WOAH Collaborative Centre Reports Activities 2022

Activities in 2022

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Centre Information

Title of WOAH Collaborating Centre	Zoonoses of Asia-Pacific
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Name of the writer:	Gongxun Zhong

TOR1 AND 2: SERVICES PROVIDED

1. Activities as a centre of research, expertise, standardisation and dissemination of techniques within the remit of the mandate given by WOAH

Epidemiology, surveillance, risk assessment	
Title of activity	Scope
	In 2022, we screened more than 2,000,000 swab samples

COVID-19 surveillance in human	collected from human in Heilongjiang province, China. Four SARS-CoV-2 viruses were isolated from the positive samples in Vero-E6 cells.
Epidemiology, surveillance, risk assessment	
Title of activity	Scope
COVID-19 surveillance in animals	In 2022, we conducted SARS-CoV-2 surveillance in various animals and environments during the COVID-19 outbreak in Heilongjiang province, China. 427 environmental samples, and swabs, feces and tissues collected from domestic and stray cats, dogs, minks, foxes, field mice and wild birds were subjected to viral RNA detection by using qRT-PCR. 10 sera collected from those animals were subjected to antibody detection including ELISA and PRNT.
zoonoses	
Title of activity	Scope
Study on the mechanism of SARS-CoV-2 infection	Loss of the furin cleavage motif in the SARS-CoV-2 spike protein reduces the virulence and transmission of SARS-CoV-2, suggesting that furin is an attractive antiviral drug target. We find that alpha-soluble NSF attachment protein (alpha-SNAP), an indispensable component of vesicle trafficking machinery, inhibits the cleavage of SARS-CoV-2 spike protein and other furin-dependent virus glycoproteins. SARS-CoV-2 infection increases the expression of alpha-SNAP, and overexpression of alpha-SNAP reduces SARS-CoV-2 infection in cells. We further reveal that alpha-SNAP is an interferon-upregulated furin inhibitor that inhibits furin function by interacting with its P domain. Our study demonstrates that alpha-SNAP, in addition to its role in vesicle trafficking, plays an important role in the host defense against furin-dependent virus infection and therefore could be a target for the development of therapeutic options for COVID-19.
zoonoses	
Title of activity	Scope
Study on the cellular entrance of SARS-CoV-2	We discovered that the S protein contains two previously unidentified Cathepsin L (CTSL) cleavage sites (CS-1 and CS-2). Both sites are highly conserved among all known SARS-CoV-2 variants. Our structural studies revealed that CTSL cleavage promoted S to adopt receptor-binding domain (RBD) "up" activated conformations, facilitating receptor-binding and membrane fusion. We confirmed that CTSL cleavage is essential during infection of all emerged SARS-CoV-2 variants by pseudovirus (PsV) infection. Furthermore, we found CTSL-specific inhibitors not only blocked infection of PsV/live virus in cells but also reduced live virus infection of ex vivo lung tissues of both human donors and human ACE2-transgenic mice. Finally, we showed that two CTSL-specific inhibitors exhibited excellent In vivo effects to prevent live virus infection in human

	ACE2-transgenic mice. Our work demonstrated that inhibition of CTSL cleavage of SARS-CoV-2 S protein is a promising approach for the development of future mutation-resistant therapy.

Veterinary medicinal products	
Title of activity	Scope
Efficacy evaluation of SARS-CoV-2 drugs	We have evaluated anti-SARS-CoV-2 activities for 7 different drugs in cell lines, mouse-adapted virus-based mouse model, and transgenic mice.

Veterinary medicinal products	
Title of activity	Scope
Study on Anti-SARS-CoV-2 drugs	The continuous emergence of severe acute respiratory coronavirus 2 (SARS-CoV-2) variants and the increasing number of breakthrough infection cases among vaccinated people support the urgent need for research and development of antiviral drugs. Viral entry is an intriguing target for antiviral drug development. We found that diltiazem, a blocker of the L-type calcium channel Cav1.2 pore-forming subunit (Cav1.2 alpha1c) and an FDA-approved drug, inhibits the binding and internalization of SARS-CoV-2, and decreases SARS-CoV-2 infection in cells and mouse lung. Cav1.2 alpha1c interacts with SARS-CoV-2 spike protein and ACE2, and affects the attachment and internalization of SARS-CoV-2. Our finding suggests that diltiazem has potential as a drug against SARS-CoV-2 infection and that Cav1.2 alpha1c is a promising target for antiviral drug development for COVID-19.

