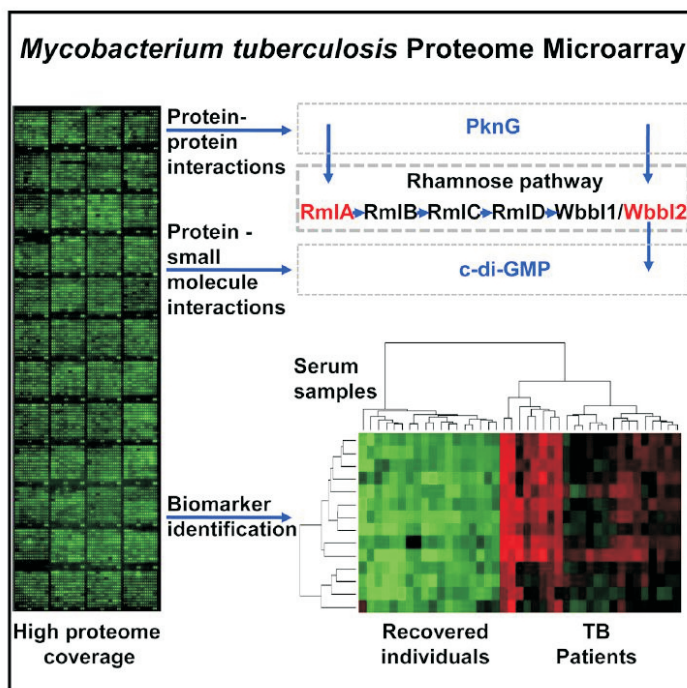


# WIV NEWSLETTER

## Chinese scientists construct the first *M. tuberculosis* proteome microarray

Tuberculosis, an ancient, yet re-emerging infectious disease, is responsible for more deaths than almost all other infectious diseases, and the vaccine, drugs and diagnostic tests currently in use are limiting the effectiveness of global efforts to prevent and control TB. The BCG vaccine, the only licensed TB vaccine, has now been in use for almost one hundred years; however, it provides only limited protection. Drugs currently used to treat TB have been in use clinically for almost half a century and bacterial drug resistance is a growing problem. In addition, current methods for detecting TB are not very effective, and the detection rate is low. Suitable biomarkers which can be used in rapid screening methods for TB are lacking.



Chinese scientists and clinical experts from the CAS Wuhan Institute of Virology, the CAS Institute of Biophysics, Shanghai Jiao Tong University, the Center for Tuberculosis Control of Guangdong Province, the CAS Institute of Hydrobiology, the Shanghai Municipal Center for Disease Control and Prevention, and TB Healthcare Biotechnology Co., Ltd., have worked together to construct the first *Mycobacterium tuberculosis* (MTB) proteome microarray, a powerful high-throughput experimental platform for basic research on TB, and published the results from their joint study in the journal *Cell Reports* on 11th Dec., 2014.

The MTB proteome microarray includes the products of 4262 *Mycobacterium tuberculosis* open-reading frames and covers 95% of the proteome. It can be used for global analysis of protein-protein interactions in studies of the interactions between human immune cells and the MTB pathogen, for analysis of protein interactions with small molecules in the global discovery of drug targets, and for high-throughput analysis of serum samples in the systematic discovery of biomarkers for use in the diagnosis of tuberculosis. The MTB proteome microarray is thus a suitable tool for enabling the systematic discovery of new immunogens and biomarkers, and will likely facilitate the development of new and efficient vaccines, drugs and diagnostic technology.

In studies to demonstrate typical applications of the proteome microarray, PknG, a protein kinase, and c-di-GMP, a small molecule that is a ubiquitous second messenger in bacteria, were found to interact with many previously unreported protein binding partners. Results indicated that both PknG phosphorylation and c-di-GMP are involved in the regulation of the MTB rhamnose synthesis pathway, an important pathway in cell wall biosynthesis. In addition, analysis of serum samples using the proteome microarray identified a panel of 14 biomarkers that can effectively distinguish between patients with active TB and those who have recovered from the disease, and thus has potential as an index for monitoring treatment outcome.

This collaborative study took five years to complete and was supported by grants from the Key Project Specialized for Infectious Diseases of the Chinese Ministry of Health, the Chinese Academy of Sciences, the National High Technology Research and Development Program of China, and the National Natural Science Foundation of China.

