IUPHAR/BPS Guide to Pharmacology CITE
https://doi.org/10.2218/gtopdb/F1034/2025.1

Coronavirus (CoV) proteins in GtoPdb v.2025.1

Stephen P.H. Alexander[1], Jonathan K. Ball[1] and Theocharis Tsoleridis[1]

1. University of Nottingham, UK

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

This is a citation summary for Coronavirus (CoV) proteins in the Guide to Pharmacology database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

GtoPdb is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts. For further details see [22].

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

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
  - Complexes
    - CoV 2'-O-methyltransferase
      https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3277
  - Targets and Subunits
    - 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 10
https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3275
CoV Non-structural protein 13
https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3261
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 Non-structural protein 16
https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3276
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. Identification of inhibitors of SARS-Cov2 M-Pro enzymatic activity using a small molecule repurposing screen DOI: 10.6019/CHEMBL4495564.
2. 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]
3. 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 *N*7-Methyltransferase by Sulfonamide-Based Bisubstrate Analogues. *J Med Chem* **65**: 6231-6249 [PMID:35439007]
4. 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]
5. Alugubelli YR, Xiao J, Khatua K, Kumar S, Sun L, Ma Y, Ma XR, Vulupala VR, Atla S and Blankenship LR *et al.*. (2024) Discovery of First-in-Class PROTAC Degraders of SARS-CoV-2 Main Protease. *J Med Chem* **67**: 6495-6507 [PMID:38608245]
6. 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]
7. 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*
8. Arnold LD, Jennings A and Keung W. (2021) Inhibitors of cysteine proteases and methods of use thereof Patent number: WO2021252644A1.
9. 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* **35**: 109133 [PMID:33984267]
10. Bai B, Belovodskiy A, Hena M, Kandadai AS, Joyce MA, Saffran HA, Shields JA, Khan MB, Arutyunova E and Lu J *et al.*. (2022) Peptidomimetic α-Acyloxymethylketone 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* **65**: 2905-2925 [PMID:34242027]
11. 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]

