中国科学院
CHINESE ACADEMY OF SCIENCES

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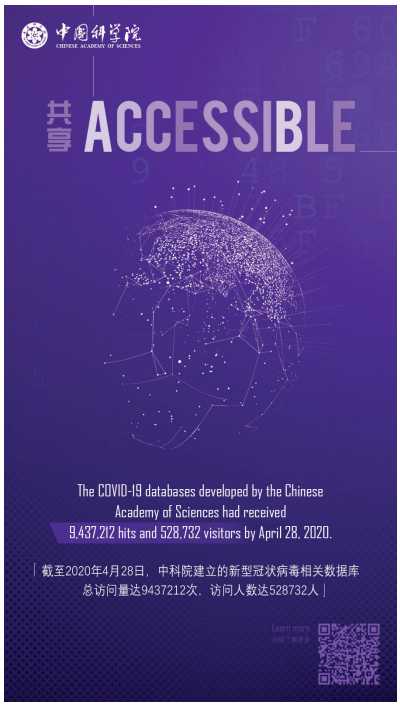
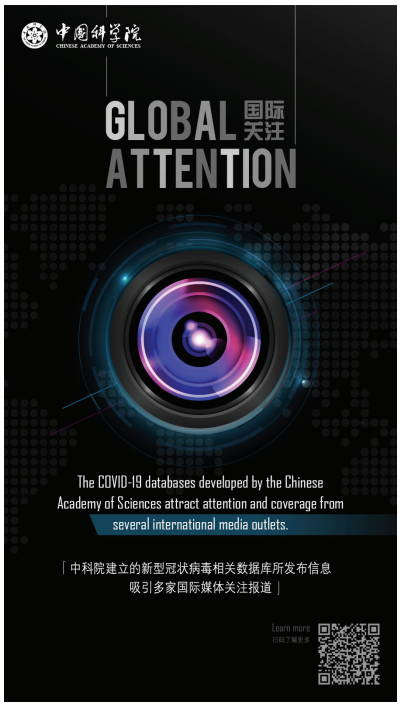
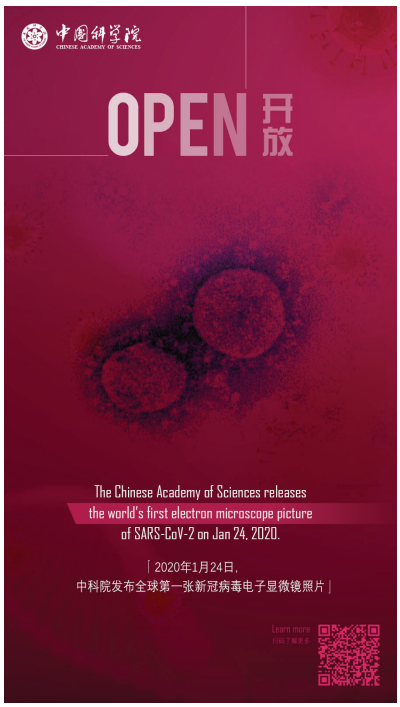
LEAD ARTICLE







CAS helps marshal global science community's COVID-19 fight

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HOT ISSUE

Oligomannate obtains IND approval from FDA for international Phase III clinical study in US

Oligomannate, a drug developed in China to improve cognitive function for those with mild to moderate Alzheimer's disease, was formally approved by the FDA for international multi-center Phase III clinical study in the U.S.. >> **PAGE 2**

RESEARCH PROGRESS

Major progress in study of N-linked glycproteomics of human serum

"Large-scale Identification of N-linked Intact Glycopeptides in Human Serum using HILIC Enrichment and Spectral Library Search" was published online in *Molecular & Cellular Proteomics* on February 29, 2020. >> **PAGE 3**

INTERNATIONAL COOPERATION

China-UK Centre of Excellence expands to tackle global challenges

The successful CAS-JIC Centre of Excellence for Plant and Microbial Science was boosted on April 29 by the signing of a new five-year agreement between the three partner institutes in Beijing, Shanghai and Norwich. >> **PAGE 5**

