WIVNewsletter
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Bat cave solves mystery of deadly SARS virus — and suggests new outbreak could occur

After a detective hunt across China, researchers chasing the origin of the deadly SARS virus have finally found their smoking gun. In a remote cave in Yunnan province, virologists have identified a single population of horseshoe bats that harbours virus strains with all the genetic building blocks of the one that jumped to humans in 2002, killing almost 800 people around the world.

The killer strain could easily have arisen from such a bat population, the researchers report in PLoS Pathogens on 30 November. They warn that the ingredients are in place for a similar disease to emerge again.

In late 2002, cases of a mystery pneumonia-like illness began occurring in Guangdong province, southeastern China. The disease, dubbed severe acute respiratory syndrome (SARS), triggered a global emergency as it spread around the world in 2003, infecting thousands of people.

Scientists identified the culprit as a strain of coronavirus and found genetically similar viruses in masked palm civets (Paguma larvata) sold in Guangdong's animal markets. Later surveys revealed large numbers of SARS-related coronaviruses circulating in China's horseshoe bats (Rhinolophus) — suggesting that the deadly strain probably originated in the bats, and later passed through civets before reaching humans. But crucial genes — for a protein that allows the virus to latch onto and infect cells — were different in the human and known bat versions of the virus, leaving room for doubt about this hypothesis.

Researchers analysed strains of SARS virus circulating in horseshoe bats, such as this one (Rhinolophus sinicus), in a cave in Yunnan province, China. Credit: Libiao Zhang /Guangdong Institute of Applied Biological Resource

To clinch the case, a team led by Shi Zheng-Li and Cui Jie of the Wuhan Institute of Virology in China sampled thousands of horseshoe bats in locations across the country. "The most challenging work is to locate the caves, which usually are in remote areas," says Cui. After finding a particular cave in Yunnan, southwestern China, in which the strains of coronavirus looked similar to human versions, the researchers spent five years monitoring the bats that lived there, collecting fresh guano and taking anal swabs.

They sequenced the genomes of 15 viral strains from the bats and found that, taken together, the strains contain all the genetic pieces that make up the human version. Although no single bat had the exact strain of SARS coronavirus that is found in humans, the analysis showed that the strains mix often. The human strain could have emerged from such mixing, says Kwok-Yung Yuen, a virologist

at the University of Hong Kong who co-discovered the SARS virus: "The authors should be congratulated for confirming what has been suspected."

But Changchun Tu, a virologist who directs the OIE Reference Laboratory for Rabies in Changchun, China, says the results are only "99%" persuasive. He would like to see scientists demonstrate in the lab that the human SARS strain can jump from bats to another animal, such as a civet. "If this could have been done, the evidence would be perfect," he says.

Another outstanding question is how a virus from bats in Yunnan could travel to animals and humans around 1,000 kilometres away in Guangdong, without causing any suspected cases in Yunnan itself. That "has puzzled me a long time", says Tu.

Cui and Shi are searching for other bat populations that could have produced strains capable of infecting humans. The researchers have now isolated some 300 bat coronavirus sequences, most not yet published, with which they will continue to monitor the virus's evolution.

And they warn that a deadly outbreak could emerge again: the cave where the elements of SARS were found is just 1 kilometre from the nearest village, and genetic mixing among the viral strains is fast. "The risk of spillover into people and emergence of a disease similar to SARS is possible," the authors write in their paper.

Although many markets selling animals in China have already been closed or restricted following outbreaks of SARS and other infectious diseases, Yuen agrees that the latest results suggest the risk is still present. "It reinforces the notion that we should not disturb wildlife habitats and never put wild animals into markets," says Yuen. Respecting nature, he argues, "is the way to stay away from the harm of emerging infections".

Source: Nature (*https://www.nature.com/articles/d41586-017-07766-9?from=timeline&isappinstalled=0)*

Scientists identify IE1 as the first potential HCMV-encoded E3 ubiquitin ligase

Congenital human cytomegalovirus (HCMV) infection is one of the most common causes of neurological disabilities in children. However, the relationship between Hes1 regulation and virus infection, in particular whether and how HCMV regulates Hes1, remained unknown.

In the present study, the research group led by Prof. LUO Minhua from Wuhan Institute of Virology of the Chinese Academy of Sciences report for the first time that HCMV infection downregulates Hes1 protein at the level in human NPCs through IE1 via a newly identified function, which may be a key mechanism that contributes to fetal brain maldevelopment caused by congenital HCMV infection.

The scientists demonstrated that HCMV infection downregulates Hes1 protein levels in infected human NPCs. Importantly, IE1 leads to Hes1 depletion by mediating Hes1 ubiquitination and proteasomal degradation

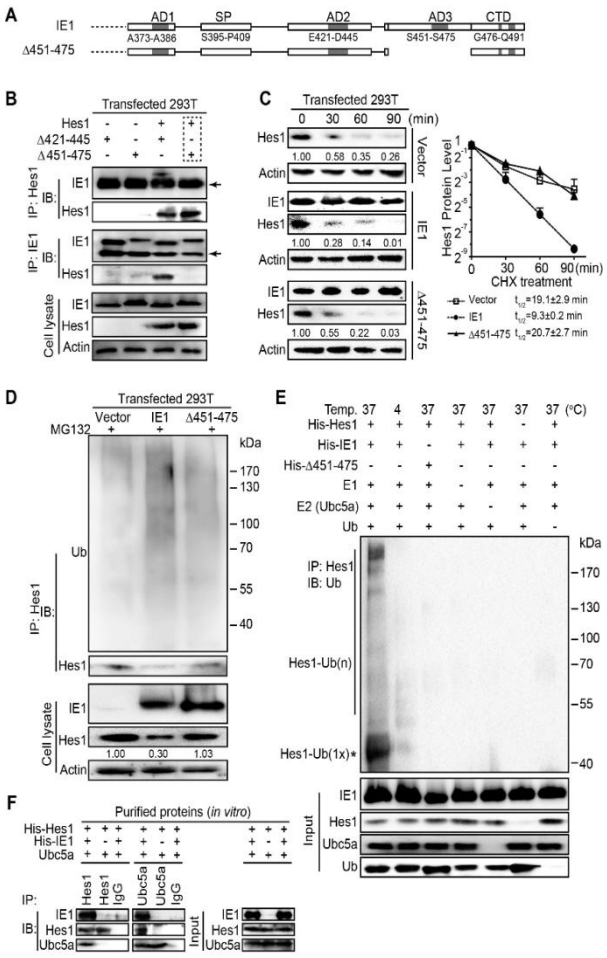
by acting as a potential E3 ubiquitin ligase. IE1 physically interacts with Hes1 via amino acids (AA) 451–475, which are also essential for IE1-mediated Hes1 ubiquitination. In addition, Sp100A, an important component of PML nuclear bodies (PML-NBs), is identified as an additional ubiquitination substrate of IE1 ubiquitination.