12. 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]
13. Bekdash R, Yoshida K, Nair MS, Qiu L, Ahdout J, Tsai HY, Uryu K, Soni RK, Huang Y and Ho DD *et al.*. (2024) Developing inhibitory peptides against SARS-CoV-2 envelope protein. *PLoS Biol* **22**: e3002522 [PMID:38483887]
14. Bobiļeva O, Bobrovs R, Kaņepe I, Patetko L, Kalniņš G, Šišovs M, Bula AL, Gri Nberga S, Borodušķis MR and Ramata-Stunda A *et al.*. (2021) Potent SARS-CoV-2 mRNA Cap Methyltransferase Inhibitors by Bioisosteric Replacement of Methionine in SAM Cosubstrate. *ACS Med Chem Lett* **12**: 1102-1107 [PMID:34257831]
15. Boby ML, Fearon D, Ferla M, Filep M, Koekemoer L, Robinson MC, COVID Moonshot Consortium‡, Chodera JD, Lee AA and London N *et al.*. (2023) Open science discovery of potent noncovalent SARS-CoV-2 main protease inhibitors. *Science* **382**: eabo7201 [PMID:37943932]
16. Bolinger AA, Li J, Xie X, Li H and Zhou J. (2024) Lessons learnt from broad-spectrum coronavirus antiviral drug discovery. *Expert Opin Drug Discov* **19**: 1023-1041 [PMID:39078037]
17. 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.
18. 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]
19. 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]
20. Breidenbach J, Lemke C, Pillaiyar T, Schäkel L, Al Hamwi G, Diett 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* **60**: 10423-10429 [PMID:33655614]
21. Breidenbach J, Voget R, Si Y, Hingst A, Claff T, Sylvester K, Wolf V, Krasniqi V, Useini A and Sträter N *et al.*. (2024) Macrocyclic Azapeptide Nitriles: Structure-Based Discovery of Potent SARS-CoV-2 Main Protease Inhibitors as Antiviral Drugs. *J Med Chem* **67**: 8757-8790 [PMID:38753594]
22. 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]
23. 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]
24. 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]
25. Carlsson J, Danielson H, Moodie L and Sandstrom A. (2022) SUBSTITUTED HYDANTOIN COMPOUNDS, METHODS FOR PREPARATION THEREOF AND USE THEREOF IN THE TREATMENT AND/OR PREVENTION OF A CORONA VIRUS DISEASE Patent number: WO2022229458.
26. Chakraborty S, Mallick D, Goswami M, Guengerich FP, Chakrabarty A and Chowdhury G. (2022) The Natural Products Withaferin A and Withanone from the Medicinal Herb *Withania somnifera* Are Covalent Inhibitors of the SARS-CoV-2 Main Protease. *J Nat Prod* **85**: 2340-2350 [PMID:36098617]
27. 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]
28. Chen IY, Moriyama M, Chang MF and Ichinohe T. (2019) Severe Acute Respiratory Syndrome Coronavirus Viroporin 3a Activates the NLRP3 Inflammasome. *Front Microbiol* **10**: 50 [PMID:30761102]
29. Chen J, Liang C, Miao K, Wu Y, Yun H and Zhang W. (2022) Aminocarbamoyl compounds for the treatment of viral infections Patent number: WO2022043374.
30. Chen X, Huang X, Ma Q, Kuzmič P, Zhou B, Zhang S, Chen J, Xu J, Liu B and Jiang H *et al.*. (2024) Preclinical evaluation of the SARS-CoV-2 M^{pro} inhibitor RAY1216 shows improved pharmacokinetics compared with nirmatrelvir. *Nat Microbiol* **9**: 1075-1088 [PMID:38553607]
31. 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*
32. 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*
33. Chia CSB, Xu W and Shuyi Ng P. (2022) A Patent Review on SARS Coronavirus Main Protease ($3CL^{pro}$) Inhibitors. *ChemMedChem* **17**: e202100576 [PMID:34651447]
34. 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]
35. 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]
36. Cockram PE, Walters BT, Lictao A, Shanahan F, Wertz IE, Foster SA and Rudolph J. (2024) Allosteric Inhibitors of the SARS-COV-2 Papain-like Protease Domain Induce Proteasomal Degradation of Its Parent Protein NSP3. *ACS Chem Biol* **19**: 22-36 [PMID:38150587]
37. Congreve MS, Christopher JA, Pickworth M, De Graff C, Higueruelo AP, Mason JS and Kulkarni SS. (2022) SARS-COV-2 MPRO INHIBITOR COMPOUNDS Patent number: WO2022129953.
38. Cooper MS, Zhang L, Ibrahim M, Zhang K, Sun X, Röske J, Göhl M, Brönstrup M, Cowell JK and Sauerhering L *et al.*. (2022) Diastereomeric Resolution Yields Highly Potent Inhibitor of SARS-CoV-2 Main Protease. *J Med Chem* **65**: 13328-13342 [PMID:36179320]
39. 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]
40. Corona A, Madia VN, De Santis R, Manelfi C, Emmolo R, Ialongo D, Patacchini E, Messore A, Amatore D and Faggioni G *et al.*. (2023) Diketo acid inhibitors of nsp13 of SARS-CoV-2 block viral replication. *Antiviral Res* **217**: 105697 [PMID:37562607]
41. Cottam EM, Whelband MC and Wileman T. (2014) Coronavirus NSP6 restricts autophagosome expansion. *Autophagy* **10**: 1426-41 [PMID:24991833]
42. Cui J and Jia J. (2021) Discovery of juglone and its derivatives as potent SARS-CoV-2 main proteinase inhibitors. *Eur J Med Chem* **225**: 113789 [PMID:34438124]