SCIENCE STORY

An honorable and unforgettable experience of life and research at CAS

Being awarded as a CAS-PIFI was a great honor and I was very excited for having the chance and opportunity to work in China in an excellent, high-qualified scientific atmosphere. >> **PAGE 6**

Edited by Bureau of International Co-operation, Chinese Academy of Sciences
CAS Newsletter – Monthly – Editorial Board: 52, Sanlihe Road, Beijing, 100864, China

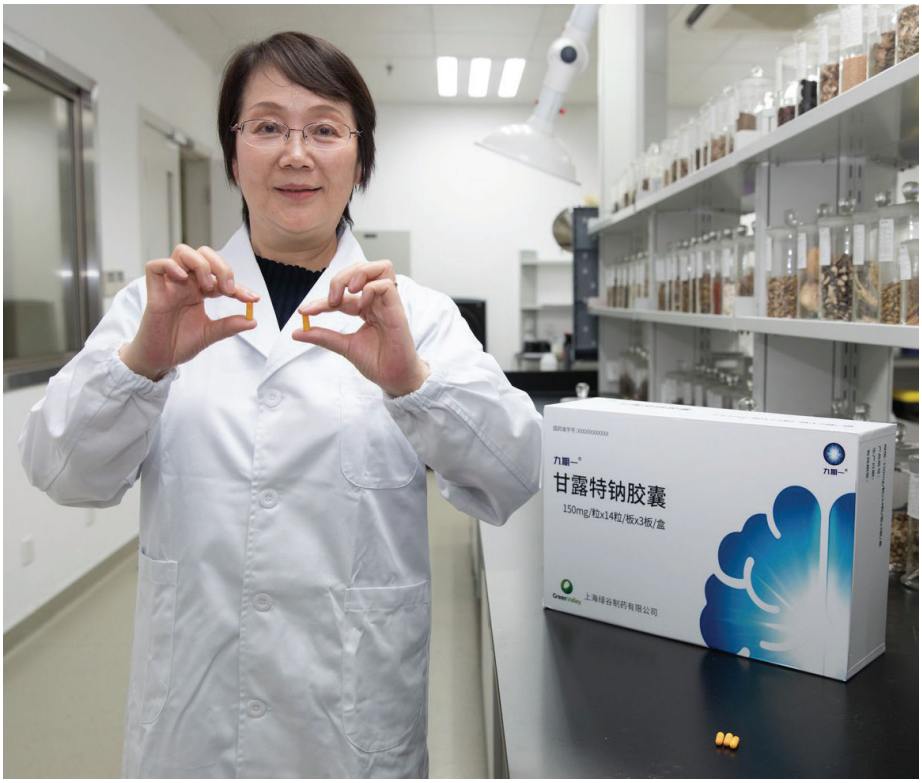
Oligomannate obtains IND approval from FDA for international Phase III clinical study in US

Oligomannate (compound code GV-971), a drug developed in China to improve cognitive function for those with mild to moderate Alzheimer's disease, was formally approved on April 8 by the US Food and Drug Administration (FDA) for international multi-center Phase III clinical study in the U.S..

A formal decision letter from the US Food and Drug Administration on the Investigational New Drug (IND) application for GV-971 indicated the "Study May Proceed" with the proposed clinical investigation in the treatment of patients with Alzheimer's disease. The IND effective date is April 3, 2020.

GV-971 was developed jointly by Ocean University of China, the Shanghai Institute of Materia Medica (SIMM) of the Chinese Academy of Sciences and Green Valley, in a 22-year study.

The leading inventor of this new medicine is Professor Geng Meiyu from SIMM.