This study not only suggests an important mechanism for fetal brain development disorders induced by congenital HCMV infection, but also reveals a novel unanticipated function of HCMV IE1 as a potential E3 ubiquitin ligase.

The results have been published in PloS Pathogens entitled "Human cytomegalovirus IE1 downregulates Hes1 in neural progenitor cells as a potential E3 ubiquitin ligase".

This work was supported by the National Natural Science Foundation of China and the National Basic Research Program of China (973 Program).

Link: *http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006542#abstract1*

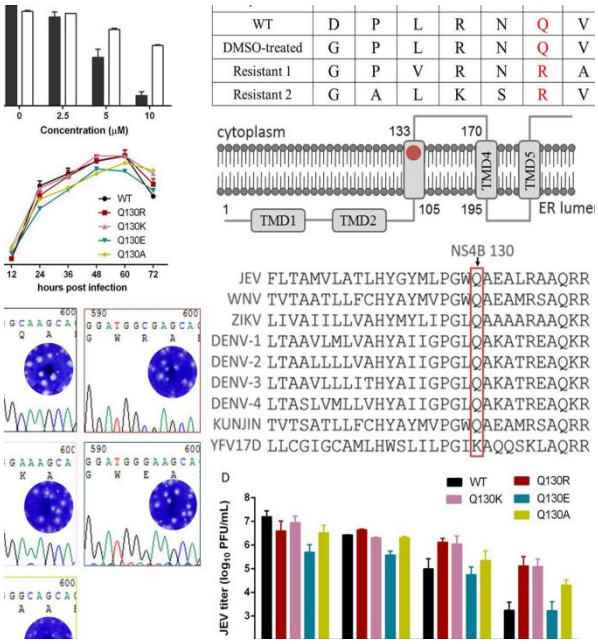


Scientists provide therapeutic possibilities for combating infections caused by flavivirus

Flavivirus pathogens are taxonomically classified in the genus Flavivirus and family Flaviviridae. These viruses comprise over 70 different pathogens such as Japanese encephalitis virus (JEV), Zika virus (ZIKV), dengue virus (DENV), West Nile virus (WNV), and yellow fever virus (YFV). Most flaviviruses are arthropod-borne and cause public health problems worldwidely. However, flavivirus-induced diseases are still pandemic and few therapies beyond intensive supportive care are currently available.

In the present study, the research group led by Prof. XIAO Gengfu from Wuhan Institute of Virology of the Chinese Academy of Sciences screened an FDA-drugs library with 1018 compounds and identified five hit drugs, especially calcium inhibitors, exerting ant 41 i-flavivirus activity that blocked viral replication. The in vivo efficacy and toxicity of manidipine were investigated with a JEV-infected mouse model and the viral target was identified by generating adaptive mutant.

Five hit drugs were identified that inhibited JEV infection with a selective index > 10. Antiviral activities of these five hit drugs against other flavivirus, including Zika virus, were also validated. As three of the five hit drugs were calcium inhibitors, additional types of calcium inhibitors were utilized that confirmed calcium was essential for JEV infection, most likely during viral replication. Adaptive mutant analysis uncovered that



WT	D	P	L	R	N	Q	V
DMSO-treated	G	P	L	R	N	Q	V
Resistant 1	G	P	V	R	N	R	A
Resistant 2	G	A	L	K	S	R	V

replacement of Q130, located in transmembrane domain 3 of the non-structural NS4B protein while relatively conserved in flavivirus, with R or K conferred JEV resistance to manidipine, a voltage-gated Ca2+ 30 channel (VGCC) inhibitor, without apparent loss of the viral growth profile.

Furthermore, manidipine was indicated to protect mice against JEV-induced lethality by decreasing viral load in brain, while abrogating histopathological changes associated with JEV infectionThe study provided novel insights into the molecular mechanisms underlying flavivirus infection, and offer new and promising therapeutic possibilities for combating infections caused by flavivirus.

The results have been published in Journal of Virology entitled "Screening of FDA-1 Approved Drugs for Inhibitors against Japanese Encephalitis Virus Infection".

This work was supported by the National Natural Sciences Foundation of China.

Link: *http://jvi.asm.org/content/early/2017/08/10/JVI.01055-17.abstract?sid%20=61e6a00f-55bb-49ad-ab65-1b7ba0cc4b3b*

Important features of protease-helicase coordination in pestivirus NS3 was revealed

Many RNA viruses encode helicases to aid their RNA genome replication and transcription by unwinding structured RNA. Being naturally fused to a protease participating in viral polyprotein processing, the NS3 helicases encoded by the Flaviviridae family viruses are quite unique. Therefore, how these two enzyme modules coordinate in a single polypeptide is of particular interest.

