WIV Newsletter
No.14 JAN 2017

Spotlight

WIV's application for Intergovernmental Project of National Key R & D Program has been approved

Recently, the application of the Intergovernmental Project of National Key Research and Development Program ("European Virus Archive goes global") submitted by Prof. Zhihong Hu in Wuhan Institute of Virology (WIV), Chinese Academy of Sciences (CAS) has been approved by the Ministry of Science and Technology (MOST). The project funding is 368.82 millions.

On April 1, 2015, WIV has officially joined the European Virus Archive goes global (EVAg) project, a part of the European Horizon 2020 Research Project, after signing the consortium agreement.

In 2009, the European Virus Archive (EVA) project started. It is a project funded by the European Union Seventh Framework Programme (FP7). The overall objective was to create and mobilize a European network of high calibre centres with the appropriate expertise, to collect, amplify, characterize, standardize, authenticate, distribute and track, mammalian and other exotic viruses. The EVA project was very successful that the EVA web-based catalogue contains 1364 well-characterized viruses and about 2000 products to the scientific community. The current project EVAg (2015-2019) is aimed at the largest global virus collection network. Now it includes an international group of 23 laboratories including 16 EU member state institutions and 7 non-EU institutions. EVAg objectives will meet the needs of scientists, worldwide, by generating a carefully authenticated animal virus collection that is larger than any existing repository, and readily available to all laboratories that meet approved ethical, safety and security standards.

Here, the approval of WIV's project application from MOST is very significant for China to introduce necessary strategic virus resources and to build international accredited standards on virus reservation and quality control. Additionally, this project will provide important resources to the scientific researches and biotechnology industries including antiviral drugs and vaccines from home and abroad, which will undoubtedly improve China's international influence in responding to emergencies in international public health effectively.

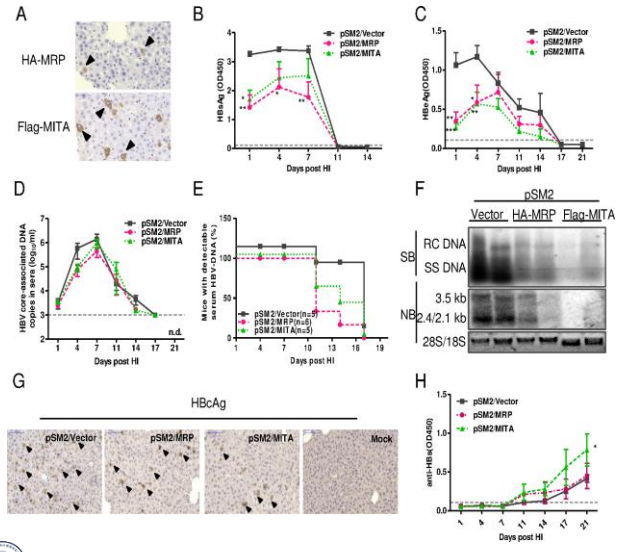
Global quantitative proteomic analysis profiles host protein expression in response to Sendai virus infection

Sendai virus is an enveloped non-segmented negative-strand RNA virus that belongs to the genus Respirovirus of the Paramyxoviridae family. As a model pathogen, SeV has been extensively studied to define the basic biochemical and molecular biologic properties of the paramyxoviruses. In addition, SeV-infected host cells were widely employed to uncover the mechanism of innate immune response.

To identify proteins involved in the SeV infection process or the SeV-induced innate immune response process, system-wide evaluations of SeV-host interactions have been performed by the Research Group of Viral Biochemistry led by Prof. Gengfu Xiao in WIV. cDNA microarray, siRNA screening and phospho-proteomic analysis suggested that multiple signaling pathways are involved in SeV infection process. Here, to study SeV-host interaction, a global quantitative proteomic analysis was performed on SeV-infected HEK 293T cells. A total of 4,699 host proteins were quantified, with 742 proteins being differentially regulated. Bioinformatics analysis indicated regulated proteins were mainly involved in "IFN-I signaling pathway" and "defense response to virus", suggesting these processes play roles in SeV infection. Further RNAi-based functional studies indicated that the regulated protein TRIM24 and TRIM27 affect SeV induced IFN-I production. Their data provided a comprehensive view of host cell response to SeV and identified host proteins involved in the SeV infection process or the SeV-induced innate immune response process.

