This report focuses on neutralizing antibodies:

1. **Epitope RBD-A as the preferred target for eliciting neutralizing antibodies**
2. **RBD-specific F(ab')2 as therapeutic candidate for SARS-CoV-2**
3. **Convalescent plasma therapy in severe COVID-19 patients: a pilot study**
4. **SARS-CoV-2 S1-Fc recombinant protein as a strong candidate for vaccine development**
5. **Two B-cell linear epitopes that are immunodominant.**
6. **Discovery of a panel of humanized single domain antibodies (sdAbs)**
7. **Generation of synthetic nanobodies, known as sybodies**
8. **The first report of a (human) monoclonal antibody that neutralizes SARS-CoV-2.** *Published in Nature Communications.*
9. **A receptor-binding domain-based (RBD) vaccine for SARS-CoV-2 could be safe and effective**
10. **Clinical grade hrsACE2 significantly blocks early stages of SARS-CoV-2 infections.** *Published in Cell.*
11. **A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2.** *Published in Science*

1. Epitope RBD-A as the preferred target for eliciting neutralizing antibodies. With the aim of nterrogating the antibody immune response against SARS-CoV-2 and discovering nAbs, Rogers et al. report a pipeline to rapidly isolate and characterize monoclonal antibodies (mAbs) from convalescent donors. A cohort of previously swab-positive SARS-CoV-2 donors was recruited for PBMC and plasma collection.

In parallel, the group developed live replicating and pseudovirus neutralization assays using a HeLa-ACE2 (Angiotensin-Converting Enzyme-2) cell line that gave robust and reproducible virus titers. Convalescent serum responses were evaluated for neutralization activity against SARS-CoV-1 and SARS-CoV-2, and eight donors were selected for mAb discovery. The selected antibodies were further tested *in vivo* using Syrian hamsters.

The results describe the isolation of highly potent nAbs to SARS-CoV-2 and demonstrate their *in vivo* efficacy in Syrian hamsters. This high throughput antibody isolation, production and characterization pipeline allowed to rapidly screen over 1000 antigen-specific antibodies and established an animal model to test protection.

Single antigen-specific memory B cells were sorted, and their corresponding variable genes were recovered and cloned using a high-throughput expression system that enabled antibody expression and characterization in under two weeks.

The authors report multiple highly potent neutralizing antibodies (nAbs) and show that passive transfer of a nAb provides protection against high-dose SARS-CoV-2 challenge in Syrian hamsters. Promising mAbs were used for further biophysical characterization and in vivo testing.

These data highlight epitope RBD-A as the preferred target for eliciting neutralizing antibodies and that corresponding increases in affinity of mAbs to RBD-A will likely result in corresponding increases in neutralization potency. The data also suggest that less potent nAbs targeting RBD-B that compete with RBD-A nAbs could, at least in principle, pose challenges for the elicitation of RBD-A nAbs. Therefore, this study suggests focussing on the RBD for vaccine design, which is supported also by previous mouse studies. This work also strongly supports a role for nAbs in prophylaxis, and potentially therapy, of COVID-19.

Source: Thomas F Rogers, Fangzhu Zhao, Deli Huang, Nathan Beutler, Robert K Abbott, Sean Callaghan, Elijah Garcia, Wan-ting He, Jonathan Hurtado, Oliver Limbo, Mara Parren,

Linghang Peng, James Ricketts, Michael K Ricciardi, Chloe Smith, Ge Song, Jordan Woehl, Linlin Yang, Stephen Rawlings, Davey M Smith, David Nemazee, John R Teijaro, James E Voss, Raiees Andrabi, Bryan Briney, Elise Landais, Devin Sok, Joseph G Jardine, Dennis Burton Rapid isolation of potent SARS-CoV-2 neutralizing antibodies and protection in a small animal mode. *Preprint.* doi: https://doi.org/10.1101/2020.05.11.088674

---

2. RBD-specific F(ab')2 as therapeutic candidate for SARS-CoV-2.

In this study, therapeutic antibodies for SARS-CoV-2, were obtained from hyper immune equine plasma. SARS-CoV-2 RBD with gram level were obtained through Chinese hamster ovary cells high-density fermentation. Horses were immunized with RBD with complete Freund's adjuvant at the first time and with incomplete Freund's adjuvant at subsequent times, via intramuscular injections. The amount of RBD was doubled for the first three times, from 3 mg to 12 mg each horse, and fixed as 12 mg per horse when boosting before each plasma collection. Receptor binding domain RBD triggered high-titer neutralizing antibodies in vivo, and immunoglobulin fragment F(ab')2 was prepared from horse antisera through removing Fc. Sera were adopted routinely after each immunization to monitor the antibody response. The binding of RBD to SARS-CoV-2 receptor, human ACE2, was verified and the efficacy of RBD in vivo was tested on mice and then on horses. Efficiency of horse antisera was tested against 11 plasma samples, randomly adopted from patients in Wuhan, China.