43. Dai W, Jochmans D, Xie H, Yang H, Li J, Su H, Chang D, Wang J, Peng J and Zhu L *et al.*. (2022) Design, Synthesis, and Biological Evaluation of Peptidomimetic Aldehydes as Broad-Spectrum Inhibitors against Enterovirus and SARS-CoV-2. *J Med Chem* **65**: 2794-2808 [PMID:33872498]
44. 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]
45. 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* **64**: 10047-10058 [PMID:34213885]
46. Dampalla CS, Kim Y, Zabiegala A, Howard DJ, Nguyen HN, Madden TK, Thurman HA, Cooper A, Liu L and Battaile KP *et al.*. (2024) Structure-Guided Design of Potent Coronavirus Inhibitors with a 2-Pyrrolidone Scaffold: Biochemical, Crystallographic, and Virological Studies. *J Med Chem* **67**: 11937-11956 [PMID:38953866]
47. 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*
48. 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]
49. 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]
50. Dang F, Bai L, Dong J, Hu X, Wang J, Paulo JA, Xiong Y, Liang X, Sun Y and Chen Y *et al.*. (2023) USP2 inhibition prevents infection with ACE2-dependent coronaviruses in vitro and is protective against SARS-CoV-2 in mice. *Sci Transl Med* **15**: eadh7668 [PMID:38055802]
51. Dayan Elshan NGR, Wolff KC, Riva L, Woods AK, Grabovyi G, Wilson K, Pedroarena J, Ghorai S, Nazarian A and Weiss F *et al.*. (2024) Discovery of CMX990: A Potent SARS-CoV-2 3CL Protease Inhibitor Bearing a Novel Warhead. *J Med Chem* **67**: 2369-2378 [PMID:38335279]
52. 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]
53. 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]
54. Devantier K, Kjaer VMS, Griffin S, Kragelund BB and Rosenkilde MM. (2024) Advancing the field of viroporins—Structure, function and pharmacology: IUPHAR Review 39 *British Journal of Pharmacology*
55. 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]
56. 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]
57. 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*
58. Elseginy SA, Fayed B, Hamdy R, Mahrous N, Mostafa A, Almehdi AM and S M Soliman S. (2021) Promising anti-SARS-CoV-2 drugs by effective dual targeting against the viral and host proteases. *Bioorg Med Chem Lett* **43**: 128099 [PMID:33984473]
59. Fàbrega-Ferrer M, Herrera-Morandé A, Muriel-Goñi S, Pérez-Saavedra J, Bueno P, Castro V, Garaigorta U, Gastaminza P and Coll M. (2022) Structure and inhibition of SARS-CoV-1 and SARS-CoV-2 main proteases by oral antiviral compound AG7404. *Antiviral Res* **208**: 105458 [PMID:36336176]
60. 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]
61. Feng K, Min YQ, Sun X, Deng F, Li P, Wang H and Ning YJ. (2021) Interactome profiling reveals interaction of SARS-CoV-2 NSP13 with host factor STAT1 to suppress interferon signaling. *J Mol Cell Biol* **13**: 760-762 [PMID:34687317]
62. Feng K, Zhang HJ, Min YQ, Zhou M, Deng F, Wang HL, Li PQ and Ning YJ. (2023) SARS-CoV-2 NSP13 interacts with host IRF3, blocking antiviral immune responses. *J Med Virol* **95**: e28881 [PMID:37314155]
63. Flury P, Krüger N, Sylvester K, Breidenbach J, Al Hamwi G, Qiao J, Chen Y, Rocha C, Serafim MSM and Barbosa da Silva E *et al.*. (2025) Design, Synthesis, and Unprecedented Interactions of Covalent Dipeptide-Based Inhibitors of SARS-CoV-2 Main Protease and Its Variants Displaying Potent Antiviral Activity. *J Med Chem* **68**: 3626-3652 [PMID:39813204]
64. 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]
65. 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]
66. 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 deISGylase Activity of SARS-CoV-2 Papain-Like Protease. *ACS Infect Dis* **6**: 2099-2109 [PMID:32428392]
67. Fung SY, Siu KL, Lin H, Chan CP, Yeung ML and Jin DY. (2022) SARS-CoV-2 NSP13 helicase suppresses interferon signaling by perturbing JAK1 phosphorylation of STAT1. *Cell Biosci* **12**: 36 [PMID:35317858]
68. Fung TS and Liu DX. (2019) Human Coronavirus: Host-Pathogen Interaction. *Annu Rev Microbiol* **73**: 529-557 [PMID:31226023]
69. 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]
70. Garnsey MR, Robinson MC, Nguyen LT, Cardin R, Tillotson J, Mashalidis E, Yu A, Aschenbrenner L, Balesano A and Behzadi A *et al.*. (2024) Discovery of SARS-CoV-2 papain-like protease (PLpro) inhibitors with efficacy in a murine infection model *bioRxiv*
71. Geng ZZ, Atla S, Shaabani N, Vulupala V, Yang KS, Alugubelli YR, Khatua K, Chen PH, Xiao J and Blankenship LR *et al.*. (2023) A Systematic Survey of Reversibly Covalent Dipeptidyl Inhibitors of the SARS-CoV-2 Main Protease. *J Med Chem* **66**: 11040-11055 [PMID:37561993]
72. Gervasoni S, Vistoli G, Talarico C, Manelfi C, Beccari AR, Studer G, Tauriello G, Waterhouse AM, Schwede T and Pedretti A. (2020) A Comprehensive Mapping of the Druggable Cavities within the SARS-CoV-2 Therapeutically Relevant Proteins by Combining Pocket and Docking Searches as Implemented in Pockets 2.0. *Int J Mol Sci* **21**: 5152 [PMID:32708196]
73. 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]

