

Coronavirus (CoV) proteins in GtoPdb v.2022.3

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Abstract

Coronaviruses are large, often spherical, enveloped, single-stranded positive-sense RNA viruses, ranging in size from 80-220 nm. Their genomes and protein structures are highly conserved. Three coronaviruses have emerged over the last 20 years as serious human pathogens: SARS-CoV was identified as the causative agent in an outbreak in 2002-2003, Middle East respiratory syndrome (MERS) CoV emerged in 2012 and the novel coronavirus SARS-CoV-2 emerged in 2019-2020. SARS-CoV-2 is the virus responsible for the infectious disease termed COVID-19 ([WHO Technical Guidance 2020](#)).

Contents

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Database links

Coronavirus (CoV) proteins

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=1034>

Introduction to Coronavirus (CoV) proteins

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=1034>

Targets

CoV Envelope protein

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3116>

CoV 3C-like (main) protease

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3111>

CoV Membrane glycoprotein

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3117>

CoV Non-structural protein 6

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3118>

CoV Non-structural protein 7b

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3123>

CoV Non-structural protein 8

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3120>

CoV Non-structural protein 14

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3198>

CoV Non-structural protein 15

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3206>

CoV Nucleoprotein

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3121>
CoV Papain-like protease

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3132>
CoV Protein 3a

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3115>
CoV Protein 7a

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3119>
CoV Protein 9b

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3122>
CoV Replicase polyprotein 1a

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3124>
CoV Replicase polyprotein 1ab

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3125>
CoV RNA-dependent RNA polymerase

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3139>
CoV Spike glycoprotein

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3114>

References

1. Adedeji AO, Marchand B, Te Velthuis AJ, Snijder EJ, Weiss S, Eoff RL, Singh K and Sarafianos SG. (2012) Mechanism of nucleic acid unwinding by SARS-CoV helicase. *PLoS ONE* **7**: e36521 [PMID:22615777]
2. Ahmed-Belkacem R, Hausdorff M, Delpal A, Sutto-Ortiz P, Colmant AMG, Touret F, Ogando NS, Snijder EJ, Canard B and Coutard B *et al.* (2022) Potent Inhibition of SARS-CoV-2 nsp14 N7-Methyltransferase by Sulfonamide-Based Bisubstrate Analogues. *J Med Chem* [PMID:35439007]
3. Ahn DG, Choi JK, Taylor DR and Oh JW. (2012) Biochemical characterization of a recombinant SARS coronavirus nsp12 RNA-dependent RNA polymerase capable of copying viral RNA templates. *Arch Virol* **157**: 2095-104 [PMID:22791111]
4. Angelini MM, Akhlaghpour M, Neuman BW and Buchmeier MJ. (2013) Severe acute respiratory syndrome coronavirus nonstructural proteins 3, 4, and 6 induce double-membrane vesicles. *mBio* **4** [PMID:23943763]
5. Anson BJ, Chapman ME, Lendy EK, Pshenychnyi S, D'Aquila RT, Satchell KJF and Mesecar AD. (2020) Broad-spectrum inhibition of coronavirus main and papain-like proteases by HCV drugs *Nature Research*
6. Arnold LD, Jennings A and Keung W. (2021) Inhibitors of cysteine proteases and methods of use thereof Patent number: WO2021252644A1.
7. Bafna K, White K, Harish B, Rosales R, Ramelot TA, Acton TB, Moreno E, Kehrer T, Miorin L and Royer CA *et al.* (2021) Hepatitis C virus drugs that inhibit SARS-CoV-2 papain-like protease synergize with remdesivir to suppress viral replication in cell culture. *Cell Rep*: 109133 [PMID:33984267]
8. Bai B, Belovodskiy A, Hena M, Kandadai AS, Joyce MA, Saffran HA, Shields JA, Khan MB, Arutyunova E and Lu J *et al.* (2021) Peptidomimetic α -Acylloxymethylketone Warheads with Six-Membered Lactam P1 Glutamine Mimic: SARS-CoV-2 3CL Protease Inhibition, Coronavirus Antiviral Activity, and *in Vitro* Biological Stability. *J Med Chem* [PMID:34242027]
9. Baker JD, Uhrich RL, Kraemer GC, Love JE and Kraemer BC. (2021) A drug repurposing screen identifies hepatitis C antivirals as inhibitors of the SARS-CoV2 main protease. *PLoS One* **16**: e0245962 [PMID:33524017]
10. Barretto N, Jukneliene D, Ratia K, Chen Z, Mesecar AD and Baker SC. (2005) The papain-like protease of severe acute respiratory syndrome coronavirus has deubiquitinating activity. *J Virol* **79**: 15189-98 [PMID:16306590]
11. Botyanszki J, Catalano G, Chong PY, Dickson H, Jin Q, Leivers A, Maynard A, Liao X, Miller J and Shotwell JB *et al.* (2018) Compounds that inhibit 3c and 3cl proteases and methods of use thereof Patent number: WO2018042343A2.
12. Bouvet M, Debarnot C, Imbert I, Selisko B, Snijder EJ, Canard B and Decroly E. (2010) In vitro reconstitution of SARS-coronavirus mRNA cap methylation. *PLoS Pathog* **6**: e1000863 [PMID:20421945]
13. Bouvet M, Imbert I, Subissi L, Gluais L, Canard B and Decroly E. (2012) RNA 3'-end mismatch excision by the severe acute respiratory syndrome coronavirus nonstructural protein nsp10/nsp14 exoribonuclease complex. *Proc Natl Acad Sci USA* **109**: 9372-7 [PMID:22635272]
14. Breidenbach J, Lemke C, Pillaiyar T, Schäkel L, Al Hamwi G, Dieltz M, Gedschold R, Geiger N, Lopez V and Mirza S *et al.* (2021) Targeting the Main Protease of SARS-CoV-2: From the Establishment of High Throughput Screening to the Design of Tailored Inhibitors. *Angew Chem Int Ed Engl* [PMID:33655614]
15. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
16. Báez-Santos YM, Barraza SJ, Wilson MW, Agius MP, Mielech AM, Davis NM, Baker SC, Larsen SD and