The results highlight RBD-specific F(ab')2 as a therapeutic candidate for SARS-CoV-2 and demonstrated that passively immunized horses with RBD is more efficient in producing nAbs than purifying antibodies from convalescent plasma after natural infection by SARS-CoV-2, implying a necessity of producing horse antisera-derived antibodies.

Results showed RBD triggered high-titer neutralizing antibodies in vivo, and immunoglobulin fragment F(ab')2 was prepared from horse antisera through removing Fc. Neutralization test demonstrated that RBD-specific F(ab')2 inhibited SARS-CoV-2 with EC50 at 0.07 μg/ml, showing a potent inhibitory effect on SARS-CoV-2. These results highlights as RBD-specific F(ab')2 as therapeutic candidate for SARS-CoV-2. Neutralization assays from mice and cell lines collectively demonstrated that RBD could be used as immunogen in triggering nAbs in vivo.

The results were, 5 out of 11 plasma samples (45%) inhibited over 50% SARS-CoV-2 with a dilution at 1:640, 2 out of 11 plasma samples (9%) inhibited over 80% SARS-CoV-2 with a dilution at 1:640, and 6 out of 11 plasma samples (55%) inhibited 80% SARS-CoV-2 needed a dilution of 1:160. Horse antisera after the third immunization inhibited 80% SARS-CoV-2 at a dilution of 1:2560. By a set of neutralization tests, F(ab')2 was found inhibiting SARS-CoV-2 with EC50 as 8.78 μg/ml and EC80 as 24.92 μg/ml (Fig 4A). Over 90% SARS-CoV-2 were inhibited under the treatment of F(ab')2 at 31.15 μg/ml, and over 50% SARS-CoV-2 were inhibited at 7.81 μg/ml, the inhibition on SARS-CoV-2 was observed with apparent dose-dependent manner.)

Neutralization test demonstrated that RBD-specific F(ab')2 inhibited SARS-CoV-2 with EC50 at 0.07 μg/ml, showing a potent inhibitory effect on SARS-CoV-2. F(ab')2 reported here validates the efficacy of RBD in triggering nAbs in vivo and is highlighted as an alternative to immunotherapy for COVID-19

Source: Xiaoyan Pan, Pengfei Zhou, Tiejiong Fan, Yan Wu, Jing Zhang, Xiaoyue Shi, Weijuan Shang, Lijuan Fang, Xiaming Jiang, Jian Shi, Yuan Sun, Shaojuan Zhao, Rui Gong,

Ze Chen, Gengfu Xiao. Immunoglobulin fragment F(ab')2 against RBD potently neutralizes SARS-CoV-2 in vitro.*Preprint.* doi: https://doi.org/10.1101/2020.04.07.029884

---

3. Convalescent plasma therapy in severe COVID-19 patients: a pilot study.

10 severe patients confirmed by real-time viral RNA test were enrolled prospectively. One dose of 200 ml convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents. The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 days after CP transfusion. The median time from onset of illness to CP transfusion was 16.5 days.

Results showed after CP transfusion, the level of neutralizing antibody increased rapidly up to 1:640 in five cases, while that of the other four cases maintained at a high level. The clinical symptoms were significantly improved along with increase of oxyhemoglobin saturation within 3 days. Several parameters tended to improve as compared to pre-transfusion, including increased lymphocyte counts (0.65×109/L vs. 0.76×109/L) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L). Radiological examinations showed varying degrees of absorption of lung lesions within 7 days. The viral load was undetectable after transfusion in seven patients who had previous viremia. No severe adverse effects were observed.