74. 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]
75. Glaser J, Sedova A, Galanie S, Kneller DW, Davidson RB, Maradzike E, Del Galdo S, Labbé A, Hsu DJ and Agarwal R *et al.*. (2022) Hit Expansion of a Noncovalent SARS-CoV-2 Main Protease Inhibitor. *ACS Pharmacol Transl Sci* **5**: 255-265 [PMID:35434531]
76. Godoy AS, Nakamura AM, Douangamath A, Song Y, Noske GD, Gawriljuk VO, Fernandes RS, Pereira HDM, Oliveira KIZ and Fearon D *et al.*. (2023) Allosteric regulation and crystallographic fragment screening of SARS-CoV-2 NSP15 endoribonuclease. *Nucleic Acids Res* **51**: 5255-5270 [PMID:37115000]
77. 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]
78. 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]
79. 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]
80. Grifagni D, Lenci E, De Santis A, Orsetti A, Barracchia CG, Tedesco F, Bellini Puglielli R, Lucarelli F, Lauriola A and Assfalg M *et al.*. (2024) Development of a GC-376 Based Peptidomimetic PROTAC as a Degrader of 3-Chymotrypsin-like Protease of SARS-CoV-2. *ACS Med Chem Lett* **15**: 250-257 [PMID:38352832]
81. Hamdy R, Fayed B, Mostafa A, Shama NMA, Mahmoud SH, Mehta CH, Nayak Y and M Soliman SS. (2021) Iterated Virtual Screening-Assisted Antiviral and Enzyme Inhibition Assays Reveal the Discovery of Novel Promising Anti-SARS-CoV-2 with Dual Activity. *Int J Mol Sci* **22** [PMID:34445763]
82. Han SH, Goins CM, Arya T, Shin WJ, Maw J, Hooper A, Sonawane DP, Porter MR, Bannister BE and Crouch RD *et al.*. (2022) 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* **65**: 2880-2904 [PMID:34347470]
83. Hanna GS, Benjamin MM, Choo YM, De R, Schinazi RF, Nielson SE, Hevel JM and Hamann MT. (2024) Informatics and Computational Approaches for the Discovery and Optimization of Natural Product-Inspired Inhibitors of the SARS-CoV-2 2'-*O*-Methyltransferase. *J Nat Prod* **87**: 217-227 [PMID:38242544]
84. 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]
85. 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]
86. 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]
87. 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-1β secretion. *Cell Res* **25**: 1285-98 [PMID:26611636]
88. Hilgenfeld R. (2014) From SARS to MERS: crystallographic studies on coronaviral proteases enable antiviral drug design. *FEBS J* **281**: 4085-96 [PMID:25039866]
89. Hirose Y, Shindo N, Mori M, Onitsuka S, Isogai H, Hamada R, Hiramoto T, Ochi J, Takahashi D and Ueda T *et al.*. (2022) Discovery of Chlorofluoroacetamide-Based Covalent Inhibitors for Severe Acute Respiratory Syndrome Coronavirus 2 3CL Protease. *J Med Chem* **65**: 13852-13865 [PMID:36229406]
90. 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]
91. 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*