Under a present study in cooperation with Prof. PAN Zishu from Wuhan University, the research group led by Prof. GONG Peng from Wuhan Institute of Virology of the Chinese Academy of Sciences report a previously unidentified conformation of pestivirus NS3 in complex with its NS4A protease cofactor segment (PCS). This conformational state is related to the protease cis-cleavage event and is optimal for the function of helicase.

In this study, the scientists have crystallized the full-length CSFV NS3 with its NS4A PCS covalently tethered to its

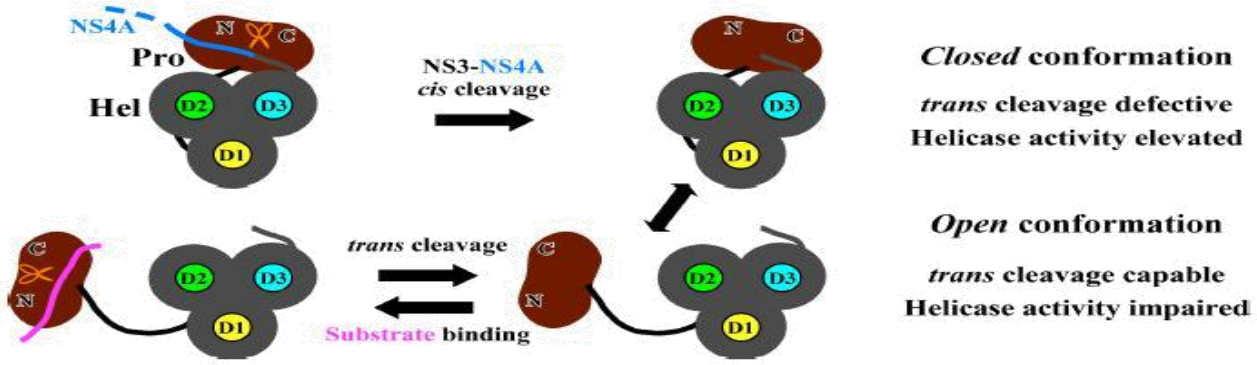
N-terminus through a flexible linker and solved its crystal structure at 2.35 Å resolution. The structure provides structural insights into pestivirus NS3-NS4A cis-cleavage and protease substrate recognition, allowing them to find evolutionary linkages between pestivirus NS3 protease and its hepacivirus and flavivirus counterparts. More importantly, the structure reveals a previously unidentified intra-molecular interface between the protease and helicase modules that may play key roles for the function of both enzymes. In vitro helicase assays and virological data further validated the functional importance of this interface and its relevance to the RNA unwinding function of the helicase.

The structural and functional analyses in this work pave a way to the further understanding of how this natural protease-helicase fusion protein works in harmony and how its different conformational states may play distinct roles to achieve versatile functions.

The results have been published in Journal of Virology entitled "The uncoupling of protease trans-cleavage and helicase activities in the pestivirus NS3".

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

Link: *http://jvi.asm.org/content/early/2017/08/17/JVI.01094-17.full.pdf+html*



A Study Showed that HRTV NSs functions as a robust antagonist of host innate immunity

Heartland virus (HRTV) is a novel phlebovirus (Phlebovirus genus, Phenuiviridae family, Bunyavirales order) associated with a severe febrile illness in humans. The original cases of HRTV infections were reported in two Missouri farmers hospitalized with fever, leukopenia, and thrombocytopenia in 2009. HRTV is genetically related to the severe fever with thrombocytopenia syndrome virus (SFTSV), also a highly pathogenic phlebovirus emerging in China and neighboring countries. The emergences of SFTSV, HRTV, and their recently discovered relatives, collectively termed the SFTSV/HRTV-group viruses, have raised new concerns to the public health worldwide. However, there is currently no vaccine or drug available against these emerging viruses. Furthermore, whether and how HRTV can interfere with the host innate immune response is unknown.

In a present study, the research group led by Prof. WANG Hualin from Wuhan Institute of

Virology of the Chinese Academy of Sciences showed that HRTV NSs (HNSs) also functions as a robust antagonist of host innate immunity, thus promoting viral replication. Although its expression appears not to induce noticeable IB formation in multiple cell lines they tested, HNSs can inhibit RLR-mediated antiviral signaling and virus-infection-triggered IFN and inflammatory cytokine expression.

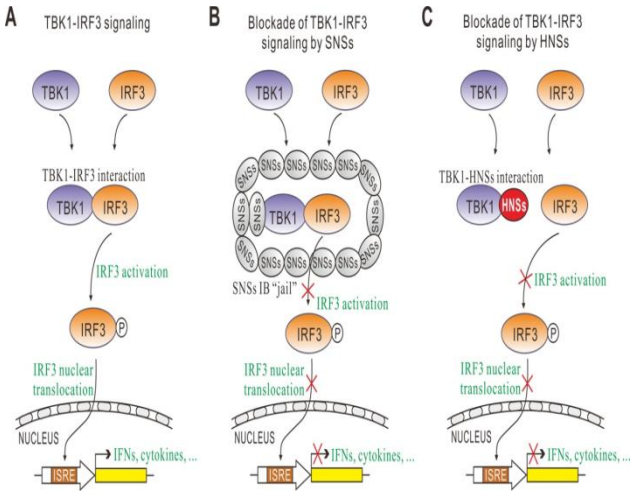
Mechanistically, the scientists found that HNSs disrupts the IFN-stimulated response element (ISRE) activation by interfering with IRF3 phosphorylation and nuclear accumulation; furthermore, HNSs interacts with TBK1 and likely hinders TBK1-IRF3 association, thus disabling IRF3 activation and IFN and cytokine induction.

In summary, this study identified HRTV NSs as a robust antagonist of the host innate immunity. HNSs strongly interacts with the host kinase TBK1 and suppresses the transcription factor IRF3 activation by obstructing the TBK1-IRF3 interaction and signaling, resulting in the blockade of IFN and inflammatory cytokine induction. These findings will benefit the better understanding of viral pathogenesis and the development of antiviral therapeutics.

