OIE Collaborating Centres Reports Activities

Activities in 2021

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Title of collaborating centre:	Zoonoses of Asia-Pacific
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ToR: To provide services to the OIE, in particular within the region, in the designated specialty, in support of the implementation of OIE policies and, where required, seek for collaboration with OIE Reference Laboratories

ToR: To identify and maintain existing expertise, in particular within its region

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

Epidemiology, surveillance, risk assessment, modelling	
Title of activity	**Scope**
COVID-19 surveillance in human	In 2021, we screened more than 6,000,000 samples collected from human in Heilongjiang province, China. 92 samples were detected positive for COVID-19. Seven SARS-CoV-2 viruses were isolated from the positive samples in Vero-E6 cells.
COVID-19 surveillance in animals	In 2021, we conducted SARS-CoV-2 surveillance in various animals and environments during the COVID-19 outbreak in Heilongjiang province, China. 369 environmental samples, and swabs and faeces collected from domestic and stray cats, dogs, minks, foxes, field mice, cows, deer, pigs, sheep, goats, poultry and wild birds were subjected to viral RNA detection using qRT-PCR. 99 sera collected from those animals were subjected to antibody detection including ELISA and PRNT.
Replication, pathogenicity, and transmission of SARS-CoV-2 in minks	We experimentally investigated and found that SARS-CoV-2 replicates efficiently in both the upper and lower respiratory tracts, and transmits efficiently in minks via respiratory droplets; pulmonary lesions caused by SARS-CoV-2 in minks are similar to those seen in humans with COVID-19. Our study indicates that minks are a useful animal model for evaluating the efficacy of drugs or vaccines against COVID-19.
Zoonoses	
Title of activity	**Scope**
The study on the cellular entrance of SARS-CoV-2	We identified a novel internalization factor mGluR2 is an internalization factor for SARS-CoV-2. Our results show that mGluR2 directly interacts with the SARS-CoV-2 spike protein and that knockdown of mGluR2 decreases internalization of SARS-CoV-2 but not cell binding. Further, mGluR2 is uncovered to cooperate with ACE2 to facilitate SARS-CoV-2 internalization through CME and mGluR2 knockout in mice abolished SARS-CoV-2 infection in the nasal turbinates and significantly reduced viral infection in the lungs. We also proved that mGluR2 is also important for SARS-CoV spike protein- and Middle East respiratory syndrome coronavirus spike protein-mediated internalization.

Generation of A Stable GFP-reporter Zika Virus System for High-throughput Screening of Zika Virus Inhibitors	We developed a stable ZIKV GFP-reporter virus system with considerably improved GFP visibility and stability. In this system a BHK-21 cell line expressing DC-SIGNR was established for high-throughput screening of compounds library to block ZIKV infection. More than 31 out of 974 tested compounds effectively decreased ZIKV reporter infection. Four selected compounds, homoharringtonine (HHT), bruceine D (BD), dihydroartemisinin (DHA) and digitonin (DGT), were further validated to inhibit wild-type ZIKV infection in cells of BHK-21 and human cell line A549, representing potential therapies for the treatment of ZIKV infection.
The study on the medicinal product for SARS-CoV-2	We evaluated the antiviral activity of GS441524 and GC376 against SARS-CoV-2 infection in a mouse-adapted SARS-CoV-2 infected mouse model. The results showed that GS441524 effectively blocked the proliferation of SARS-CoV-2 in the mouse upper and lower respiratory tracts, and low-dose combined application of GS441524 with GC376 could effectively protect mice against SARS-CoV-2 infection.
The study on the mechanism of rabies virus replication	We identified a new partner for RABV M proteins and establish a new role of ATP6V1A by promoting virion uncoating during RABV replication. We mapped the protein interactome between RABV M and human host factors, and found that ATP6V1A facilitated RABV replication in the dissociation of incoming viral M proteins during viral uncoating.
The study on virulence-related gene of brucella	We analyzed the transcriptional change of avirulent strain Brucella melitensis M5-90 (B. melitensis M5-90) during macrophage infection using RNA-seq technology. We detected 601 significant changed genes of which 428 were upregulated after infection. Our study provided a view of transcriptional landscape of B. melitensis M5-90 intracellular, and found L31 gene is required for the full virulence of B. melitensis.
The study on virulence-related gene of brucella	We defined an ECF sigma bcrS and its cognate anti-sigma factor abcS and their regulons in Brucella melitensis M28. AbcS is required for the maintenance of persistent infection, while bcrS is dispensable in a mouse infection model. Collectively, we conclude that BcrS and AbcS influence expression of multiple genes responsible for Brucella virulence traits.
The study on vesicular trafficking in Toxoplasma gondii	We analyzed the localization of SNAREs and investigated their roles in vesicular trafficking in Toxoplasma gondii. The conditional ablation of ER- and Golgi-residing SNAREs caused severe defects in the secretory system, and an R-SNARE (TgVAMP4-2) that is targeted to the apicoplast. We provides the first mention of a SNARE located on endosymbiotic organelles that functions in vesicular trafficking in eukaryotes.
Diagnosis, biotechnology and laboratory	
Title of activity	**Scope**
Development of biological and diagnostic reagents for SARS-CoV-2 detection	We have generated antigens, antisera, and monoclonal antibodies for development of SARS-CoV-2 detection and diagnostic technology for humans and animals.