This study showed CP therapy was well tolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases. **The optimal dose and time point, as well as the clinical benefit of CP therapy, needs further investigation in larger well-controlled trials.**

Source: Kai Duan, Bende Liu, Cesheng Li, Huajun Zhang, Ting Yu, Jieming Qu, Min Zhou, Li Chen, Shengli Meng, Yong Hu, Cheng Peng, Mingchao Yuan, Jinyan Huang, Zejun Wang, Jianhong Yu, Xiaoxiao Gao, Dan Wang, Xiaoqi Yu, Li Li, Jiayou Zhang, Xiao Wu, Bei Li, Yanping Yu, Wei Chen, Yan Peng, Yeqin Hu, Lianzhen Lin, Xuefei Liu, Shihe Huang, Zhijun Zhou, Lianghao Zhang, Yue Wang, Zhi Zhang, Kun Deng, Zhiwu Xia, Qin Gong, Wei Zhang, Xiaobei Zheng, Ying Liu, Huichuan Yang, Dongbo Zhou, Ding Yu, Jifeng Hou, Zhengli Shi, Saijuan Chen, Zhu Chen, Xin-xin Zhang, Xiaoming Yang The feasibility of convalescent plasma therapy in severe COVID-19 patients: a pilot study. *Preprint*. doi: https://doi.org/10.1101/2020.03.16.20036145

---

4. SARS-CoV-2 S1-Fc recombinant protein as a strong candidate for vaccine development

This study aim was to optimize and test a stable CHO cell line expressing 50 mg/L of SARS-CoV-2 S1-Fc and examine the immunogenicity of CHO-expressed recombinant SARS-CoV-2 S1-Fc fusion protein in mice, rabbits, and monkeys as a potential candidate for a COVID-19 vaccine.

Results showed the stable CHO cell line expressing 50 mg/L of S1-Fc and a 3,000 L Bioreactor can produce 3 million doses of human COVID-19 vaccine every 10 days, making it an accessible and affordable option for worldwide vaccinationS1-Fc fusion protein is extremely immunogenic, as evidenced by strong antibody titers observed by day 7. Strong virus neutralizing activity was observed on day 14 in rabbits immunized with the S1-Fc fusion

protein using a pseudovirus neutralization assay. In less than 20 days and three injections of the S1-Fc fusion protein, two monkeys developed higher virus neutralizing titers than a recovered COVID-19 patient in a live SARS-CoV-2 infection assay. **CHO-expressed S1-Fc protein is very immunogenic in various animals and can rapidly induce strong antibody production.** These data strongly suggests that the CHO-expressed SARS-CoV-2 S1-Fc recombinant protein could be a strong candidate for vaccine development against COVID-19.

Source: Wenlin Ren, Hunter Sun, George F. Gao, Jianxin Chen, Sean Sun, Rongqing Zhao, Guang Gao, Yalin Hu, Gan Zhao, Yuxin Chen, Xia Jin, Feng Fang, Jinggong Chen, Qi Wang, Sitao Gong, Wen Gao, Yufei Sun, Junchi Su, Ailiang He, Xin Cheng, Min Li, Chenxi Xia, Maohua Li, Le Sun Recombinant SARS-CoV-2 spike S1-Fc fusion protein induced high levels of neutralizing responses in nonhuman primates. *Preprint.* doi: https://doi.org/10.1101/2020.04.21.052209

---

5. Two B-cell linear epitopes that are immunodominant.

In this report, using pools of overlapping linear peptides and functional assays, Poh et al. present two immunodominant regions on the spike glycoprotein that were highly recognized by neutralizing antibodies in the sera of COVID-19 convalescent patients.

The method involved the study of antibody profiles of COVID-19 patients, and the identification of two immunodominant linear B-cell epitopes on the S glycoprotein of SARS-CoV-2 that are crucial in controlling infection. A total of 25 convalescence serum samples collected during the current COVID-19 outbreak in Singapore were screened at 1:1000 dilution for neutralizing antibodies against a pseudo-typed lentivirus expressing SARS-CoV-2 S glycoprotein tagged with a 8 luciferase reporter

Results showed of the 25 patients tested, six patients with sufficient amount of serum samples that displayed a good neutralizing activity were selected for further functional characterization. Sera from all patients showed similar IC50, ranging from a titer of 694 to 836, except patient 20, who showed the strongest neutralizing activity with an IC50 of 1603.

