WIV Newsletter
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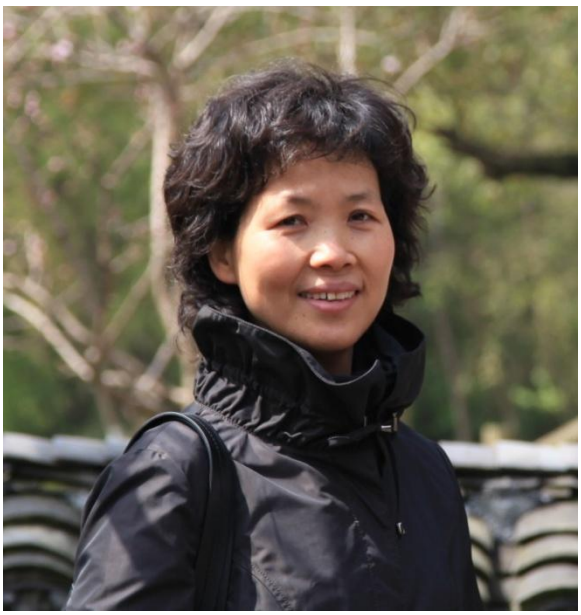
Spotlight

Prof. SHI Zhengli elected a fellow of the American Academy of Microbiology

On Jan 28, the American Academy of Microbiology elected 109 new Fellows in 2019. The “Class of 2019" represents fellows from China, the U.S., France, Ireland, the Netherlands, Israel, Korea, and etc. Prof. SHI Zhengli from Wuhan Institute of Virology (WIV), Chinese Academy of Sciences (CAS) has been elected a Fellow of the American Academy of Microbiology.

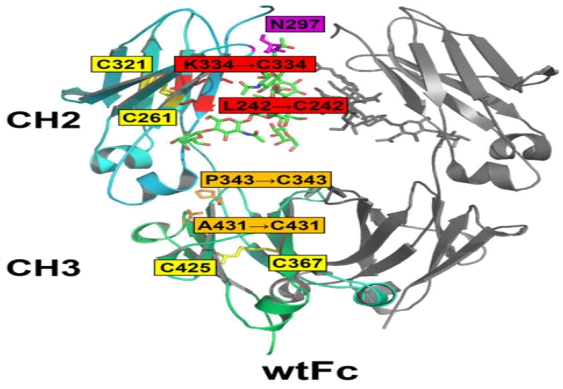
Prof. SHI is the Director of the Center of Emerging Infectious Diseases at WIV, Director of the Key Laboratory of Special Pathogens and Biosafety of CAS, and the Editor-in-Chief of Virologica Sinica. She received her Ph.D from Montpellier University II, France, in 2000.



Her researches focus on molecular epidemiology and interspecies infection mechanism of emerging viruses of zoonotic origin especially those from bats. She has made distinguished and pioneering achievement in discovery and characterization of important bat-borne viruses. She identified the bat origin of Severe Acute Respiratory Syndrome (SARS) and has made crucial contributions to prevention and control of zoonotic emerging infectious disease in China. She had got over 120 publications including research articles on Science, Nature, Cell Host & Microbe, PLoS Pathogens, etc. She won the first prize of Natural Science Award of Hubei Province in 2017 and the second prize of National Natural Science Award in 2018.

Fellows of the American Academy of Microbiology, an honorific leadership group within the American Society for Microbiology (ASM), are elected annually through a highly selective, peer-review process, based on their records of scientific achievement and original contributions that have advanced microbiology. Formed in 1955, the ASM is the largest single life science society. Its mission is to promote and advance the microbial sciences. Now there are over 2,400 Fellows representing all subspecialties of the microbial sciences and involved in basic and applied research, teaching, public health, industry, and government service.

Scientists constructed three human IgG1 Fc mutants for better clinical performance



Fc-based therapeutic proteins include therapeutic antibodies and Fc-fusion proteins. Therapeutic monoclonal antibodies (mAbs) with high affinity and specificity are now widely used in treatment of cancer, immune disorders, viral infection and other diseases. Fc-fusion proteins are also emerging as promising biopharmaceuticals because of the additional benefits from Fc fragment.