Veterinary medicinal products	
Title of activity	Scope
Study on Anti-coronovirus drugs	Based on cryo-electron microscopy and biochemical approaches, gossypol (GOS) is identified from 881 natural products to directly block SARS-CoV-2 RdRp, thus inhibiting SARS-CoV-2 replication in both cellular and mouse infection models. GOS also acts as a potent inhibitor against the SARS-CoV-2 variant of concern (VOC) and exerts same inhibitory effects toward mutated RdRps of VOCs as the RdRp of the original SARS-CoV-2. Moreover, the RdRp inhibitor GOS has broad-spectrum anti-coronavirus activity against alphacoronaviruses (porcine epidemic diarrhea virus and swine acute diarrhea syndrome coronavirus), betacoronaviruses (SARS-CoV-2), gammacoronaviruses (avian infectious bronchitis virus), and deltacoronaviruses (porcine deltacoronavirus). The findings demonstrate that GOS may serve as a promising lead compound for combating the ongoing COVID-19 pandemic and other coronavirus outbreaks.

Vaccines

Title of activity	Scope
R&D of SARS-CoV vaccine	We developed an effective vaccine against coronavirus and influenza virus infection. Herein, we used the influenza virus as a vector to express the SARS-CoV-2 spike receptor-binding domain (RBD) and hemagglutinin-esterase-fusion (HEF) protein of the influenza C virus. The chimeric viruses could stably express the HEF protein and the SARS-CoV-2 spike RBD at a high level. BALB/c mice, infected with the chimeric virus, exhibited mild clinical symptoms, yet produced high specific antibody levels against RBD and HEF, including neutralizing antibodies. Importantly, high neutralizing antibodies could be retained in the sera of mice for at least 20 weeks. Altogether, our data provided a new strategy for developing safe and effective COVID-19 and influenza virus vaccines.
Vaccines	
Title of activity	Scope
Approval of brucella gene deletion marker live vaccine	In 2022, the brucella gene deletion marker live vaccine product jointly developed by Harbin Veterinary Research Institute of Chinese Academy of Agricultural Sciences and others for 18 years was approved and launched in China.
Vaccines	
Title of activity	Scope
COVID-19 vaccine	We developed a rapid response SARS vaccine to provide protection for human populations. We constructed a recombinant chimeric vesicular stomatitis virus (VSV) VSVDeltaG-SARS, in which the glycoprotein (G) gene is replaced with the SARS-CoV S gene. The results of safety trials revealed that VSVDeltaG-SARS is safe and effective in mice at a dose of 1 x 10(6) TCID(50). More importantly, only a single-dose immunization can provide high-level neutralizing antibodies and robust T cell responses to non-human primate animal models. Thus, our data indicate that VSVDeltaG-SARS can be used as a rapid response vaccine candidate, providing a foundation for the new coronavirus disease in the future.

TOR3: HARMONISATION OF STANDARDS

2. Proposal or development of any procedure that will facilitate harmonisation of international regulations applicable to the main fucus area for which you were designated

Proposal title	Scope/Content	Applicable area

4. Did your Collaborating Centre maintain a network with other WOAH Collaborating Centres (CC), Reference Laboratories (RL), or organisations designated for the same specialty, to coordinate scientific and technical studies?

No

TOR4 AND 5: NETWORKING AND COLLABORATION

5. Did your Collaborating Centre maintain a network with other WOAH Collaborating Centres, Reference laboratories, or organisations in other disciplines, to coordinate scientific and technical studies?

Yes

Name of OIE CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
the OIE cc- of Biotechnology-based Diagnosis of Infectious Diseases in Veterinary Medicine National Veterinary Institute, Sweden	Sweden	Europe	To have cooperation on the research of swine fever

TOR6: EXPERT CONSULTANTS

6. Did your Collaborating Centre place expert consultants at the disposal of WOAH?

Yes

NAME OF EXPERT	KIND OF CONSULTANCY	SUBJECT
Jingfei Wang	Conselor	Presentation of "Unknown pathogen laboratory diagnosis process" in the meeting of "WOAH Regional virtual training on swine diseases laboratory diagnosis"

TOR7: SCIENTIFIC AND TECHNICAL TRAINING

7. Did your Collaborating Centre provide advice/services to requests from Members in your main focus area?

8. Did your Collaborating Centre provide scientific and technical training, within the remit of the mandate given by WOAH, to personnel from WOAH Members?