92. 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]
93. Hou N, Shuai L, Zhang L, Xie X, Tang K, Zhu Y, Yu Y, Zhang W, Tan Q and Zhong G *et al.*. (2023) Development of Highly Potent Noncovalent Inhibitors of SARS-CoV-2 3CLpro. *ACS Cent Sci* **9**: 217-227 [PMID:36844503]
94. Huang C, Shuai H, Qiao J, Hou Y, Zeng R, Xia A, Xie L, Fang Z, Li Y and Yoon C *et al.*. (2023) A new generation M^{pro} inhibitor with potent activity against SARS-CoV-2 Omicron variants. *Signal Transduct Target Ther* **8**: 128 [PMID:36928316]
95. 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*
96. 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]
97. Inniss NL, Kozic J, Li F, Rosas-Lemus M, Minasov G, Rybáček J, Zhu Y, Pohl R, Shuvalova L and Rulíšek L *et al.*. (2023) Discovery of a Druggable, Cryptic Pocket in SARS-CoV-2 nsp16 Using Allosteric Inhibitors. *ACS Infect Dis* **9**: 1918-1931 [PMID:37728236]
98. Inniss NL, Rzhetskaya M, Ling-Hu T, Lorenzo-Redondo R, Bachta KE, Satchell KJF and Hultquist JF. (2024) Activity and inhibition of the SARS-CoV-2 Omicron nsp13 R392C variant using RNA duplex unwinding assays. *SLAS Discov* **29**: 100145 [PMID:38301954]
99. 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*
100. Keum YS and Jeong YJ. (2012) Development of chemical inhibitors of the SARS coronavirus: viral helicase as a potential target. *Biochem Pharmacol* **84**: 1351-8 [PMID:22935448]
101. Khalili Yazdi A, Li F, Devkota K, Perveen S, Ghiabi P, Hajian T, Bolotokova A and Vedadi M. (2021) A High-Throughput Radioactivity-Based Assay for Screening SARS-CoV-2 nsp10-nsp16 Complex. *SLAS Discov* **26**: 757-765 [PMID:33874769]
102. 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]
103. 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]
104. 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]
105. 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]
106. 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]
107. 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]
108. Kocek H, Chalupská D, Dejmek M, Dvořáková A, Zgarbová M, Šála M, Chalupský K, Krafčíková P, Otava T and Drexler M *et al.*. (2024) Discovery of highly potent SARS-CoV-2 nsp14 methyltransferase inhibitors based on adenosine 5'-carboxamides. *RSC Med Chem* **15**: 3469-76 [PMID:39220762]
109. Konno S, Kobayashi K, Senda M, Funai Y, Seki Y, Tamai I, Schäkel L, Sakata K, Pillaiyar T and Taguchi A *et al.*. (2022) 3CL Protease Inhibitors with an Electrophilic Arylketone Moiety as Anti-SARS-CoV-2 Agents. *J Med Chem* **65**: 2926-2939 [PMID:34313428]
110. 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]
111. Krafcikova P, Silhan J, Nencka R and Boura E. (2020) Structural analysis of the SARS-CoV-2 methyltransferase complex involved in RNA cap creation bound to sinefungin. *Nat Commun* **11**: 3717 [PMID:32709887]
112. 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* **65**: 12500-12534 [PMID:36169610]
113. 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]
114. 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]
115. Lee C, Lee JM, Lee NR, Jin BS, Jang KJ, Kim DE, Jeong YJ and Chong Y. (2009) Aryl diketoacids (ADK) selectively inhibit duplex DNA-unwinding activity of SARS coronavirus NTPase/helicase. *Bioorg Med Chem Lett* **19**: 1636-8 [PMID:19233643]
116. 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]
117. Li F, Ghiabi P, Hajian T, Klima M, Li ASM, Khalili Yazdi A, Chau I, Loppnau P, Kutera M and Seitova A *et al.*. (2023) SS148 and WZ16 inhibit the activities of nsp10-nsp16 complexes from all seven human pathogenic coronaviruses. *Biochim Biophys Acta Gen Subj* **1867**: 130319 [PMID:36764586]
118. Li X and Song Y. (2024) Perspective for Drug Discovery Targeting SARS Coronavirus Methyltransferases: Function, Structure and Inhibition. *J Med Chem* **67**: 18642-18655 [PMID:39478665]
119. Liang C, Xin L, Tian L, Xia J, Qin N, Li J, Qiang T, Li H, Wang X and Xie X *et al.*. (2022) Protacs targeting coronavirus 3CL protease and preparation method and application thereof Patent number: US11530195B1.
120. Liang C, Xin L, Tian L, Xia J, Qin N, Li J, Qiang T, Li H, Wang X and Xie X *et al.*. (2022) Protacs based on VHL ligand targeting coronavirus 3CL protease and preparation method and application thereof Patent number: US11518759B1.
121. 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]
122. Liu H, Iketani S, Zask A, Khanizeman N, Bednarova E, Forouhar F, Fowler B, Hong SJ, Mohri H and Nair MS *et al.*. (2022) Development of optimized drug-like small molecule inhibitors of the SARS-CoV-2 3CL protease for treatment of COVID-19. *Nat Commun* **13**: 1891 [PMID:35393402]
123. Liu R, Xu Y, Hua L, Zhou J, Deng H, Chu X and Ding S. (2023) 3CL PROTEASE SMALL-MOLECULE INHIBITOR FOR TREATING OR PREVENTING CORONAVIRUS INFECTION, AND USE THEREOF Patent number: WO2023011443.
124. 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]
125. 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]
126. 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]
127. 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]
128. Luttens 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* **144**: 2905-2920 [PMID:35142215]
129. 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]
130. 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* **40**: e108249 [PMID:34296442]
131. 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]
132. Marx SK, Mickolajczyk KJ, Craig JM, Thomas CA, Pfeffer AM, Abell SJ, Carrasco JD, Franzi MC, Huang JR and Kim HC *et al.*. (2023) Observing inhibition of the SARS-CoV-2 helicase at single-nucleotide resolution. *Nucleic Acids Res* **51**: 9266-9278 [PMID:37560916]
133. Matos-Hernández ML, Samples R, Dyer G, Casimir Montán VM, Morales-Colón CA, Salvino JM, Montaner LJ, Cassel JA, Messick TE and Tietjen I *et al.*. (2024) Metabolomic Analysis and Antiviral Screening of a Marine Algae Library Yield Jobosic Acid (2,5-Dimethyltetradecanoic Acid) as a Selective Inhibitor of SARS-CoV-2. *J Nat Prod* [PMID:38781491]
134. McGovern-Gooch KR, Mani N, Gotchev D, Ardzinski A, Kowalski R, Sheraz M, Micolochick Steuer HM, Tercero B, Wang X and Wasserman A *et al.*. (2024) Biological characterization of