Unfortunately, both mAbs and Fc-fusion proteins might be unstable and susceptible to aggregation, which may not meet the requirements for therapy in vivo. Therefore, in the field of the development of recombinant therapeutic proteins, control and prevention of unfolding and aggregation are essential for ensuring efficacy and safety. As the common part of all the full-size mAbs and Fc-fusion proteins, Fc fragment is an attractive target for optimization. In a present study, three Fc mutants with additional disulfide bonds in CH2 domain, CH3 domain and both CH2 and CH3 domains were designed by the research group led by Prof. GONG Rui in Wuhan Institute of Virology of Chinese Academy of Sciences.

A series of experiments were performed for comparison of stability, aggregation resistance and function of these Fc mutants with wildtype Fc. The roles of engineered disulfide bonds in different Fc domains to the stability, aggregation resistance and function have been comprehensively elucidated. The most stable and aggregation-resistant mutants in CH2 and CH3 domains with reservation of Fc-mediated function could be used for modification of Fc-based therapeutics toward better clinical outcomes.

This study gives a comprehensive elucidation of structural and functional effects caused by additional disulfide bonds in the Fc fragment, which is important for Fc engineering toward the desired clinical performance.

The results have been published in the Journal of Biological Chemistry entitled "Comprehensive elucidation of the structural and functional roles of engineered disulfide bonds in antibody Fc fragment".

This work was supported by Key Program of Chinese Academy of Sciences Grant (ZDRW-ZS-2016-4), National Key Research and Development Program of China Grant (2016YFC1202902), National Natural Science Foundation of China Young Scientists Program Grant (81302690), and Novo Nordisk–Chinese Academy of Sciences Research Fund Grant (NNCAS-2014-10).

Link: *http://www.jbc.org/content/293/49/19127.abstract*

Scientists characterized a bat filovirus belonging to a new genus, Dianlovirus

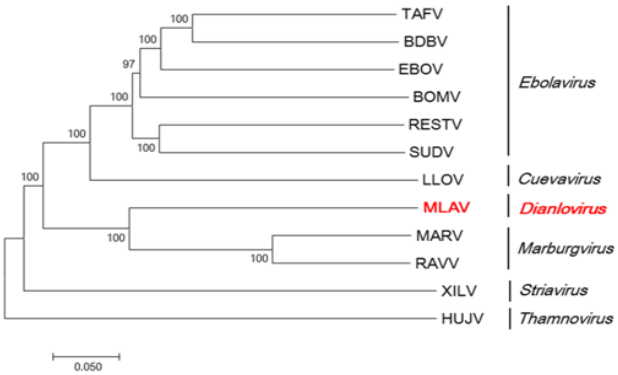
Filoviruses, especially Ebola virus (EBOV) and Marburg virus (MARV), are notoriously pathogenic and capable of causing severe hemorrhagic fever diseases in humans with high lethality. The risk of future outbreaks of filoviruses is drawing increasing concern as other bat-borne filoviruses such as Lloviu virus and Bombali virus were globally discovered with great genetic diversity.

In a recent study published in Nature Microbiology, Prof. SHI Zhengli from Wuhan Institute of Virology of Chinese Academy of Sciences, collaborating with Prof. WANG Linfa from Duke-NUS Medical School, Singapore, reported the discovery of Měnglà virus (MLAV), a new filovirus named after the location where it was found.

Researchers found MLAV in Rousettus bats in Yunnan Province.

According to this study, the coding-complete genome of MLAV shares 32-54% nucleotide sequence identity with known filoviruses. Besides, the low genomic sequence identity, the divergent phylogenic relationship with previously reported filoviruses as well as its unique gene overlapping pattern suggest that MLAV most likely represents a new genus within the Filoviridae family, which is termed Dianlovirus by researchers.

The finding provided evidence that bats harbor a large number of genetically diverse filoviruses across a wide range of locations



globally. Similar to other filoviruses, MLAV uses NPC1 as entry receptor. Using the chimeric minigenome system, the MLAV replication complex is functional and exchangeable with that from EBOV or MARV.

Bats play important roles in ecosystem through pollinating native and agricultural crops, reducing insect pests that damage crops, and consuming mosquitoes and other pests that feed on people and livestock.

"Killing or disturbing bats in their natural habitats could actually increase the risk of transmission of this new virus, and the best way for prevention of bat-borne diseases is to reduce exposure to the bats," Prof. SHI Zhengli said. "The purpose of this study is to discover new virus before it may spillover to humans, but not to incite panic of the public or a fear of bats, which is totally unnecessary."

Researchers from Yunnan Institute of Endemic Diseases Control and Prevention, Dali University, Guangdong Institute of Applied Biological Resources, and Wuhan University also participated in this study.

Link: *https://www.nature.com/articles/s41564-018-0328-y*

Scientists Dissect Dynamic Uncoating of Individual Influenza Viruses in Infected Cells

During virus infection, uncoating is a key step to release the viral genome into host cells, and this step is an attractive antiviral target. However, virus uncoating, especially influenza A virus (IAV), which contains an unusual genome of eight segmented RNAs, has been a poorly understood process due to limitation in applicable methodology for detecting this transient and dynamic event.

In a study, Prof. CUI Zongqiang from Wuhan Institute of Virology of the Chinese Academy of Sciences has reported a novel approach to allow the studying of the dynamic uncoating of individual IAV in live cells.

In this approach, quantum dots (QDs) with the single-particle sensitivity were site-specifically conjugated to the viral ribonucleoprotein complexes (vRNPs) and encapsulated in IAV particles during virus assembly.

By incorporating differently colored QD-vRNP segments or by combining internal QD encapsulation with QD surface decoration into single virions, the researchers also constructed multi-color IAV particles.

Using single-particle tracking, the researchers monitored viral uncoating of individual influenza viruses in real time.

Around 30% of IAV particles fused with late endosomes, a cellular sorting compartment, and shed their coats in the region surrounding the host nucleus within 30-90 minutes of infection.

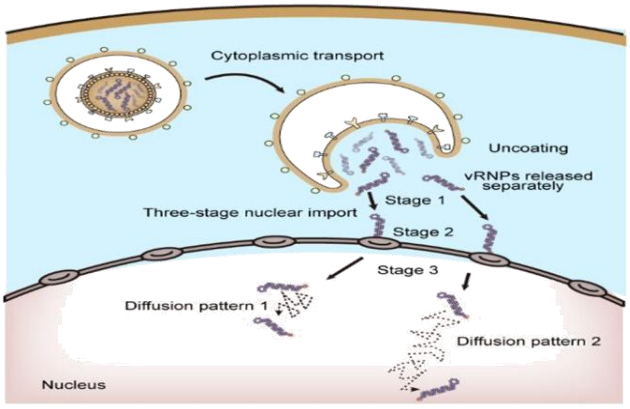
VRNPs from each virion separated into distinct units and entered the nucleus in a three-step process and displayed two diffusion patterns when inside the nucleus.

The scientists have developed a new method for studying of IAV uncoating, and believe that the findings unveil a critical step in IAV infection and may aid the development of therapeutic strategies.

The results have been published in PNAS entitled "Real-time dissection of dynamic uncoating of individual influenza viruses".

This work was supported by the Strategic Priority Research Program of the Chinese Academy of Sciences, the National Key Research and Development Program of China, the National Natural Science Foundation of China, and the Youth Innovation Promotion Association of the Chinese Academy of Sciences.

Link: *https://www.pnas.org/content/116/7/2577*



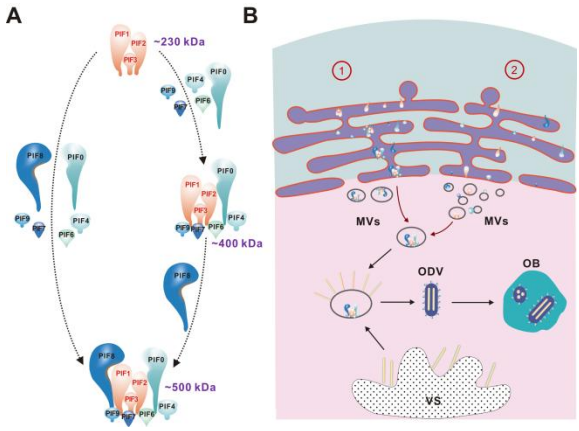
Researchers revealed PIF complex formation and intracellular transport

Baculoviruses are rod-shaped, large dsDNA viruses that infect insects from the families Lepidoptera, Hymenoptera, and Diptera. Entry of baculovirus in host insects is mediated by a per os infectivity factor (PIF) complex on the envelope of occlusion-derived virus.

The mechanism of PIF complex assembly is still largely unknown. Knowledge of the composition and structure of the PIF complex is fundamental to understanding its mode of action.

In a present study, the research group led by Prof. HU Zhihong from Wuhan Institute of Virology of the Chinese Academy of Sciences provided a complete list of proteins (nine) in the PIF complex.

In this study, the researchers systematically investigated the composition assembly and function of the baculovirus PIF complex to understand its role in virus entry. Multiple approaches including blue native (BN) PAGE, liquid chromatography-tandem mass spectrometry, and Western blot analysis were used to obtain a complete list of components of the PIF complex.



Different from previous knowledge in the field, they found that the core-complex was revised to ~230 kDa in size and consisting of PIF1-3 but not PIF4. Their results provided a likely complete list of PIF complex components, revised previous understanding of the core-complex, and shed light on the process of complex assembly and intracellular transport.

The results have been published in Journal of Virology entitled "Baculovirus per os Infectivity Factor Complex: Components and Assembly". “This will be a landmark paper in the baculovirus field,” the peer reviewer said.

This work was supported by the Key Research Program of Frontier Sciences of the Chinese Academy of Sciences, the Strategic Priority Research Program of the Chinese Academy of Sciences, the National Natural Science Foundation of China and the Virology Key Frontier Science Program of the State Key Laboratory of Virology.

Link: *https://jvi.asm.org/content/93/6/e02053-18.long*

Scientists revealed the multistep SFTSV entry process and the dynamic virus–host interactions involved

The Bunyavirales is one of the largest groups of RNA viruses, which encompasses more than 350 members distributed among nine families. Severe fever with thrombocytopenia syndrome virus (SFTSV), an emerging bunyavirus in the genus Phlebovirus, was first identified in China in 2009, with a high case fatality rate of up to 30%.

Although some critical entry steps have been investigated, a comprehensive picture of the bunyavirus entry process remains to be depicted. There is an urgent need for developing effective approaches for unraveling dynamic entry process of bunyaviruses.

In a joint study, the research groups from Huazhong University of Science and Technology and Wuhan Institute of Virology of the Chinese Academy of Sciences dissected the dynamic molecular process of SFTSV entry and penetration via quantum dot (QD)-based single-particle tracking and multicolor imaging.

The researchers showed that SFTSV is internalized into the host cell via the recruitment of clathrin onto the plasma membrane for clathrin-coated pit formation. Then the virus-containing clathrin-coated vesicles deliver SFTSV particles and membranes to Rab5+ EEs, and further to Rab7+ LEs, a common mechanism of cytoplasmic delivery also shared by other bunyaviruses, such as Uukunniemi virus, the Rift Valley fever virus and Crimean-Congo hemorrhagic fever virus (CCHFV).