SARS-CoV-2 diagnostic assay development	We have developed various diagnostic assays for SARS-CoV-2 detection, including -Deep sequencing and bio-information analyses -qRT-PCR detection and genome sequencing -Virus isolation -Double Antigen Sandwich ELISA for antibody detection regardless of species -PRNT assay for anti-SARS-CoV-2 neutralization antibody detection -Immunofluorescence assay for viral antigen detection in cells -Immunohistochemical assay for viral antigen detection in tissues
Characterization of anti-p54 monoclonal antibodies and establishment of cELISA for African swine fever virus diagnosis.	We produced and characterize five p54 monoclonal antibodies and developed a monoclonal antibody-based competitive enzyme-linked immunosorbent assay (cELISA) for rapid and convenient ASFV antibody detection, with an excellent agreement when compared to other commercially available blocking ELISA (kappa value = 0.912) and showed no reaction to other swine pathogens.
Vaccines	
Title of activity	**Scope**
R&D of SARS-CoV-2 vaccines for animals	We have developed subunit, adenovirus type-5-vectored, NDV-vectored, MVA-vectored and attenuated rabies virus-vectored SARS-CoV-2 candidate vaccines for R&D of SARS-CoV-2 vaccines for animals, such as cats, minks, and other potential animals need to be protected. We will continue to evaluating the efficacy of single candidate vaccines or their combinations in animals in cats, dogs, minks, ferrets, and other potential susceptible animals.
Efficacy evaluation of SARS-CoV-2 drugs	We have evaluated anti-SARS-CoV-2 activities for 35 different drugs in cell lines, mouse-adapted virus-based mouse model, transgenic mice, ferrets and minks.
COVID-19 vaccine	We identified a novel linear and broadly neutralizing peptide in the S2 protein of SARS-CoV-2. This linear peptide (1147SFKEELDKYFKNHTSP1162) is conserved across SARS-CoV, BatCoV RaTG13, SARS-CoV-2, and SARS-CoV-2 variants. mAbs targeting this peptide efficiently neutralized SARS-CoV-2 and SARS-CoV S-pseudovirus as well as wild-type SARS-CoV-2. These antibodies also inhibited both S-mediated cell-cell membrane fusion and viral spread among cells. Antibodies targeting the peptide may neutralize both SARS-CoV-2 and SARS-CoV by preventing fusion between the virus and cell membrane.
Study on COVID-19 vaccine for animals	We found that a spike protein-based subunit vaccine largely prevented SARS-CoV-2 replication and lung damage caused by SARS-CoV-2 infection in minks. Vaccination is a potential strategy to prevent minks from transmitting SARS-CoV-2.

ToR : To propose or develop methods and procedures that facilitate harmonisation of international standards and guidelines applicable to the designated specialty

2. Proposal or development of any procedure that will facilitate harmonisation of international regulations applicable to the surveillance and control of animal diseases, food safety or animal

welfare

Proposal title	Scope/Content	Applicable area
		☐Surveillance and control of animal diseases ☐Food safety ☐Animal welfare

ToR: To establish and maintain a network with other OIE Collaborating Centres designated for the same specialty, and should the need arise, with Collaborating Centres in other disciplines

ToR: To carry out and/or coordinate scientific and technical studies in collaboration with other centres, laboratories or organisations

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

Yes

Name of OIE CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
Surveillance and Control of animal protozoan Diseases	Japan	☐Africa ☐Americas ☒Asia and Pacific ☐Europe ☐Middle East	Co-publish a research Paper

4. Did your Collaborating Centre maintain a network with other OIE 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	☐Africa ☐Americas ☐Asia and Pacific ☒Europe ☐Middle East	To have cooperation on the research of swine fever
RL of Marek's Disease	UK	☐Africa ☐Americas ☐Asia and Pacific ☒Europe ☐Middle East	Apply for a joint project

ToR: To place expert consultants at the disposal of the OIE.