Yes

a) Technical visit :

b) Seminars : 30

c) Hands-on training courses:

d) Internships (>1 month) :

TYPE OF TECHNICAL TRAINING PROVIDED (A, B, C OR D)	CONTENT	COUNTRY OF ORIGIN OF THE EXPERT(S) PROVIDED WITH TRAINING	NO. PARTICIPANTS FROM THE CORRESPONDING COUNTRY
	Provided traing by the first China-Kazakhstan Graduate Academic forum on Preventive Veterinary Technology	China	30

TOR8: SCIENTIFIC MEETINGS

9. Did your Collaborating Centre organise or participate in the organisation of scientific meetings related to your main focus area on behalf of WOAH?

Yes

NATIONAL/INTERNATIONAL	TITLE OF EVENT	CO-ORGANISER	DATE (MM/YY)	LOCATION	NO. PARTICIPANTS
International	The International Symposium on Animal Diseases and Zoonosis	Jiangsu Co-innovation Centre for important animal diseases and zoonoses	2022-11-10	Virtual/Yangzhou, China	200
International	14th ANNUAL MEETING EPIZONE	Participants in the meeting	2022-05-09	Virtual	1000
International	IABS Meeting on High Pathogenicity Avian Influenza Vaccination Strategies to prevent and control HPAI : Removing unnecessary barriers for usages	International Alliance for Biological Standarization	2022-10-25	Paris, France	200
International	Workshop for the OIE avian disease network in east Asia	WOAH	2022-04-21	Virtual	200
International	89th general session of WOAH	WOAH	2022-05-25	Paris, France	200

TOR9: DATA AND INFORMATION DISSEMINATION

10. Publication and dissemination of any information within the remit of the mandate given by WOAH that may be useful to Members of WOAH

a) Articles published in peer-reviewed journals:

1. Wang W, Li W, Wen Z, Wang C, Liu W, Zhang Y, Liu J, Ding T, Shuai L, Zhong G, Bu Z, Qu L, Ren M, Li F. 2022. Gossypol Broadly Inhibits Coronaviruses by Targeting RNA-Dependent RNA Polymerases. Adv Sci (Weinh) 9:e2203499.