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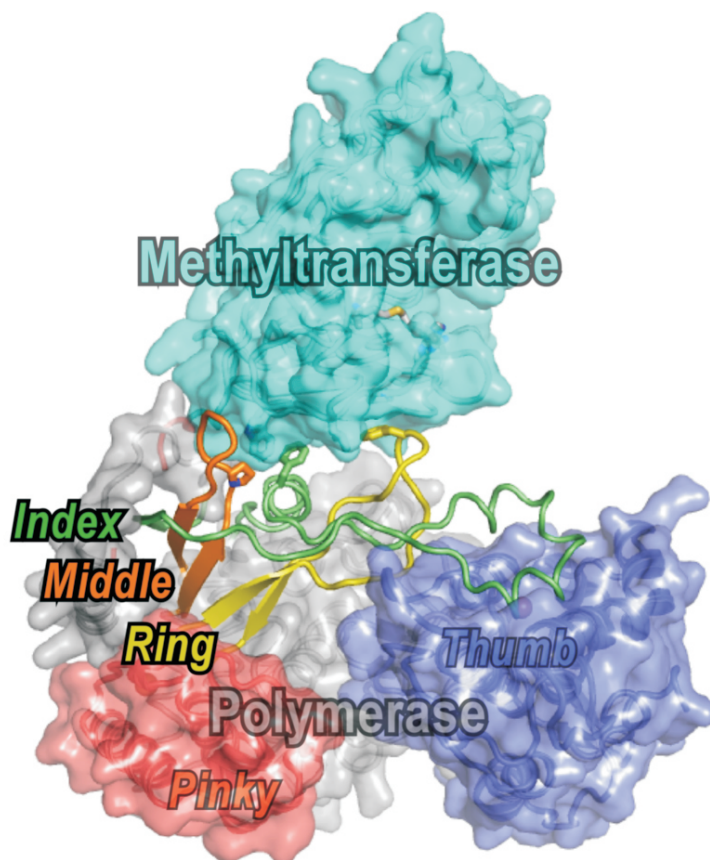
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## Progress in structure and function of flavivirus replication protein NS5

In the past two years, the collaborative research teams led by Prof. Peng Gong and Prof. Bo Zhang have published three papers focusing on the regulation between the methyltransferase and polymerase modules of flavivirus NS5. Since the report of the first flavivirus NS5 methyltransferase crystal structure (EMBO J 2002), scientists have made tremendous efforts in getting a full-length structure also including the polymerase. The breakthrough was made by the Gong group that reported the first full-length crystal structure revealing a conserved interface between the two enzyme modules (PLoS Pathog 2013). Soon after, the Zhang Group validated the function of the interface in the level of virus replication and discovered novel sites that may also participate in the auto-regulation of NS5 (PLoS Negl Trop Dis 2014). To more specifically address the interface regulation on polymerase catalysis, recombinant NS5 and its interface mutants were compared in finely designed polymerase assays. The data suggested that the interface interactions were relevant in both initiation and elongation of RNA synthesis (J Virol 2015). Collectively, the work done by these two groups has made significant contribution to the understanding of NS5 that plays key roles in flavivirus life cycle.

Founded in Nov 2011, the Gong group focuses on important human pathogens such as hepatitis C virus (HCV), Japanese encephalitis virus (JEV), enterovirus 71 (EV71), and investigates the mechanism of catalysis and regulation of viral polymerases through macromolecule crystallography and biochemical approaches.



Crystal structure of the full-length Japanese encephalitis virus NS5



## Virologica Sinica awarded 2014 “The Highest International Impact Academic Journals of China”

Released on December 16, 2014, Virologica Sinica, sponsored by Wuhan Institute of Virology and Chinese Society for Microbiology, was awarded “The Highest International Impact Academic Journals of China” (HII-CAJ, Top 5% STM journals of China) in 2014 China's academic journal impact (CAJ) report, and it was the second time that the Journal was awarded this title after 2013.

The annual report of CAJ is jointly conducted by International Evaluation Research Center of China Literature, China Academic Journals Electronic Publishing House and Library of Tsinghua University. The report adopts big data analysis method and covers about 14,000 kinds of journals (including SCI-JCR journals) in its statistical range.