- Mesecar AD. (2014) X-ray structural and biological evaluation of a series of potent and highly selective inhibitors of human coronavirus papain-like proteases. *J Med Chem* **57**: 2393-412 [PMID:24568342]
17. Cao L, Goreshnik I, Coventry B, Case JB, Miller L, Kozodoy L, Chen RE, Carter L, Walls AC and Park YJ *et al.* (2020) De novo design of picomolar SARS-CoV-2 miniprotein inhibitors. *Science* **370**: 426-431 [PMID:32907861]
 18. Chamakuri S, Lu S, Ucisik MN, Bohren KM, Chen YC, Du HC, Faver JC, Jimmidi R, Li F and Li JY *et al.* (2021) DNA-encoded chemistry technology yields expedient access to SARS-CoV-2 M^{pro} inhibitors. *Proc Natl Acad Sci U S A* **118** [PMID:34426525]
 19. Chen IY, Moriyama M, Chang MF and Ichinohe T. (2019) Severe Acute Respiratory Syndrome Coronavirus Viroprotein 3a Activates the NLRP3 Inflammasome. *Front Microbiol* **10**: 50 [PMID:30761102]
 20. Chen J, Liang C, Miao K, Wu Y, Yun H and Zhang W. (2022) Aminocarbonyl compounds for the treatment of viral infections Patent number: WO2022043374.
 21. Cheng Y-W, Chao T-L, Li C-L, Chen P-J, Chang S-Y and Yeh S-H. (2020) Furin Inhibitors Block SARS-CoV-2 Spike Protein Cleavage to Suppress Virus Production and Cytopathic Effects *Cell Reports*
 22. Chi Y, Yan R, Zhang J, Zhang G, Zhang Y, Hao M, Zhang Z, Fan P, Dong Y and Yang Y *et al.* (2020) A neutralizing human antibody binds to the N-terminal domain of the Spike protein of SARS-CoV-2 *Science*
 23. Chia CSB, Xu W and Ng PS. (2021) A patent review on SARS coronavirus main protease (3CL_{pro}) inhibitors. *ChemMedChem* [PMID:34651447]
 24. Chinese SARS Molecular Epidemiology Consortium. (2004) Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science* **303**: 1666-9 [PMID:14752165]
 25. Chuck CP, Chen C, Ke Z, Wan DC, Chow HF and Wong KB. (2013) Design, synthesis and crystallographic analysis of nitrile-based broad-spectrum peptidomimetic inhibitors for coronavirus 3C-like proteases. *Eur J Med Chem* **59**: 1-6 [PMID:23202846]
 26. Congreve MS, Christopher JA, Pickworth M, De Graff C, Higuero AP, Mason JS and Kulkarni SS. (2022) SARS-COV-2 MPRO INHIBITOR COMPOUNDS Patent number: WO2022129953.
 27. Cornillez-Ty CT, Liao L, Yates 3rd JR, Kuhn P and Buchmeier MJ. (2009) Severe acute respiratory syndrome coronavirus nonstructural protein 2 interacts with a host protein complex involved in mitochondrial biogenesis and intracellular signaling. *J Virol* **83**: 10314-8 [PMID:19640993]
 28. Cottam EM, Whelband MC and Wileman T. (2014) Coronavirus NSP6 restricts autophagosome expansion. *Autophagy* **10**: 1426-41 [PMID:24991833]
 29. Dai W, Jochmans D, Xie H, Yang H, Li J, Su H, Chang D, Wang J, Peng J and Zhu L *et al.* (2021) Design, Synthesis, and Biological Evaluation of Peptidomimetic Aldehydes as Broad-Spectrum Inhibitors against Enterovirus and SARS-CoV-2. *J Med Chem* [PMID:33872498]
 30. Dai W, Zhang B, Jiang XM, Su H, Li J, Zhao Y, Xie X, Jin Z, Peng J and Liu F *et al.* (2020) Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease. *Science* **368**: 1331-1335 [PMID:32321856]
 31. Dampalla CS, Kim Y, Bickmeier N, Rathnayake AD, Nguyen HN, Zheng J, Kashipathy MM, Baird MA, Battaile KP and Lovell S *et al.* (2021) Structure-Guided Design of Conformationally Constrained Cyclohexane Inhibitors of Severe Acute Respiratory Syndrome Coronavirus-2 3CL Protease. *J Med Chem* [PMID:34213885]
 32. Dampalla CS, Rathnayake AD, Galasiti Kankanamalage AC, Kim Y, Perera KD, Nguyen HN, Miller MJ, Madden TK, Picard HR and Thurman HA *et al.* (2022) Structure-Guided Design of Potent Spirocyclic Inhibitors of Severe Acute Respiratory Syndrome Coronavirus-2 3C-like Protease *Journal of Medicinal Chemistry*
 33. Dampalla CS, Rathnayake AD, Perera KD, Jesri AM, Nguyen HN, Miller MJ, Thurman HA, Zheng J, Kashipathy MM and Battaile KP *et al.* (2021) Structure-Guided Design of Potent Inhibitors of SARS-CoV-2 3CL Protease: Structural, Biochemical, and Cell-Based Studies. *J Med Chem* **64**: 17846-17865 [PMID:34865476]
 34. Dampalla CS, Zheng J, Perera KD, Wong LR, Meyerholz DK, Nguyen HN, Kashipathy MM, Battaile KP, Lovell S and Kim Y *et al.* (2021) Postinfection treatment with a protease inhibitor increases survival of mice with a fatal SARS-CoV-2 infection. *Proc Natl Acad Sci U S A* **118** [PMID:34210738]
 35. de Vries RD, Schmitz KS, Bovier FT, Noack D, Haagmans BL, Biswas S, Rockx B, Gellman SH, Alabi CA and de Swart RL *et al.* (2020) Intranasal fusion inhibitory lipopeptide prevents direct contact SARS-CoV-2 transmission in ferrets. *bioRxiv* [PMID:33173865]
 36. DeDiego ML, Alvarez E, Almazán F, Rejas MT, Lamirande E, Roberts A, Shieh WJ, Zaki SR, Subbarao K and Enjuanes L. (2007) A severe acute respiratory syndrome coronavirus that lacks the E gene is attenuated in vitro and in vivo. *J Virol* **81**: 1701-13 [PMID:17108030]
 37. Devaraj SG, Wang N, Chen Z, Chen Z, Tseng M, Barretto N, Lin R, Peters CJ, Tseng CT and Baker SC *et al.* (2007) Regulation of IRF-3-dependent innate immunity by the papain-like protease domain of the severe acute respiratory syndrome coronavirus. *J Biol Chem* **282**: 32208-21 [PMID:17761676]
 38. Dong S, Sun J, Mao Z, Wang L, Lu YL and Li J. (2020) A guideline for homology modeling of the proteins from