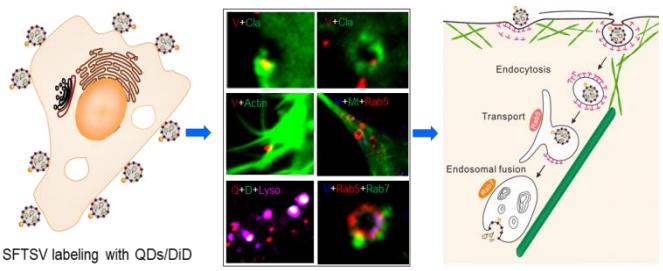
The intracellular trafficking of SFTSV is dependent on the two different kinds of cytoskeleton in sequence: first on actin filaments at the cell periphery, subsequently switching to microtubules toward the cell interior.

It has been demonstrated that cytoskeletons are also involved in hantavirus and CCHFV entry, suggesting that cytoskeleton might be generally involved in bunyavirus transport. For the vast majority of virions, acid-activated penetration was triggered at pH5.6 in LEs.

This study enriches the understanding of the entry mechanisms of bunyaviruses, and provides potential targets for SFTS prevention and control.

The results have been published in small entitled "Single-Particle Tracking Reveals the Sequential Entry Process of the Bunyavirus Severe Fever with Thrombocytopenia Syndrome Virus".

Link: *https://onlinelibrary.wiley.com/doi/full/10.1002/smll.201803788*



SFTSV labeling with QDs/DiD

WIV delegation paid a visit to University of Karachi, Pakistan

On Jan 14-15, invited by Prof. Muhammad Iqbal Choudhary, the Director of International Center for Chemistry and Biological Sciences (ICCBS) in University of Karachi, Pakistan, Prof. GONG Peng, the Deputy Director General and other 5 research fellow from Wuhan Institute of Virology (WIV), Chinese Academy of Sciences (CAS) paid a visit to ICCBS. Prof. Atta-Rahman, the Chairman of the United Nations Committee on Science, Technology and Innovation, President of the Network of Academies of Science of Islamic Countries, Foreign Academician of the Chinese Academy of Sciences (CAS), and the Professor Emeritus of University of Karachi, and Prof. Choudhary met the WIV delegation.

During the visit, the scientists held active discussions on the bilateral cooperation in research on rapid molecular diagnostics of viral infections, drug discovery developments and vaccines, molecular virology, genomics and computational research for virology, infectious diseases surveillance, and prevention and control of emerging viral diseases along the China-Pakistan Economic Corridor under the "Belt and Road" Initiative. It was agreed that WIV and ICCBS will try to build the joint research unit, organize the bilateral annual meeting, and strengthen the personnel training and students' cultivation in the future.

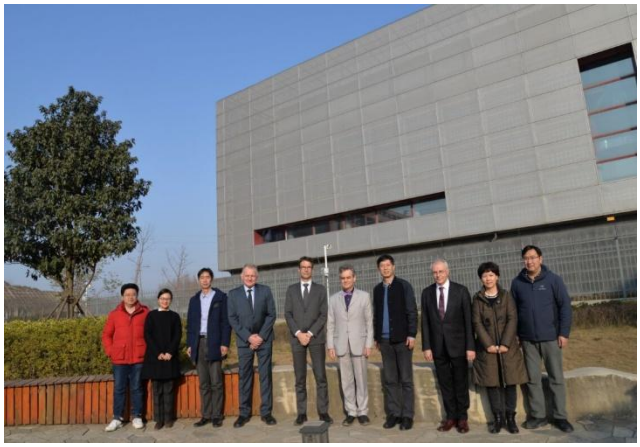
French Delegation visited Wuhan National Biosafety Laboratory, CAS

On Jan 24, Mr. Olivier GUYONVARCH, the Consul General of France in Wuhan, Mr. Pierre LEMOND, the Counselor from the Embassy of France in China, and Mr. Yann MOREAU, the new Science and Technology Attaché from Consulate General of France in Wuhan visited Wuhan National Biosafety Laboratory (Wuhan P4 Laboratory), Chinese Academy of Sciences (CAS). Prof. GONG Peng, the Deputy Director General of Wuhan Institute of Virology (WIV), CAS, accompanied by Prof. YUAN Zhiming, the Director of Wuhan P4 Laboratory, Prof. SHI Zhengli and Prof. SONG Donglin, the Deputy Directors of Wuhan P4 Laboratory, and Mr. Rene COURCOL, the International Technical Expert for the P4 Project met the delegation.

