peaked during the third week of the disease. The virus-specific antibody responses included IgG, IgM, and IgA, but IgA contributed to virus neutralization to a greater extent compared with IgG. Specific IgA serum concentrations decreased notably 1 month after the onset of symptoms, but

neutralizing IgA remained detectable in saliva for a longer time (days 49 to 73 post-symptoms). These results represent a critical observation given the emerging information as to the types of antibodies associated with optimal protection against reinfection and whether vaccine regimens should consider targeting a potent but potentially short-lived IgA response.

Copyright © 2021 The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. Distributed under a Creative Commons Attribution License 4.0 (CC BY).

Figures

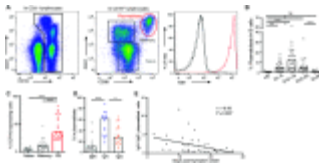


Fig. 1. Plasmablast dynamics after SARS-CoV-2 infection.

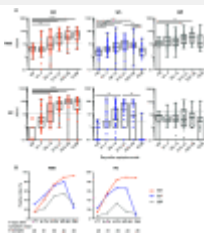


Fig. 2. Antibody response kinetics to SARS-CoV-2...

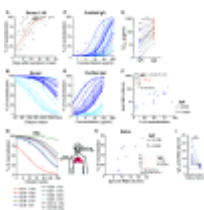


Fig. 3. Neutralizing activity of serum, BAL...

Similar articles

- [Enhanced SARS-CoV-2 neutralization by dimeric IgA.](#)

Wang Z, Lorenzi JCC, Muecksch F, Finkin S, Viant C, Gaebler C, Cipolla M, Hoffmann HH, Oliveira TY, Oren DA, Ramos V, Nogueira L, Michailidis E, Robbiani DF, Gazumyan A, Rice CM, Hatzioannou T, Bieniasz PD, Caskey M, Nussenzweig MC. *Sci Transl Med*. 2021 Jan 20;13(577):eabf1555. doi: 10.1126/scitranslmed.abf1555. Epub 2020 Dec 7. PMID: 33288661 **Free PMC article.**

- [Comparative analyses of SARS-CoV-2 binding \(IgG, IgM, IgA\) and neutralizing antibodies from human serum samples.](#)

Mazzini L, Martinuzzi D, Hyseni I, Benincasa L, Molesti E, Casa E, Lapini G, Piu P, Trombetta CM, Marchi S, Razzano I, Manenti A, Montomoli E. *J Immunol Methods*. 2021 Feb;489:112937. doi: 10.1016/j.jim.2020.112937. Epub 2020 Nov 28. PMID: 33253698 **Free PMC article.**

- [Screening for SARS-CoV-2 antibodies in convalescent plasma in Brazil: Preliminary lessons from a voluntary convalescent donor program.](#)

Wendel S, Kutner JM, Machado R, Fontão-Wendel R, Bub C, Fachini R, Yokoyama A, Candelaria G, Sakashita A, Achkar R, Hamerschlak N, Scuracchio P, Amaral M, Dal Ben M, Araujo D, Soares C, Camargo A, Kallás E, Durigon E, Reis LF, Rizzo LV. *Transfusion*. 2020 Dec;60(12):2938-2951. doi: 10.1111/trf.16065. Epub 2020 Sep 16. PMID: 32935877 **Free PMC article.**

- [IgA Antibodies and IgA Deficiency in SARS-CoV-2 Infection.](#)

Quinti I, Mortari EP, Fernandez Salinas A, Milito C, Carsetti R. *Front Cell Infect Microbiol*. 2021 Apr 6;11:655896. doi: 10.3389/fcimb.2021.655896. eCollection 2021. PMID: 33889552 **Free PMC article.** Review.

- [Humoral Immunity against SARS-CoV-2 and the Impact on COVID-19 Pathogenesis.](#)

Lee E, Oh JE. *Mol Cells*. 2021 Jun 30;44(6):392-400. doi: 10.14348/molcells.2021.0075. PMID: 34059562 **Free PMC article.** Review.