- newly discovered betacoronavirus, 2019 novel coronavirus (2019-nCoV). *J Med Virol* **92**: 1542-1548 [PMID:32181901]
39. Drayman R, DeMarco JK, Jones KA, Azizi S-A, Froggatt HM, Tan K, Maltseva NI, Chen S, Nicolaescu V and Dvorkin S *et al.*. (2021) Masitinib is a broad coronavirus 3CL inhibitor that blocks replication of SARS-CoV-2 *Science*
 40. Fan H, Ooi A, Tan YW, Wang S, Fang S, Liu DX and Lescar J. (2005) The nucleocapsid protein of coronavirus infectious bronchitis virus: crystal structure of its N-terminal domain and multimerization properties. *Structure* **13**: 1859-68 [PMID:16338414]
 41. Frazier MN, Dillard LB, Krahn JM, Perera L, Williams JG, Wilson IM, Stewart ZD, Pillon MC, Deterding LJ and Borgnia MJ *et al.*. (2021) Characterization of SARS2 Nsp15 nuclease activity reveals it's mad about U. *Nucleic Acids Res* **49**: 10136-10149 [PMID:34403466]
 42. Frazier MN, Wilson IM, Krahn JM, Butay KJ, Dillard LB, Borgnia MJ and Stanley RE. (2022) Flipped over U: structural basis for dsRNA cleavage by the SARS-CoV-2 endoribonuclease. *Nucleic Acids Res* **50**: 8290-8301 [PMID:35801916]
 43. Freitas BT, Durie IA, Murray J, Longo JE, Miller HC, Crich D, Hogan RJ, Tripp RA and Pegan SD. (2020) Characterization and Noncovalent Inhibition of the Deubiquitinase and delSGylase Activity of SARS-CoV-2 Papain-Like Protease. *ACS Infect Dis* **6**: 2099-2109 [PMID:32428392]
 44. Fung TS and Liu DX. (2019) Human Coronavirus: Host-Pathogen Interaction. *Annu Rev Microbiol* **73**: 529-557 [PMID:31226023]
 45. Gao Y, Yan L, Huang Y, Liu F, Zhao Y, Cao L, Wang T, Sun Q, Ming Z and Zhang L *et al.*. (2020) Structure of the RNA-dependent RNA polymerase from COVID-19 virus. *Science* **368**: 779-782 [PMID:32277040]
 46. Ghosh AK, Gong G, Grum-Tokars V, Mulhearn DC, Baker SC, Coughlin M, Prabhakar BS, Sleeman K, Johnson ME and Mesecar AD. (2008) Design, synthesis and antiviral efficacy of a series of potent chloropyridyl ester-derived SARS-CoV 3CLpro inhibitors. *Bioorg Med Chem Lett* **18**: 5684-8 [PMID:18796354]
 47. Ghosh AK, Raghavaiah J, Shahabi D, Yadav M, Anson BJ, Lendy EK, Hattori SI, Higashi-Kuwata N, Mitsuya H and Mesecar AD. (2021) Indole Chloropyridinyl Ester-Derived SARS-CoV-2 3CLpro Inhibitors: Enzyme Inhibition, Antiviral Efficacy, Structure-Activity Relationship, and X-ray Structural Studies. *J Med Chem* **64**: 14702-14714 [PMID:34528437]
 48. Godoy AS, Nakamura AM, Douangamath A, Song Y, Noske GD, Gawriljuk VO, Fernandes RS, Pereira HDM, Oliveira KIZ and Fearon D *et al.*. (2022) Allosteric regulation and crystallographic fragment screening of SARS-CoV-2 NSP15 endoribonuclease *bioRxiv*
 49. Gong YN, Tsao KC, Hsiao MJ, Huang CG, Huang PN, Huang PW, Lee KM, Liu YC, Yang SL and Kuo RL *et al.*. (2020) SARS-CoV-2 genomic surveillance in Taiwan revealed novel ORF8-deletion mutant and clade possibly associated with infections in Middle East. *Emerg Microbes Infect* **9**: 1457-1466 [PMID:32543353]
 50. Gordon CJ, Tchesnokov EP, Woolner E, Perry JK, Feng JY, Porter DP and Götte M. (2020) Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency. *J Biol Chem* **295**: 6785-6797 [PMID:32284326]
 51. Gordon DE, Jang GM, Bouhaddou M, Xu J, Obernier K, White KM, O'Meara MJ, Rezelj VV, Guo JZ and Swaney DL *et al.*. (2020) A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature* **583**: 459-468 [PMID:32353859]
 52. Han SH, Goins CM, Arya T, Shin WJ, Maw J, Hooper A, Sonawane DP, Porter MR, Bannister BE and Crouch RD *et al.*. (2021) Structure-Based Optimization of ML300-Derived, Noncovalent Inhibitors Targeting the Severe Acute Respiratory Syndrome Coronavirus 3CL Protease (SARS-CoV-2 3CL^{pro}). *J Med Chem* [PMID:34347470]
 53. Hansen J, Baum A, Pascal KE, Russo V, Giordano S, Wloga E, Fulton BO, Yan Y, Koon K and Patel K *et al.*. (2020) Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail. *Science* **369**: 1010-1014 [PMID:32540901]
 54. Harcourt BH, Jukneliene D, Kanjanahaluethai A, Bechill J, Severson KM, Smith CM, Rota PA and Baker SC. (2004) Identification of severe acute respiratory syndrome coronavirus replicase products and characterization of papain-like protease activity. *J Virol* **78**: 13600-12 [PMID:15564471]
 55. Hattori SI, Higashi-Kuwata N, Hayashi H, Allu SR, Raghavaiah J, Bulut H, Das D, Anson BJ, Lendy EK and Takamatsu Y *et al.*. (2021) A small molecule compound with an indole moiety inhibits the main protease of SARS-CoV-2 and blocks virus replication. *Nat Commun* **12**: 668 [PMID:33510133]
 56. He WT, Wan H, Hu L, Chen P, Wang X, Huang Z, Yang ZH, Zhong CQ and Han J. (2015) Gasdermin D is an executor of pyroptosis and required for interleukin-1 β secretion. *Cell Res* **25**: 1285-98 [PMID:26611636]
 57. Hilgenfeld R. (2014) From SARS to MERS: crystallographic studies on coronaviral proteases enable antiviral drug design. *FEBS J* **281**: 4085-96 [PMID:25039866]
 58. Hoffman RL, Kania RS, Brothers MA, Davies JF, Ferre RA, Gajiwala KS, He M, Hogan RJ, Kozminski K and Li LY *et al.*. (2020) Discovery of Ketone-Based Covalent Inhibitors of Coronavirus 3CL Proteases for the Potential