Cooperation

On the symposium, Prof. YUAN Zhiming expressed his heartfelt gratitude to the French side for its long-term support and assistance to the construction of Wuhan P4 laboratory. Mr. Rene Courcol made a phased work report on the construction of the laboratory's quality control system and the comparative study of the procedural documents of the Chinese and French laboratories. The organization of the next meeting of the Sino-French Steering Committee, the sharing of related resources between China and France, and the import of positive pressure protective clothing from P4 laboratories had been deeply exchanged and discussed. The French side indicated that it will actively promote exchanges between the two sides.

Prof. Gong Peng said that Wuhan P4 Laboratory, as one of the important achievements in the cooperation between China and France in the field of prevention and control of emerging infectious diseases, had been widely supported by the Chinese and French governments. This meeting has enhanced mutual understanding and proposed a lot of constructive opinions, which will effectively promote the cooperation between the two sides to achieve substantive progress and results in the future.



Science Tips

DNA tests of Lassa virus mid-outbreak helped Nigeria target its response

Probiotics didn't shorten bouts of stomach flu in kids, two large studies found. Image by SHAROMKA/SHUTTERSTOCK

There's no sorrier sight than a puking preschooler. That's the conclusion I recently reached around 2 a.m. as my poor 4-year-old heaved into the dim abyss. Luckily, her bout with the stomach flu was brief, and she was feeling better by the next day.

Stomach flu, also known as gastroenteritis, is a common affliction caused by bacteria or

Science Tips

viruses that inflame the gut. Though mercifully short, the misery this brings is complete, for both the sufferer and the person charged with scrubbing chunks out of sheets, carpet and a stuffed toy cupcake.

So when presented with something that could potentially cut short the puking, any parent would jump at the chance. That's the promise of probiotics, "good" bacteria (typically in pill form) that some people think might help restore the irritated gut and get kids feeling better faster. But according to two big studies (here and here) of puking kids and probiotics, parents should save their money for something else.

For both studies, scientists studied kids ages 3 months to 4 years who came to an emergency department with acute gastroenteritis. In addition to receiving regular care, these kids took either a probiotic or placebo for five days. Then the researchers tallied up the kids' symptoms to see if those who got the live bugs fared better than those who received a placebo. Long story short, the scientists found absolutely no differences.

The trials used different bacteria as probiotics. One used Lactobacillus rhamnosus, sold as products such as Culturelle, and the other used that bacteria plus Lactobacillus helveticus, a combination sold as Lacidofil. Neither of the formulations cut puking or other symptoms short. The kids had about the same duration of diarrhea (about two days) and missed the same amount of daycare (two days on average).

As far as studies go, these results, both published November 22 in the New England Journal of Medicine, are pretty clear: Probiotics didn't help puking kids feel better faster. Of course, it's possible that certain types of probiotics are good for other things, as an editorial in the same issue of the NEJM points out.

Scientists have been studying whether probiotics can curb colic in babies, with some hints that helpful bacteria may reduce crying in breastfed babies (though the jury is still out). Other bacteria might also help newborns at risk of developing dangerous infections, as a recent study on babies in rural India suggests.

But when it comes to gastroenteritis in kids, probiotics' benefits don't seem to be there. If you're desperate and willing to throw money at the problem, go ahead and buy your poor puking kid some probiotics. There's no evidence they hurt, and it might make you feel like you're doing something. Still, you're probably better off spending your money on juice and popsicles.

Source:
ScienceNews- https://www.sciencenews.org/blog/growth-curve/probiotics-vomiting-kids-stomach-flu