The results have been published in Journal of Biological Chemistry entitled "Heartland virus NSs protein disrupts host defenses by blocking the TBK1 kinase–IRF3 transcription factor interaction and signaling required for interferon induction".

This work was supported by the National Natural Science Foundation of China, the strategic priority research program of the Chinese Academy of Sciences, the National Basic Research Program (973 Program) of China, the Science and Technology Basic Work Program, the National Key Research and Development Program of China, European Union's Horizon 2020 project European Virus Archive goes global (EVAg), the Hubei Provincial Natural Science Foundation of China, and the "One-Three-Five" Research Program of Wuhan Institute of Virology.

Link: *http://europepmc.org/abstract/MED/28848048*



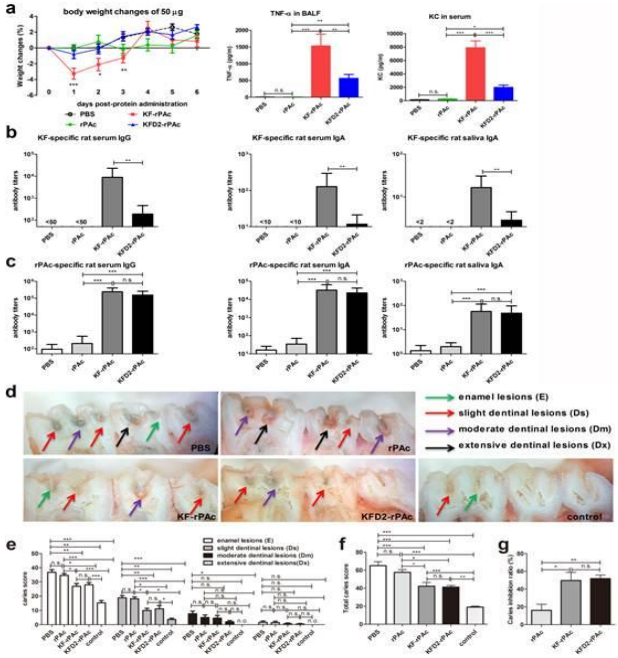
Scientists produced a second-generation flagellin-rPAc fusion protein, KFD2-rPAc

Dental caries, one of the most common global chronic diseases distributed unevenly among populations, is still a major oral health problem in most industrialized countries. It affects 60–90% of school-age children and the vast majority of adults, thus an anti-caries vaccine has long been attractive for broad-based dental health in caries prevention, and in the treatment of large infected populations. Dental lesions of caries usually result from the localized dissolution and destruction of teeth caused primarily by Streptococcus mutans (S. mutans) infections.

Research Progress

In a present study, the research group led by Prof. YAN Huimin from Wuhan Institute of Virology of the Chinese Academy of Sciences characterized the second-generation flagellin-rPAc fusion protein, a vaccine candidate designed to avoid an undesired flagellin-specific antibody response and inflammatory side effects while inducing efficacious antibodies against PAc and providing high protective efficacy against dental caries.

To reduce the immunogenicity of flagellin, the scientists constructed a second-generation flagellin-rPAc fusion protein, KFD2-rPAc, in which rPAc replaced D2/D3, the main antigenicity domains of KF. Results in this study demonstrated that the immunogenicity of flagellin itself is substantially reduced in KFD2-rPAc. KFD2-rPAc induced over 10-fold less flagellin-specific antibody responses in mice and rats. The significantly lowered immunogenicity of flagellin partly makes KFD2-rPAc more feasible for multiple administrations without interference by pre-existed antibodies.



In conclusion, KFD2-rPAc, the second-generation flagellin-rPAc fusion protein, induced low potential systemic inflammatory responses and low flagellin-specific antibody responses, but high immune protection against caries. These advantages make KFD2-rPAc a promising anti-caries vaccine candidate.

The results have been published in Scientific Reports entitled "Second-generation Flagellin-rPAc Fusion Protein, KFD2-rPAc, Shows High Protective Efficacy against Dental Caries with Low Potential Side Effects".

This work was supported by grants from the National Natural Science Foundation of China, the “One-Three-Five” Strategic Planning Program of Wuhan Institute of Virology of Chinese Academy of Sciences, and grants from Deutsche Forschungsgemeinschaft.

Link: *https://www.nature.com/articles/s41598-017-10247-8#Ack1*

Chinese Researchers Reveal the Function of Prion Protein in Tumorigenesis

Prion protein (PrP) is a glycosylphosphatidylinositol anchored protein widely expressed in central nervous system, lymphoreticular system and GI tract. It has been attributed to neurodegenerative diseases such as prion disease and alzheimers disease. However, normal functions of PrP remains in-completely understood.

Recently, more and more papers reported that PrP is up-regulated in many types of cancers and contributes to tumorigenesis. In the cases of pancreatic ductal adenocarcinoma,

breast cancer, and gastric cancer, expression of PrP is the biomarker for poor prognosis of the patients.

New research carried out by scientists at the Center for Molecular Virology, Wuhan Institute of Virology of the Chinese Academy of Sciences, investigated the role of PrP in melanoma and pancreatic cancer tumorigenesis.

Their study was published online on September 12th in Journal of Biological Chemistry entitled "Prion protein is required for tumor necrosis factor α (TNFα)-triggered nuclear factor κB (NF-κB) signaling and cytokine production".

"Working with M2 melanoma cell line and BxPC-3 pancreatic ductal adenocarcinoma cell line, we successfully deleted PRNP gene using Crispr/Cas9 technique. Treatment of PrP expressing and PrP null M2 cells with TNFα revealed that only M2 cells expressing PrP showed TNF receptor (TNFR) response, resulting in NFκb signaling. To prove that there is functional interplay between PrP and TNFR, we also down regulated PrP expression with siRNA or we rescued the PrP expression in PrP null M2 cells by transducing PrP expression, we found indeed that PrP is required for the activation of NFκb signaling", said WU Guiru, the first author of the paper.