Geng Meiyu, key inventor of the drug GV-971, also a researcher of Shanghai Institute of Materia Medica under Chinese Academy of Sciences, shows the sample model of the new drug in Shanghai.
[IMAGE: BLOOMBERG]

The drug GV-971 is an orally administered mixture of acidic linear oligosaccharides derived from a marine brown algae. Preclinical studies on its mechanism of action shows that GV-971 can improve cognitive function by reshaping the balance of gastrointestinal microbiota and inhibiting abnormal increase of specific metabolites of gut microbiota, thus reducing peripheral and central inflammation, β-amyloid deposition and hyperphosphorylation of Tau protein. A growing body of evidence reveals that gut microbiota is highly correlated with the incidence of Parkinson's disease, depression, autism and other central nervous system diseases.

Oligomannate obtained conditional approval from the China NMPA for improving the cognitive function of patients living with mild to moderate Alzheimer's disease on November 2, 2019, and was launched in China on December 29, 2019.

The international Phase III clinical trial of GV-971 plans to enroll more than 2,000 patients with mild to moderate Alzheimer's disease, and consists of a 12-month double-blind treatment period and a six-month open-label period. The trial study will be conducted at 200 sites in North America, Europe and the Asia-Pacific regions including China, and is planned to be completed in 2024. New drug application (NDA) submission is expected by 2025.