Sera from recalled SARS patients could neutralize SARS-CoV, but not the SARS-CoV-2 pseudotyped lentiviruses. Moreover, COVID-19 patients sera could strongly detect SARS-CoV S library pool S51, which partially overlaps with SARS-CoV-2 pool S21. This region encompasses the fusion peptide, which is highly conserved among coronaviruses, suggesting a potential pan-coronavirus epitope at this location. Further assessment of individual peptides within pools S14 and S21 narrowed down the specific region of interest to peptides S14P5 and S21P2, respectively. Recognition of these regions was stronger for the peptides of SARS-CoV-2 than SARS-CoV. Sera that were depleted for antibodies targeting either peptides S14P5, S21P2, or S14P5+S21P2 led to a significantly reduced ability to neutralize SARS-CoV-2 pseudovirus infection, as compared to the non-depleted sera controls. These results demonstrate that the **two B-cell linear epitopes identified in this study are immunodominant. One is highly specific to SARS-CoV-2, and the other is a potential pan-coronavirus target.**

Source: Chek Meng Poh, Guillaume Carissimo, Bei Wang, Siti Naqiah Amrun, Cheryl Yi-Pin Lee, Rhonda Sin-Ling Chee, Nicholas Kim-Wah Yeo, Wen-Hsin Lee, Yee-Sin Leo, Mark I-Cheng Chen, Seow-Yen Tan, Louis Yi Ann Chai, Shirin Kalimuddin, Siew-Yee Thien, Barnaby Edward Young, David C. Lye, Cheng-I Wang, Laurent Renia, Lisa F.P. Ng Potent neutralizing antibodies in the sera of convalescent COVID-19 patients are directed against

conserved linear epitopes on the SARS-CoV-2 spike protein. *Preprint.* doi: https://doi.org/10.1101/2020.03.30.015461

---

6. Discovery of a panel of humanized single domain antibodies (sdAbs)

Single domain antibodies (sdAbs), have been investigated as important therapeutic alternatives against viral infection because of their high yield, low cost and intrinsic stability. Using SARS-CoV-2 spike RBD as a bait, we have discovered a panel of humanized single domain antibodies (sdAbs). Single domain antibodies (sdAbs), namely nanobodies, were initially identified from 69 camelids or cartilaginous fish heavy-chain only antibodies devoid of light chains, where antigen-binding is mediated exclusively by a single variable domain (VHH). To enrich for SARS-CoV-2 RBD binding sdAbs, we performed four rounds of biopanning using a lab owned, full synthetic, humanized phage display library with recombinant RBD protein. After phage ELISA identification of 480 clones, a number of sdAbs exhibited an excellent affinity for SARS-CoV-2 RBD.

Results showed five distinctive sdAd sequences (1E2, 2F2, 3F11, 4D8 and 5F8) were cloned into a prokaryotic expression vector and recombinant sdAb proteins were purified by nickel-charged sepharose affinity chromatography. These sdAbs revealed binding kinetics with the equilibrium dissociation constant (KD) of 0.7~33 nM. The monomeric sdAbs showed half maximal inhibitory concentration (IC50) of 0.003~0.3 μg/mL in pseudotyped particle neutralization assay, and 0.23~0.50 μg/mL in authentic SARS-CoV-2 neutralization assay. Competitive ligand-binding data suggested that the sdAbs either completely blocked or significantly inhibited the association between SARS-CoV-2 RBD and viral entry receptor ACE2. Finally, they showed that fusion of the human IgG1 Fc to sdAbs improved their neutralization activity by tens of times.

These results reveal the novel SARS-CoV-2 RBD targeting sdAbs and pave a road for antibody drug development.

Notes: Since the mature COVID-19 animal 198 models have not been developed, this study did not involve in vivo studies. Used: The Vero (African green monkey kidney), HEK293T (human kidney epithelial), 293F, 210 Calu-3 (human lung adenocarcinoma) cells.

Source: Xiaojing Chi, Xiuying Liu, Conghui Wang, Xinhui Zhang, Lili Ren, Qi Jin, Jianwei Wang, View ORCID ProfileWei Yang Humanized Single Domain Antibodies Neutralize SARS-CoV-2 by Targeting Spike Receptor Binding Domain. *Preprint.* doi: https://doi.org/10.1101/2020.04.14.042010

---

7. Generation of synthetic nanobodies, known as sybodies

This study reports the generation of synthetic nanobodies, known as sybodies, against the receptor-binding domain (RBD) of SARS-CoV-2. In an expeditious process taking only twelve working days, sybodies were selected entirely in vitro from three large combinatorial libraries, using ribosome and phage display. They obtained six strongly enriched sybody pools against the isolated RBD and identified 63 unique anti-RBD sybodies which also interact in the context of the full-length SARS-CoV-2 spike protein.