2. Fan Y, Chen W, Jiang C, Zhang X, Sun Y, Liu R, Wang J, Yang D, Zhao D, Bu Z, He X. 2022. Host Responses to Live-Attenuated ASFV (HLJ/18-7GD). Viruses 14.
3. Wang L, Fu D, Tesfagaber W, Li F, Chen W, Zhu Y, Sun E, Wang W, He X, Guo Y, Bu Z, Zhao D. 2022. Development of an ELISA Method to Differentiate Animals Infected with Wild-Type African Swine Fever Viruses and Attenuated HLJ/18-7GD Vaccine Candidate. Viruses 14.
4. Kong D, Wen Z, Su H, Ge J, Chen W, Wang X, Wu C, Yang C, Chen H, Bu Z. 2022. Corrigendum to "Newcastle disease virus vectored Nipah encephalitis vaccines induce B and T cell responses in mice and long-lasting neutralizing antibodies in pigs" [Virology 432 (2012) 327-335]. Virology 573:176-177.
5. Zhao Y, Zhao L, Li Y, Liu Q, Deng L, Lu Y, Zhang X, Li S, Ge J, Bu Z, Ping J. 2022. An influenza virus vector candidate vaccine stably expressing SARS-CoV-2 receptor-binding domain produces high and long-lasting neutralizing antibodies in mice. Vet Microbiol 271:109491.
6. Zhao MM, Zhu Y, Zhang L, Zhong G, Tai L, Liu S, Yin G, Lu J, He Q, Li MJ, Zhao RX, Wang H, Huang W, Fan C, Shuai L, Wen Z, Wang C, He X, Chen Q, Liu B, Xiong X, Bu Z, Wang Y, Sun F, Yang JK. 2022. Novel cleavage sites identified in SARS-CoV-2 spike protein reveal mechanism for cathepsin L-facilitated viral infection and treatment strategies. Cell Discov 8:53.
7. Shan D, Tang X, Liu R, Pan D, Wang X, Ge J, Wen Z, Bu Z. 2022. Immunogenicity of a recombinant VSV-Vectored SARS-CoV vaccine induced robust immunity in rhesus monkeys after single-dose immunization. Virol Sin 37:248-255.
8. Wang X, Luo J, Wen Z, Shuai L, Wang C, Zhong G, He X, Cao H, Liu R, Ge J, Hua R, Sun Z, Wang X, Wang J, Bu Z. 2022. Diltiazem inhibits SARS-CoV-2 cell attachment and internalization and decreases the viral infection in mouse lung. PLoS Pathog 18:e1010343.
9. Zhu W, Meng K, Zhang Y, Bu Z, Zhao D, Meng G. 2021. Lateral Flow Assay for the Detection of African Swine Fever Virus Antibodies Using Gold Nanoparticle-Labeled Acid-Treated p72. Front Chem 9:804981.
10. Wang J, Luo J, Wen Z, Wang X, Shuai L, Zhong G, Wang C, Sun Z, Chen W, Ge J, Liu R, Wang X, Bu Z. 2022. Alpha-Soluble NSF Attachment Protein Prevents the Cleavage of the SARS-CoV-2 Spike Protein by Functioning as an Interferon-Upregulated Furin Inhibitor. mBio 13:e0244321.
11. Zhao G, Li T, Liu X, Zhang T, Zhang Z, Kang L, Song J, Zhou S, Chen X, Wang X, Li J, Huang L, Li C, Bu Z, Zheng J, Weng C. 2022. African swine fever virus cysteine protease pS273R inhibits pyroptosis by noncanonically cleaving gasdermin D. J Biol Chem 298:101480.
12. Li J, Bai Y, Li F, Zhang Y, Xie Q, Zhang L, Hua L, Xiong Q, Shan Y, Bu Z, Shao G, Feng Z, Zhao D, Liu F. 2022. Rapid and ultra-sensitive detection of African swine fever virus antibody on site using QDM based-ASFV immunosensor (QAIS). Anal Chim Acta 1189:339187.
13. Chen M, Wang MH, Shen XG, Liu H, Zhang YY, Peng JM, Meng F, Wang TY, Bai YZ, Sun MX, Tian ZJ, Yin X, Cai XH, Tang YD. 2022. Neuropilin-1 Facilitates Pseudorabies Virus Replication and Viral Glycoprotein B Promotes Its Degradation in a Furin-Dependent Manner. J Virol 96:e0131822.
14. Cui XY, Xia DS, Huang XY, Tian XX, Wang T, Yang YB, Wang G, Wang HW, Sun Y, Xiao YH, Tian ZJ, Cai XH, An TQ. 2022. Recombinant characteristics, pathogenicity, and viral shedding of a novel PRRSV variant derived from twice inter-lineage recombination. Vet Microbiol 271:109476.
15. Fu J, Zhao L, Pang Y, Chen H, Yamamoto H, Chen Y, Li Z, Mizushima N, Jia H. 2022. Apicoplast biogenesis mediated by ATG8 requires the ATG12-ATG5-ATG16L and SNAP29 complexes in Toxoplasma gondii. Autophagy:1-19.
16. Sun M, Hou L, Song H, Lyu C, Tang YD, Qin L, Liu Y, Wang S, Meng F, Cai X. 2022. The relationship between autophagy and apoptosis during pseudorabies virus infection. Front Vet Sci 9:1064433.
17. Wang B, Zhang J, Liu X, Chai Q, Lu X, Yao X, Yang Z, Sun L, Johnson SF, Schwartz RC, Zheng YH. 2022. Protein disulfide isomerases (PDIs) negatively regulate ebolavirus structural glycoprotein expression in the endoplasmic reticulum (ER) via the autophagy-lysosomal pathway. Autophagy 18:2350-2367.

b) International conferences:

c) National conferences:

d) Other (Provide website address or link to appropriate information):

11. What have you done in the past year to advance your area of focus, e.g. updated technology?

The highlight of our work in 2022 were the approval and launch of brucella gene deletion marker live vaccine, as well as the studies on SARS-CoV-2 including sruveillance, R&D of vaccines and anti-viral drugs, and fundamental research.

12. Additional comments regarding your report: