WIV Newsletter
No.17 JUL 2017

Spotlight

1st International Workshop on Biosafety Laboratory Management and Experimental Techniques First Announcement

The 1st International Workshop on Biosafety Laboratory Management and Experimental Techniques organized by Wuhan Institute of Virology (WIV), Chinese Academy of Sciences (CAS), will be held from October 18 to 28, 2017 in Wuhan, China. This workshop is designed for laboratory managers and directors, research and laboratory staff who plan to carry out infectious disease research in biosafety facilities from countries along the "One Belt, One Road" region, especially from the developing countries. The workshop will address key aspects of biosafety and provide practical training in high level biosafety laboratories (BSL).

Objectives:

- Learn the key components (risk recognition, risk assessment and risk mitigation) of a biorisk management system.
- Acquire knowledge on contagious pathogens and hands-on experience of safe operations in biosafety laboratories.
- Know basic design principles of biosafety laboratories.

Venue: Wuhan Institute of Virology, CAS

Trainees: Less than 20 people

Language: English

Topics:

- Introduction to Biosafety
- Laboratory Biosafety Management System
- Biorisk Assessment Contents and Methods
- Basic Etiology of Contagious Pathogens
- Protection Classes and Key Facilities of Biosafety Laboratory
- Biosafety Operation Norms
- Biosafety Management on Animal Experiments
- Preservation, Transportation and Management of Bacterial and Viral Strains

Notice:

- The application deadline is September 30, 2017. An application letter and applicant's resume are required. WIV, CAS will select the final attendee according to applicants' resumes and other relevant information

and inform the result as soon as possible.
- The cost of training will be fully supported by WIV, CAS.

Contact:
Please email application letter and resume to :

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Scientists investigated the effect of ORF7 deletion on varicella-zoster virus replication cycle

The neurological damage caused by varicella-zoster virus (VZV) reactivation is commonly manifested as clinical problems. Thus, identifying viral neurovirulent genes and characterizing their functions are important for relieving VZV related neurological complications. ORF7 has been previously identified as a potential neurotropic gene, but its involvement in VZV replication is unclear.

In a joint study with Prof. ZHU Hua from Rutgers New Jersey Medical School, Prof. LUO Minhua from Wuhan Institute of Virology of the Chinese Academy of Sciences demonstrate that the ORF7 protein is a component of the tegument layer of VZV virions.

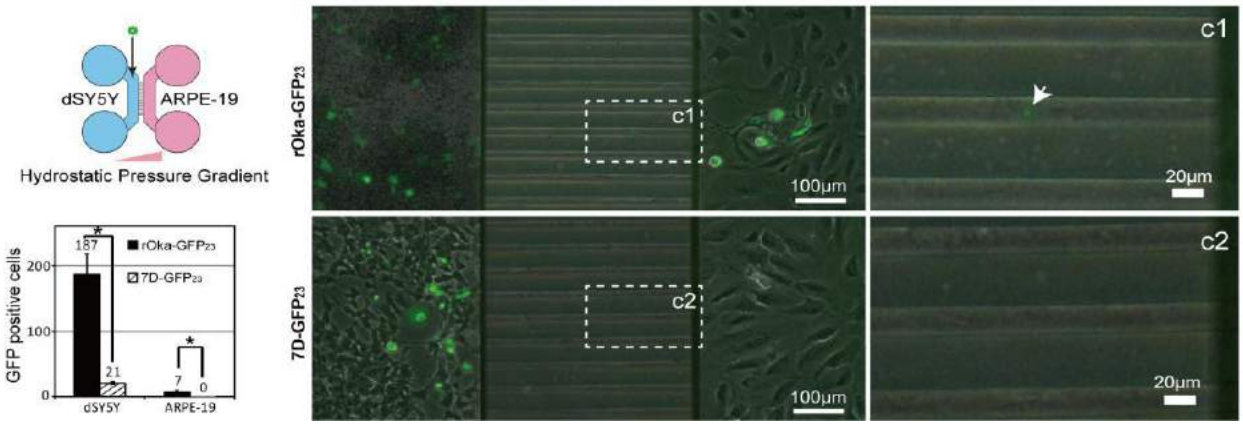
In this study, to decode the function of pORF7, distinct cells including the epithelium cell ARPE-19, neural progenitor cells (NPCs), differentiated NPCs (dNPCs), neuroblastoma SH-SY5Y (SY5Y) and differentiated SH-SY5Y (dSY5Y) were used. The scientists analyzed the effect of ORF7 deletion on the viral replication processes, including viral entry, viral gene expression and genome replication, viral particle assembly and envelopment, and intercellular viral spread. Results revealed that pORF7 participates in VZV cytoplasmic envelopment in neuronal cells which could be a target for the attenuation of VZV neurovirulence.

ORF7 deletion attenuates the VZV replication in ARPE-19 cells and NPCs, and severely impairs viral replication and neurovirulence in differentiated neuronal cells. 7D shows impaired trans-neuronal transmission, and impaired capacity for producing intact virions in neurons and for spreading to neighboring neurons or innervated non-neuronal cells. These results suggest that 7D could be a basis for a safer vaccine.

The results have been published in Journal of Virology entitled "ORF7 of Varicella-Zoster Virus Is Required for Viral Cytoplasmic Envelopment in Differentiated Neuronal Cells".

This work was supported by National Natural Science Foundation of China (NSFC) projects and the National Basic Research Program of China (973 Program). Researchers from National Institute of Diagnostics and Vaccine Development in Infectious Diseases (Xiamen University) and College of Life Sciences of Wuhan University also participated in this study.

Link: *http://jvi.asm.org/content/early/2017/03/23/JVI.00127-17.long*



Scientists generated a serial of recombinant viruses for neuronal circuit tracing

Damage of brain connectome in neurodegenerative diseases remains unclear. Revealing the differences and abnormalities of neuronal circuits between healthy individuals and patients with PD or AD will contribute to understanding the mechanism(s) of these diseases. Mapping the brain connectome requires appropriate tracing tools, but the anterograde tracing tools are underdevelopment, and particularly, the monosynaptic anterograde tracer is still lacking.

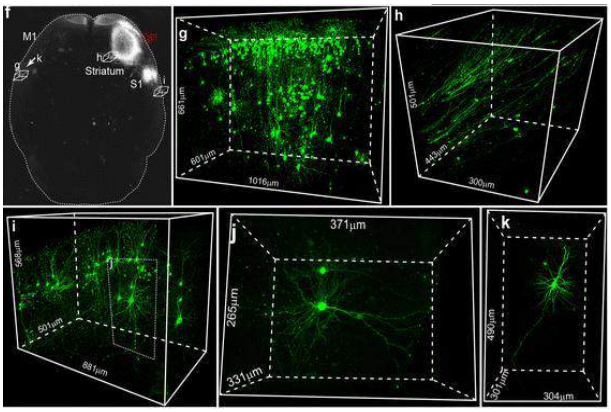
In a joint study with Prof. XU Fuqiang from Wuhan Institute of Physics and Mathematics of the Chinese Academy of Sciences, the research group led by Prof. LUO Minhua from Wuhan Institute of Virology of the Chinese Academy of Sciences created the anterograde multi- and monosynaptic tracers derived from HSV-1 H129 strain.

Based on the bacterial artificial chromosome of H129, the scientists have generated a serial of recombinant viruses for neuronal circuit tracing. Among them, H129-G4 was obtained by inserting binary tandemly connected GFP cassettes into the H129 genome, and H129-ΔTK-tdT was obtained by deleting the thymidine kinase (TK) gene and adding tdTomato coding gene to the H129 genome. Then the obtained viral tracers were tested in vitro and in vivo for the tracing capacity.

They introduced a potential novel anterograde monosynaptic tracer H129-ΔTK-tdT and a bright anterograde multisynaptic tracer H129-G4. With helper virus complementarily expressing TK, H129-ΔTK-tdT can potentially transmit to the postsynaptic neurons, and enable visualization of direct projection targets of either a given brain

nucleus or a specific neuron type. H129-G4 may label the multisynaptic projection circuit with high labeling intensify, which helps to visualize the details of neuron morphology along the circuits.