Link: *https://www.ncbi.nlm.nih.gov/pubmed/28067018*

Scientists reveal that MITA/STING plays an important role in triggering HBV specific adaptive immune responses



An efficient clearance of hepatitis B virus (HBV) requires the coordinated work of both the innate and adaptive immune responses. MITA/STING, an adapter protein of the innate immune signaling pathways, plays a key role in regulating innate and adaptive immune responses to DNA virus infection. Previously, the Research Group of Molecular Biology of Hepatitis Viruses and Gene Therapy led by Prof. Xinwen Chen in WIV identified an alternatively spliced isoform of MITA/STING, called MITA-related protein (MRP), and found that MRP could specifically block MITA-mediated interferon (IFN) induction while retaining the ability to activate NF-κB.

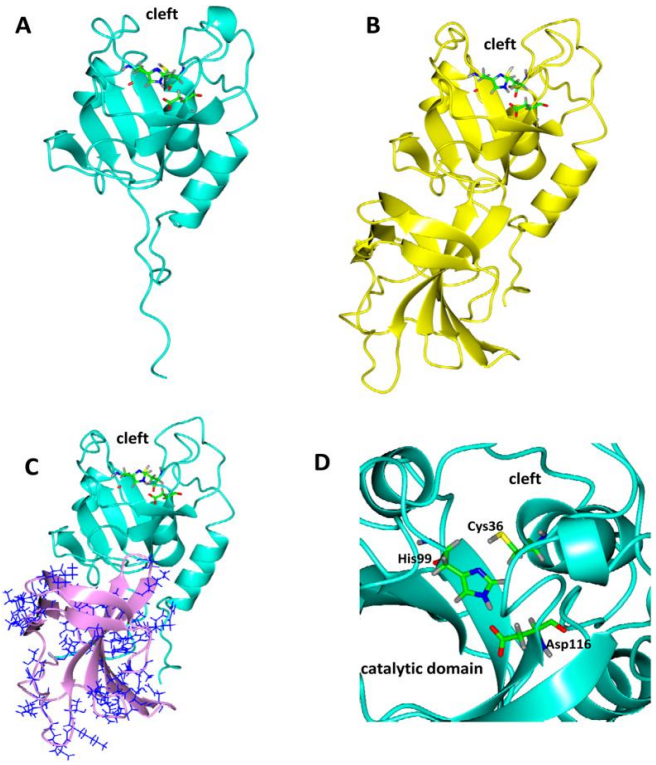
Here, the scientists from WIV asked whether MITA/STING and MRP were able to control the HBV replication. Both MITA/STING and MRP significantly inhibited HBV replication in vitro. MITA overexpression stimulated IRF3-IFN pathway; while MRP overexpression activated NF-κB pathway, suggesting these two isoforms may inhibit HBV replication through different ways. Using a hydrodynamic injection (HI) mouse model, we found that HBV replication was reduced following MITA/STING and MRP expression vectors in mice and was enhanced by the knockout of MITA/STING (MITA/STING-/-). The HBV specific humoral and CD8+ T cell responses were impaired in MITA/STING deficient mice, suggesting the participation of MITA/STING in the initiation of host adaptive immune responses. In summary, their data suggest that MITA/STING and MRP contribute to HBV control via modulation of the innate and adaptive responses.

Link: *http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0169701*

A useful antibacterial to combat Methicillin-resistant Stanphylococcus aureus is represented

Methicillin-resistant Staphylococcus aureus (MRSA) is one of the most threatening pathogens due to its multi-drug resistance (MDR) and strong biofilm-forming capacity.