It is anticipated that compact binders such as these sybodies could feasibly be developed into an inhalable drug that can be used as a convenient prophylaxis against COVID-19. Moreover, generation of polyvalent antivirals, via fusion of anti-RBD sybodies to additional

small binders recognizing secondary epitopes, could enhance the therapeutic potential and guard against escape mutants. They present full sequence information and detailed protocols for the identified sybodies, as a freely accessible resource.

The study has attempted to provide a complete account of the generation of these molecules, including full sequences and detailed methods, such that other researchers may contribute to their ongoing analysis. They will update the report as they further characterize the identified sybodies, in terms of affinities, scaled-up purification yields, and their potential to neutralize SARS-CoV-2 infections.

Source: Justin D. Walter, Cedric A.J. Hutter, Iwan Zimmermann, Jennifer Earp, Pascal Egloff, Michèle Sorgenfrei, Lea M. Hürlimann, Imre Gonda, Gianmarco Meier, Sille Remm, Sujani Thavarasah, Philippe Plattet, Markus A. Seeger Synthetic nanobodies targeting the SARS-CoV-2 receptor-binding domain. *Preprint.* doi: https://doi.org/10.1101/2020.04.16.045419

---

8. The first report of a (human) monoclonal antibody that neutralizes SARS-CoV-2.

Source: Chunyan Wang, Wentao Li, Dubravka Drabek, Nisreen M.A. Okba, Rien van Haperen, Albert D.M.E. Osterhaus, Frank J.M. van Kuppeveld, Bart L. Haagmans, Frank Grosveld, Berend-Jan Bosch A human monoclonal antibody blocking SARS-CoV-2 infection. Nature Comms. https://www.nature.com/articles/s41467-020-16256-y https://doi.org/10.1101/2020.03.11.987958

The aim was to identify and test neutralizing antibodies against SARS-CoV-2 infection. In order to identify SARS-CoV-2-neutralizing antibodies, ELISA-(cross)reactivity was assessed of antibody-containing supernatants of a collection of 51 SARS-S hybridoma's derived from immunized transgenic H2L2 mice that encode chimeric immunoglobulins with human variable heavy and light chains and constant regions of rat origin.

(47D11) exhibited cross-neutralizing activity of SARS-S and SARS2-S pseudotyped VSV infection. The chimeric 47D11 H2L2 antibody was reformatted to a fully human immunoglobulin, by cloning of the human variable heavy and light chain regions into a human IgG1 isotype backbone.

This is the first report of a (human) monoclonal antibody that neutralizes SARS-CoV-2. 47D11 binds a conserved epitope on the spike RBD explaining its ability to cross-neutralize SARS-CoV and SARS-CoV-2, using a mechanism that is independent of receptor-binding inhibition. This antibody will be useful for development of antigen detection tests and serological assays targeting SARS-CoV-2. It offers the potential to prevent and/or treat COVID-19.

---

9. A receptor-binding domain-based (RBD) vaccine for SARS-CoV-2 could be safe and effective

The authors have shown before that the SARS-CoV-1 RBD that an immunoadhesin form of this RBD neutralized S-protein mediated entry with a 50% inhibitor concentration (IC50) of ~10 nM (Wong et al., 2004). This construct, RBD-Fc, also efficiently raised antibodies in mice capable of neutralizing SARS-CoV-1 variants with distinct RBD sequences (He et al., 2006; He et al., 2004). This raised the possibility that an RBD-based SARS-CoV-2 vaccine could be also effective against virus throughout the current COVID-19 pandemic.

They tested the SARS-CoV-2 RBD ability to trigger neutralizing antibody response in rodents. The authors produced and purified the SARS-CoV-2 RBD, fused to the Fc domain as an expedient for rapid purification. This RBD fusion protein was conjugated to a Keyhole limpet hemocyanin (KLH) carrier protein and mixed with the AS01 adjuvant formulation. This was injected into 4 female Sprague-Dawley rats with a schedule of seven increasing (2.5-fold) doses, one each day, ultimately administering a total of 500 µg of the SARSCoV RBD-Fc. Blood was harvested from each of the four rats immediately before inoculation (day 0), and at 5-day intervals starting at day 10 after the first inoculation. Serial dilutions of day-0 and day-40 sera were measured for their ability to neutralize retroviruses pseudotyped with the SARS-CoV-2 S protein (SARS2-PV) as well as ability to mediate antibody-dependent enchancement.