See all similar articles

Cited by 292 articles

- [Teleost swim bladder, an ancient air-filled organ that elicits mucosal immune responses.](#)

Yu Y, Huang Z, Kong W, Dong F, Zhang X, Zhai X, Cheng G, Zhan M, Cao J, Ding L, Han G, Takizawa F, Ding Y, Oriol Sunyer J, Xu Z. *Cell Discov.* 2022 Apr 5;8(1):31. doi: 10.1038/s41421-022-00393-3. PMID: 35379790

- [Glomerular Disease in Temporal Association with SARS-CoV-2 Vaccination: A Series of 29 Cases.](#)

Caza TN, Cassol CA, Messias N, Hannoudi A, Haun RS, Walker PD, May RM, Seipp RM, Betchick EJ, Amin H, Ziadie MS, Haderlie M, Eduwu-Okwuwa J, Vancea I, Seek M, Elashi EB, Shenoy G, Khalillullah S, Flaxenburg JA, Brandt J, Diamond MJ, Frome A, Kim EH, Schlessinger G, Ulozas E, Weatherspoon JL, Hoerschgen ET, Fabian SL, Bae SY, Iqbal B, Chouhan KK, Karam Z, Henry JT, Larsen CP. *Kidney360.* 2021 Sep 16;2(11):1770-1780. doi: 10.34067/KID.0005372021. eCollection 2021 Nov 25. PMID: 35372991 **Free PMC article.**

- [Leveraging Antibody, B Cell and Fc Receptor Interactions to Understand Heterogeneous Immune Responses in Tuberculosis.](#)

Carpenter SM, Lu LL. *Front Immunol.* 2022 Mar 17;13:830482. doi: 10.3389/fimmu.2022.830482. eCollection 2022. PMID: 35371092 **Free PMC article.** Review.

- [Comorbidities and clinical complications associated with SARS-CoV-2 infection: an overview.](#)

Gupta A, Marzook H, Ahmad F. *Clin Exp Med.* 2022 Apr 1:1-19. doi: 10.1007/s10238-022-00821-4. Online ahead of print. PMID: 35362771 **Free PMC article.** Review.

- [Heterologous Immune Responses of Serum IgG and Secretory IgA Against the Spike Protein of Endemic Coronaviruses During Severe COVID-19.](#)

Smit WL, van Tol S, van der Wal S, van Vulpen F, la Grouw S, van Lelyveld L, Limonard G, Bossink A, Godeke GJ, Shrestha S, Reimerink J, Eggink D, Reusken C, Heron M, Thijsen S. *Front Immunol.* 2022 Mar 9;13:839367. doi:

10.3389/fimmu.2022.839367. eCollection 2022.PMID: 35355988 **Free PMC article.**

See all "Cited by" articles

References

1.
 0. Su S., Wong G., Shi W., Liu J., Lai A. C. K., Zhou J., Liu W., Bi Y., Gao G. F., Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol.* 24, 490–502 (2016). - [PMC](#) - [PubMed](#)
2.
 0. Long Q.-X., Liu B.-Z., Deng H.-J., Wu G.-C., Deng K., Chen Y.-K., Liao P., Qiu J.-F., Lin Y., Cai X.-F., Wang D.-Q., Hu Y., Ren J.-H., Tang N., Xu Y.-Y., Yu L.-H., Mo Z., Gong F., Zhang X.-L., Tian W.-G., Hu L., Zhang X.-X., Xiang J.-L., Du H.-X., Liu H.-W., Lang C.-H., Luo X.-H., Wu S.-B., Cui X.-P., Zhou Z., Zhu M.-M., Wang J., Xue C.-J., Li X.-F., Wang L., Li Z.-J., Wang K., Niu C.-C., Yang Q.-J., Tang X.-J., Zhang Y., Liu X.-M., Li J.-J., Zhang D.-C., Zhang F., Liu P., Yuan J., Li Q., Hu J.-L., Chen J., Huang A.-L., Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat. Med.* 26, 845–848 (2020). - [PubMed](#)
3.
 0. Guo L., Ren L., Yang S., Xiao M., Chang D., Yang F., Dela Cruz C. S., Wang Y., Wu C., Xiao Y., Zhang L., Han L., Dang S., Xu Y., Yang Q.-W., Xu S.-Y., Zhu H.-D., Xu Y.-C., Jin Q., Sharma L., Wang L., Wang J., Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin. Infect. Dis.* 71, 778–785 (2020). - [PMC](#) - [PubMed](#)
4.
 0. Okba N. M. A., Müller M. A., Li W., Wang C., GeurtsvanKessel C. H., Corman V. M., Lamers M. M., Sikkema R. S., de Bruin E., Chandler F. D., Yazdanpanah Y., Le Hingrat Q., Descamps D., Houhou-Fidouh N., Reusken C. B. E. M., Bosch B.-J., Drosten C., Koopmans M. P. G., Haagmans B. L., Severe acute respiratory syndrome coronavirus 2-specific antibody responses in coronavirus disease patients. *Emerg. Infect. Dis.* 26, 1478–1488 (2020). - [PMC](#) - [PubMed](#)
5.
 0. Mazanec M. B., Coudret C. L., Fletcher D. R., Intracellular neutralization of influenza virus by immunoglobulin A anti-hemagglutinin monoclonal antibodies. *J. Virol.* 69, 1339–1343 (1995). - [PMC](#) - [PubMed](#)

6.
 0. Mazanec M. B., Kaetzel C. S., Lamm M. E., Fletcher D., Peterra J., Nedrud J. G., Intracellular neutralization of Sendai and influenza viruses by IgA monoclonal antibodies. *Adv. Exp. Med. Biol.* 371A, 651–654 (1995).
- [PubMed](#)
7.
 0. Planque S., Salas M., Mitsuda Y., Siencyk M., Escobar M. A., Mooney J. P., Morris M.-K., Nishiyama Y., Ghosh D., Kumar A., Gao F., Hanson C. V., Paul S., Neutralization of genetically diverse HIV-1 strains by IgA antibodies to the gp120-CD4-binding site from long-term survivors of HIV infection. *AIDS* 24, 875–884 (2010). - [PMC](#) - [PubMed](#)
8.
 0. Devito C., Hinkula J., Kaul R., Lopalco L., Bwayo J. J., Plummer F., Clerici M., Broliden K., Mucosal and plasma IgA from HIV-exposed seronegative individuals neutralize a primary HIV-1 isolate. *AIDS* 14, 1917–1920 (2000). - [PubMed](#)
9.
 0. Liew F. Y., Russell S. M., Appleyard G., Brand C. M., Beale J., Cross-protection in mice infected with influenza A virus by the respiratory route is correlated with local IgA antibody rather than serum antibody or cytotoxic T cell reactivity. *Eur. J. Immunol.* 14, 350–356 (1984).
- [PubMed](#)
10.
 0. Asahi-Ozaki Y., Yoshikawa T., Iwakura Y., Suzuki Y., Tamura S.-i., Kurata T., Sata T., Secretory IgA antibodies provide cross-protection against infection with different strains of influenza B virus. *J. Med. Virol.* 74, 328–335 (2004). - [PubMed](#)
11.
 0. Aina A., Tamura S.-i., Suzuki T., van Riet E., Ito R., Odagiri T., Tashiro M., Kurata T., Hasegawa H., Intranasal vaccination with an inactivated whole influenza virus vaccine induces strong antibody responses in serum and nasal mucus of healthy adults. *Hum. Vaccin. Immunother.* 9, 1962–1970 (2013). - [PMC](#) - [PubMed](#)
12.
 0. See R. H., Zakhartchouk A. N., Petric M., Lawrence D. J., Mok C. P. Y., Hogan R. J., Rowe T., Zitzow L. A., Karunakaran K. P., Hitt M. M., Graham F. L., Prevec L., Mahony J. B., Sharon C., Auperin T. C., Rini J. M., Tingle A. J., Scheifele D. W., Skowronski D. M., Patrick D. M., Voss T. G., Babiuk L.