These novel anterograde tracers offer novel tools for projectome mapping, and complement the existing neuronal circuit tracing tool box.



The results have been published in Molecular Neurodegeneration entitled "Anterograde monosynaptic transneuronal tracers derived from herpes simplex virus 1 strain H129 ".

This work was supported by the National Program on Key Basic Research Project and the National Natural Science Foundation of China. Researchers from Wuhan National Laboratory for Optoelectronics, Peking University, Beijing Normal University and Kunming University of Science and Technology also participated in this study.

Link: *https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-017-0179-7*

Researchers established a novel strategy to mineralize inorganic nanoparticles inside the viral protein cage

Mineralization templated by bio-nanostructures has been a focus in the field of nanomaterial synthesis of late. Various bio-nanostructures (e.g., protein nanocages, nanotubes, and nanowires) have been investigated for the templated synthesis of nanomaterials and have been found to offer excellent control over the morphology and properties of the target.

As a well-known class of nanoplatforms, protein nanocages have received intense attention for the biomineralization of nanomaterials. Protein nanocages are assembled from multiple copies of protein subunits with a spherical shape, generally 10–200 nm in diameter and an inner cavity. Several advantages of protein nanocages including well-defined structures with monodispersity, controllable assembly, and convenient preparation and modification, make them suitable templates for the controlled fabrication of nanomaterials.

In a joint study with Prof. ZHANG Xian'en from Institute of Biophysics of the Chinese Academy of Sciences, the research group led by Prof. LI Feng from Wuhan Institute of Virology of the Chinese Academy of Sciences put forward a simple route to circumvent such a limitation: encapsulation of a preformed nanoparticles (NP) as the seed via self-assembly, followed by the growth of an outer metal layer. Using such a method, they succeeded in mineralizing size-tunable Au NPs and Au@Ag core–shell NPs (<10 nm in diameter) with narrow size distributions inside the virus-based NPs of simian virus 40.

In this work, ELD of a metal layer onto a

pre-encapsulated AuNP core inside a protein nanocage was achieved. Enlarged AuNPs and Au@Ag core–shell NPs with narrow size distributions were synthesized, with the thickness of the deposited layer being finely tuned under confinement by the protein nanocage by controlling the input of metal precursors, as evidenced by UV–Vis spectroscopy, agarose gel electrophoresis, TEM, and EDS.

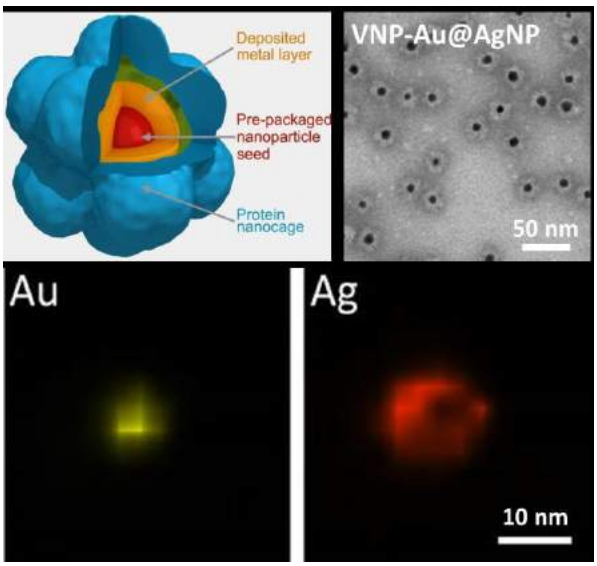
The method demonstrated in this work is unique in directly encapsulating preformed NPs as the seed through self-assembly, instead of synthesizing the seed inside the protein nanocages. Therefore, it does not need the introduction of ion affinity tags via protein modification. Most importantly, it circumvents the limitation that only gentle reaction conditions can be used for seed synthesis inside protein cages to avoid protein damage, opening up the possibility that many more kinds of chemically synthesized NPs could be used as seeds for mineralization inside protein nanocages.

The method provides a new way to fabricate hybrid bio-inorganic NPs with tailored components and structures for a variety of applications.

The results have been published in Nano Research entitled " Reaction inside a viral protein nanocage: Mineralization on a nanoparticle seed after encapsulation via self-assembly ".

This work was supported by the National Natural Science Foundation of China and the Key Research Program of the Chinese Academy of Sciences.

Link: *https://link.springer.com/article/10.1007/s12274-017-1541-3*

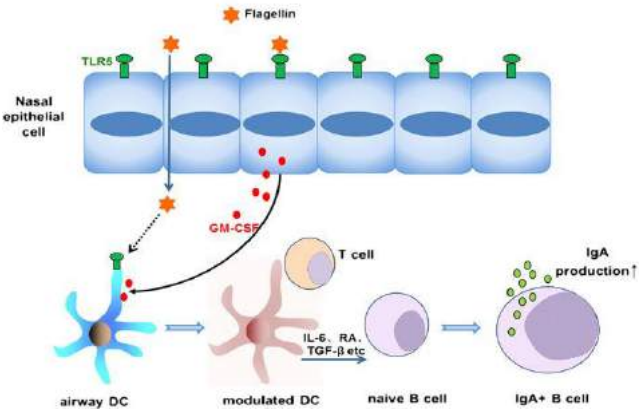


Scientists confirmed that GM-CSF derived from NECs play an important role in TLR5-mediated DC activation and subsequent IgA enhancement

The TLR5 agonist flagellin has been proven as an effective mucosal adjuvant, in addition to its systemic adjuvant activity, when administered via the i.n. route, which can prominently increase a protective IgA response. However, the mechanism by which flagellin drives a mucosal immune response when acting as an i.n. adjuvant remains elusive.

In a present study, the research group led by Prof. YAN Huimin from Wuhan Institute of Virology of the Chinese Academy of Sciences focused on the mechanism of the airway dendritic cells (DCs) modulation and subsequent IgA enhancement. Their study

confirmed that direct flagellin stimulation was insufficient to activate DCs and enhance DC-mediated IgA response. Using an in vitro system for culturing mouse primary NECs (mNECs), they found that NECs play an important role in TLR5-mediated DC activation and IgA enhancement. Flagellin-activated NECs secreted certain cytokines, particularly GM-CSF, and these conveyed the TLR5 signal of NECs to mucosal DCs, resulting in the subsequent IgA responses.



This study helps to understand TLR5-mediated immune activation in the airway and provide insight into a new function of epithelial GM-CSF in modulating immune responses.

The results have been published in Journal of Leukocyte Biology entitled "Nasal epithelial GM-CSF contributes to TLR5-mediated modulation of airway dendritic cells and subsequent IgA response" under the Frontline Science Section as "Leading Edge Research".

This work was supported by grants from the National Natural Science Foundation of China, National Science and Technology Major Project on Major Infectious Diseases, Ministry of Science and Technology of China (973 Program), and Grants of Deutsche Forschungsgemeinschaft.

Link: *http://www.jleukbio.org/content/early/2017/05/18/jlb.3HI0816-368RR.abstract*

Scientists demonstrate RNAi as an antiviral immunity in mammals

RNAi is an evolutionarily conserved post-transcriptional gene silencing mechanism in eukaryotes, and has been well recognized as an antiviral immunity in fungi, plants, and invertebrates. In the process of antiviral RNAi, viral dsRNA replicative intermediates generated during RNA virus replication are recognized and processed by Dicer into siRNAs. These virus-derived siRNAs (vsiRNAs) are then transferred into RNA-induced silencing complex (RISC), to direct the cleavage of cognate viral RNAs. However, whether RNAi can function as an antiviral defense in mammals, particularly in differentiated mammalian somatic cells, remains unclear for decades.

In collaboration with Dr. QIN Cheng-Feng from Beijing Institute of Microbiology and Epidemiology, the researchers from Dr. ZHOU Xi's group at the State Key Laboratory of Virology, Wuhan Institute of Virology of the Chinese Academy of Sciences, have reported that RNAi can be induced and suppressed by human enterovirus 71 (HEV71), and indeed function as an antiviral immunity in mammals.

HEV71 infection in infants and young children causes hand-foot-and-mouth disease and severe neurological manifestations, and has emerged as one of the major global threats to public health. In this work, Dr. ZHOU Xi and his colleagues identified the nonstructural protein 3A of HEV71 as the viral suppressor of RNAi (VSR) that inhibits vsiRNA biogenesis. When the VSR activity of 3A was

impaired, the VSR-deficient viruses effectively triggered RNAi response in both mammalian cells and mice, producing abundant vsiRNAs. These vsiRNAs are Dicer-dependently produced from viral dsRNA, loaded into RISC, and fully active to degrade cognate viral RNAs.

The VSR-deficient mutants of HEV71 are significantly restricted in human somatic cells and mice, while Dicer deficiency successfully restored HEV71 infection independently of type I interferon (IFN-I) response. Their findings highlight that RNAi can indeed function as an antiviral immunity in mammals. And it uncovers for the first time the detailed mechanism by which a human RNA virus evades antiviral RNAi both in vitro and in vivo.

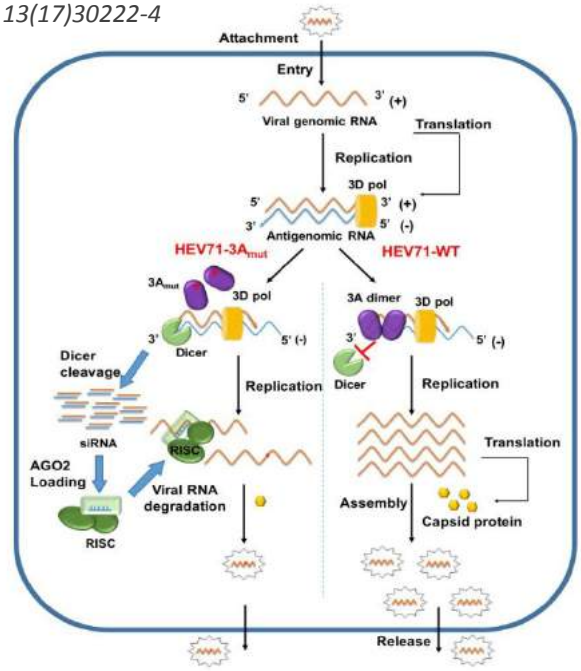
The results have been published on June 20 in Immunity entitled "Human virus-derived small RNAs can confer antiviral immunity in mammals".

"This work defines RNAi as a novel antiviral immune pathway in mammals. Given the evolutionary conservation of RNAi in all eukaryotes, RNAi evolves from the simplest eukaryotic organisms to human beings, and keeps combating against viruses," said Dr. QIU Yang, the first author of the paper.

"Our study is a conceptual advance in antiviral immunity, and should inspire and attract more scientists to this field," said Dr. ZHOU Xi.

This work was supported by the NSFC Excellent Young Scientist Fund, CAS Strategic Priority Research Program, and Newton Advanced Fellowship of the Royal Society. Researchers from Wuhan University and the Institute of Biochemistry and Cell Biology of CAS also participated in this study.

Link: *http://www.cell.com/immunity/fulltext/S1074-7613(17)30222-4*



NSF Delegation paid a visit to WIV

On 20 June 2017, Dr. Nancy S. Sung, the Head of the U.S. National Science Foundation's (NSF) China office, Dr. Samuel Scheiner, the Program Director in the Division of Environmental Biology at the U.S. National Science Foundation where he heads the Ecology & Evolution of Infectious Disease (EEID) program, and Mr. Bo Sun, the Science Program Specialist at the NSF China Office visited Wuhan Institute of Virology and attended the exchanges meeting.

On the meeting, Prof. Yanyi Wang, Deputy Director of WIV, delivered the welcome

address to the NSF Delegation. Dr. Samuel Scheiner briefed the focus, goal, scope and etc. of the Ecology and Evolution of Infectious Diseases program. After the visit and exchange, it is believed that the Sino-U.S. participants shall initiate the collaboration under the program, and it is a shared vision that we will make further endeavor and work closely to boost the cooperative partnership on studies in emerging infectious disease in more depth, so as to make greater contributions to human health and well-being.