Prof. Hongping Wei and his research group from WIV described the screening of a novel chimeolysin (ClyF) that was active against planktonic and biofilm MRSA. Biochemical tests showed that ClyF was active against all S. aureus clinical isolates tested under planktonic and biofilm conditions. Structure analysis revealed that ClyF has an enhanced thermostability and pH tolerance than its parental lysin Pc by forming a hydrophobic cleft in the catalytic domain and an Ig-like structure in the cell-wall binding domain. A single intraperitoneally or topically administration of ClyF showed good MRSA removing efficacy in mouse models of bacteremia and burn wound infection, respectively. Their data collectively demonstrated that ClyF has good bactericidal activity against planktonic and biofilm MRSA both in vitro and in vivo, and therefore represents a useful antibacterial to combat MDR S. aureus.



Link: *http://www.nature.com/articles/srep40182*

Research Progress

Sub-ICs of anti-folates can potentiate bactericidal effects of other antimicrobial agents in various bacteria

Synergies between sulfonamides and other antimicrobial agents have long been reported, but the reason still remains unclear. Previously, Vilchèze et al. found that, sulfamethoxazole (SMX) could potentiate the bacterialcidal activity of isoniazid (INH) and rifampin (RIF) in Mycobacterium tuberculosis.

This study was operated by the research group led by Prof. Jiaoyu Deng in WIV under the collaboration with University of Chinese Academy of Sciences and Institute of Biophysics, CAS. To test if this was also the case in other bacteria, the ability to potentiate bactericidal effect of RIF by SMX was evaluated in Escherichia coli, Staphylococcus aureus, Salmonella typhimurium and Mycobacterium smegmatis. And the ability to potentiate bactericidal effect of streptomycin (SM) by SMX was also evaluated in E. coli and M. Smegmatis. Susceptibility tests and drug exposure experiments were performed for RIF and SM in the presence of sub-ICs of SMX. In drug exposure experiments, 10 mg l-1 of 7,8-dihydropteroic acid (DHP) was used to reverse the effect of SMX. In the presence of sub-ICs of SMX, MIC of RIF for E. coli and M. smegmatis decreased 2 and 16 fold, respectively. In the drug exposure experiments, addition of sub-ICs of SMX suppressed the growth of RIF and SM resistant population in a pool of susceptible bacteria, and the effects of SMX could be reversed by DHP. Besides, they also found that, sub-ICs of para-aminosalicylic acid (PAS) could bactericidal effects of INH, RIF and SM in M. tuberculosis. Taken together, their data suggest that, sub-ICs of anti-folates can potentiate bactericidal effects of other antimicrobial agents in various bacteria.

Link: *http://www.nature.com/ja/journal/vaop/ncurrent/full/ja2016159a.html*

International Cooperation

Call for Applications – 2017 CAS-TWAS President's Fellowship Programme for Doctoral Candidates

According to an agreement between CAS and The World Academy of Sciences (TWAS) for the advancement of science in developing countries, up to 200 students/scholars from all over the world will be sponsored to study in China for doctoral degrees for up to 4 years. Under this Programme, students who are non--Chinese citizens have the opportunity to pursue doctoral degrees at the University of Chinese Academy of Sciences (UCAS), the University of

Science and Technology of China (USTC) or Institutes of CAS around China. For the further information about the general conditions, financial support and application, please contact Ms. Pei Pingping in The Graduate Office through yjs@wh.iov.cn.

Foreign experts under the EMERGENGES 2016 Program paid visits to WIV

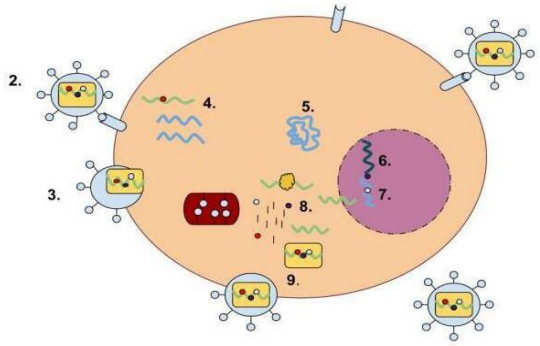
On Dec. 12, 2016, Dr. Maria Dolores Fernandez-GARCIA from Institut Pasteur de Dakar (Senegal) visited WIV and gave an academic presentation.