- A., Gauldie J., Roper R. L., Brunham R. C., Finlay B. B., Comparative evaluation of two severe acute respiratory syndrome (SARS) vaccine candidates in mice challenged with SARS coronavirus. *J. Gen. Virol.* 87, 641–650 (2006). - [PubMed](#)
- 13.
0. Kim M. H., Kim H. J., Chang J., Superior immune responses induced by intranasal immunization with recombinant adenovirus-based vaccine expressing full-length Spike protein of Middle East respiratory syndrome coronavirus. *PLOS ONE* 14, e0220196 (2019).
- [PMC](#) - [PubMed](#)
- 14.
0. Fink K., Origin and function of circulating plasmablasts during acute viral infections. *Front. Immunol.* 3, 78 (2012). - [PMC](#) - [PubMed](#)
- 15.
0. Xiong N., Fu Y., Hu S., Xia M., Yang J., CCR10 and its ligands in regulation of epithelial immunity and diseases. *Protein Cell* 3, 571–580 (2012). - [PMC](#) - [PubMed](#)
- 16.
0. Mei H. E., Yoshida T., Sime W., Hiepe F., Thiele K., Manz R. A., Radbruch A., Dörner T., Blood-borne human plasma cells in steady state are derived from mucosal immune responses. *Blood* 113, 2461–2469 (2009).
- [PubMed](#)
- 17.
0. Thevarajan I., Nguyen T. H. O., Koutsakos M., Druce J., Caly L., van de Sandt C. E., Jia X., Nicholson S., Catton M., Cowie B., Tong S. Y. C., Lewin S. R., Kedzierska K., Breadth of concomitant immune responses prior to patient recovery: A case report of non-severe COVID-19. *Nat. Med.* 26, 453–455 (2020). - [PMC](#) - [PubMed](#)
- 18.
0. Miyara M., Charuel J.-L., Mudumba S., Wu A., Ghillani-Dalbin P., Amoura Z., Burlingame R. W., Musset L., Detection in whole blood of autoantibodies for the diagnosis of connective tissue diseases in near patient testing condition. *PLOS ONE* 13, e0202736 (2018).
- [PMC](#) - [PubMed](#)
- 19.
0. Mudumba S., de Alba S., Romero R., Cherwien C., Wu A., Wang J., Gleeson M. A., Iqbal M., Burlingame R. W., Photonic ring resonance is a

versatile platform for performing multiplex immunoassays in real time. *J. Immunol. Methods* 448, 34–43 (2017). - [PubMed](#)

20.

0. Grzelak L., Temmam S., Planchais C., Demeret C., Tondeur L., Huon C., Guivel-Benhassine F., Staropoli I., Chazal M., Dufloo J., Planas D., Buchrieser J., Rajah M. M., Robinot R., Porrot F., Albert M., Chen K.-Y., Crescenzo-Chaigne B., Donati F., Anna F., Souque P., Gransagne M., Bellalou J., Nowakowski M., Backovic M., Bouadma L., Le Fevre L., Le Hingrat Q., Descamps D., Pourbaix A., Laouénan C., Ghosn J., Yazdanpanah Y., Besombes C., Jolly N., Pellerin-Fernandes S., Cheny O., Ungeheuer M.-N., Mellon G., Morel P., Rolland S., Rey F. A., Behillil S., Enouf V., Lemaitre A., Créach M.-A., Petres S., Escriou N., Charneau P., Fontanet A., Hoen B., Bruel T., Eloit M., Mouquet H., Schwartz O., van der Werf S., A comparison of four serological assays for detecting anti-SARS-CoV-2 antibodies in human serum samples from different populations. *Sci. Transl. Med.* 12, eabc3103 (2020). - [PMC](#) - [PubMed](#)

21.