- Therapeutic Treatment of COVID-19. *J Med Chem* **63**: 12725-12747 [PMID:33054210]
59. Hoffmann M, Arora P, Groß R, Seidel A, Hörnich BF, Hahn AS, Krüger N, Graichen L, Hofmann-Winkler H and Kempf A *et al.*. (2021) SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies *Cell*
 60. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH and Nitsche A *et al.*. (2020) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* **181**: 271-280.e8 [PMID:32142651]
 61. Huo J, Zhao Y, Ren J, Zhou D, Duyvesteyn HME, Ginn HM, Carrique L, Malinauskas T, Ruza RR and Shah PNM *et al.*. (2020) Neutralisation of SARS-CoV-2 by destruction of the prefusion Spike. *Cell Host and Microbe*
 62. Imbert I, Guillemot JC, Bourhis JM, Bussetta C, Coutard B, Egloff MP, Ferron F, Gorbalenya AE and Canard B. (2006) A second, non-canonical RNA-dependent RNA polymerase in SARS coronavirus. *EMBO J* **25**: 4933-42 [PMID:17024178]
 63. Jin Z, Du X, Xu Y, Deng Y, Liu M, Zhang B, Li X, Zhang L, Peng C and Duan Y. (2020) Structure of Mpro from COVID-19 virus and discovery of its inhibitors *bioRxiv*
 64. Kim C, Ryu DK, Lee J, Kim YI, Seo JM, Kim YG, Jeong JH, Kim M, Kim JI and Kim P *et al.*. (2021) A therapeutic neutralizing antibody targeting receptor binding domain of SARS-CoV-2 spike protein. *Nat Commun* **12**: 288 [PMID:33436577]
 65. Kim SS, Sze L, Liu C and Lam KP. (2019) The stress granule protein G3BP1 binds viral dsRNA and RIG-I to enhance interferon- β response. *J Biol Chem* **294**: 6430-6438 [PMID:30804210]
 66. Kim SY, Jin W, Sood A, Montgomery DW, Grant OC, Fuster MM, Fu L, Dordick JS, Woods RJ and Zhang F *et al.*. (2020) Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. *Antiviral Res* **181**: 104873 [PMID:32653452]
 67. Kim Y, Jedrzejczak R, Maltseva NI, Wilamowski M, Endres M, Godzik A, Michalska K and Joachimiak A. (2020) Crystal structure of Nsp15 endoribonuclease NendoU from SARS-CoV-2. *Protein Sci* **29**: 1596-1605 [PMID:32304108]
 68. Kim Y, Wower J, Maltseva N, Chang C, Jedrzejczak R, Wilamowski M, Kang S, Nicolaescu V, Randall G and Michalska K *et al.*. (2021) Tipiracil binds to uridine site and inhibits Nsp15 endoribonuclease NendoU from SARS-CoV-2. *Commun Biol* **4**: 193 [PMID:33564093]
 69. Kirchdoerfer RN and Ward AB. (2019) Structure of the SARS-CoV nsp12 polymerase bound to nsp7 and nsp8 co-factors. *Nat Commun* **10**: 2342 [PMID:31138817]
 70. Konno S, Kobayashi K, Senda M, Funai Y, Seki Y, Tamai A, Schakel L, Sakata K, Pillaiyar T and Taguchi A *et al.*. (2021) 3CL Protease Inhibitors with an Electrophilic Arylketone Moiety as Anti-SARS-CoV-2 Agents *Journal of Medicinal Chemistry* [PMID:34313428]
 71. Konno S, Thanigaimalai P, Yamamoto T, Nakada K, Kakiuchi R, Takayama K, Yamazaki Y, Yakushiji F, Akaji K and Kiso Y *et al.*. (2013) Design and synthesis of new tripeptide-type SARS-CoV 3CL protease inhibitors containing an electrophilic arylketone moiety. *Bioorg Med Chem* **21**: 412-24 [PMID:23245752]
 72. La Monica G, Bono A, Lauria A and Martorana A. (2022) Targeting SARS-CoV-2 Main Protease for Treatment of COVID-19: Covalent Inhibitors Structure-Activity Relationship Insights and Evolution Perspectives. *J Med Chem* [PMID:36169610]
 73. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, Zhang Q, Shi X, Wang Q and Zhang L *et al.*. (2020) Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature* **581**: 215-220 [PMID:32225176]
 74. Law PTW, Wong CH, Au TCC, Chuck CP, Kong SK, Chan PKS, To KF, Lo AWI, Chan JYW and Suen YK *et al.*. (2005) The 3a protein of severe acute respiratory syndrome-associated coronavirus induces apoptosis in Vero E6 cells. *J Gen Virol* **86**: 1921-1930 [PMID:15958670]
 75. Lee CC, Kuo CJ, Ko TP, Hsu MF, Tsui YC, Chang SC, Yang S, Chen SJ, Chen HC and Hsu MC *et al.*. (2009) Structural basis of inhibition specificities of 3C and 3C-like proteases by zinc-coordinating and peptidomimetic compounds. *J Biol Chem* **284**: 7646-55 [PMID:19144641]
 76. Lindner HA, Lytvyn V, Qi H, Lachance P, Ziomek E and Ménard R. (2007) Selectivity in ISG15 and ubiquitin recognition by the SARS coronavirus papain-like protease. *Arch Biochem Biophys* **466**: 8-14 [PMID:17692280]
 77. Liu X, Zhang Z, Ruan J, Pan Y, Magupalli VG, Wu H and Lieberman J. (2016) Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores. *Nature* **535**: 153-8 [PMID:27383986]
 78. Liu ZS, Cai H, Xue W, Wang M, Xia T, Li WJ, Xing JQ, Zhao M, Huang YJ and Chen S *et al.*. (2019) G3BP1 promotes DNA binding and activation of cGAS. *Nat Immunol* **20**: 18-28 [PMID:30510222]
 79. Lokugamage KG, Narayanan K, Huang C and Makino S. (2012) Severe acute respiratory syndrome coronavirus protein nsp1 is a novel eukaryotic translation inhibitor that represses multiple steps of translation initiation. *J Virol* **86**: 13598-608 [PMID:23035226]
 80. Lu W, Zheng BJ, Xu K, Schwarz W, Du L, Wong CK, Chen J, Duan S, Deubel V and Sun B. (2006) Severe

- acute respiratory syndrome-associated coronavirus 3a protein forms an ion channel and modulates virus release. *Proc Natl Acad Sci USA* **103**: 12540-5 [PMID:16894145]
81. Lutgens A, Gullberg H, Abdurakhmanov E, Vo DD, Akaberi D, Talibov VO, Nekhotiaeva N, Vangeel L, De Jonghe S and Jochmans D *et al.*. (2022) Ultralarge Virtual Screening Identifies SARS-CoV-2 Main Protease Inhibitors with Broad-Spectrum Activity against Coronaviruses. *J Am Chem Soc* [PMID:35142215]
 82. Ma C, Sacco MD, Hurst B, Townsend JA, Hu Y, Szeto T, Zhang X, Tarbet B, Marty MT and Chen Y *et al.*. (2020) Boceprevir, GC-376, and calpain inhibitors II, XII inhibit SARS-CoV-2 viral replication by targeting the viral main protease. *Cell Res* **30**: 678-692 [PMID:32541865]
 83. Ma J, Zhu F, Zhao M, Shao F, Yu D, Ma J, Zhang X, Li W, Qian Y and Zhang Y *et al.*. (2021) SARS-CoV-2 nucleocapsid suppresses host pyroptosis by blocking Gasdermin D cleavage. *EMBO J*: e108249 [PMID:34296442]
 84. Ma Y, Wu L, Shaw N, Gao Y, Wang J, Sun Y, Lou Z, Yan L, Zhang R and Rao Z. (2015) Structural basis and functional analysis of the SARS coronavirus nsp14-nsp10 complex. *Proc Natl Acad Sci U S A* **112**: 9436-41 [PMID:26159422]
 85. Miknis ZJ, Donaldson EF, Umland TC, Rimmer RA, Baric RS and Schultz LW. (2009) Severe acute respiratory syndrome coronavirus nsp9 dimerization is essential for efficient viral growth. *J Virol* **83**: 3007-18 [PMID:19153232]
 86. Milligan JC, Zeisner TU, Papageorgiou G, Joshi D, Soudy C, Ulferts R, Wu M, Lim CT, Tan KW and Weissmann F *et al.*. (2021) Identifying SARS-CoV-2 antiviral compounds by screening for small molecule inhibitors of Nsp5 main protease. *Biochem J* **478**: 2499-2515 [PMID:34198327]
 87. Minakshi R, Padhan K, Rani M, Khan N, Ahmad F and Jameel S. (2009) The SARS Coronavirus 3a protein causes endoplasmic reticulum stress and induces ligand-independent downregulation of the type 1 interferon receptor. *PLoS ONE* **4**: e8342 [PMID:20020050]
 88. Minskaia E, Hertzog T, Gorbalenya AE, Campanacci V, Cambillau C, Canard B and Ziebuhr J. (2006) Discovery of an RNA virus 3'->5' exoribonuclease that is critically involved in coronavirus RNA synthesis. *Proc Natl Acad Sci USA* **103**: 5108-13 [PMID:16549795]
 89. Molecular Partners. Molecular Partners pipeline page
 90. Muth D, Corman VM, Roth H, Binger T, Dijkman R, Gottula LT, Gloza-Rausch F, Balboni A, Battilani M and Rihtarič D *et al.*. (2018) Attenuation of replication by a 29 nucleotide deletion in SARS-coronavirus acquired during the early stages of human-to-human transmission. *Sci Rep* **8**: 15177 [PMID:30310104]
 91. Nakagawa K, Narayanan K, Wada M and Makino S. (2018) Inhibition of Stress Granule Formation by Middle East Respiratory Syndrome Coronavirus 4a Accessory Protein Facilitates Viral Translation, Leading to Efficient Virus Replication. *J Virol* **92** [PMID:30068649]
 92. Nelson CA, Pekosz A, Lee CA, Diamond MS and Fremont DH. (2005) Structure and intracellular targeting of the SARS-coronavirus Orf7a accessory protein. *Structure* **13**: 75-85 [PMID:15642263]
 93. Nieto-Torres JL, Verdía-Báguena C, Jimenez-Guardeño JM, Regla-Nava JA, Castaño-Rodríguez C, Fernandez-Delgado R, Torres J, Aguilera VM and Enjuanes L. (2015) Severe acute respiratory syndrome coronavirus E protein transports calcium ions and activates the NLRP3 inflammasome. *Virology* **485**: 330-9 [PMID:26331680]
 94. Ogando NS, Zevenhoven-Dobbe JC, van der Meer Y, Bredenbeek PJ, Posthuma CC and Snijder EJ. (2020) The Enzymatic Activity of the nsp14 Exoribonuclease Is Critical for Replication of MERS-CoV and SARS-CoV-2. *J Virol* **94** [PMID:32938769]
 95. Oh CK, Nakamura T, Beutler N, Zhang X, Piña-Crespo J, Talantova M, Ghatak S, Trudler D, Carnevale LN and McKercher SR *et al.*. (2022) Targeted protein S-nitrosylation of ACE2 inhibits SARS-CoV-2 infection. *Nat Chem Biol* [PMID:36175661]
 96. Osipiuk J, Azizi SA, Dvorkin S, Endres M, Jedrzejczak R, Jones KA, Kang S, Kathayat RS, Kim Y and Lisnyak VG *et al.*. (2021) Structure of papain-like protease from SARS-CoV-2 and its complexes with non-covalent inhibitors. *Nat Commun* **12**: 743 [PMID:33531496]
 97. Osipiuk J, Wydorski PM, Lanham BT, Tesar C, Endres M, Engle E, Jedrzejczak R, Mullapudi V, Michalska K and Fidelis K *et al.*. (2022) Dual domain recognition determines SARS-CoV-2 PLpro selectivity for human ISG15 and K48-linked di-ubiquitin. *bioRxiv* [PMID:35547846]
 98. Otava T, Šála M, Li F, Fanfrlík J, Devkota K, Perveen S, Chau I, Pakarian P, Hobza P and Vedadi M *et al.*. (2021) The Structure-Based Design of SARS-CoV-2 nsp14 Methyltransferase Ligands Yields Nanomolar Inhibitors. *ACS Infect Dis* **7**: 2214-2220 [PMID:34152728]
 99. Outlaw VK, Bovier FT, Mears MC, Cajimat MN, Zhu Y, Lin MJ, Addetia A, Lieberman NAP, Peddu V and Xie X *et al.*. (2020) Inhibition of Coronavirus Entry *In Vitro* and *Ex Vivo* by a Lipid-Conjugated Peptide Derived from the SARS-CoV-2 Spike Glycoprotein HRC Domain. *mBio* **11** [PMID:33082259]
 100. Owen DR, Allerton CMN, Anderson AS, Aschenbrenner L, Avery M, Berritt S, Boras B, Cardin RD, Carlo A and

