WOAH Collaborative Centre Reports Activities 2023

Activities in 2023

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Centre Information

Title of WOAH Collaborating Centre	Zoonoses of Asia-Pacific
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Name of the writer:	Dr. 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

Category	Title of activity	Scope
Disease control (true)	Development of Highly Potent Noncovalent Inhibitors of SARS-CoV-2 3CLpro.	The 3C-like protease (3CLpro) is an essential enzyme for the replication of SARS-CoV-2 and other coronaviruses and thus is a target for coronavirus drug discovery. Nearly all inhibitors of coronavirus 3CLpro reported so far are covalent inhibitors. Here, we report the development of specific, noncovalent inhibitors of 3CLpro. The most potent one, WU-04, effectively blocks SARS-CoV-2 replications in human cells with EC(50) values in the 10-nM range. WU-04 also inhibits the 3CLpro of SARS-CoV and MERS-CoV with high potency, indicating that it is a pan-inhibitor of coronavirus 3CLpro. WU-04 showed anti-SARS- CoV-2 activity similar to that of PF-07321332 (Nirmatrelvir) in K18-hACE2 mice when the same dose was administered orally. Thus, WU-04 is a promising drug candidate for coronavirus treatment.
		The swine pathogens porcine reproductive and respiratory syndrome virus (PRRSV) and Streptococcus suis have both been reported to cause damage to the immune organs. Inguinal lymph node (ILN) injury has been reported in PRRSV-infected pigs with secondary S. suis infection. In this study,

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Epidemiology, surveillance, risk assessment, (true)	Co-infection of Streptococcus suis and highly pathogenic porcine reproductive and respiratory syndrome virus in piglets.	secondary S. suis infection after highly pathogenic (HP)-PRRSV infection caused more severe clinical symptoms, mortality, and ILN lesions. Histopathological lesions were seen in ILNs with a marked decrease in lymphocyte numbers. Terminal deoxynucleotidyl transferase (TdT)-mediated de- oxyuridine triphosphate (dUTP)-biotin nick end- labeling (TUNEL) assays revealed that HP-PRRSV strain HuN4 alone induced ILN apoptosis, but dual- infection with S. suis strain BM0806 induced greater levels of apoptosis. Besides, we found that some HP- PRRSV-infected cells underwent apoptosis. Furthermore, anti-caspase-3 antibody staining confirmed that ILN apoptosis was mainly induced by a caspase-dependent pathway. Pyroptosis was also observed in HP-PRRSV-infected cells, and there was more pyroptosis in piglets infected with HP-PRRSV alone compared with those with secondary S. suis infection, and HP-PRRSV-infected cells underwent pyroptosis. Altogether, this is the first report to identify pyroptosis in ILNs and which signaling pathway is related to ILN apoptosis in single or dual- infected piglets. These results contribute to a better understanding of the pathogenic mechanisms during secondary S. suis infection.	
Zoonoses (true)	Novel Conserved Neutralizing Epitope on the Receptor-Binding Domain of the SARS-CoV-2 Spike Protein.	We have identified a broad-spectrum neutralizing antibody and its highly conserved epitope in the receptor-binding domain (RBD) of the spike protein (S) S1 subunit of SARS-CoV-2. First, nine monoclonal antibodies (MAbs) against the RBD or S1 were generated; of these, one RBD-specific MAb, 22.9-1, was selected for its broad RBD-binding abilities and neutralizing activities against SARS-CoV-2 variants. An epitope of 22.9-1 was fine-mapped with overlapping and truncated peptide fusion proteins. The core sequence of the epitope, (405)D(N)EVR(S)QIAPGQ(414), was identified on the internal surface of the up-state RBD. The epitope was conserved in nearly all variants of concern of SARS- CoV-2. MAb 22.9-1 and its novel epitope could be beneficial for research on broad-spectrum prophylactic vaccines and therapeutic antibody drugs.	
Diagnosis, biotechnology and laboratory (true)	Development of a rapid reverse genetics system for coronavirus based on TAR cloning in yeast.	Reverse genetics has become an indispensable tool to gain insight into the pathogenesis of viruses and the development of vaccines. The yeast-based synthetic genomics platform has demonstrated the novel capabilities to genetically reconstruct different viruses. In this study, a transformation-associated recombination (TAR) system in yeast was used to rapidly rescue different strains of feline infectious peritonitis virus, which causes a deadly disease of cats for which there is no effective vaccine. Using this system, the viruses could be rescued rapidly and stably without multiple cloning steps. Considering its speed and ease of manipulation in virus genome assembly, the reverse genetics system developed in this study will facilitate the research of the coronaviruses and the vaccine development.	
Vaccines (true)	Application of Brucella gene deletion vaccine (M5-90 Δ 26 strain).	Brucella gene deletion vaccine (M5-90 Δ 26 strain) was licenced In 2023 and applied in animals in Inner Mongolia, Xinjiang, Ningxia, Gansu provinces of China.	

disease control (true)	ldentification of a broad-spectrum neutralizing antibodies and its highly conserved epitope of SARS-CoV-2 variants	We have identified a broad-spectrum neutralizing antibody and its highly conserved epitope in the receptor-binding domain (RBD) of the spike protein (S) S1 subunit of SARS-CoV-2. First, nine monoclonal antibodies (MAbs) against the RBD or S1 were generated; of these, one RBD-specific MAb, 22.9-1, was selected for its broad RBD-binding abilities and neutralizing activities against SARS-CoV-2 variants. An epitope of 22.9-1 was fine-mapped with overlapping and truncated peptide fusion proteins. The core sequence of the epitope, (405)D(N)EVR(S)QIAPGQ(414), was identified on the internal surface of the up-state RBD. The epitope was conserved in nearly all variants of concern of SARS- CoV-2. MAb 22.9-1 and its novel epitope could be beneficial for research on broad-spectrum prophylactic vaccines and therapeutic antibody drugs.
Epidemiology, surveillance, risk assessment, (true)	Identification of virulence Factor in Pasteurella multocida.	Identification of the relevant virulence factors is therefore essential for understanding its pathogenicity. Pmorf0222, encoding the PM0222 protein, is located on a specific prophage island of the pathogenic strain C48-1 of P. multocida. Its role in the pathogenesis of P. multocida infection is still unknown. The proinflammatory cytokine plays an important role in P. multocida infection; therefore, murine peritoneal exudate macrophages were treated with the purified recombinant PM0222, which induced the secretion of tumor necrosis factor alpha (TNF-alpha) and interleukin-1beta (IL-1beta) via the Toll-like receptor 1/2 (TLR1/2)-nuclear factor kappa B (NF-kappaB)/mitogen-activated protein kinase (MAPK) signaling and inflammasome activation. Additionally, the mutant strain and complemented strain were evaluated in the mouse model with P. multocida infection, and PM0222 was identified as a virulence factor, which was secreted by outer membrane vesicles of P. multocida. Further results revealed that Pmorf0222 affected the synthesis of the capsule, adhesion, serum sensitivity, and biofilm formation. Thus, we identified Pmorf0222 as a novel virulence factor in the C48-1 strain of P. multocida, explaining the high pathogenicity of this pathogenic strain.
Epidemiology, surveillance, risk assessment, (true)	PE12 interaction with TLR4 promotes intracellular survival of Mycobacterium tuberculosis by suppressing inflammatory response.	NLRP3, a member of the NLRs family, plays a significant role in conferring resistance against Mycobacterium tuberculosis (MTB) infection. Conversely, MTB evades innate immune killing by impeding the activation of the NLRP3 inflammasome, although the precise mechanism remains uncertain. In this study, we have identified PE12 (Rv1172c), a member of the PE/PPE family proteins, as an extracellular protein of MTB. PE12 interacts with Toll like receptor 4 (TLR4) in macrophages, forming the PE12-TLR4 complex which subsequently inhibits the transcription and expression of NLRP3. As a result, the transcription and secretion of IL-1beta are reduced through the PE12-TLR4-NLRP3-IL-1beta immune pathway. In vitro and in vivo experiments using a PE12-deficient strain (H37RvDeItaPE12) demonstrate a weakening of the suppression of the inflammatory response to MTB infection. Our findings highlight the role of the PE12 protein in not only inhibiting the transcription and release of inflammatory cytokines but also