Virologica Sinica, founded in 1986, is the only journal of the Chinese Society for Microbiology published in English. The Journal publishes peer-reviewed research articles and reviews on the latest developments in all branches of virology, welcomes studies on virus discovery, viral pathogenesis, virus-host

interaction, vaccine development, antiviral agents and therapies, and virus related bio-techniques, and serves as a platform for the communication and exchange of academic information and ideas in an international context.

No publishing/page charges to authors, and all submissions are handled electronically, via ScholarOne online submission and review system. The journal is published by Springer-Verlag Press, and abstracted/indexed in: PubMed/Medline, Scopus, BIOSIS, EMBASE, Google Scholar, ect.

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## The 3rd National Industrial Summit Forum on Insect Virus Pesticides

On 21 Nov. 2014, the 3rd National Industrial Summit Forum on Insect Virus Pesticides was held as scheduled in WIV, CAS. More than 200 represents and technicians from related enterprises attended the forum.

On this forum, the following issues were discussed in depth, namely, popularization and application of green prevention and control technology, the history and status quo of China's insect virus pesticides, and the objective of green agriculture prevention and control.

To seek better ways of cooperation and strive for win-win situations and make great contributions to promoting crop and food protection, the Strategy Union for the Prevention and Control of Biological Pesticides and three-dimensional green prevention and control technology was officially established on the forum, which was consisted of voluntary enterprises and entities who committed to research, development, manufacturing, and service of biosafety prevention and control.



The 3rd National Industrial Summit Forum on Insect Virus Pesticides

The broad-spectrum virus pesticides, whose key technology was provided by WIV, have been applied to 21 provinces, such as Jiangxi, Shanghai, Hunan, Hubei, Guangdong, Guangxi, Hainan, Xinjiang, Liaoning, etc. As the most widely applied virus pesticides in the world nowadays, our broad-spectrum virus pesticides effectively prevent and control various kinds of pests.

## The Training Course for Emerging Infectious Diseases and Biosafety Management



the Training Course for Emerging Infectious Diseases and Biosafety Management

On 20 Oct. 2014, the Training Course for Emerging Infectious Diseases and Biosafety Management was held in WIV, CAS, for the sake of improving the managerial and technological capability of emerging infectious diseases and biosafety management of the institute. Over 180 stuff members from managerial, scientific, and support offices participated in the training course.

As a part of further education under the guidance of the institute's strategic planning, the training course, which centers on biosafety and biotechnology development, the spread, prevention and control of emerging infectious diseases, and laboratory safety management, touches upon four topics, including macro-biosafety laws and regulations, the scientific popularization, diagnostic and prevention and control strategies of emerging infectious diseases, biosafety management and operation norms in the laboratory, and network information security of the institute.

During the training, the biosafety academic symposium of the institute was held, on which the development strategies of biosafety system, the framework of biosafety education and training of the institute, and biosafety training plan of the institute were discussed in depth. The symposium put an emphasis on the importance of biosafety training, set up the draft of biosafety training outline, and put forward constructive suggestions for biosafety management and systematic training of the institute.

WIV will continue to promote biosafety training, striving to grow to be the world-renowned base for specialized technology training and S&T service.

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## Prof. Yanyi WANG wins Distinguished Young Scholar

In 2014, Prof. Yanyi WANG from WIV was awarded as Distinguished Young Scholars, which was funded by National Natural Science Foundation of China.

By identifying critical signaling components and regulatory molecules in the virus-triggered signaling pathways leading to induction of type I IFNs and proinflammatory cytokines, including VISA, WDR5, WWP2 and A20, and revealing roles of the E3 ubiquitin ligases TRIM8 and MIB1 in signaling mediated by the proinflammatory cytokines TNF and IL-1, she makes great contributions to our understanding of the molecular mechanisms of antiviral innate immunity and inflammation, and exerts profound impact in this field internationally.

Prof. Yanyi WANG has published 17 papers in international journals, including 1 in *Mol. Cell*, *Cell Host Microbe* and 3 in *PNAS* as a first/corresponding author. These publications have been cited for more than 1170 times by others. She received the Young Scholar Award from the Chinese Society for Immunology, and was an awardee of the 10000 Talent Plan--Outstanding Young Talents.