- Coffman KJ *et al.*. (2021) An oral SARS-CoV-2 M^{pro} inhibitor clinical candidate for the treatment of COVID-19. *Science* **374**: 1586-1593 [PMID:34726479]
101. Pakrashy S, Mandal PK, Dey SK, Choudhury SM, Alasmay FA, Almalki AS, Islam MA and Dolai M. (2022) Design of a Structurally Novel Multipotent Drug Candidate by the Scaffold Architecture Technique for ACE-II, NSP15, and M^{pro} Protein Inhibition: Identification and Isolation of a Natural Product to Prevent the Severity of Future Variants of Covid 19 and a Colorectal Anticancer Drug. *ACS Omega* **7**: 33408-33422 [PMID:36157758]
102. Pathak N, Chen YT, Hsu YC, Hsu NY, Kuo CJ, Tsai HP, Kang JJ, Huang CH, Chang SY and Chang YH *et al.*. (2021) Uncovering Flexible Active Site Conformations of SARS-CoV-2 3CL Proteases through Protease Pharmacophore Clusters and COVID-19 Drug Repurposing. *ACS Nano* **15**: 857-872 [PMID:33373194]
103. Pei P, Qin H, Chen J, Wang F, He C, He S, Hong B, Liu K, Qiao RZ and Fan H *et al.*. (2021) Computational design of ultrashort peptide inhibitors of the receptor-binding domain of the SARS-CoV-2 S protein. *Brief Bioinform* [PMID:34180984]
104. Peng Q, Peng R, Yuan B, Zhao J, Wang M, Wang X, Sun Y, Fan Z, Qi J and Gao GF *et al.*. (2020) Structural and biochemical characterization of nsp12-nsp7-nsp8 core polymerase complex from SARS-CoV-2 *Cell Reports*
105. Pervushin K, Tan E, Parthasarathy K, Lin X, Jiang FL, Yu D, Vararattanavech A, Soong TW, Liu DX and Torres J. (2009) Structure and inhibition of the SARS coronavirus envelope protein ion channel. *PLoS Pathog* **5**: e1000511 [PMID:19593379]
106. Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, Storgaard M, Al Khalili S and Simonsen L. (2020) Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. *Lancet Infect Dis* **20**: e238-e244 [PMID:32628905]
107. Pfefferle S, Krähling V, Ditt V, Grywna K, Mühlberger E and Drosten C. (2009) Reverse genetic characterization of the natural genomic deletion in SARS-Coronavirus strain Frankfurt-1 open reading frame 7b reveals an attenuating function of the 7b protein in-vitro and in-vivo. *Virology* **6**: 131 [PMID:19698190]
108. Pillaiyar T, Manickam M, Namasivayam V, Hayashi Y and Jung SH. (2016) An Overview of Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) 3CL Protease Inhibitors: Peptidomimetics and Small Molecule Chemotherapy. *J Med Chem* **59**: 6595-628 [PMID:26878082]
109. Pillon MC, Frazier MN, Dillard LB, Williams JG, Kocaman S, Krahn JM, Perera L, Hayne CK, Gordon J and Stewart ZD *et al.*. (2021) Cryo-EM structures of the SARS-CoV-2 endoribonuclease Nsp15 reveal insight into nuclease specificity and dynamics. *Nat Commun* **12**: 636 [PMID:33504779]
110. PostEra AI. MPro Activity Data
111. Pruijssers AJ and Denison MR. (2019) Nucleoside analogues for the treatment of coronavirus infections. *Curr Opin Virol* **35**: 57-62 [PMID:31125806]
112. Qiao J, Li YS, Zeng R, Liu FL, Luo RH, Huang C, Wang YF, Zhang J, Quan B and Shen C *et al.*. (2021) SARS-CoV-2 M^{pro} inhibitors with antiviral activity in a transgenic mouse model. *Science* [PMID:33602867]
113. Rappazzo CG, Tse LV, Kaku CI, Wrapp D, Sakharkar M, Huang D, Deveau LM, Yockachonis TJ, Herbert AS and Battles MB *et al.*. (2021) Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody. *Science* **371**: 823-829 [PMID:33495307]
114. Rashid F, Xie Z, Suleman M, Shah A, Khan S and Luo S. (2022) Roles and functions of SARS-CoV-2 proteins in host immune evasion. *Front Immunol* **13**: 940756 [PMID:36003396]
115. Rathnayake AD, Zheng J, Kim Y, Perera KD, Mackin S, Meyerholz DK, Kashipathy MM, Battaile KP, Lovell S and Perlman S *et al.*. (2020) 3C-like protease inhibitors block coronavirus replication in vitro and improve survival in MERS-CoV-infected mice. *Sci Transl Med* **12** [PMID:32747425]
116. Ratia K, Pegan S, Takayama J, Sleeman K, Coughlin M, Baliji S, Chaudhuri R, Fu W, Prabhakar BS and Johnson ME *et al.*. (2008) A noncovalent class of papain-like protease/deubiquitinase inhibitors blocks SARS virus replication. *Proc Natl Acad Sci USA* **105**: 16119-24 [PMID:18852458]
117. Riva L, Yuan S, Yin X, Martin-Sancho L, Matsunaga N, Pache L, Burgstaller-Muehlbacher S, De Jesus PD, Teriete P and Hull MV *et al.*. (2020) Discovery of SARS-CoV-2 antiviral drugs through large-scale compound repurposing *Nature*
118. Rosas-Lemus M, Minasov G, Shuvalova L, Inniss NL, Kiryukhina O, Brunzelle J and Satchell KJF. (2020) High-resolution structures of the SARS-CoV-2 2'-O-methyltransferase reveal strategies for structure-based inhibitor design *Science Signaling* **13**: eabe1202
119. Ruch TR and Machamer CE. (2012) The coronavirus E protein: assembly and beyond. *Viruses* **4**: 363-82 [PMID:22590676]
120. Saikatendu KS, Joseph JS, Subramanian V, Clayton T, Griffith M, Moy K, Velasquez J, Neuman BW, Buchmeier MJ and Stevens RC *et al.*. (2005) Structural basis of severe acute respiratory syndrome coronavirus ADP-ribose-1"-phosphate dephosphorylation by a conserved domain of nsP3. *Structure* **13**: 1665-75