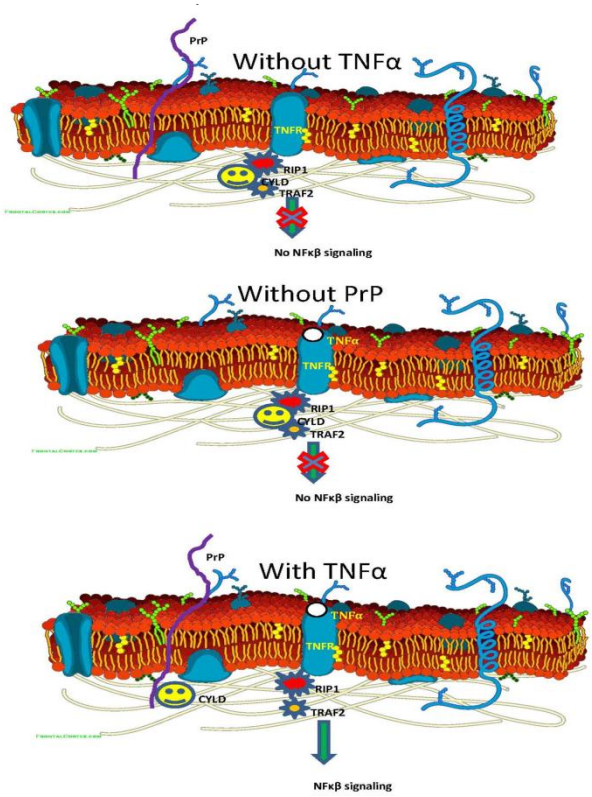
"To identify the mechanism of PrP regulating NFκb signaling, we performed co-immunoprecipitation of PrP with monoclonal antibody specific for PrP. We found that CYLD, a de-ubiquitinase that co-purified with PrP. In addition, treatment with TNFα enhanced the co-location and co-purification of PrP and CYLD, suggesting that PrP by pulling CYLD away from TNFR complex stimulated NFκb signaling. Indeed, we found that interaction between CYLD and RIP1 or interaction between CYLD and Traf2 were reduced only when PrP was present and only when the cells were treated with TNFα. Accordingly, we found that TNFα treatment resulted in significantly reduce poly-ubiquitinated RIP1 or Traf2 in the absence of PrP compared to when PrP is present", Ms. WU added.

"Based on our results, we propose a model to explain how PrP responds to TNFα to enhance tumorigenesis", said Dr. LI Chaoyang, a principal investigator and the corresponding author of the paper.

"Our work is of great interest not only to the specific field of prion biology, but also to the broader readership interested in cancer biology", he added.

The study was supported by grants from the National Natural Science Foundation of China, by Strategic Priority Research Program A of the Chinese Academy of Sciences, and by Ministry of Science and Technology of China.

Link: *http://www.jbc.org/content/early/2017/09/13/jb*



Scientists found that three conserved regions play important roles in the enzymatic activity and function of P33

Sulfhydryl oxidase catalyzes disulfide bond formation of substrate proteins. P33, a baculovirus-encoded sulfhydryl oxidase, is different from other cellular and viral sulfhydryl oxidases, bearing unique features in tertiary and quaternary structure organizations.

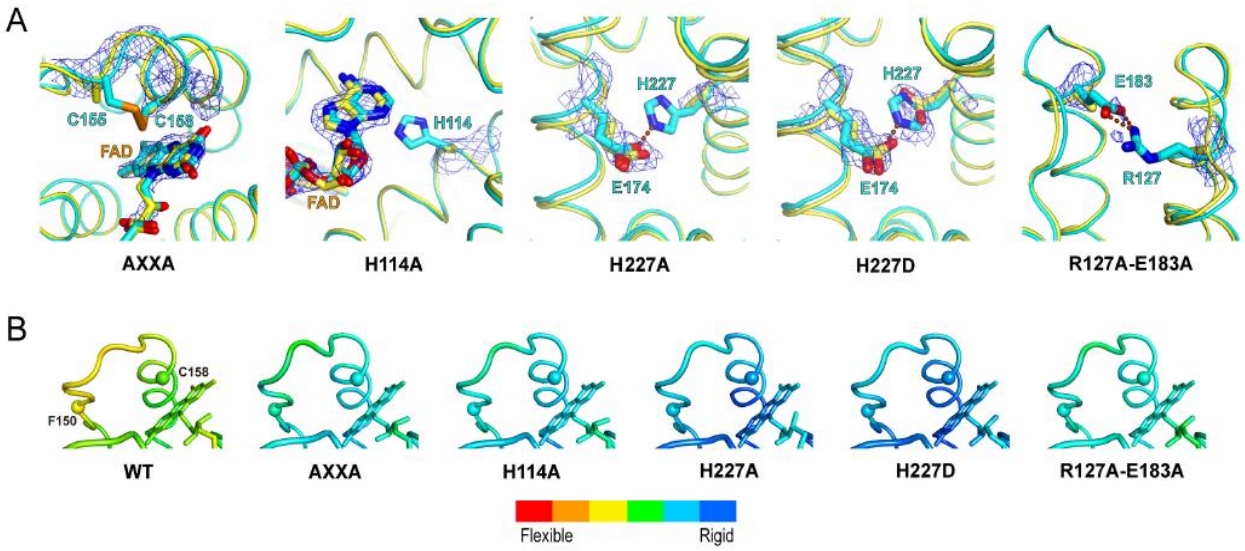
To better understand the structural and functional relationship of P33, a series of point mutations in three conserved regions were generated and their biological functions were studied by the research group led by Prof. HU Zhihong and the research group led by Prof. GONG Peng from Wuhan Institute of Virology of the Chinese Academy of Sciences. The sulfhydryl oxidase activities of these mutants were biochemically tested in vitro. Correspondingly, recombinant viruses were constructed to study the biological function of the mutants in vivo. Crystal structures of wild-type (wt) and representative P33 mutants were also resolved to aid the analyses of the functional data.