Prof. Yanyi WANG

## Racing Deathly Ebola

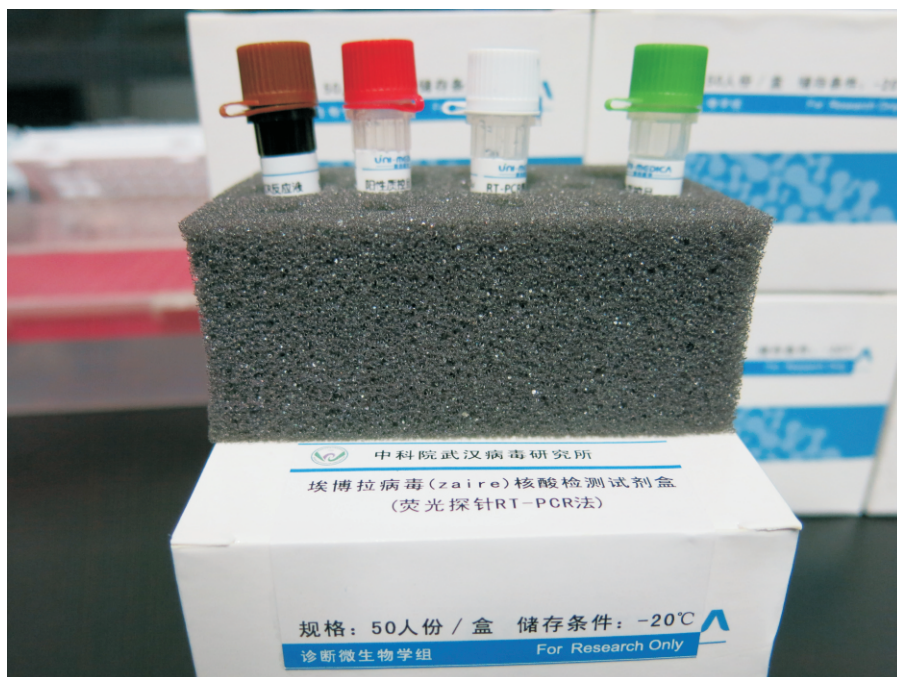
The stern situation of the current outbreak of Ebola hemorrhagic fever has caught intensive attention from the leadership of CAS. Leaders of multiple CAS institutes were convened to discuss proper deployment of R&D activities at the Academy. Subsequently a tentative plan for emergency research projects was formed aiming at tackling key problems existing in the prevention and control of this deadly disease. The plan involves aspects of Ebola virus research, including detection of the virus, therapeutic antibodies, infection and immunology, anti-virus medicine, and structure of viral proteins.

### Battle in Wuhan

Wuhan Institute of Virology (WIV), CAS, is an important arena of this life-and-death battle against Ebola. According to Prof. CHEN Xinwen, Director of WIV, as part of this emergency plan, the institute will devote itself to establishing and optimizing the detection techniques of antigens and antibodies of Ebola virus.

Researchers in WIV expect to successfully develop antigen test kits suitable for field screening and IgM/IgG antibody test kits suitable for lab diagnosis of infection. Also, they are developing a type of test kits for general detection, targeting the RNA of the Zaire and five other strains, based on fluorescent quantitative PCR technique.

Meanwhile, they will also develop a system of pseudoviral particles, a novel system of infectious virus-like particles and a minimum replicon for Ebola virus. Subsequently an expression system based on VEEV replicon will make it possible for them to express the GP and VP40 proteins of Ebola virus, and produce pseudoviral particles free of viral genes. They will also be able to construct a cell line for stable expression of Ebola GP proteins. From these proteins virus-like particles with single-infectivity can be assembled. They are also eager to succeed in observing the minimum replicon's replication in the cell, to apply it in the high throughput screening of anti-virus drugs.



### "We Are Ready"

Actually, WIV has already compiled a set of RT-PCT technical standard for detection of Ebola virus and successfully developed the EBOV nucleic acid test kits. Both have been sent to the ports in Guangdong China to test their efficacy in the local inspection and quarantine practice. WIV has also established a series of techniques for virus detection, including serological detection methods for Zaire and Reston strains, TaqMan RT-PCR methods aimed at detecting the nucleic acid of highly infectious viruses like Ebola and Marburg viruses, and a technique for antibody detection capable of detecting the virus' nucleoprotein. They have also succeeded in expressing soluble antigens in vitro, based on which they have prepared single/multiple antigenic peptides and further obtained monoclonal antibodies of Ebola and Marburg virus with good specificity and high affinity. Also, WIV has programmed a species of yellow fever virus that can express Ebola GP proteins, and accordingly conducted immunity experiments in mice.