Results suggest that a receptor-binding domain-based (RBD) vaccine for SARS-CoV-2 could be safe, effective and that it is unlikely to promote pathogenicity through conventional antibody dependent enhancement (ADE) mechanisms. These data suggested that antibodies to the RBD domain of SARS-CoV-1 potently neutralize SARS-CoV-1 S-protein-mediated entry in rat, and the presence of anti-RBD antibodies correlates with neutralization in SARS-CoV-2 convalescent sera.

Source: Brian D. Quinlan, Huihui Mou, Lizhou Zhang, Yan Guo, Wenhui He, Amrita Ojha, Mark S. Parcells, Guangxiang Luo, Wenhui Li, Guocai Zhong, Hyeryun Choe, Michael Farzan. The SARS-CoV-2 receptor-binding domain elicits a potent neutralizing response without antibody-dependent enhancement *Preprint*. doi: https://doi.org/10.1101/2020.04.10.036418

---

10. Clinical grade hrsACE2 significantly blocks early stages of SARS-CoV-2 infections

This study shows that clinical grade hrsACE2 can significantly block early stages of SARS-CoV-2 infections. Using a soluble recombinant human and murine ACE2, Kidney & blood vessel organoids, Vero E6 cells with human rsACE2 and murine rsACE2.

Results show that SARS-CoV-2 can be infected and can replicate in Kidney & blood vessel organoids. The clinical grade hrsACE2 reduced SARS-CoV-2 recovery from Vero cells by a factor of 1,000– 5,000. An equivalent mouse rsACE2 had no effect. They also show that SARS-CoV-2 can directly infect engineered human blood vessel organoids and human kidney organoids, which can be inhibited by hrsACE2. These data demonstrate that hrsACE2 can significantly block early stages of SARS-CoV-2 infections.

Source: Monteil V, Kwon H, Prado P, Hagelkrüys A, Wimmer RA, Stahl M, Leopoldi A, Garreta E, Hurtado Del Pozo C, Prosper F, Romero JP, Wirnsberger G, Zhang H, Slutsky AS, Conder R, Montserrat N, Mirazimi A, Penninger JM. Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2. *Cell.* https://www.cell.com/cell/pdf/S0092-8674(20)30399-8.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420303998%3Fshowall%3Dtrue

---

11. A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2.

In this study they used COVID-19 virus RBD protein as bait to isolate specific single memory B-cells from COVID-19 convalescent patient peripheral blood mononuclear cells (PBMCs).

Neutralisation assay was done using Vero cell like. hACE2 transgenic mice model was established and supplied by Institute for Laboratory Animal Resources, NIFDC. Twelve female hACE2 transgenic mice (5-6 weeks old) were divided into three groups with four mice in each group.

Results showed successful isolation of four human-origin monoclonal antibodies from a convalescent patient, all of which displayed neutralization abilities. B38 and H4 blocked the binding between virus S-protein RBD and cellular receptor ACE2. A competition assay indicated their different epitopes on the RBD, making them a potential virus-targeting MAb-pair to avoid immune escape in future clinical applications. Further, a therapeutic study in a mouse model validated that these antibodies could reduce virus titers in infected lungs. The RBD-B38 complex structure revealed that most residues on the epitope overlap with the RBD-ACE2 binding interface, explaining the blocking effect and neutralizing capacity. These results provide support for antibody-based therapeutics and provide a structural basis for rational vaccine design.

Source: Yan Wu, Feiran Wang, Chenguang Shen, Weiyu Peng, Delin Li, Cheng Zhao, Zhaohui Li , Shihua Li, Yuhai Bi, Yang Yang, Yuhuan Gong, Haixia Xiao, Zheng Fan, Shuguang Tan, Guizhen Wu, Wenjie Tan, Xuancheng Lu, Changfa Fan, Qihui Wang, Yingxia Liu, Chen Zhang, Jianxun Qi, George Fu Gao, Feng Gao, Lei Liu. A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2. *Science.* https://science.sciencemag.org/content/early/2020/05/12/science.abc2241

This report was contributed to by Anna Bajur and Georgina Ellison-Hughes