Their results showed that the three conserved regions, i.e. the active site, dimer interface and the R127-E183 salt bridge, are key regions of P33 and play significant roles in virus morphogenesis and oral infectivity.

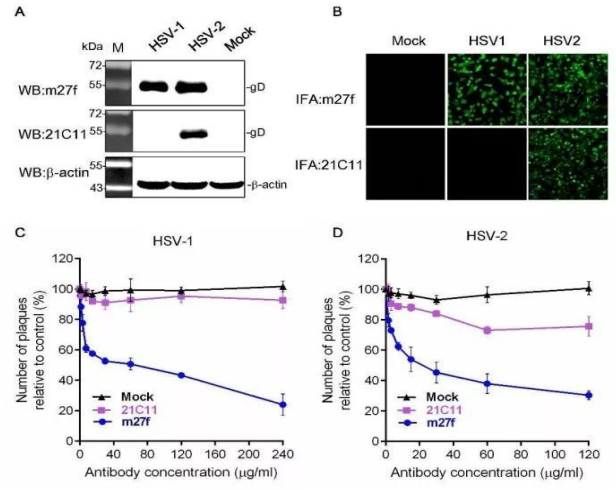
The results have been published in Journal of Virology entitled "Three conserved regions in baculovirus sulfhydryl oxidase, P33, are critical for enzymatic activity and function ".

This research was supported by the grants from the National Natural Science Foundation of China, the Strategic Priority Research Program of the Chinese Academy of Sciences, the National Key Basic Research Program of China, the Keyresearch projects of frontier science, Chinese academy of sciences, the National Key R&D Program of China and the Virology Key Frontier Science Program of State Key Laboratory of Virology.

Link: *http://jvi.asm.org/content/early/2017/09/08/JVI.01158-17.full.pdf+html*



A novel neutralizing mAb m27f whose epitope located in the pro-fusion domain of gD was generated



Herpes simplex virus (HSV) is a prevalent worldwide human pathogen that infects epithelial cells before it establishes latency in trigeminal or sacral nerve root ganglia, causing mucocutaneous lesions, keratitis, and encephalitis. The development of vaccines and novel therapeutic strategies against HSV has become very urgent.

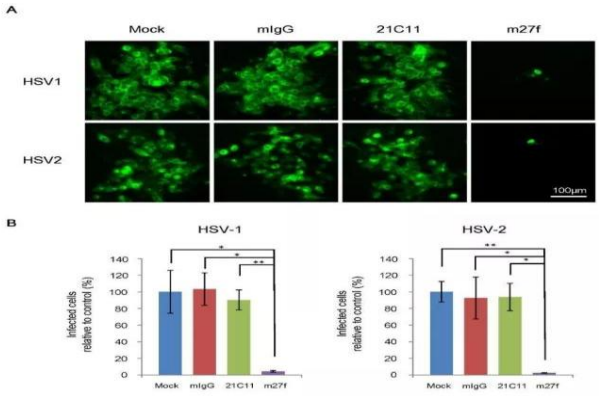
Glycoprotein D (gD) is the most abundant glycoprotein on the virion and the major stimulus for virus-neutralizing antibodies of HSV. For both vaccine design and novel therapeutic strategies, it is important to study epitopes on gD that stimulate virus-neutralizing antibodies.

In a present study led by Prof. WANG Hualin in Wuhan Institute of Virology of Chinese Academy of Sciences, the scientists found a novel monoclonal antibody (mAb), m27f, targeting to glycoprotein D (gD) of HSV-2, which also has cross-reactivity against HSV-1 gD. M27f was found to recognize a new continuous epitope (residues 292 to 297) within the pro-fusion domain of HSV and possesses a high level of virus-neutralizing activity. It showed a high degree of neutralizing activity against both HSV-1 and HSV-2, completely abrogated viral cell-to-cell spread, and inhibited syncytium formation in vitro. In addition, it also exhibited highly therapeutic effects in a HSV-2 infected mouse model, implying its high potential for adaptation as protective or therapeutic interventions.

In conclusion, their results have demonstrated for the first time that mAb m27f targeting a new continuous epitope (residues 292 to 297) within the pro-fusion domain has a high level of virus-neutralizing activity. These finding will enrich the HSV glycoprotein D-specific neutralizing antibodies and will facilitate the development of vaccine design or novel therapeutic strategies.

The results have been published in Antiviral Research entitled "A novel glycoproteinD-specific monoclonal antibody neutralizes herpes simplex virus". This work was supported by the National Science Foundation of China; the National Key Research and Development Program from the Ministry of Science and Technology of China; and the European Union's Horizon 2020 EVAg project.

Link: *https://link.springer.com/article/10.1007%2Fs13238-017-0471-x*



Scientists provide direct evidence of the Emuc pathogenicity in vivo for the first time

Ebola virus (EBOV) is one of the most virulent pathogens to humans. Recently, the largest-ever outbreak of Ebola virus disease (EVD) in West Africa, 2013–2016, resulted in the unprecedented damage to human health and social economy. However, there is currently no licensed vaccine or antiviral available against EVD. Clinically, EBOV infection can result in exaggerated inflammatory responses and multiorgan damage, although the pathogenesis (including the inflammatory pathogenesis) and the viral virulence factor(s) involved in the excessive inflammation induction and viral pathogenicity are largely unclear.