Notably, WIV researchers detected antibodies of Ebola-like virus in a number of bat species when conducting epidemiological studies on emerging virus carried by bats in 2012. Given the theory that bats could be possible natural hosts of Ebola virus, the researchers warned that this might suggest that bats in China could carry filiform virus related to Ebola (Yuan et al., *Virology Journal*, 2012, 9:236).

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## The 6th International Symposium on Emerging Viral Diseases Control



On 29-31 Oct. 2014, the 6th International Symposium on Emerging Viral Diseases Control was held by WIV. More than 100 experts from America, Britain, Australia, Singapore, Hong Kong, Taiwan, and mainland China attended the symposium.

On the opening ceremony, Prof. Xinwen Chen, the Director General of WIV, delivered the opening address, in which he pointed out that as a qualified academic exchange activity, this symposium, which focuses on the cutting-edge issues of emerging viral diseases, will put forward new ideas for the research on emerging viral diseases control. The symposium is divided into four academic sessions, including Emerging Viruses and Viral Epidemiology, Antiviral and Vaccine, Emerging Viruses and Viral Therapeutic, Viral Replication. 28 experts delivered speeches in the symposium.

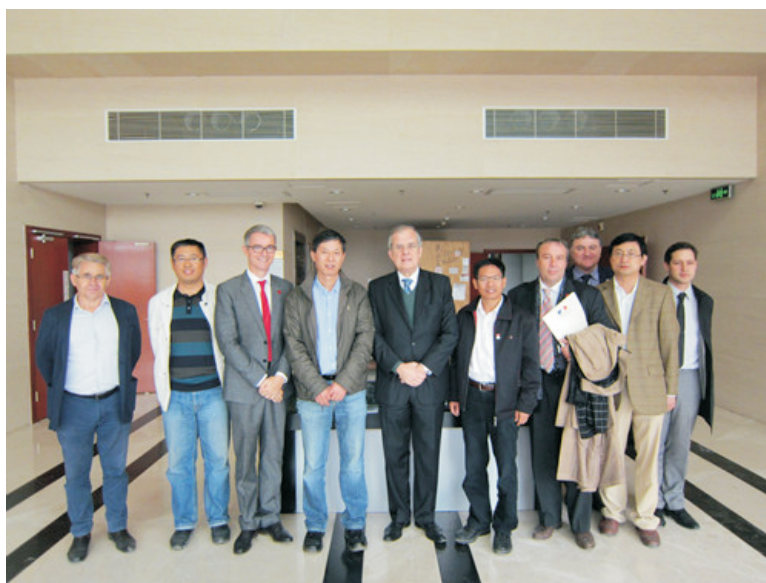
Up to now, 6 international Symposium on Emerging Viral Diseases Control have been held, all of which provides face-to face communication opportunities for experts and scholars in the field of emerging viral diseases at home and abroad and facilitates the development of emerging viral diseases control.

### French Ambassador visited WIV

On 29 Oct. 2014, French ambassador, Mr. Maurice GOURDAULT-MONTAGNE, who took office in August, 2014, visited Zhengdian Park of WIV, CAS.

Prof. Xinwen Chen, Director of WIV, CAS, briefed the research areas of WIV and the Sino-French cooperation on public health emergency response over the years. Prof. Zhiming Yuan, Director of Wuhan Branch, CAS, introduced the current progress of the project, the comparative research on Sino-French biosafety management rules and regulations, personnel training, and the exchange and collaboration on the prevention and control of emerging infectious diseases between the two countries.

Mr. Maurice GOURDAULT-MONTAGNE spoke highly of the progress and the achievements made by two sides in the field of the prevention and control of emerging infectious diseases. It is the fact that 2014 is the 50th year since the establishment of the diplomatic relations of the two countries. French government attaches great attention to the cooperative agreement of the two sides. It is our common wish that the two countries can continue to work closely together to enhance the strategic cooperative partnership in all round, thus, making greater contributions to humankind in the field of the prevention and control of emerging infectious diseases.



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