[PMID:16271890]

121. Schindewolf C, Lokugamage K, Vu M, Johnson BA, Scharton D, Plante JA, Kalveram BK, Crocquet-Valdes PA, Sotcheff SL and Jaworski E *et al.*. (2022) SARS-CoV-2 Uses Nonstructural Protein 16 to Evade Restriction by IFIT1 and IFIT3 *bioRxiv*
122. Schuller M, Correy GJ, Gahbauer S, Fearon D, Wu T, Diaz RE, Young ID, Martins LC, Smith DH and Schulze-Gahmen U *et al.*. (2021) Fragment binding to the Nsp3 macrodomain of SARS-CoV-2 identified through crystallographic screening and computational docking *Science Advances* **7**: eabf8711
123. Schäfer A, Martinez DR, Won JJ, Moreira FR, Brown AJ, Gully KL, Kalla R, Chun K, Du Pont V and Babusis D *et al.*. (2021) Therapeutic efficacy of an oral nucleoside analog of remdesivir against SARS-CoV-2 pathogenesis in mice. *bioRxiv* [PMID:34545367]
124. Shahid M and Shahzad-UI-Hussan S. (2020) Structural insights of key enzymes into therapeutic intervention against SARS-CoV-2. *J Struct Biol* **213**: 107690 [PMID:33383190]
125. Shan H, Liu J, Shen J, Dai J, Xu G, Lu K, Han C, Wang Y, Xu X and Tong Y *et al.*. (2021) Development of potent and selective inhibitors targeting the papain-like protease of SARS-CoV-2. *Cell Chem Biol* [PMID:33979649]
126. Sharma A, Kaur M, Yadav P, Singh G and Barnwal RP. (2022) Expediting the drug discovery for ideal leads against SARS-CoV-2 via molecular docking of repurposed drugs. *J Biomol Struct Dyn*: 1-17 [PMID:36165445]
127. Shen Z, Ratia K, Cooper L, Kong D, Lee H, Kwon Y, Li Y, Alqarni S, Huang F and Dubrovskiy O *et al.*. (2021) Design of SARS-CoV-2 PLpro Inhibitors for COVID-19 Antiviral Therapy Leveraging Binding Cooperativity. *J Med Chem* [PMID:34665619]
128. Shen Z, Ratia K, Cooper L, Kong D, Lee H, Kwon Y, Li Y, Alqarni S, Huang F and Dubrovskiy O *et al.*. (2021) Potent, Novel SARS-CoV-2 PLpro Inhibitors Block Viral Replication in Monkey and Human Cell Cultures. *bioRxiv* [PMID:33594371]
129. Shi CS, Qi HY, Boularan C, Huang NN, Abu-Asab M, Shelhamer JH and Kehrl JH. (2014) SARS-coronavirus open reading frame-9b suppresses innate immunity by targeting mitochondria and the MAVS/TRAF3/TRAF6 signalosome. *J Immunol* **193**: 3080-9 [PMID:25135833]
130. Shin D, Mukherjee R, Grewe D, Bojkova D, Baek K, Bhattacharya A, Schulz L, Widera M, Mehdipour AR and Tascher G *et al.*. (2020) Papain-like protease regulates SARS-CoV-2 viral spread and innate immunity. *Nature* **587**: 657-662 [PMID:32726803]
131. Singh Tomar PP and Arkin IT. (2020) SARS-CoV-2 E protein is a potential ion channel that can be inhibited by Gliclazide and Memantine. *Biochem Biophys Res Commun* **530**: 10-14 [PMID:32828269]
132. Snijder EJ, Decroly E and Ziebuhr J. (2016) The Nonstructural Proteins Directing Coronavirus RNA Synthesis and Processing. *Adv Virus Res* **96**: 59-126 [PMID:27712628]
133. Su YCF, Anderson DE, Young BE, Linster M, Zhu F, Jayakumar J, Zhuang Y, Kalimuddin S, Low JGH and Tan CW *et al.*. (2020) Discovery and Genomic Characterization of a 382-Nucleotide Deletion in ORF7b and ORF8 during the Early Evolution of SARS-CoV-2. *mBio* **11** [PMID:32694143]
134. Surya W, Li Y, Verdià-Bàguena C, Aguilera VM and Torres J. (2015) MERS coronavirus envelope protein has a single transmembrane domain that forms pentameric ion channels. *Virus Res* **201**: 61-6 [PMID:25733052]
135. Tan H, Hu Y, Jadhav P, Tan B and Wang J. (2022) Progress and Challenges in Targeting the SARS-CoV-2 Papain-like Protease. *J Med Chem* [PMID:35620927]
136. Tan YJ, Fielding BC, Goh PY, Shen S, Tan TH, Lim SG and Hong W. (2004) Overexpression of 7a, a protein specifically encoded by the severe acute respiratory syndrome coronavirus, induces apoptosis via a caspase-dependent pathway. *J Virol* **78**: 14043-7 [PMID:15564512]
137. Tanner JA, Watt RM, Chai YB, Lu LY, Lin MC, Peiris JS, Poon LL, Kung HF and Huang JD. (2003) The severe acute respiratory syndrome (SARS) coronavirus NTPase/helicase belongs to a distinct class of 5' to 3' viral helicases. *J Biol Chem* **278**: 39578-82 [PMID:12917423]
138. te Velthuis AJ, van den Worm SH and Snijder EJ. (2012) The SARS-coronavirus nsp7+nsp8 complex is a unique multimeric RNA polymerase capable of both de novo initiation and primer extension. *Nucleic Acids Res* **40**: 1737-47 [PMID:22039154]
139. ter Meulen J, van den Brink EN, Poon LL, Marissen WE, Leung CS, Cox F, Cheung CY, Bakker AQ, Bogaards JA and van Deventer E *et al.*. (2006) Human monoclonal antibody combination against SARS coronavirus: synergy and coverage of escape mutants. *PLoS Med* **3**: e237 [PMID:16796401]
140. Thanigaimalai P, Konno S, Yamamoto T, Koiwai Y, Taguchi A, Takayama K, Yakushiji F, Akaji K, Chen SE and Naser-Tavakolian A *et al.*. (2013) Development of potent dipeptide-type SARS-CoV 3CL protease inhibitors with novel P3 scaffolds: design, synthesis, biological evaluation, and docking studies. *Eur J Med Chem* **68**: 372-84 [PMID:23994330]
141. Thanigaimalai P, Konno S, Yamamoto T, Koiwai Y, Taguchi A, Takayama K, Yakushiji F, Akaji K, Kiso Y and Kawasaki Y *et al.*. (2013) Design, synthesis, and biological evaluation of novel dipeptide-type SARS-CoV 3CL