AB-343, a novel and potent SARS-CoV-2 M^{pro} inhibitor with pan-coronavirus activity. *Antiviral Res* **232**: 106038 [PMID:39577571]
135. Mehyar N. (2023) Coronaviruses SARS-CoV, MERS-CoV, and SARS-CoV-2 helicase inhibitors: a systematic review of *invitro* studies. *J Virus Erad* **9**: 100327 [PMID:37363132]
136. Meyer C, Garzia A, Miller MW, Huggins DJ, Myers RW, Hoffmann HH, Ashbrook AW, Jannath SY, Liverton N and Kargman S *et al.*. (2025) Small-molecule inhibition of SARS-CoV-2 NSP14 RNA cap methyltransferase. *Nature* **637**: 1178-1185 [PMID:39663451]
137. 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]
138. 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]
139. 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]
140. Minskaia E, Hertzig 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]
141. Mitsuya H, Tamamura H and Kuwata N. (2023) COMPOUND EXHIBITING PHYSIOLOGICAL ACTIVITY SUCH AS ANTIVIRAL ACTIVITY Patent number: WO2023286844.
142. Molecular Partners. Molecular Partners pipeline page
143. 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]
144. 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]
145. 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]
146. Newman JA, Douangamath A, Yadzani S, Yosaatmadja Y, Aimon A, Brandão-Neto J, Dunnett L, Gorrie-Stone T, Skyner R and Fearon D *et al.*. (2021) Structure, mechanism and crystallographic fragment screening of the SARS-CoV-2 NSP13 helicase. *Nat Commun* **12**: 4848 [PMID:34381037]
147. Nieman JA, Lemieux MJ, Tyrrell DL, Bai B, Belovodskiy A, Hena M, Kandadai AS and Joyce MA. (2022) RNA VIRUS INHIBITOR COMPOUNDS AND USES THEREOF Patent number: WO2022133588.
148. Nieto-Torres JL, Verdiá-Báguena C, Jimenez-Guardeño JM, Regla-Nava JA, Castaño-Rodriguez C, Fernandez-Delgado R, Torres J, Aguilella 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]
149. Nigam AK, Hurley MFD, Fengling Li F, Konkoľová E, Klíma M, Trylčová J, Pollice R, Çinaroğlu SS, Levin-Konigsberg R and Handjaya J *et al.*. (2024) Application of established computational techniques to identify potential SARS-CoV-2 Nsp14-MTase inhibitors in low data regimes *Digital Discovery* **3**: 1327-1341
150. 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]
151. Oh CK, Nakamura T, Beutler N, Zhang X, Piña-Crespo J, Talantova M, Ghatak S, Trudler D, Carnevale LN and McKercher SR *et al.*. (2023) Targeted protein S-nitrosylation of ACE2 inhibits SARS-CoV-2 infection. *Nat Chem Biol* **19**: 275-283 [PMID:36175661]
152. 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]
153. 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]
154. 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]
155. 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]
156. 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]
157. Owen DR, Pettersson MY, Reese MR, Sammona MF, Tuttle JB and Yang Q. (2022) Antiviral heteroaryl ketone derivatives Patent number: WO2022013684A1.
158. Owen DR, Reese MR, Sammons MF, Tuttle JB, Verhoest PR and Yang Q. (2022) Nitrile-Containing Antiviral Compounds Patent number: US20220257563A1.
159. Pakrashy S, Mandal PK, Dey SK, Choudhury SM, Alasmary 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]
160. 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]
161. Pei P, Qin H, Chen J, Wang F, He C, He S, Hong B, Liu K, Qiao R 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* **22** [PMID:34180984]
162. 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*
163. 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]
164. 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]
165. 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. *Virol J* **6**: 131 [PMID:19698190]
166. 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]
167. 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]
168. PostEra AI. MPro Activity Data
169. Previti S, Ettari R, Calcaterra E, Roggia M, Natale B, Weldert AC, Müller-Ruttloff C, Salisch F, Irto A and Cigala RM *et al.*. (2024) Identification of Dual Inhibitors Targeting Main Protease (M^{pro}) and Cathepsin L as Potential Anti-SARS-CoV-2 Agents. *ACS Med Chem Lett* **15**: 602-609 [PMID:38746883]
170. Pruijssers AJ and Denison MR. (2019) Nucleoside analogues for the treatment of coronavirus infections. *Curr Opin Virol* **35**: 57-62 [PMID:31125806]
171. 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* **371**: 1374-1378 [PMID:33602867]
172. Ramsey JR, Shelton PMM, Heiss TK, Olinares PDB, Vostal LE, Soileau H, Grasso M, Casebeer SW, Adaniya S and Miller M *et al.*. (2024) Using a Function-First "Scout Fragment"-Based Approach to Develop Allosteric Covalent Inhibitors of Conformationally Dynamic Helicase Mechanoenzymes. *J Am Chem Soc* **146**: 62-67 [PMID:38134034]
173. 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]
174. 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]
175. 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]
176. 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]
177. 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*
178. Rogovoy B, Kysil V, Berishvili V, Pauza CD, Zapata JC, Moreno SMM, Li A, Orry A, Lam PCH and Abagyan R. (2023) Compounds for treatment of a coronavirus infection Patent number: WO2023245166A2.
179. Rona G, Zeke A, Miwatani-Minter B, de Vries M, Kaur R, Schinlever A, Garcia SF, Goldberg HV, Wang H and Hinds TR *et al.*. (2022) The NSP14/NSP10 RNA repair complex as a Pan-coronavirus therapeutic target. *Cell Death Differ* **29**: 285-292 [PMID:34862481]
180. 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. *Sci Signal* **13** [PMID:32994211]
181. 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
182. Ruch TR and Machamer CE. (2012) The coronavirus E protein: assembly and beyond. *Viruses* **4**: 363-82 [PMID:22590676]
183. Sacco MD, Ma C, Lagarias P, Gao A, Townsend JA, Meng X, Dube P, Zhang X, Hu Y and Kitamura N *et al.*. (2020) Structure and inhibition of the SARS-CoV-2 main protease reveal strategy for developing dual inhibitors against M^{pro} and cathepsin L. *Sci Adv* **6** [PMID:33158912]
184. 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]
185. Sanders BC, Pokhrel S, Labbe AD, Mathews II, Cooper CJ, Davidson RB, Phillips G, Weiss KL, Zhang Q and O'Neill H *et al.*. (2023) Potent and selective covalent inhibition of the papain-like protease from SARS-CoV-2. *Nat Commun* **14**: 1733 [PMID:36977673]
186. Sato J, Shibayama H, Hirai K, Uno Y, Uehara S, Yonezawa S, Kurahashi K and Kojima E. (2023) Uracil derivative having viral growth inhibitory activity and pharmaceutical composition containing same Patent number: WO2023195530A1.
187. 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*
188. 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
189. 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]
190. Shahid M and Shahzad-Ul-Hussan S. (2021) Structural insights of key enzymes into therapeutic intervention against SARS-CoV-2. *J Struct Biol* **213**: 107690 [PMID:33383190]
191. 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* **28**: 855-865.e9 [PMID:33979649]
192. Sharma A, Kaur M, Yadav P, Singh G and Barnwal RP. (2023) Expediting the drug discovery for ideal leads against SARS-CoV-2 via molecular docking of repurposed drugs. *J Biomol Struct Dyn* **41**: 7949-7965 [PMID:36165445]
193. Shen Z, Li Y, Zhu J, Huang Q, Yin J, Xu Y, Wu A, Su W and Kuai L. (2023) VIRUS MAIN PROTEASE INHIBITOR, PREPARATION METHOD THEREFOR, AND USE Patent number: WO2023283831.
194. Shen Z, Ratia K, Cooper L, Kong D, Lee H, Kwon Y, Li Y, Alqarni S, Huang F and Dubrovskyi O *et al.*. (2022) Design of SARS-CoV-2 PLpro Inhibitors for COVID-19 Antiviral Therapy Leveraging Binding Cooperativity. *J Med Chem* **65**: 2940-2955 [PMID:34665619]
195. Shen Z, Ratia K, Cooper L, Kong D, Lee H, Kwon Y, Li Y, Alqarni S, Huang F and Dubrovskyi O *et al.*. (2021) Potent, Novel SARS-CoV-2 PLpro Inhibitors Block Viral Replication in Monkey and Human Cell Cultures. *bioRxiv* [PMID:33594371]
196. 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]
197. 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]
198. Shiryaev V and Klimochkin Y. (2024) Computer-aided Design of Wide-spectrum Coronavirus Helicase NSP13 Cage Inhibitors: A Molecular Modelling Approach. *Curr Comput Aided Drug Des* **20**: 1027-1041 [PMID:37921184]
199. Shurtleff VW, Layton ME, Parish CA, Perkins JJ, Schreier JD, Wang Y, Adam GC, Alvarez N, Bahmanjah S and Bahnck-Teets CM *et al.*. (2024) Invention of MK-7845, a SARS-CoV-2 3CL Protease Inhibitor Employing a Novel Difluorinated Glutamine Mimic. *J Med Chem* **67**: 3935-3958 [PMID:38365209]
200. Singh I, Li F, Fink EA, Chau I, Li A, Rodriguez-Hernández A, Glenn I, Zapatero-Belinchón FJ, Rodriguez ML and Devkota K *et al.*. (2023) Structure-Based Discovery of Inhibitors of the SARS-CoV-2 Nsp14 N7-Methyltransferase *J Med Chem*
201. 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]
202. 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]
203. 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]
204. Sui C, Xiao T, Zhang S, Zeng H, Zheng Y, Liu B, Xu G, Gao C and Zhang Z. (2022) SARS-CoV-2 NSP13 Inhibits Type I IFN Production by Degradation of TBK1 via p62-Dependent Selective Autophagy. *J Immunol* **208**: 753-761 [PMID:34996837]
205. Surya W, Li Y, Verdià-Bàguena C, Aguilella 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]
206. Tan B, Sacco M, Tan H, Li K, Joyce R, Zhang X, Chen Y and Wang J. (2023) Exploring diverse reactive warheads for the design of SARS-CoV-2 main protease inhibitors. *Eur J Med Chem* **259**: 115667 [PMID:37482021]
207. Tan B, Zhang X, Ansari A, Jadhav P, Tan H, Li K, Chopra A, Ford A, Chi X and Ruiz FX *et al.*. (2024) Design of a SARS-CoV-2 papain-like protease inhibitor with antiviral efficacy in a mouse model. *Science* **383**: 1434-1440 [PMID:38547259]
208. 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* **65**: 7561-7580 [PMID:35620927]
209. 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]
210. 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]
211. 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]
212. 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]
213. 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]
214. 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]
215. 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*
216. 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]
217. 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]
218. Tong X, Keung W, Arnold LD, Stevens LJ, Pruijssers AJ, Kook S, Lopatin U, Denison M and