5. Did your Collaborating Centre place expert consultants at the disposal of the OIE?

Yes

Name of expert	Kind of consultancy	Subject
Dr. CHEN Hualan	Conselor	The prevention and control of avian influenza in China. To participant in the OIE/FAO Regional Expert Network Meeting and Workshop for Avian Diseases in Asia and the Pacific on 29-30 September 2021 (virtual)
Dr. QI Xiaole	Conselor	Infectious bursal disease prevention and control technology in China. To participant in the OIE/FAO Regional Expert Network Meeting and Workshop for Avian diseases in Asia and the Pacific
Dr. AN Tongqin	Conselor	Bioinformatics Analysis of PRRSV. To participant in OIE Virtual Event: Diagnosis and Control of Porcine Reproductive and Respiratory Syndrome

ToR: To provide, within the designated specialty, scientific and technical training to personnel from OIE Member Countries

6. Did your Collaborating Centre provide scientific and technical training, within the remit of the mandate given by the OIE, to personnel from OIE Member Countries?

Yes
a) Technical visits: 0
b) Seminars: 2
c) Hands-on training courses: 0
d) Internships (>1 month): 0

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
b	Training on prevention and control of the key animal diseases	Egypt	50
b	Training on prevention and control of avian influenza in China	Egypt	50

ToR: To organise and participate in scientific meetings and other activities on behalf of the OIE

7. Did your Collaborating Centre organise or participate in the organisation of scientific meetings on behalf of the OIE?

Yes

National/International	Title of event	Co-organiser	Date (mm/yy)	Location	No. Participants
International	International Symposium on Important Animal Diseases and Zoonoses	Yangzhou University	12/2021	Yangzhou, China (zoom video conference)	100
International	Food and Agriculture Organization of the United Nations& Nanjing Agricultural University One Health Global Experts Symposium	FAO	12/2021	Zoom video conference	100
International	Regional Expert Network Meeting and Workshop for Avian Diseases in Asia and the Pacific on 29-30 September 2021 (virtual)	OIE, FAO	09/2021	Hokkaido, Japan (video conference)	100
International	Virtual Mini-symposium on Zoonotic Disease and 12th International Symposium of Integrative Zoology (ISIZ)	International Symposium of Integrative Zoology	04/2021	video conference	200
International	International Veterinary Vaccinology Network Virtual Symposium: Vaccines for Poultry	One Health Poultry Hub	02/2021	video conference	100

ToR: To collect, process, analyse, publish and disseminate data and information relevant to the designated specialty

8. Publication and dissemination of any information within the remit of the mandate given by the OIE that may be useful to Member Countries of the OIE

a) Articles published in peer-reviewed journals: 22

1. Liu X, Li F, Zhang J, Wang L, Wang J, Wen Z, Wang Z, Shuai L, Wang X, Ge J, Zhao D, Bu Z. The ATPase ATP6V1A facilitates rabies virus replication by promoting virion uncoating and interacting with the viral matrix protein. J Biol Chem. 2021 Jan-Jun;296:100096. doi: 10.1074/jbc.RA120.014190. PubMed PMID: 33208464; PubMed Central PMCID: PMCPMC7949080.
2. Zhang JW, Wang H, Liu J, Ma L, Hua RH, Bu ZG. Generation of A Stable GFP-reporter Zika Virus System for High-throughput Screening of Zika Virus Inhibitors. Virol Sin. 2021 Jun;36(3):476-489. doi: 10.1007/s12250-020-00316-0. PubMed PMID: 33231855; PubMed Central PMCID: PMCPMC8257822.
3. Yan X, Hu S, Yang Y, Xu D, Liu W, Li G, Cai W, Bu Z. Proteomics Investigation of the Time Course Responses of RAW264.7 Macrophages to Infections With the Wild-Type and Twin-Arginine Translocation Mutant Strains of Brucella melitensis. Front Cell Infect Microbiol. 2021;11:679571. doi: 10.3389/fcimb.2021.679571. PubMed PMID: 34195100; PubMed Central PMCID: PMCPMC8238042.
4. Xu D, Zhao J, Jiang L, Song J, Zong S, Yan X, Liu H, Zhang H, Hu S, Bu Z. Comparison of transcriptional change of B. melitensis M5-90 after macrophage infection highlights the role of ribosome gene L31 in virulence. Vet Microbiol. 2021 Feb;253:108951. doi: 10.1016/j.vetmic.2020.108951. PubMed PMID: 33373884.
5. Wang J, Yang G, Wang X, Wen Z, Shuai L, Luo J, Wang C, Sun Z, Liu R, Ge J, He X, Hua R, Wang X, Yang X, Chen W, Zhong G, Bu Z. SARS-CoV-2 uses metabotropic glutamate receptor subtype 2 as an internalization factor to infect cells. Cell Discov. 2021 Dec 14;7(1):119. doi: 10.1038/s41421-021-00357-z. PubMed PMID: 34903715; PubMed Central PMCID: PMCPMC8668938.
6. Wang J, Yang G, Wang X, Wen Z, Shuai L, Luo J, Wang C, Sun Z, Liu R, Ge J, He X, Hua R, Wang X, Yang X, Chen W, Zhong G, Bu Z. Author Correction: SARS-CoV-2 uses metabotropic glutamate receptor subtype 2 as an internalization factor to infect cells. Cell Discov. 2021 Dec 27;7(1):124. doi: 10.1038/s41421-021-00365-z. PubMed PMID: 34961770; PubMed Central PMCID: PMCPMC8710923.
7. Tesfagaber W, Wang L, Tsegay G, Hagoss YT, Zhang Z, Zhang J, Huangfu H, Xi F, Li F, Sun E, Bu Z, Zhao D. Characterization of Anti-p54 Monoclonal Antibodies and Their Potential Use for African Swine Fever Virus Diagnosis. Pathogens. 2021 Feb 7;10(2). doi: 10.3390/pathogens10020178. PubMed PMID: 33562314; PubMed Central PMCID: PMCPMC7915713.
8. Sun E, Zhang Z, Wang Z, He X, Zhang X, Wang L, Wang W, Huang L, Xi F, Huangfu H, Tsegay G, Huo H, Sun J, Tian Z, Xia W, Yu X, Li F, Liu R, Guan Y, Zhao D, Bu Z. Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020. Sci China Life Sci. 2021 May;64(5):752-765. doi: 10.1007/s11427-021-1904-4. PubMed PMID: 33655434.
9. Sun E, Huang L, Zhang X, Zhang J, Shen D, Zhang Z, Wang Z, Huo H, Wang W, Huangfu H, Wang W, Li F, Liu R, Sun J, Tian Z, Xia W, Guan Y, He X, Zhu Y, Zhao D, Bu Z. Genotype I African swine fever viruses emerged in domestic pigs in China and caused chronic infection. Emerg Microbes Infect. 2021 Dec;10(1):2183-2193. doi: 10.1080/22221751.2021.1999779. PubMed PMID: 34709128; PubMed Central PMCID: PMCPMC8635679.
10. Shuai L, Zhong G, Yuan Q, Wen Z, Wang C, He X, Liu R, Wang J, Zhao Q, Liu Y, Huo N, Deng J, Bai J, Wu H, Guan Y, Shi J, Tian K, Xia N, Chen H, Bu Z. Replication, pathogenicity, and transmission of SARS-CoV-2 in minks. Natl Sci Rev. 2021 Mar;8(3):nwaa291. doi: 10.1093/nsr/nwaa291. PubMed PMID: 34676095; PubMed Central PMCID: PMCPMC7798852.
11. Shi Y, Shuai L, Wen Z, Wang C, Yan Y, Jiao Z, Guo F, Fu ZF, Chen H, Bu Z, Peng G. The preclinical inhibitor GS441524 in combination with GC376 efficaciously inhibited the proliferation of SARS-CoV-2 in the mouse respiratory tract. Emerg Microbes Infect. 2021 Dec;10(1):481-492. doi: 10.1080/22221751.2021.1899770. PubMed PMID: 33691601; PubMed Central PMCID: PMCPMC7993387.
12. Nan FL, Zhang H, Nan WL, Xie CZ, Ha Z, Chen X, Xu XH, Qian J, Qiu XS, Ge JY, Bu ZG, Zhang Y, Lu HJ, Jin NY. Lentogenic NDV V protein inhibits IFN responses and represses cell apoptosis. Vet Microbiol. 2021 Oct;261:109181. doi: 10.1016/j.vetmic.2021.109181. PubMed PMID: 34399297.
13. Zhu W, Meng K, Zhang Y, Bu Z, Zhao D, Meng G. Lateral Flow Assay for the Detection of African Swine Fever Virus Antibodies Using Gold Nanoparticle-Labeled Acid-Treated p72. Front Chem. 2021;9:804981. doi: 10.3389/fchem.2021.804981. PubMed PMID: 35047481; PubMed Central PMCID: PMCPMC8761911.
14. Li T, Zhao G, Zhang T, Zhang Z, Chen X, Song J, Wang X, Li J, Huang L, Wen L, Li C, Zhao D, He X, Bu Z, Zheng J, Weng C. African Swine Fever Virus pE199L Induces Mitochondrial-Dependent Apoptosis. Viruses. 2021 Nov 8;13(11). doi: 10.3390/v13112240. PubMed PMID: 34835046; PubMed Central PMCID: PMCPMC8617669.
15. Li T, Kan Q, Ge J, Wan Z, Yuan M, Huang Y, Xie Q, Yang Y, Shao H, Li X, Ye L, Qin A, Bu Z, Liu P, Ye J. A novel linear and broadly neutralizing peptide in the SARS-CoV-2 S2 protein for universal vaccine development. Cell Mol Immunol. 2021 Nov;18(11):2563-2565. doi: 10.1038/s41423-021-00778-6. PubMed PMID: 34645942; PubMed Central PMCID: PMCPMC8513545.
16. Li J, Song J, Kang L, Huang L, Zhou S, Hu L, Zheng J, Li C, Zhang X, He X, Zhao D, Bu Z, Weng C. pMGF505-7R determines pathogenicity of African swine fever virus infection by inhibiting IL-1beta and type I IFN production. PLoS Pathog. 2021 Jul;17(7):e1009733. doi: 10.1371/journal.ppat.1009733. PubMed PMID: 34310655; PubMed Central PMCID: PMCPMC8341718.
17. Cao S, Yang J, Fu J, Chen H, Jia H. The Dissection of SNAREs Reveals Key Factors for Vesicular Trafficking to the Endosome-like Compartment and Apicoplast via the Secretory System in Toxoplasma gondii. mBio. 2021 Aug

31;12(4):e0138021. doi: 10.1128/mBio.01380-21. PubMed PMID: 34340555; PubMed Central PMCID: PMCPMC8406237.
18. Li F, Luo M, Zhou W, Li J, Jin X, Xu Z, Juan L, Zhang Z, Li Y, Liu R, Li Y, Xu C, Ma K, Cao H, Wang J, Wang P, Bu Z, Jiang Q. Single cell RNA and immune repertoire profiling of COVID-19 patients reveal novel neutralizing antibody. Protein Cell. 2021 Oct;12(10):751-755. doi: 10.1007/s13238-020-00807-6. PubMed PMID: 33237441; PubMed Central PMCID: PMCPMC7686823.
19. Huang L, Xu W, Liu H, Xue M, Liu X, Zhang K, Hu L, Li J, Liu X, Xiang Z, Zheng J, Li C, Chen W, Bu Z, Xiong T, Weng C. African Swine Fever Virus pI215L Negatively Regulates cGAS-STING Signaling Pathway through Recruiting RNF138 to Inhibit K63-Linked Ubiquitination of TBK1. J Immunol. 2021 Dec 1;207(11):2754-2769. doi: 10.4049/jimmunol.2100320. PubMed PMID: 34759016.
20. Fakri FZ, Bamouh Z, Elmejdoub S, Elkarhat Z, Tadlaoui K, Chen W, Bu Z, Elharrak M. Long term immunity against Peste Des Petits Ruminants mediated by a recombinant Newcastle disease virus vaccine. Vet Microbiol. 2021 Oct;261:109201. doi: 10.1016/j.vetmic.2021.109201. PubMed PMID: 34399299.
21. Chai Q, Li S, Collins MK, Li R, Ahmad I, Johnson SF, Frabutt DA, Yang Z, Shen X, Sun L, Hu J, Hultquist JF, Peterlin BM, Zheng YH. HIV-1 Nef interacts with the cyclin K/CDK13 complex to antagonize SERINC5 for optimal viral infectivity. Cell Rep. 2021 Aug 10;36(6):109514. doi: 10.1016/j.celrep.2021.109514. PubMed PMID: 34380030; PubMed Central PMCID: PMCPMC8385645.
22. Li H, Hu S, Yan X, Yang Y, Liu W, Bu Z, Li G, Cai W. An Extracytoplasmic Function Sigma/Anti-Sigma Factor System Regulates Hypochlorous Acid Resistance and Impacts Expression of the Type IV Secretion System in Brucella melitensis. J Bacteriol. 2021 May 20;203(12):e0012721. doi: 10.1128/JB.00127-21. PubMed PMID: 33820796; PubMed Central PMCID: PMCPMC8315932.

b) International conferences: 0

c) National conferences: 0

d) Other
(Provide website address or link to appropriate information): 0

9. Additional comments regarding your report:

No