		mediating the killing of MTB escape macrophages through TLR4 and inducing lung injury in MTB- infected mice. These results provide evidence that PE12 plays a significant role in the inhibition of the host immune response by MTB.
Epidemiology, surveillance, risk assessment, (true)	Analysis of avian influenza A (H3N8) viruses in poultry from China and their zoonotic potential.	Two human cases of avian influenza A (H3N8) virus infection were reported in China in 2022. To characterise H3N8 viruses circulating in China in September 2021-May 2022. We sampled poultry and poultry-related environments in 25 Chinese provinces. In total, 98 H3N8 avian influenza virus isolates were retrieved from 38,639 samples; genetic analysis of 31 representative isolates revealed 17 genotypes. Viruses belonging to 10 of these genotypes had six internal genes originating from influenza A (H9N2) viruses. These reassorted viruses could be found in live poultry markets and comprised the strains responsible for the two human infections. A subset of nine H3N8 viruses (including six reassorted) that replicated efficiently in mice bound to both avian-type and human-type receptors in vitro. Three reassorted viruses were shed by chickens for up to 9 days, replicating efficiently in their upper respiratory tract. Five reassorted viruses with H9N2 virus internal genes, causing two human infections, occurred in live poultry markets in China. The low pathogenicity of H3N8 viruses in poultry allows their continuous circulation with potential for reassortment. Careful monitoring of spill-over infections in humans is important to strengthen early-warning systems and maintain influenza pandemic preparedness.
Epidemiology, surveillance, risk assessment, (true)	Deletion of H240R Gene Attenuates the Virulence of African Swine Fever Virus (ASFV) by Enhancing NLRP3-Mediated Inflammatory Responses.	We found that ASFV pH240R strongly inhibits transcription, maturation, and secretion of interleukin-1beta (IL-1beta). Importantly, pH240R not only targeted NF-kappaB signaling but also impaired NLRP3 inflammasome activation. In this mechanism, pH240R interacted with NF-kappa-B essential modulator (NEMO), a component of inhibitor of kappa B kinase (IKK) complex and subsequently reduced phosphorylation of IkappaBalpha and p65. In addition, pH240R bonded to NLRP3 to inhibit NLRP3 inflammasome activation, resulting in reduced IL-1beta production. As expected, infection with H240R-deficient ASFV (ASFV-DeltaH240R) induced more inflammatory cytokine expression both in vitro and in vivo than its parental ASFV HLJ/18 strain. Consistently, H240R deficiency reduced the viral pathogenicity in pigs compared with its parental strain. These findings reveal that the H240R gene is an essential virulence factor, and deletion of the H240R gene affects the pathogenicity of ASFV HLJ/18 by enhancing antiviral inflammatory responses, which provides insights for ASFV immune evasion mechanisms and development of attenuated live vaccines and drugs for prevention and control of ASF.
		S. suis serotype 9 avirulent strain W7119 induced higher levels of adhesion and pro-inflammatory cytokines in PAM-Tang cells than the S. suis serotype 2 virulent strain 700794. Prolonged incubation with S. suis caused more cytotoxic cell damage, and the

Epidemiology, surveillance, risk assessment, (true)	Study of Streptococcus suis Strains of different virulence in porcine alveolar macrophage-Tang cells.	virulent strain induced higher levels of cytotoxicity to PAM-Tang cells. The virulent strain also induced higher levels of apoptosis in PAM-Tang cells, as shown by terminal deoxynucleotidyl transferase (TdT)-mediated dUTP-biotin nick end labeling (TUNEL) assay. In addition, it is the first report of virulent and avirulent S. suis inducing PAM-Tang polarization towards pro-inflammatory M1 macrophages and p53- and caspase-dependent apoptosis in PAMs. Taken together, this study contributes to a better understand of interactions between macrophages and S. suis isolates of different virulence, and confirms that PAM-Tang cells provide a long-term, renewable resource for investigating macrophage infections with bacteria.
Zoonoses (true)	The study on the cellular entrance of Rabies and SARS-CoV-2 viruses.	We demonstrate that mGluR2 facilitates RABV internalization in vitro and infection in vivo. We found that transferrin receptor 1 (TfR1) interacts with mGluR2 and internalizes with mGluR2 and RABV in the same clathrin-coated pit. Knockdown of TfR1 blocks agonist-triggered internalization of mGluR2. Importantly, TfR1 also interacts with the SARS-CoV-2 spike protein and is important for SARS-CoV-2 internalization. Our findings identify a novel axis (mGluR2-TfR1 axis) used by RABV and SARS-CoV-2 for entry, and reveal TfR1 as a potential target for therapeutics against RABV and SARS-CoV-2.
Zoonoses (true)	The study on the life cycle of Toxoplasma gondii.	Exocytosis is a key active process in cells by which proteins are released in bulk via the fusion of exocytic vesicles with the plasma membrane. Soluble N- ethylmaleimide-sensitive factor attachment protein receptor (SNARE) protein-mediated vesicle fusion with the plasma membrane is essential in most exocytotic pathways. In mammalian cells, the vesicular fusion step of exocytosis is normally mediated by Syntaxin-1 (Stx1) and SNAP25 family proteins (SNAP25 and SNAP23). However, in Toxoplasma gondii, a model organism of Apicomplexa, the only SNAP25 family protein, with a SNAP29-like molecular structure, is involved in vesicular fusion at the apicoplast. We reveal that an unconventional SNARE complex comprising TgStx1, TgStx20, and TgStx21 mediates vesicular fusion at the plasma membrane. This complex is essential for the exocytosis of surface proteins and vesicular fusion at the apical annuli in T. gondii.
Zoonoses (true)	The study on the mechanism of Toxoplasma gondii infection.	We found that the ATG12-ATG5-ATG16L complex exists in Toxoplasma gondii (Tg). This complex is localized on isolated structures at the periphery of the apicoplast dependent on TgATG16L. Inducible depletion of TgATG12, TgATG5, or TgATG16L caused loss of the apicoplast and affected parasite growth. We found that a putative soluble N-ethylmaleimide sensitive factor attachment protein receptor (SNARE) protein, synaptosomal-associated protein 29 (TgSNAP29, Qbc SNARE), is required to maintain the apicoplast in T. gondii. TgSNAP29 depletion disrupted TgATG8 localization at the apicoplast. Additionally, we identified a putative ubiquitin- interacting motif-docking site (UDS) of TgATG8. Mutation of the UDS site abolished TgATG8 localization on the apicoplast but not lipidation. These findings suggest that the TgATG12-TgATG5- TgATG16L complex is required for biogenesis of the

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		apicoplast, in which TgATG8 is translocated to the apicoplast via vesicles in a SNARE -dependent manner in T. gondii.
Zoonoses (true)	Study of virulence of porcine Shiga toxin- producing enterotoxigenic Escherichia coli.	Enterotoxigenic Escherichia coli (ETEC) cause severe diarrhea in humans and animals, leading to death and huge economic loss worldwide. Thus, elucidation of ETEC's pathogenic mechanisms will provide powerful data for the discovery of drugs serving as prevention or therapeutics against ETEC- caused diarrheal diseases. Here, we report that ArcA plays an essential role in the pathogenicity and virulence regulation in ETEC by positively regulating the expression of several key virulence factors including F18 fimbriae, heat-labile and heat-stable toxins, Shiga toxin 2e, and hemolysin, under microaerobic conditions and in vivo. Moreover, we found that positive regulation of several virulence genes by ArcA requires a global repressor H-NS (histone-like nucleoid structuring), implying that ArcA may exert positive effects by antagonizing H- NS. Collectively, our data established a key role for ArcA in the pathogenicity of porcine ETEC and ETEC strains isolated from human infections. Moreover, our work reveals another layer of regulation in relation to oxygen control of virulence factors in ETEC.
Zoonoses (true)	Broad antagonism of coronaviruses nsp5 to evade the host antiviral responses by cleaving POLDIP3.	Coronaviruses (CoVs) are a family of the largest RNA viruses that typically cause respiratory, enteric, and hepatic diseases in animals and humans, imposing great threats to the public safety and animal health. In this study, downregulation of DNA polymerase delta interacting protein 3 (POLDIP3) was confirmed in PDCoV infected IPEC-J2 cells by isobaric tags for relative and absolute quantification (iTRAQ) and Western blotting analysis. An antagonistic strategy was revealed that PDCoV encoded nonstructural protein 5 (nsp5) was responsible for POLDIP3 reduction via its 3C-like protease cleavage of POLDIP3 at the glutamine acid 176 (Q176), facilitating PDCoV infection due to the loss of antiviral effects of the cleaved fragments. Collectively, we unveiled a new antagonistic strategy evolved by PDCoV to counteract antiviral innate immunity by nsp5-mediated POLDIP3 cleavage, eventually ensuring productive virus replication. Importantly, we further demonstrated that nsp5s from PEDV and TGEV harbor the conserved function to cleave porcine POLDIP3 at the Q176 to despair POLDIP3-mediated antiviral effects. In addition, nsp5 from SARS-CoV-2 also cleaves human POLDIP3. Therefore, we speculate that coronaviruses employ similar POLDIP3 cleavage mechanisms mediated by nsp5 to antagonize the host antiviral responses to sustain efficient virus infection.
Diagnosis, biotechnology and laboratory (true)	Development and application of ELISA kit for Brucella antibody detection kit.	An ELISA kit for Brucella antibody detection based on bp26 protein was development and applied in animals in Inner Mongolia, Xinjiang, Ningxia, Gansu provinces of China.
Diagnosis, biotechnology and laboratory (true)	Development and application of Colloid gold test strip for Brucella antigen detection.	A colloid gold test strip for Brucella antigen detection based on bp26 protein antibodies was development and applied in animals in Inner Mongolia, Xinjiang, Ningxia, Gansu provinces of China.
		Streptococcus suis serotype 2 is a zoonotic pathogen

Diagnosis, biotechnology and laboratory (true)	A CRISPR-Cas12a-based platform facilitates the detection and serotyping of Streptococcus suis serotype 2.	that causes septicemia, arthritis, and meningitis in pigs and humans. In this study, we developed a high- fidelity detection and serotyping platform for S. suis serotype 2 based on recombinase polymerase amplification (RPA) and a clustered regularly interspaced short palindromic repeat (CRISPR)- Cas12a system called Cards-SSJ/K. Cards-SSJ had a detection limit of 10 CFU, takes <60 min, and no cross-reaction was found with other S. suis serotypes, closely related Streptococcus spp., or common pig pathogens, and Cards-SSK could differentiate serotype 2 from serotype 1/2. Results from Cards-SSJ and qPCR were equivalent in detecting S. suis serotype 2 in tissue samples. Analysis indicated that despite a relatively high reagent cost compared to PCR and qPCR, Cards-SSJ was less time-consuming and had low requirements for equipment and personnel. Thus, it is an excellent method for point- of-care detection for S. suis serotype 2.
Vaccines (true)	A candidate subunit vaccine against Mycobacterium avium subspecies paratuberculosis.	Mycobacterium avium subspecies paratuberculosis (MAP) causes paratuberculosis (PTB), which is a granulomatous enteritis in ruminants that threatens the dairy industry's healthy development and public health safety worldwide. Because the commercial inactivated vaccines are not completely protective and interfere with bovine tuberculosis diagnostics, we tested four fusion proteins, namely 66NC, 66CN, 90NC, and 90CN, which were constructed with MAP3527, Ag85B, and Hsp70 of MAP in different tandem combinations. Notably, 66NC, which encodes a 66 kDa fusion protein that combines in linear order MAP3527(N40-232), Ag85B(41-330), and MAP3527(C231-361,) induced a powerful and specific IFN-gamma response. Immunization of C57BL/6 mice with the 66NC fusion protein formulated in Montanide ISA 61 VG adjuvant generated robust Th1, Th2, and Th17 type immune responses and strong antibody responses. The 66NC vaccine protected C57BL/6 mice against virulent MAP K-10 infection. This resulted in a reduction of bacterial load and improvement of pathological damage in the liver and intestine, in addition to a reduction of body weight loss; significantly better protection than the reported 74 F vaccine was also induced. Furthermore, vaccine efficacy correlated with the levels of IFN- gamma-, TNF-alpha-, and IL-17A-secreting antigen- specific CD4(+) and CD8(+) T lymphocytes as well as with serum IFN-gamma and TNF-alpha levels after vaccination. These results demonstrate that recombinant protein 66NC is an efficient candidate for further development into a protective vaccine in terms of inducing specific protection against MAP.
Vaccines (true)	Analysis of the conserved protective epitopes of hemagglutinin on influenza A viruses.	The conserved protective epitopes of hemagglutinin (HA) are essential to the design of a universal influenza vaccine and new targeted therapeutic agents. Over the last 15 years, numerous broadly neutralizing antibodies (bnAbs) targeting the HA of influenza A viruses have been isolated from B lymphocytes of human donors and mouse models, and their binding epitopes identified. This work has brought new perspectives for identifying conserved protective epitopes of HA. We succinctly analyzed and summarized the antigenic epitopes and functions of more than 70 kinds of bnAb. The highly conserved protective epitopes are concentrated on

		five regions of HA: the hydrophobic groove, the receptor-binding site, the occluded epitope region of the HA monomers interface, the fusion peptide region, and the vestigial esterase subdomain. Our analysis clarifies the distribution of the conserved protective epitope regions on HA and provides distinct targets for the design of novel vaccines and therapeutics to combat influenza A virus infection.
Vaccines (true)	A novel viral vaccine platform based on engineered transfer RNA.	We used anticodon-engineered transfer RNAs (ACE- tRNAs) as powerful precision switches to control the replication of PTC-containing viruses. We showed that ACE-tRNAs display higher potency of reading through PTCs than genetic code expansion (GCE) technology. Interestingly, ACE-tRNA has a site preference that may influence its read-through efficacy. We further attempted to use ACE-tRNAs as a novel viral vaccine platform. Using a human immunodeficiency virus type 1 (HIV-1) pseudotyped virus as an RNA virus model, we found that ACE- tRNAs display high potency for read-through viral PTCs and precisely control their production. Pseudorabies virus (PRV), a herpesvirus, was used as a DNA virus model. We found that ACE-tRNAs display high potency for reading through viral PTCs and precisely controlling PTC-containing virus replication. In addition, PTC-engineered PRV completely attenuated and lost virulence in mice in vivo, and immunization with PRV containing a PTC elicited a robust immune response and provided complete protection against wild-type PRV challenge. Overall, replication-controllable PTC- containing viruses based on ACE-tRNAs provide a new strategy to rapidly attenuate virus infection and prime robust immune responses. This technology can be used as a platform for rapidly developing viral vaccines 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	
Specification for the description and determination of pig biological indicators	Specification for experimental animals	Laboratory expertise	
Technical specifications for caesarean section for acquisition of SPF pigs	Specification for experimental animals	Laboratory expertise	
Specification for sterile feeding of piglets	Specification for experimental animals	Laboratory expertise	
Basic operation specifications for poultry	Specification for experimental animals	Laboratory expertise	

3. In exercising your activities, have you identified any regulatory research needs* relevant for WOAH?

No

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?

Yes	
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Name of WOAH CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
Surveillance and Control of animal protozoan Diseases	Japan	Asia and Pasific	To cooperate in the research for surveillance and control of animal protozoan diseases
Biotechnology-based Diagnosis of Infectious Diseases	Sweden	Europe	To have cooperation on the research of zoonoses and other animal diseases

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?

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Name of WOAH CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
the WOAH 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
RL of Marek's Disease	UK	Europe	To have cooperation on the research of Marek's Disease

TOR6: EXPERT CONSULTANTS

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

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NAME OF EXPERT	KIND OF CONSULTANCY	SUBJECT
Dr. CHEN Hualan	Conselor	Highly pathogenic avian influenzacontrol in China. To participant in the WOAH Regional Workshop for Avian Disease Prevention and Control in Asia and the Pacific. Qingdao, People's Republic of China August 30, 2023
Dr. ZHAO Dongming	Conselor	Control measures for Afrian swine fever (ASF) in China. To participant in the WOAH Fifth Regional Workshop on Swine Disease Control in Asia. Beijing, People's Republic of China 21-22 Nov 2023
Dr. ZHAO Dongming	Conselor	Update on vaccine development. To participant in WOAH/FAO Global Consultations on African Swine Fever Control. Rome, 12 Dec 2023

Dr. CHEN Hualan	Conselor	Control highly pathogenic avian influenzaby vaccination. To participate in The Regional Quadripartite (FAO, UNEP, WHO and WOAH) for Asia-Pacific joint webinar on "Zoonotic influenza", 8-9May 2023
Dr. CHEN Hualan	Conselor	Highly pathogenic avian influenza control : the strategy in China. To participate in the 12th Asia Pacific Poultry Conference. Nanjing, China. 1-3 Nov 2023
Dr. LIU Shengwang	Conselor	Vaccine and prevention and control of chicken infectious bronchitis. To participate in the 12th Asia Pacific Poultry Conference. Nanjing, China. 1-3 Nov 2023
Dr. ZHAO Dongming	Conselor	Updates on ASFV Virology from China. To participate in the Global African Swine Fever Research Alliance Gap Analysis. Manila, Philippines. 5 Dec 2023.

TOR7: SCIENTIFIC AND TECHNICAL TRAINING

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

Yes

We maintain a Joint Laboratory of Animal Diseases Prevention and Control with Cairo University. We provided advice and diagnostic technique for prevention of zoonoses and other avian diseases, and vaccines against highly pathogenic avian influenza to Egypt.

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 : 0
- b) Seminars : 10

c) Hands-on training courses: 0

d) Internships (>1 month) : 3

TYPE OF TECHNICAL TRAINING PROVIDED (A, B, C OR D)	CONTENT		NO. PARTICIPANTS FROM THE CORRESPONDING COUNTRY
D	provided scientific and technical training in research and overall preventive veterinary techniques	Parkistan	3
В	Seminar for China-Kazakhstan Joint Laboratory of Agricultural Science we maintained	Kazakhstan	3
В	Seminar for China-Burundi joint One-health laboratory of animal disease prevention and control	Burundi	5
В	Seminar for prevention and control of African Swine Fever	Russia	1
В	Seminar for prevention and control of zoonotic parasite disease	Japan	1

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?

ATIONAL/INTERNATIONAL	TITLE OF EVENT	CO-ORGANISER	DATE (MM/YY)	LOCATION	NO. PARTICIPANTS
International	WOAH Regional Workshop for Avian Disease Prevention and Control in Asia and the Pacific	WOAH	2023-08-30	Qingdao, China	100
International	WOAH Fifth Regional Workshop on Swine Disease Control in Asia	WOAH	2023-11-21	Beijing, China	100
International	Global Consultations on African Swine Fever Control.	WOAH, FAO	2023-12-12	Rome, Italy	100
International	The Regional Quadripartite (FAO, UNEP, WHO and WOAH) for Asia-Pacific joint webinar on "Zoonotic influenza"	FAO, UNEP, WHO and WOAH	2023-05-08	webinar	100
International	International Symposium for Classical Swine Fever	Huazhong Agricultural University, China Institute of Veterinary Drug Control	2023-11-28	Wuhan, China	500
International	The Fourth International Conference on Veterinary Testing and Diagnosis	China Agricultural University	2023-03-29	Chongqin, China	500
International	2023 GARAD GLOBAL ALLIANCE FOR RESEARCHON AVIAN DISEASES	The Global Alliance for Research on Avian Diseases	2023-05-22	Guildford, UK	100
International	2023 Annual Meeting of Overseas Chinese Society of Microbiology	The Overseas Chinese Society for Microbiology	2023-07-07	Changchun, China	200
International	2023 NAPRRS/NC229: International Conference of Swine Viral Diseases	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	2023-11-30	Chicago, USA	100
International	EMI Symposium 2023	EMI OXFORD RESEARCH GROUP	2023-12-06	On-line	100
International	Global African Swine Fever Research Alliance Gap Analysis	FAO/WOAH	2023-12-12	Manila, Philippines	100

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. Cao H, Gu H, Kang H, Jia H. 2023. Development of a rapid reverse genetics system for feline coronavirus based on TAR cloning in yeast. Front Microbiol 14:1141101. 2. Chen X, Zheng J, Li T, Liu C, Bao M, Wang X, Li X, Li J, Huang L, Zhang Z, Weng C. 2023. Coreceptor AXL Facilitates African Swine Fever Virus Entry via Apoptotic Mimicry. J Virol 97:e0061623.

3. Cui P, Shi J, Yan C, Wang C, Zhang Y, Zhang Y, Xing X, Chen Y, Zhang J, Liu L, Zeng X, Tian G, Li C, Suzuki Y, Deng G, Chen H. 2023. Analysis of avian influenza A (H3N8) viruses in poultry and their zoonotic potential, China, September 2021 to May 2022. Euro Surveill 28.

4. Fu J, Zhao L, Pang Y, Chen H, Yamamoto H, Chen Y, Li Z, Mizushima N, Jia H. 2023. Apicoplast biogenesis mediated by ATG8 requires the ATG12-ATG5-ATG16L and SNAP29 complexes in Toxoplasma gondii. Autophagy 19:1258-1276.

5. Fu J, Zhao L, Yang J, Chen H, Cao S, Jia H. 2023. An unconventional SNARE complex mediates exocytosis at the plasma membrane and vesicular fusion at the apical annuli in Toxoplasma gondii. PLoS Pathog 19:e1011288.

6. Hagoss YT, Shen D, Zhang Z, Li F, Bu Z, Zhao D. 2023. Novel Epitopes Mapping of African Swine Fever Virus CP312R Protein Using Monoclonal Antibodies. Viruses 15.

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7. Hou N, Shuai L, Zhang L, Xie X, Tang K, Zhu Y, Yu Y, Zhang W, Tan Q, Zhong G, Wen Z, Wang C, He X, Huo H, Gao H, Xu Y, Xue J, Peng C, Zou J, Schindewolf C, Menachery V, Su W, Yuan Y, Shen Z, Zhang R, Yuan S, Yu H, Shi PY, Bu Z, Huang J, Hu Q. 2023. Development of Highly Potent Noncovalent Inhibitors of SARS-CoV-2 3CLpro. ACS Cent Sci 9:217-227.

8. Hua RH, Zhang SJ, Niu B, Ge JY, Lan T, Bu ZG. 2023. A Novel Conserved Linear Neutralizing Epitope on the Receptor-Binding Domain of the SARS-CoV-2 Spike Protein. Microbiol Spectr 11:e0119023.

9. Huang L, Chen W, Liu H, Xue M, Dong S, Liu X, Feng C, Cao S, Ye G, Zhou Q, Zhang Z, Zheng J, Li J, Zhao D, Wang Z, Sun E, Chen H, Zhang S, Wang X, Zhang X, He X, Guan Y, Bu Z, Weng C. 2023. African Swine Fever Virus HLJ/18 CD2v Suppresses Type I IFN Production and IFN-Stimulated Genes Expression through Negatively Regulating cGMP-AMP Synthase-STING and IFN Signaling Pathways. J Immunol 210:1338-1350.

10. Huang L, Liu H, Ye G, Liu X, Chen W, Wang Z, Zhao D, Zhang Z, Feng C, Hu L, Yu H, Zhou S, Zhang X, He X, Zheng J, Bu Z, Li J, Weng C. 2023. Deletion of African Swine Fever Virus (ASFV) H240R Gene Attenuates the Virulence of ASFV by Enhancing NLRP3-Mediated Inflammatory Responses. J Virol 97:e0122722.

11. Jiang F, Yang Y, Mao Z, Cai W, Li G. 2023. ArcA positively regulates the expression of virulence genes and contributes to virulence of porcine Shiga toxin-producing enterotoxigenic Escherichia coli. Microbiol Spectr 11:e0152523.

12. Jiao C, Wang B, Chen P, Jiang Y, Liu J. 2023. Analysis of the conserved protective epitopes of hemagglutinin on influenza A viruses. Front Immunol 14:1086297.

13. Jiao S, Li C, Liu H, Xue M, Zhou Q, Zhang L, Liu X, Feng C, Ye G, Liu J, Li J, Huang L, Xiong T, Zhang Z, Weng C. 2023. Porcine reproductive and respiratory syndrome virus infection inhibits NF-kappaB signaling pathway through cleavage of IKKbeta by Nsp4. Vet Microbiol 282:109767.

14. Li S, Wang C, Tang YD, Qin L, Chen T, Wang S, Bai Y, Cai X, Wang S. 2023. Interaction between Porcine Alveolar Macrophage-Tang Cells and Streptococcus suis Strains of Different Virulence: Phagocytosis and Apoptosis. Microorganisms 11.

15. Li T, Li X, Wang X, Chen X, Zhao G, Liu C, Bao M, Song J, Li J, Huang L, Rong J, Tian K, Deng J, Zhu J, Cai X, Bu Z, Zheng J, Weng C. 2023. African swine fever virus pS273R antagonizes stress granule formation by cleaving the nucleating protein G3BP1 to facilitate viral replication. J Biol Chem 299:104844.

16. Liu X, Qi S, Yin X. 2023. Morphogenesis of Hepatitis E Virus. Adv Exp Med Biol 1417:159-169.

17. Mao D, Song X, Ma D, Hu S, Zhang Z, Wang J, He X. 2023. Bile duct hamartoma in a dog. J Comp Pathol 207:45-49.

18. Qin L, Meng F, He H, Li S, Zhang H, Sun Y, Zhang W, An T, Cai X, Wang S. 2023. Inflammation plays a critical role in damage to the bronchiolar epithelium induced by Trueperella pyogenes in vitro and in vivo. Infect Immun 91:e0027323.

19. Shao M, Cui N, Tang Y, Chen F, Cui Y, Dang G, Liu S. 2023. A candidate subunit vaccine induces protective immunity against Mycobacterium avium subspecies paratuberculosis in mice. NPJ Vaccines 8:72.

20. Wang S, Xu M, Yang K, Zhang Y, Li S, Tang YD, Wang J, Leng C, An T, Cai X. 2023. Streptococcus suis contributes to inguinal lymph node lesions in piglets after highly pathogenic porcine reproductive and respiratory syndrome virus infection. Front Microbiol 14:1159590.

21. Wang TY, Meng FD, Sang GJ, Zhang HL, Tian ZJ, Zheng H, Cai XH, Tang YD. 2023. A novel viral vaccine platform based on engineered transfer RNA. Emerg Microbes Infect 12:2157339.

22. Wang X, Wen Z, Cao H, Luo J, Shuai L, Wang C, Ge J, Wang X, Bu Z, Wang J. 2023. Transferrin Receptor Protein 1 Cooperates with mGluR2 To Mediate the Internalization of Rabies Virus and SARS-CoV-2. J Virol 97:e0161122.

23. Wu Y, Li M, Tian J, Yan H, Pan Y, Shi H, Shi D, Chen J, Guo L, Feng L. 2023. Broad antagonism of coronaviruses nsp5 to evade the host antiviral responses by cleaving POLDIP3. PLoS Pathog 19:e1011702.

24. Xu T, Zheng Y, Liu B, Kou M, Jiang Q, Liu J, Kang H, Yang M, Guo D, Qu L. 2023. Pmorf0222, a Virulence Factor in Pasteurella multocida, Activates Nuclear Factor Kappa B and Mitogen-Activated Protein Kinase via Toll-Like Receptor 1/2. Infect Immun 91:e0019322.

25. Ye G, Liu H, Liu X, Chen W, Li J, Zhao D, Wang G, Feng C, Zhang Z, Zhou Q, Zheng J, Bu Z, Weng C, Huang L. 2023. African Swine Fever Virus H240R Protein Inhibits the Production of Type I Interferon through Disrupting the Oligomerization of STING. J Virol 97:e0057723.

26. Zhang J, Cui Y, Zang X, Feng T, Chen F, Wang H, Dang G, Liu S. 2023. PE12 interaction with TLR4 promotes intracellular survival of Mycobacterium tuberculosis by suppressing inflammatory response. Int J Biol Macromol 253:127547.

27. Zhang SJ, Liu J, Niu B, Zhu YM, Zhao DM, Chen WY, Liu RQ, Bu ZG, Hua RH. 2023. Comprehensive mapping of antigenic linear B-cell epitopes on K205R protein of African swine fever virus with monoclonal antibodies. Virus Res 328: 199085.

28. Zhao D, Sun E, Huang L, Ding L, Zhu Y, Zhang J, Shen D, Zhang X, Zhang Z, Ren T, Wang W, Li F, He X, Bu Z. 2023. Highly lethal genotype I and II recombinant African swine fever viruses detected in pigs. Nature communications 14:3096.

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? Especially, vaccine. Brucella gene deletion vaccine (M5-90 Δ 26 strain) was licenced In 2023 and applied in animals in Inner Mongolia, Xinjiang, Ningxia, Gansu provinces of China.

12. Additional comments regarding your report: *No.*