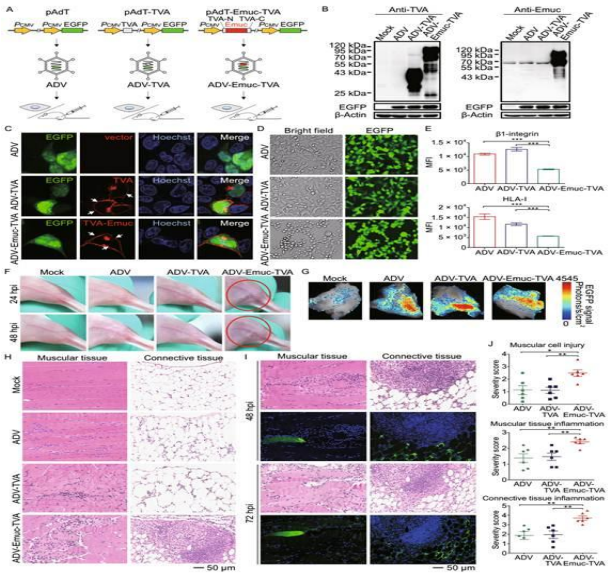
To investigate the potential pathogenic effects of Emuc both in vitro and in vivo, the research group led by Prof. WANG Hualin from Wuhan Institute of Virology of the Chinese Academy of Sciences designed an experiment of adenovirus-mediated gene delivery to cultured cells and mice. The data confirm the effects of Emuc observed in transient transfection assays and suggest that the viral vector efficiently mediated gene expression and functioning by transduction to the cultured cells. Furthermore, the scientists conducted gene delivery of the adenoviral vectors to BALB/c mice for further exploring the effects of Emuc in vivo and observed that Emuc expression specifically caused disease, though temporarily, in the context of local transduction by the replication-deficient adenovirus.

In summary, their study demonstrated that Emuc can not only induce morphological change of adherent cells in vitro but also distinct cell and tissue damage and acute inflammation in mouse muscles, revealing and characterizing the Emuc pathogenicity both in vitro and in vivo. These findings provide direct evidence of the Emuc pathogenicity in vivo for the first time and also critical clues on EBOV pathogenesis and particularly the inflammatory pathogenesis.

The results have been published in Protein & Cell entitled "Ebola virus mucin-like glycoprotein (Emuc) induces remarkable acute inflammation and tissue injury: evidence for Emuc pathogenicity in vivo".

This work was supported by the National Natural Science Foundation of China, the National Basic Research Program (973 Program), the Science and Technology Basic Work Program, the National Key Research and Development Program of China, the strategic priority research program of the Chinese Academy of Sciences and the Hubei Provincial Natural Science Foundation of China.

Link: *https://www.sciencedirect.com/science/article/pii/S0166354217304710*



2017 International Workshop on Biosafety Laboratory Management and Experimental Techniques was held successfully

From October 18 to 28, "2017 International Workshop on Biosafety Laboratory Management and Experimental Techniques" was held in Wuhan, Hubei by Wuhan Institute of Virology, Chinese Academy of Sciences. More than 20 trainees from China, Pakistan, Kazakhstan, Thailand, Sri Lanka, Egypt, Kenya, Serbia, Hungary and other countries attended the workshop.

At the opening ceremony, Mr. Zhang Shizhuan, the Director of Division of Asian and African Affairs in Bureau of International Cooperation, Chinese Academy of Sciences, extended a warm welcome to all the guests participating in the workshop. He pointed out that timely and effective response to the outbreaks of newly-emergent pandemics and safeguarding the laboratory biosafety are the common goals and responsibilities of all governments and scientists along the "Belt and Road". Chinese Academy of Sciences will promote biosecurity cooperation among countries in this region under the "Belt and Road Initiative". It is hoped that this workshop can train key technical personnel in the prevention and control of emerging infectious diseases in relevant countries and contribute to the cause of human health.

The training courses specially invited senior experts from Wuhan Institute of Virology and Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences to introduce six theoretical courses including biosafety laboratory, laboratory biosafety management system, biorisk assessment, basic etiology of contagious pathogens, protection classes and key facilities of biosafety laboratory, preservation, transportation and management of bacterial and viral strains as well as two practical contents on biosafety operation norms and animal experiments.

This workshop relies on the Wuhan National Biosafety (Level 4) Laboratory of Chinese Academy of Sciences and has a basis of cooperation around the Sino-Africa Joint Research Center of CAS, the Southeast Asian, Biodiversity Research Institute of CAS and the Pasteur Network.

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 "Belt and Road", especially from the developing countries. The trainees learned 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, and know basic design principles of biosafety laboratories. These experiences not only help to expand their research knowledge in the field of biosafety, but also lay the foundation for further expansion of cooperation channels and establishment of cooperative relations.

WIV organized the 6th European Virus Archive goes global Annual Conference

Recently, "the 6th European Virus Archive goes global Annual Conference" was held in Wuhan, Hubei. As the conference chairs, Professor Hu Zhihong from Wuhan Institute of Virology, Chinese Academy of Sciences, and Professor Jean-Louis ROMETTE, the General Coordinator of Horizon 2020-EVAg Project of the European Union, invited more than 30 international experts from 15 countries including China, France, Britain and Germany to attend the conference.

Professor Wang Yanyi, the Deputy Director General of Wuhan institute of Virology, Mr. Olivier GUYONVARCH, the Consul-General of France in Beijing, Mr. Mark WATCHORN, the Deputy Consul-General of Britain in China, and Mr. Gong Xiucheng from Wuhan Association for Science and Technology delivered speeches.