0. Buchrieser J., Dufloo J., Hubert M., Monel B., Planas D., Rajah M. M., Planchais C., Porrot F., Guivel-Benhassine F., Van der Werf S., Casartelli N., Mouquet H., Bruel T., Schwartz O., Syncytia formation by SARS-CoV-2-infected cells. *EMBO J.* 39, e106267 (2020). - [PMC](#) - [PubMed](#)

22.

0. Brann D. H., Tsukahara T., Weinreb C., Lipovsek M., Van den Berge K., Gong B., Chance R., Macaulay I. C., Chou H.-J., Fletcher R. B., Das D., Street K., de Bezieux H. R., Choi Y.-G., Risso D., Dudoit S., Purdom E., Mill J. S., Hachem R. A., Matsunami H., Logan D. W., Goldstein B. J., Grubb M. S., Ngai J., Datta S. R., Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia. *Sci. Adv.* 6, eabc5801 (2020). - [PubMed](#)

23.

0. L. Fodouliau, J. Tuberosa, D. Rossier, B. N. Landis, A. Carleton, I. Rodriguez, SARS-CoV-2 receptor and entry genes are expressed by sustentacular cells in the human olfactory neuroepithelium. *bioRxiv* 2020.03.31.013268 [Preprint]. 2 April 2020. 10.1101/2020.03.31.013268. - [DOI](#)

24.

0. Reynolds H. Y., Immunoglobulin G and its function in the human respiratory tract. *Mayo Clin. Proc.* 63, 161–174 (1988). - [PubMed](#)

- 25.
0. Waldman R. H., Jurgensen P. F., Olsen G. N., Ganguly R., Johnson J. E. III, Immune response of the human respiratory tract. I. Immunoglobulin levels and influenza virus vaccine antibody response. *J. Immunol.* 111, 38–41 (1973). - [PubMed](#)
- 26.
0. Ejemel M., Li Q., Hou S., Schiller Z. A., Tree J. A., Wallace A., Amcheslavsky A., Kurt Yilmaz N., Buttigieg K. R., Elmore M. J., Godwin K., Coombes N., Toomey J. R., Schneider R., Ramchetty A. S., Close B. J., Chen D.-Y., Conway H. L., Saeed M., Ganesa C., Carroll M. W., Cavacini L. A., Klempner M. S., Schiffer C. A., Wang Y., A cross-reactive human IgA monoclonal antibody blocks SARS-CoV-2 spike-ACE2 interaction. *Nat. Commun.* 11, 4198 (2020). - [PMC](#) - [PubMed](#)
- 27.
0. Boehm M. K., Woof J. M., Kerr M. A., Perkins S. J., The Fab and Fc fragments of IgA1 exhibit a different arrangement from that in IgG: A study by X-ray and neutron solution scattering and homology modelling. *J. Mol. Biol.* 286, 1421–1447 (1999). - [PubMed](#)
- 28.
0. Muramatsu M., Yoshida R., Yokoyama A., Miyamoto H., Kajihara M., Maruyama J., Nao N., Manzoor R., Takada A., Comparison of antiviral activity between IgA and IgG specific to influenza virus hemagglutinin: Increased potential of IgA for heterosubtypic immunity. *PLOS ONE* 9, e85582 (2014). - [PMC](#) - [PubMed](#)
- 29.
0. Wec A. Z., Wrapp D., Herbert A. S., Maurer D. P., Haslwanter D., Sakharkar M., Jangra R. K., Dieterle M. E., Lilov A., Huang D., Tse L. V., Johnson N. V., Hsieh C.-L., Wang N., Nett J. H., Champney E., Burnina I., Brown M., Lin S., Sinclair M., Johnson C., Pudi S., Bortz R. III, Wirchnianski A. S., Laudermilch E., Florez C., Fels J. M., O'Brien C. M., Graham B. S., Nemazee D., Burton D. R., Baric R. S., Voss J. E., Chandran K., Dye J. M., McLellan J. S., Walker L. M., Broad neutralization of SARS-related viruses by human monoclonal antibodies. *Science* 369, 731–736 (2020). - [PMC](#) - [PubMed](#)
- 30.
0. Wang Z., Lorenzi J. C. C., Muecksch F., Finkin S., Viant C., Gaebler C., Cipolla M., Hoffmann H.-H., Oliveira T. Y., Oren D. A., Ramos V., Nogueira L., Michailidis E., Robbiani D. F., Gazumyan A., Rice C. M.,