Kwong AD. (2023) Evaluation of *in vitro* antiviral activity of SARS-CoV-2 M^{pro} inhibitor pomotrelvir and cross-resistance to nirmatrelvir resistance substitutions. *Antimicrob Agents Chemother* **67**: e0084023 [PMID:37800975]

219. Turlington M, Chun A, Tomar S, Eggler 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]
220. 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]
221. Van Damme E, Abeywickrema P, Yin Y, Xie J, Jacobs S, Mann MK, Doijen J, Miller R, Piassek M and Marsili S *et al.*. (2025) A small-molecule SARS-CoV-2 inhibitor targeting the membrane protein. *Nature* [PMID:40140563]
222. 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.
223. 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]
224. Vasilenko N, Moshynskyy I and Zakhartchouk A. (2010) SARS coronavirus protein 7a interacts with human Ap4A-hydrolase. *Virol J* **7**: 31 [PMID:20144233]
225. Vazquez C, Swanson SE, Negatu SG, Dittmar M, Miller J, Ramage HR, Cherry S and Jurado KA. (2021) SARS-CoV-2 viral proteins NSP1 and NSP13 inhibit interferon activation through distinct mechanisms. *PLoS One* **16**: e0253089 [PMID:34166398]
226. Vithani N, Ward MD, Zimmerman MI, Novak B, Borowsky JH, Singh S and Bowman GR. (2021) SARS-CoV-2 Nsp16 activation mechanism and a cryptic pocket with pan-coronavirus antiviral potential. *Biophys J* **120**: 2880-2889 [PMID:33794150]
227. 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]
228. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT and Veesler D. (2020) Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell* **181**: 281-292.e6 [PMID:32155444]
229. 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]
230. 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* **18**: 945-953 [PMID:33637958]
231. Wang X, Gotchev D, Fan KY, Vega MM, Mani N, McGovern-Gooch K, Cuconati A, Tercero B, Wang X and Carpino P *et al.*. (2024) Rational Design of Macrocyclic Noncovalent Inhibitors of SARS-CoV-2 M^{pro} from a DNA-Encoded Chemical Library Screening Hit That Demonstrate Potent Inhibition against Pan-Coronavirus Homologues and Nirmatrelvir-Resistant Variants. *J Med Chem* **67**: 19623-19667 [PMID:39453309]
232. Wang Y, Anirudhan V, Du R, Cui Q and Rong L. (2021) RNA-dependent RNA polymerase of SARS-CoV-2 as a therapeutic target. *J Med Virol* **93**: 300-310 [PMID:32633831]
233. Wazir S, Parviainen TAO, Pfannenstiel JJ, Duong MTH, Cluff D, Sowa ST, Galera-Prat A, Ferraris D, Maksimainen MM and Fehr AR *et al.*. (2024) Discovery of 2-Amide-3-methylester Thiophenes that Target SARS-CoV-2 Mac1 and Repress Coronavirus Replication, Validating Mac1 as an Antiviral Target. *J Med Chem* **67**: 6519-6536 [PMID:38592023]
234. Wei D, Hu T, Zhang Y, Zheng W, Xue H, Shen J, Xie Y and Aisa HA. (2021) Potency and pharmacokinetics of GS-441524 derivatives against SARS-CoV-2. *Bioorg Med Chem* **46**: 116364 [PMID:34450570]
235. 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* **24**: 1522-1533 [PMID:34675436]
236. 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*
237. 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]
238. White MA, Lin W and Cheng X. (2020) Discovery of COVID-19 Inhibitors Targeting the SARS-CoV-2 Nsp13 Helicase. *J Phys Chem Lett* **11**: 9144-9151 [PMID:33052685]