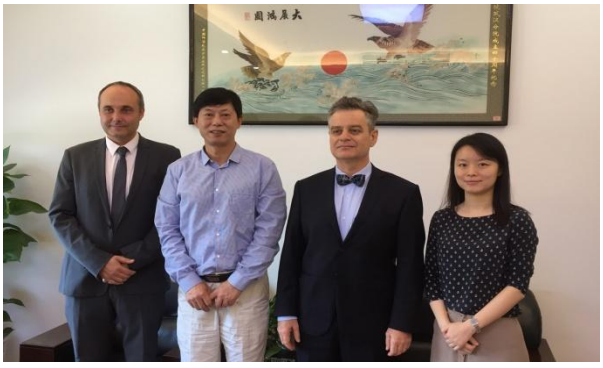
At the meeting, the experts discussed the research hot spots in the field of virology, demonstrated the latest scientific and technological achievements in the field of preservation of virus resources. The conference promoted the establishment of international standards for virus resources, and enhanced the cooperation in international exchanges of resources and construction of global emergency response capabilities. After the meeting, under the guidance of Professor Yuan Zhiming, the Director General of Wuhan Branch of Chinese Academy of Sciences and the Director of Wuhan National Biosafety Laboratory, all participants visited the Laboratory, and conducted a positive communication and constructive discussion on the introduction of high-pathogenic virus resources and personnel training.

The new Consul General of France in Wuhan paid a visit to WIV

On the morning of September 12, Mr. Olivier GUYONVARCH, the new Consul General of France in Wuhan, visited Wuhan Institute of Virology, Chinese Academy of Sciences to discuss about the cooperation in prevention and control of emerging infectious diseases between China and France. Prof. Wang Yanyi, the Deputy Director General of Wuhan institute of Virology, met with Mr. GUYONVARCH, accompanied by Prof. Yuan Zhiming, the Director of Wuhan P4 Laboratory.

During the discussion, Prof. Yuan Zhiming introduced the achievements and progress made by China and France in building Wuhan P4 laboratory in terms of laws, regulations and standards for biosafety, prevention and control of emerging infectious diseases, and

Cooperation



personnel training. He hoped that in the future, with the support of the French Ministry of Foreign Affairs, Ministry of Science and Technology and other departments, Wuhan P4 Laboratory can further strengthen the scientific cooperation with Lyon P4 Laboratory to establish a good partnership, apply for relevant scientific research projects together and strive to achieve more in the field of academic research.

Mr. GUYONVARCH fully affirmed the positive contribution made by China in the Sino-French cooperation. He said the French government pays close attention to the future cooperation between the two sides on high-level biosafety laboratories and newly-launched scientific cooperation plan in the prevention and control of emerging infectious diseases. The French government will pool its efforts with all parties to give maximum support to the cooperation between the two sides and hopes that scientists from China and France will make joint efforts to promote scientific research and contribute to the cause of public health in the world.

Science Tips

Human study supports theory on why dengue can be worse the next time around

Et tu, antibody? In humans, dengue can be more severe the second time around. Now, a study implicates an immune system treachery as the culprit.

The study suggests that the amount of anti-dengue antibodies a person has matters. In a 12-year study of Nicaraguan children, low levels of dengue antibodies left over in the blood from a prior infection increased the risk of getting a life-threatening form of the disease the next time around, researchers report online November 2 in Science.

Four related viruses cause dengue. The theory that antibodies protective against one type of dengue can collude with a different type of the virus to make a second infection worse was proposed in the 1960s. Such antibody-dependent enhancement has been shown in cells and lab animals. But “there’s been this controversy for five decades about, does this antibody-dependent enhancement really happen in dengue” in humans, says coauthor Eva Harris, a viral immunologist at the University of California, Berkeley’s School of Public Health. “And this says, yes, it does.”

About 2.5 billion people live where there is a risk of dengue infection. The virus infects 50 million to 100 million people every year, the World Health Organization estimates, but many cases go unreported. Infection with the mosquito-transmitted virus often leads to no symptoms, but can cause fever, joint and muscle pain and other flulike symptoms. The most severe form, which affects about half a million people annually, can include internal bleeding, respiratory distress or organ failure, and may be fatal.

Getting sick with one of the four virus

Science Tips

types can protect against a future infection of the same type. But in some cases, the theory goes, leftover antibodies from the first illness can actually help the second infection invade cells, increasing the risk of severe dengue disease.

"This study provides support for this idea that antibodies under certain conditions can be bad and actually cause severe disease when people are infected with dengue," says viral immunologist Sujan Shresta of the La Jolla Institute for Allergy and Immunology in California. The next step, she says, is to learn more about the antibodies involved and see whether the findings hold up in other populations.

From 2004 to 2016, Harris and her colleagues studied more than 6,500 children aged 2 to 14 in Managua, Nicaragua. The researchers took blood samples each year, at a time when the kids were healthy, and assessed their antibody levels. The scientists also monitored which kids developed dengue and how severe the disease was.

An analysis showed that kids with a specific low range of anti-dengue antibodies had around a 7½ times higher risk of developing the most severe form of the disease than those who had either no antibodies or a high amount. The team's test couldn't tell what kind of dengue antibodies each child had. Harris and colleagues are now working on characterizing the antibodies measured in their test, to learn what makes them protective or harmful.

The new study supports the theory of antibody-dependent enhancement in humans, says Anna Durbin, an infectious diseases physician at Johns Hopkins Bloomberg School of Public Health. But she also argues that the risk of developing severe disease depends on the quality of the antibody — that is, how potent it is — as much as, or more than, the quantity. "A number in and of itself doesn't tell you a whole lot."

Source: ScienceNews (https://www.sciencenews.org/article/human-study-supports-theory-why-dengue-can-be-worse-next-time-around)

Express News

Prof. Shi Peiyong was selected as a member of the Overseas Expert Board of Chinese Academy of Sciences

Recently, the Bureau of Personnel of Chinese Academy of Sciences announced the member list of the 2017 Overseas Expert Board. The selected candidate from University of Texas Medical School, Prof. Shi Peiyong, recommended by Wuhan Institute of Virology, Chinese Academy of Sciences, was on the list. The "Overseas Expert Board" is an important part of personnel introduction engineering in the Chinese Academy of Sciences. The project annually subsidizes about 40 outstanding scholars engaged in scientific research and teaching in well-known overseas universities, research institutes or high-tech enterprises to carry out scientific research cooperation, scientific advice and appraisal work to CAS affiliated institutes.