- Hatzioannou T., Bieniasz P. D., Caskey M., Nussenzweig M. C., Enhanced SARS-CoV-2 neutralization by dimeric IgA. *Sci. Transl. Med.* 13, eabf1555 (2021). - [PMC](#) - [PubMed](#)
31. 0. Burnett D., Immunoglobulins in the lung. *Thorax* 41, 337–344 (1986). - [PMC](#) - [PubMed](#)
32. 0. Stockley R. A., Mistry M., Bradwell A. R., Burnett D., A study of plasma proteins in the sol phase of sputum from patients with chronic bronchitis. *Thorax* 34, 777–782 (1979). - [PMC](#) - [PubMed](#)
33. 0. Iversen R., Snir O., Stensland M., Kroll J. E., Steinsbø Ø., Korponay-Szabó I. R., Lundin K. E. A., de Souza G. A., Sollid L. M., Strong clonal relatedness between serum and gut IgA despite different plasma cell origins. *Cell Rep.* 20, 2357–2367 (2017). - [PMC](#) - [PubMed](#)
34. 0. Bunker J. J., Erickson S. A., Flynn T. M., Henry C., Koval J. C., Meisel M., Jabri B., Antonopoulos D. A., Wilson P. C., Bendelac A., Natural polyreactive IgA antibodies coat the intestinal microbiota. *Science* 358, eaan6619 (2017). - [PMC](#) - [PubMed](#)
35. 0. Dullaers M., Li D., Xue Y., Ni L., Gayet I., Morita R., Ueno H., Palucka K. A., Banchereau J., Oh S., A T cell-dependent mechanism for the induction of human mucosal homing immunoglobulin A-secreting plasmablasts. *Immunity* 30, 120–129 (2009). - [PMC](#) - [PubMed](#)
36. 0. Nakayama T., Hieshima K., Izawa D., Tatsumi Y., Kanamaru A., Yoshie O., Cutting edge: Profile of chemokine receptor expression on human plasma cells accounts for their efficient recruitment to target tissues. *J. Immunol.* 170, 1136–1140 (2003). - [PubMed](#)
37. 0. Mora J. R., Iwata M., Eksteen B., Song S.-Y., Junt T., Senman B., Otipoby K. L., Yokota A., Takeuchi H., Ricciardi-Castagnoli P., Rajewsky K., Adams D. H., von Andrian U. H., Generation of gut-homing IgA-secreting B cells by intestinal dendritic cells. *Science* 314, 1157–1160 (2006). - [PubMed](#)
- 38.