239. 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]
240. 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]
241. Wiser C, Kim B and Ascano M. (2019) G3BP1 enhances cytoplasmic DNA pattern recognition. *Nat Immunol* **20**: 5-7 [PMID:30538338]
242. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, Meng J, Zhu Z, Zhang Z and Wang J *et al.*. (2020) Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. *Cell Host Microbe* **27**: 325-328 [PMID:32035028]
243. Węglarz-Tomczak E, Tomczak JM, Talma M and Brul S. (2020) Ebselen as a highly active inhibitor of PLProCoV2 *bioRxiv*
244. 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]
245. 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]
246. 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]
247. 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]
248. 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]
249. Xu JB, Guan WJ, Zhang YL, Qiu ZE, Chen L, Hou XC, Yue J, Zhou YY, Sheng J and Zhao L *et al.*. (2024) SARS-CoV-2 envelope protein impairs airway epithelial barrier function and exacerbates airway inflammation via increased intracellular Cl^- concentration. *Signal Transduct Target Ther* **9**: 74 [PMID:38528022]
250. 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]
251. Yadav PD, Mendiratta SK, Mohandas S, Singh AK, Abraham P, Shete A, Bandyopadhyay S, Kumar S, Parikh A and Kalita P *et al.*. (2021) ZRC3308 Monoclonal Antibody Cocktail Shows Protective Efficacy in Syrian Hamsters against SARS-CoV-2 Infection. *Viruses* **13**: 2424 [PMID:34960695]
252. 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]
253. 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]
254. 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]
255. 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]
256. 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]
257. 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]
258. 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
259. 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*
260. Yu MS, Lee J, Lee JM, Kim Y, Chin YW, Jee JG, Keum YS and Jeong YJ. (2012) Identification of myricetin and scutellarein as novel chemical inhibitors of the SARS coronavirus helicase, nsP13. *Bioorg Med Chem Lett* **22**: 4049-54 [PMID:22578462]

261. 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]
262. 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]
263. Zavoronkovs A, Ivanenkov YA and Zagribelnyy B. (2021) Sars-cov-2 inhibitors having covalent modifications for treating coronavirus infections Patent number: WO2021219089A1.
264. 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*
265. 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*
266. Zhang CH, Spasov KA, Reilly RA, Hollander K, Stone EA, Ippolito JA, Liosi ME, 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 Med Chem Lett* **12**: 1325-1332 [PMID:34408808]
267. Zhang CH, 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 Cent Sci* **7**: 467-475 [PMID:33786375]
268. 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]
269. 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]
270. 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*
271. 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]
272. 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]
273. Zhang Z, Nomura N, Muramoto Y, Ekimoto T, Uemura T, Liu K, Yui M, Kono N, Aoki J and Ikeguchi M *et al.*. (2022) Structure of SARS-CoV-2 membrane protein essential for virus assembly. *Nat Commun* **13**: 4399 [PMID:35931673]
274. Zhao Y, Fang C, Zhang Q, Zhang R, Zhao X, Duan Y, Wang H, Zhu Y, Feng L and Zhao J *et al.*. (2022) Crystal structure of SARS-CoV-2 main protease in complex with protease inhibitor PF-07321332. *Protein Cell* **13**: 689-693 [PMID:34687004]
275. 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]
276. 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*
277. 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]
278. Zou H, Zhu W, Liu L, Wang W, Xu S and Li Z. (2023) Pyrrolidine antiviral compound Patent number: WO2023093834A1.