In her report, Dr. Maria Dolores Fernandez-GARCIA talked about the frontline experience of the Pasteur Institute of Dakar during viral outbreaks, Ebola, Zika, Yellow Fever, Polio and non-polio enteroviruses as examples. According to her, from 2014 to 2016, the laboratory supported local governments during the infectious disease outbreaks including Ebola, Zika and Yellow Fever, coordinated the collection, analysis of microbiological and epidemiological data, developed molecular and serological diagnostic tools, traced the evolutionary history of the viruses, sequenced the genomes, and paved the way for ambitious research projects that will support the management of health crises and the development of future strategies for prevention.

On Dec. 16, 2016, Dr. Herve Bourhy from Institut Pasteur paid a visit to WIV. He talked about the bat lyssaviruses in Europe. In his report, bats are reservoir hosts of numerous emerging viruses that can cross the species barrier to infect other wild and domestic animals, and also humans. These include lyssaviruses, the agents of rabies, that probably originated in bats and progressively diverged from a common ancestor to infect many recipient host species. To date, bats were found to serve as reservoirs of 13 of the 15 lyssavirus species described so far. In Europe, four of these lyssavirus species, namely European bat lyssavirus types 1 and 2 (EBLV-1 and EBLV-2, respectively), Bokeloh bat lyssavirus (BBLV), West Caucasian bat virus (WCBV) and one tentative species, Lleida bat lyssavirus, circulate among several bat species.

The EMERGENGES 2016 Program launched by the French Embassy in China supports French-Chinese cooperation in emergent infectious diseases. The two scientists are selected as French representatives under this program to visit China.

Retroviruses, a Family That Includes HIV, Evolved During the Early Paleozoic Era



Researchers from Oxford University have discovered that retroviruses have existed since the early Paleozoic Era, half a billion years ago. Scientists believed that they had evolved more recently and the team's findings are providing new insights into the evolution of viruses, including HIV. Retroviridae is an odd family of viruses that includes a cancer-causing virus called the human T cell leukemia virus as well as the human immunodeficiency virus (HIV). Retroviruses incorporate their genetic material into the host cell they've infected, just like any other virus.

A team of scientists studied the closest relatives of retroviruses, the so-called "foamy" viruses. These viruses, which are common in mammals, contain bits of genetic material from retroviruses. These sequences of viral DNA were used in combination with modern phylogenetic techniques to study the evolution of the Retroviridae family.

The team was surprised to learn that retroviruses date back to at least 450 million years ago, during the early Paleozoic Era. This shows that they must have originated in the ocean when vertebrates were first evolving. Scientists believed they had evolved much more recently, making the findings especially important.

Retroviruses evolved about half a billion years ago, which makes Retroviridae one of the oldest viral families that still exists. They originated in a marine setting, before modern vertebrates had evolved. This new information will provide researchers with a fuller picture of how retroviruses evolved and changed over time. By fully understanding this strange group of viruses, scientists may be better equipped to study HIV and other retroviruses that are dangerous to humans.

Source: *Natural Science News*

WIV organized an internal academic exchange meeting

On Jan 11-12, 2017, WIV and Sun Simiao Colloquium jointly organized an internal academic exchange meeting. 31 principle investigators from different research groups gave excellent oral reports during the meeting.

This meeting focused on the research progresses and the future plans from the research groups in WIV, which attracted more than one hundred attendees and improved effectively the internal academic exchanges and stimulated the scientific innovation.

Wuhan Institute of Virology
Chinese Academy of Sciences