- protease inhibitors: structure-activity relationship study. *Eur J Med Chem* **65**: 436-47 [PMID:23747811]
142. The COVID Moonshot Consortium, Achdout H, Aimon A, Bar-David E, Barr H, Ben-Shmuel A, Bennett J, Boby ML, Borden B and Bowman GR *et al.*. (2021) Open Science Discovery of Oral Non-Covalent SARS-CoV-2 Main Protease Inhibitor Therapeutics *bioRxiv*
 143. Thoms M, Buschauer R, Ameismeier M, Koepke L, Denk T, Hirschenberger M, Kratzat H, Hayn M, Mackens-Kiani T and Cheng J *et al.*. (2020) Structural basis for translational shutdown and immune evasion by the Nsp1 protein of SARS-CoV-2. *Science* **369**: 1249-1255 [PMID:32680882]
 144. Tian X, Li C, Huang A, Xia S, Lu S, Shi Z, Lu L, Jiang S, Yang Z and Wu Y *et al.*. (2020) Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody. *Emerg Microbes Infect* **9**: 382-385 [PMID:32065055]
 145. Turlington M, Chun A, Tomar S, Egglar A, Grum-Tokars V, Jacobs J, Daniels JS, Dawson E, Saldanha A and Chase P *et al.*. (2013) Discovery of N-(benzo[1,2,3]triazol-1-yl)-N-(benzyl)acetamido)phenyl) carboxamides as severe acute respiratory syndrome coronavirus (SARS-CoV) 3CLpro inhibitors: identification of ML300 and noncovalent nanomolar inhibitors with an induced-fit binding. *Bioorg Med Chem Lett* **23**: 6172-7 [PMID:24080461]
 146. Unoh Y, Uehara S, Nakahara K, Nobori H, Yamatsu Y, Yamamoto S, Maruyama Y, Taoda Y, Kasamatsu K and Suto T *et al.*. (2022) Discovery of S-217622, a Noncovalent Oral SARS-CoV-2 3CL Protease Inhibitor Clinical Candidate for Treating COVID-19. *J Med Chem* **65**: 6499-6512 [PMID:35352927]
 147. Vandyck K, Raboisson P, Beigelman L, Serebryany V, Stoycheva A, Bardiot D, Boland S and Marchand A. (2021) Anti-viral compounds for treating coronavirus, picornavirus, and norovirus infections Patent number: WO2021252491A1.
 148. Vankadara S, Wong YX, Liu B, See YY, Tan LH, Tan QW, Wang G, Karuna R, Guo X and Tan ST *et al.*. (2021) A head-to-head comparison of the inhibitory activities of 15 peptidomimetic SARS-CoV-2 3CLpro inhibitors. *Bioorg Med Chem Lett* **48**: 128263 [PMID:34271072]
 149. Vasilenko N, Moshynskyy I and Zakhartchouk A. (2010) SARS coronavirus protein 7a interacts with human Ap4A-hydrolase. *Virology* **407**: 31 [PMID:20144233]
 150. Vuong W, Khan MB, Fischer C, Arutyunova E, Lamer T, Shields J, Saffran HA, McKay RT, van Belkum MJ and Joyce MA *et al.*. (2020) Feline coronavirus drug inhibits the main protease of SARS-CoV-2 and blocks virus replication. *Nat Commun* **11**: 4282 [PMID:32855413]
 151. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT and Velesler D. (2020) Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell* **181**: 281-292.e6 [PMID:32155444]
 152. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z, Lu G, Qiao C, Hu Y and Yuen KY *et al.*. (2020) Structural and Functional Basis of SARS-CoV-2 Entry by Using Human ACE2. *Cell* **181**: 894-904.e9 [PMID:32275855]
 153. Wang W, Zhou Z, Xiao X, Tian Z, Dong X, Wang C, Li L, Ren L, Lei X and Xiang Z *et al.*. (2021) SARS-CoV-2 nsp12 attenuates type I interferon production by inhibiting IRF3 nuclear translocation. *Cell Mol Immunol* [PMID:33637958]
 154. Wang Y, Anirudhan V, Du R, Cui Q and Rong L. (2020) RNA-dependent RNA polymerase of SARS-CoV-2 as a therapeutic target. *J Med Virol* [PMID:32633831]
 155. Wenzel J, Lampe J, Müller-Fielitz H, Schuster R, Zille M, Müller K, Krohn M, Körbelin J, Zhang L and Özorhan Ü *et al.*. (2021) The SARS-CoV-2 main protease M^{Pro} causes microvascular brain pathology by cleaving NEMO in brain endothelial cells. *Nat Neurosci* [PMID:34675436]
 156. Westberg M, Su Y, Zou X, Ning L, Hurst B, Tarbet B and Lin MZ. (2021) Rational design of a new class of protease inhibitors for the potential treatment of coronavirus diseases *bioRxiv*
 157. Westendorf K, Wang L, Žentelis S, Foster D, Vaillancourt P, Wiggin M, Lovett E, van der Lee R, Hendle J and Pustilnik A *et al.*. (2022) LY-CoV1404 (bebtelovimab) potently neutralizes SARS-CoV-2 variants. *bioRxiv* [PMID:33972947]
 158. Wilson IM, Frazier MN, Li JL, Randall TA and Stanley RE. (2022) Biochemical Characterization of Emerging SARS-CoV-2 Nsp15 Endoribonuclease Variants. *J Mol Biol* **434**: 167796 [PMID:35995266]
 159. Wilson L, McKinlay C, Gage P and Ewart G. (2004) SARS coronavirus E protein forms cation-selective ion channels. *Virology* **330**: 322-31 [PMID:15527857]
 160. Wiser C, Kim B and Ascano M. (2019) G3BP1 enhances cytoplasmic DNA pattern recognition. *Nat Immunol* **20**: 5-7 [PMID:30538338]
 161. Węglarz-Tomczak E, Tomczak JM, Talma M and Brul S. (2020) Ebselen as a highly active inhibitor of PLProCoV2 *bioRxiv*
 162. Xia S, Liu M, Wang C, Xu W, Lan Q, Feng S, Qi F, Bao L, Du L and Liu S *et al.*. (2020) Inhibition of SARS-CoV-2 (previously 2019-nCoV) infection by a highly potent pan-coronavirus fusion inhibitor targeting its spike protein that harbors a high capacity to mediate membrane fusion. *Cell Res* **30**: 343-355 [PMID:32231345]
 163. Xia S, Yan L, Xu W, Agrawal AS, Algaissi A, Tseng CK, Wang Q, Du L, Tan W and Wilson IA *et al.*. (2019) A

- pan-coronavirus fusion inhibitor targeting the HR1 domain of human coronavirus spike. *Sci Adv* **5**: eaav4580 [PMID:30989115]
164. Xia Z, Sacco M, Hu Y, Ma C, Meng X, Zhang F, Szeto T, Xiang Y, Chen Y and Wang J. (2021) Rational Design of Hybrid SARS-CoV-2 Main Protease Inhibitors Guided by the Superimposed Cocrystal Structures with the Peptidomimetic Inhibitors GC-376, Telaprevir, and Boceprevir. *ACS Pharmacol Transl Sci* **4**: 1408-1421 [PMID:34414360]
165. Xiang Y, Nambulli S, Xiao Z, Liu H, Sang Z, Duprex WP, Schneidman-Duhovny D, Zhang C and Shi Y. (2020) Versatile and multivalent nanobodies efficiently neutralize SARS-CoV-2. *Science* **370**: 1479-1484 [PMID:33154108]
166. Xie Y, Yin W, Zhang Y, Shang W, Wang Z, Luan X, Tian G, Aisa HA, Xu Y and Xiao G *et al.*. (2021) Design and development of an oral remdesivir derivative VV116 against SARS-CoV-2. *Cell Res* **31**: 1212-1214 [PMID:34584244]
167. Xu K, Zheng BJ, Zeng R, Lu W, Lin YP, Xue L, Li L, Yang LL, Xu C and Dai J *et al.*. (2009) Severe acute respiratory syndrome coronavirus accessory protein 9b is a virion-associated protein. *Virology* **388**: 279-85 [PMID:19394665]
168. Yan R, Zhang Y, Li Y, Xia L, Guo Y and Zhou Q. (2020) Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science* **367**: 1444-1448 [PMID:32132184]
169. Yang H, Xie W, Xue X, Yang K, Ma J, Liang W, Zhao Q, Zhou Z, Pei D and Ziebuhr J *et al.*. (2005) Design of wide-spectrum inhibitors targeting coronavirus main proteases. *PLoS Biol* **3**: e324 [PMID:16128623]
170. Yang KS, Ma XR, Ma Y, Alugubelli YR, Scott DA, Vatansever EC, Drelich AK, Sankaran B, Geng ZZ and Blankenship LR *et al.*. (2020) A Speedy Route to Multiple Highly Potent SARS-CoV-2 Main Protease Inhibitors. *bioRxiv* [PMID:32766582]
171. Yang S, Chen SJ, Hsu MF, Wu JD, Tseng CT, Liu YF, Chen HC, Kuo CW, Wu CS and Chang LW *et al.*. (2006) Synthesis, crystal structure, structure-activity relationships, and antiviral activity of a potent SARS coronavirus 3CL protease inhibitor. *J Med Chem* **49**: 4971-80 [PMID:16884309]
172. Yang W, Ru Y, Ren J, Bai J, Wei J, Fu S, Liu X, Li D and Zheng H. (2019) G3BP1 inhibits RNA virus replication by positively regulating RIG-I-mediated cellular antiviral response. *Cell Death Dis* **10**: 946 [PMID:31827077]
173. Yin W, Mao C, Luan X, Shen DD, Shen Q, Su H, Wang X, Zhou F, Zhao W and Gao M *et al.*. (2020) Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir. *Science* **368**: 1499-1504 [PMID:32358203]
174. Yoshimoto FK. (2020) The Proteins of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2 or n-COV19), the Cause of COVID-19 *The Protein Journal volume* **39**: 198–216
175. Young BE, Fong S-W, Chan Y-H, Mak T-M, Ang LW and Anderson DE. (2020) Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study *The Lancet*
176. Yuan M, Wu NC, Zhu X, Lee CD, So RTY, Lv H, Mok CKP and Wilson IA. (2020) A highly conserved cryptic epitope in the receptor binding domains of SARS-CoV-2 and SARS-CoV. *Science* **368**: 630-633 [PMID:32245784]
177. Zaher NH, Mostafa MI and Altaher AY. (2020) Design, synthesis and molecular docking of novel triazole derivatives as potential CoV helicase inhibitors. *Acta Pharm* **70**: 145-159 [PMID:31955138]
178. Zhang C-H, Spasov KA, Reilly RA, Hollander K, Stone EA, Ippolito JA, Liosi M-A, Deshmukh MG, Tirado-Rives J and Zhang S *et al.*. (2021) Optimization of Triarylpyridinone Inhibitors of the Main Protease of SARS-CoV-2 to Low-Nanomolar Antiviral Potency *ACS Medicinal Chemistry Letters*
179. Zhang C-H, Stone EA, Deshmukh M, Ippolito JA, Ghahremanpour MM, Tirado-Rives J, Spasov KA, Zhang S, Takeo Y and Kudalkar SN *et al.*. (2021) Potent Noncovalent Inhibitors of the Main Protease of SARS-CoV-2 from Molecular Sculpting of the Drug Perampanel Guided by Free Energy Perturbation Calculations *ACS Central Science*
180. Zhang L, Li L, Yan L, Ming Z, Jia Z, Lou Z and Rao Z. (2018) Structural and Biochemical Characterization of Endoribonuclease Nsp15 Encoded by Middle East Respiratory Syndrome Coronavirus. *J Virol* **92** [PMID:30135128]
181. Zhang L, Lin D, Kusov Y, Nian Y, Ma Q, Wang J, von Brunn A, Leyssen P, Lanko K and Neyts J *et al.*. (2020) α -Ketoamides as Broad-Spectrum Inhibitors of Coronavirus and Enterovirus Replication: Structure-Based Design, Synthesis, and Activity Assessment. *J Med Chem* **63**: 4562-4578 [PMID:32045235]
182. Zhang L, Lin D, Sun X, Curth U, Drosten C, Sauerhering L, Backer S, Rox K and Hilgenfeld R. (2020) Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α -ketoamide inhibitors *Science*
183. Zhang L, Lin D, Sun X, Curth U, Drosten C, Sauerhering L, Becker S, Rox K and Hilgenfeld R. (2020) Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α -ketoamide inhibitors.

- Science* **368**: 409-412 [[PMID:32198291](#)]
184. Zhang R, Wang K, Lv W, Yu W, Xie S, Xu K, Schwarz W, Xiong S and Sun B. (2014) The ORF4a protein of human coronavirus 229E functions as a viroporin that regulates viral production. *Biochim Biophys Acta* **1838**: 1088-95 [[PMID:23906728](#)]
 185. Zhao Y, Fang C, Zhang Q, Zhang R, Zhao X, Duan Y, Wang H, Zhu Y, Feng L and Zhao J *et al.*. (2021) Crystal structure of SARS-CoV-2 main protease in complex with protease inhibitor PF-07321332. *Protein Cell* [[PMID:34687004](#)]
 186. Zhu W, Chen CZ, Gorshkov K, Xu M, Lo DC and Zheng W. (2020) RNA-Dependent RNA Polymerase as a Target for COVID-19 Drug Discovery. *SLAS Discov* **25**: 1141-1151 [[PMID:32660307](#)]
 187. Zhu W, Xu M, Chen CZ, Guo H, Shen M, Hu X, Shinn P, Klumpp-Thomas C, Michael SG and Zheng W. (2020) Identification of SARS-CoV-2 3CL Protease Inhibitors by a Quantitative High-throughput Screening. *ACS Pharmacol Transl Sci*
 188. Zost SJ, Gilchuk P, Case JB, Binshtein E, Chen RE, Nkolola JP, Schäfer A, Reidy JX, Trivette A and Nargi RS *et al.*. (2020) Potently neutralizing and protective human antibodies against SARS-CoV-2. *Nature* **584**: 443-449 [[PMID:32668443](#)]