The Ecology and Evolution of Infectious Diseases program supports research on the ecological, evolutionary, and socio-ecological principles and processes that influence the transmission dynamics of infectious diseases. The central theme of submitted projects must be quantitative or computational understanding of pathogen transmission dynamics. The intent is discovery of principles of infectious disease transmission and testing mathematical or computational models that elucidate infectious disease systems. Projects should be broad, interdisciplinary efforts that go beyond the scope of typical studies. They should focus on the determinants and interactions of transmission among humans, non-human animals, and/or plants. This includes, for example, the spread of pathogens; the influence of environmental factors such as climate; the population dynamics and genetics of reservoir species or hosts; the cultural, social, behavioral, and economic dimensions of disease transmission.

For more details about the EEID Program: *https://www.nsf.gov/pubs/2016/nsf16592/nsf16592.htm*

CAS President's International Fellowship Initiative (PIFI)

CAS offers a package of international fellowships, collectively called the PIFI program to support highly-qualified international scientists and postgraduate students to work and study at CAS institutions and strengthen their scientific collaboration with CAS researchers. The PIFI program is available for four categories of international researchers and students: distinguished scientists, visiting scientists, postdoctoral researchers and international PhD students.

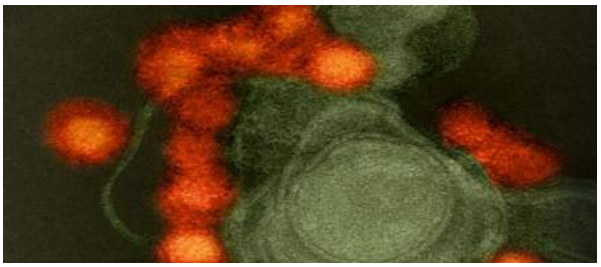
For more details: http://english.cas.cn/cooperation/fellowships/201503/t20150313_145274.shtml

Science Tips

Women's wellness: Learn more about Zika if you're traveling

The Zika infection in pregnant women can cause severe birth defects in their babies. So the U.S. CDC recommends that all pregnant women avoid traveling to areas where there is an outbreak of Zika virus.

"The current recommendation is men should not get a woman pregnant for six months, after the man has traveled to a Zika area, and women should not get pregnant for eight weeks, if they've traveled to a Zika area," says infectious diseases internist Dr. Mary Jo Kasten of the Mayo Clinic Travel Clinic. She suggests using a repellent with deet and says you can also use clothing that's been pretreated with an insecticide called permethrin. She says age is a strong factor. "If I had an adult patient saying 'I'm afraid to go to Brazil, because I might get Zika' but they're a 50-year-old woman, and there's no chance of them getting pregnant, I would say, 'You don't really need to worry.' Your risk of getting something like dengue or other things is much higher than getting sick from some other mosquito-borne illness or other travel-related problem than Zika," says Kasten. "However, if you were a 24-year-old woman interested in getting pregnant in the next six months, then Zika needs to really be on your radar, and you should really reconsider."



Again, the recommendation is if women travel to a Zika-endemic area, they should not get pregnant for eight weeks. If their partner, or any sex partner, has traveled to a Zika-endemic area, it's recommended the woman not get pregnant for six months. As researchers work on a vaccine, Kasten says it appears they're making faster progress with Zika than with other vaccines.

Source: https://medicalxpress.com/news/2017-07-women-wellness-zika-youre.html

Express News

Upcoming event - The 6th European Virus Archive goes global Annual Conference

The 6th European Virus Archive goes global Annual Conference, jointly organized by Wuhan Institute of Virology, Hubei Society for Microbiology, State Key Laboratory of Virology and *Virologica Sinica* will be held on October 16-18, 2017 in Wuhan, China.

Conference Chairs:

- HU Zhihong (Priciple Investigator, WIV, CAS)
- Jean-Louis Romette (Professor, Aix-Marseille Université)

Conference Sessions:

- International standard of virus resources;
- Global cooperation of virus resources;
- Emergency response of emerging viral diseases;
- Research progress and trend of emerging infectious disease.