0. Lin M., Du L., Brandtzaeg P., Pan-Hammarström Q., IgA subclass switch recombination in human mucosal and systemic immune compartments. *Mucosal Immunol.* 7, 511–520 (2014). - [PubMed](#)
- 39.
0. He B., Xu W., Santini P. A., Polydorides A. D., Chiu A., Estrella J., Shan M., Chadburn A., Villanacci V., Plebani A., Knowles D. M., Rescigno M., Cerutti A., Intestinal bacteria trigger T cell-independent immunoglobulin A2 class switching by inducing epithelial-cell secretion of the cytokine APRIL. *Immunity* 26, 812–826 (2007). - [PubMed](#)
- 40.
0. Berkowska M. A., Driessen G. J. A., Bikos V., Grosserichter-Wagener C., Stamatopoulos K., Cerutti A., He B., Biermann K., Lange J. F., van der Burg M., van Dongen J. J. M., van Zelm M. C., Human memory B cells originate from three distinct germinal center-dependent and - independent maturation pathways. *Blood* 118, 2150–2158 (2011). - [PMC](#) - [PubMed](#)
- 41.
0. Ju B., Zhang Q., Ge J., Wang R., Sun J., Ge X., Yu J., Shan S., Zhou B., Song S., Tang X., Yu J., Lan J., Yuan J., Wang H., Zhao J., Zhang S., Wang Y., Shi X., Liu L., Zhao J., Wang X., Zhang Z., Zhang L., Human neutralizing antibodies elicited by SARS-CoV-2 infection. *Nature* 584, 115–119 (2020). - [PubMed](#)
- 42.
0. Shi R., Shan C., Duan X., Chen Z., Liu P., Song J., Song T., Bi X., Han C., Wu L., Gao G., Hu X., Zhang Y., Tong Z., Huang W., Liu W. J., Wu G., Zhang B., Wang L., Qi J., Feng H., Wang F.-S., Wang Q., Gao G. F., Yuan Z., Yan J., A human neutralizing antibody targets the receptor binding site of SARS-CoV-2. *Nature* 584, 120–124 (2020). - [PubMed](#)
- 43.
0. Lu X., Zhang L., Du H., Zhang J., Li Y. Y., Qu J., Zhang W., Wang Y., Bao S., Li Y., Wu C., Liu H., Liu D., Shao J., Peng X., Yang Y., Liu Z., Xiang Y., Zhang F., Silva R. M., Pinkerton K. E., Shen K., Xiao H., Xu S., Wong G. W. K.; Chinese Pediatric Novel Coronavirus Study Team , SARS-CoV-2 infection in children. *N. Engl. J. Med.* 382, 1663–1665 (2020). - [PMC](#) - [PubMed](#)
- 44.
0. Zimmermann P., Curtis N., Coronavirus infections in children including COVID-19: An overview of the epidemiology, clinical features, diagnosis,

treatment and prevention options in children. *Pediatr. Infect. Dis. J.* 39, 355–368 (2020). - [PMC](#) - [PubMed](#)

45.

0. Sterlin D., Fadlallah J., Adams O., Fieschi C., Parizot C., Dorgham K., Rajkumar A., Autaa G., El-Kafsi H., Charuel J.-L., Juste C., Jönsson F., Candela T., Wardemann H., Aubry A., Capito C., Brisson H., Tresallet C., Cummings R. D., Larsen M., Yssel H., von Gunten S., Gorochov G., Human IgA binds a diverse array of commensal bacteria. *J. Exp. Med.* 217, e20181635 (2020). - [PMC](#) - [PubMed](#)

46.

0. M. Norman, T. Gilboa, A. F. Ogata, A. M. Maley, L. Cohen, Y. Cai, J. Zhang, J. E. Feldman, B. M. Hauser, T. M. Caradonna, B. Chen, A. G. Schmidt, G. Alter, R. C. Charles, E. T. Ryan, D. R. Walt, Ultra-sensitive high-resolution profiling of anti-SARS-CoV-2 antibodies for detecting early seroconversion in COVID-19 patients. medRxiv 2020.04.28.20083691. (2020).

47.

0. Yu H.-q., Sun B.-q., Fang Z.-f., Zhao J.-c., Liu X.-y., Li Y.-m., Sun X.-z., Liang H.-f., Zhong B., Huang Z.-f., Zheng P.-y., Tian L.-f., Qu H.-q., Liu D.-c., Wang E.-y., Xiao X.-j., Li S.-y., Ye F., Guan L., Hu D.-s., Hakonarson H., Liu Z.-g., Zhong N.-s., Distinct features of SARS-CoV-2-specific IgA response in COVID-19 patients. *Eur. Respir. J.* 56, 2001526 (2020). - [PMC](#) - [PubMed](#)

48.

0. Iglesias M. C., Mollier K., Beignon A.-S., Souque P., Adotevi O., Lemonnier F., Charneau P., Lentiviral vectors encoding HIV-1 polyepitopes induce broad CTL responses in vivo. *Mol. Ther.* 15, 1203–1210 (2007). - [PubMed](#)