Source: Chinese Academy of Sciences

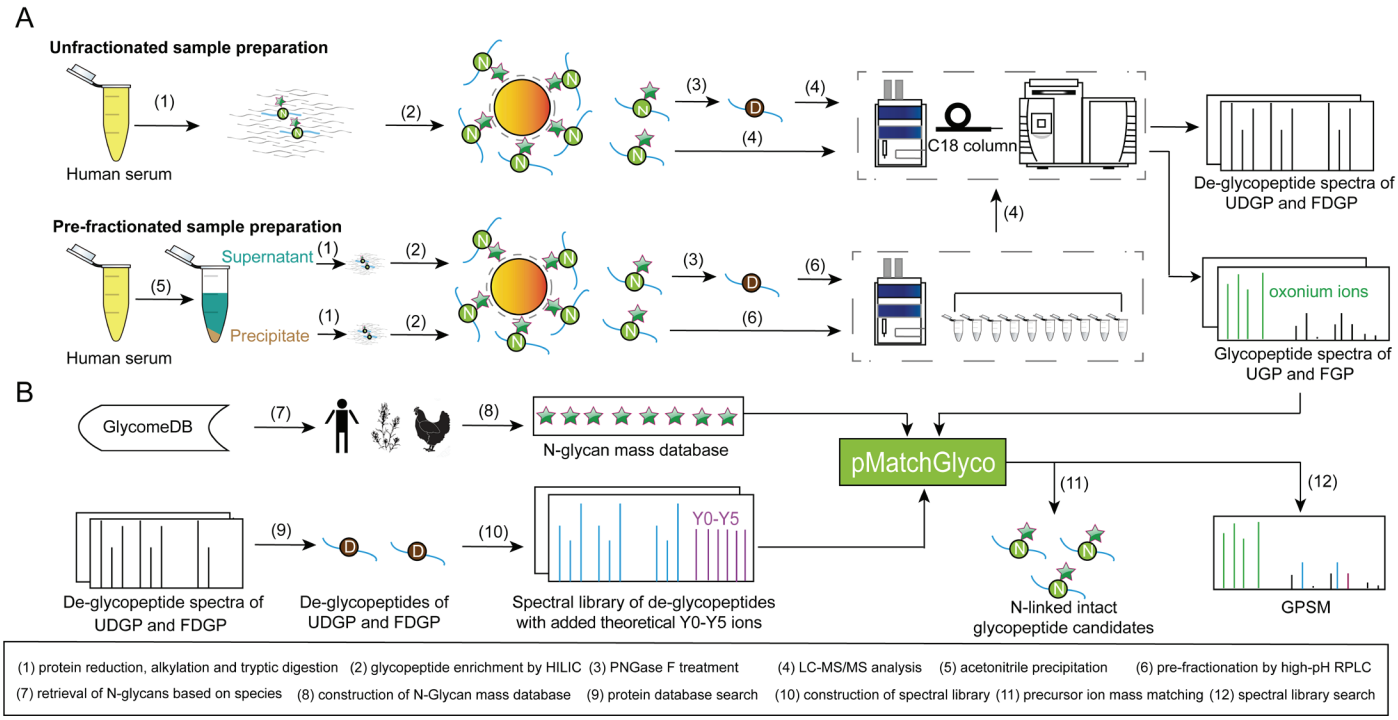


Figure: The strategy and experimental design for the identification of N-linked intact glycopeptides from N-linked glycoproteins in human serum
A: Protein & N-linked intact glycopeptide samples processing with or without fractionation
B: Data analysis workflow for N-linked intact glycopeptide identification [IMAGE: DR. YANG FUQUAN'S GROUP]

Major progress in study of N-linked glycproteomics of human serum

"Large-scale Identification of N-linked Intact Glycopeptides in Human Serum using HILIC Enrichment and Spectral Library Search" was published online in *Molecular & Cellular Proteomics* on February 29, 2020. The work was finished by Professor Yang Fuquan's group at the Institute of Biophysics, Chinese Academy of Sciences and Professor Fu Yan's group at the Academy of Mathematics and Systems Science, Chinese Academy of Sciences.

Glycosylation is one of the most important and prevalent post-translational modifications of proteins. Protein glycosylation plays vital roles in cells, including determination of protein folding, trafficking and stability, as well as regulation of various biological processes such as cell growth, cell-cell communication, cell-matrix interactions, viral replication and immune defense. Aberrant protein glycosylation is associated with the pathological progression of many diseases, including cancer, neuro degenerative disorders, pulmonary diseases, blood disorders, and genetic diseases. Most glycoproteins are potential drug targets and disease related biomarkers.

Protein glycosylation mainly includes N-linked glycosylation and O-linked glycosylation, with N-linked glycosylation accounting for about 70 percent. N-linked glycoproteins are widely distributed, ranging from the surfaces of various types of cells to different human body fluids such as serum, cerebrospinal fluid and urine. Glycoproteins secreted in body fluids are thought to provide a detailed window into the state of health of an individual. These features make glycoproteins a highly interesting class of proteins for clinical and biological research. Protein glycosylation is exceptionally complex, characterized by macroheterogeneity and microheterogeneity, and makes glycoproteomics studies extremely challenging. N-glycoproteomics of human serum is more challenging due to a wide dynamic range of serum protein abundances, low abundance of N-glycoproteins, lack of a complete serum N-glycan database and existence of proteoforms.

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Breakthrough achieved on Shenguang II Upgrade Facility

Research on fast ignition carried out on the Shenguang II Upgrade (SGIIU) high power laser facility under development by the Shanghai Institute of Optics and Fine Mechanics (SIOM), Chinese Academy of Sciences, recently led to a major breakthrough on indirect-drive fast-ignition fusion. The result was published in *Nature Physics*.

As the first physical experiment platform in China to support fast ignition for laser inertial confinement fusion (ICF) research, the SGIIU started its run-in in 2016 after nearly ten years of development. The device is composed of eight beams of ten-thousand joule nanosecond (ns) laser and one-kilojoule picosecond laser (ps). The ns laser has the ability to make precise adjustments to the whole beam such as arbitrary pulse shaping and smooth focal spot creation. The ps beam's focal spot can reach <25μm, with power density >1019W/cm^2 and beam contrast >108, while the pulse is adjustable between 0.5~10ps.

With its excellent output performance such as high energy, high focus power density, high aiming accuracy, high synchronization accuracy, and ps beam combined with ns beams for shooting, the SGIIU can satisfy complex physical experiments and widely serve laser nuclear fusion fast ignition, laboratory astrophysics, laser driven particle beams, nuclear medicine, plasma physics and other frontier research areas. It has already gained a series of important achievements.

In this new experiment, by using indirect laser driven fast ignition to obtain a high level of implosion neutron production, the research team innovatively used an indirect shooting method to pre-compress the target on the SGIIU, which overcame many defects of traditional fast ignition and increased the implosion neutron yield by 280 times, significantly improving fast ignition energy coupling efficiency.

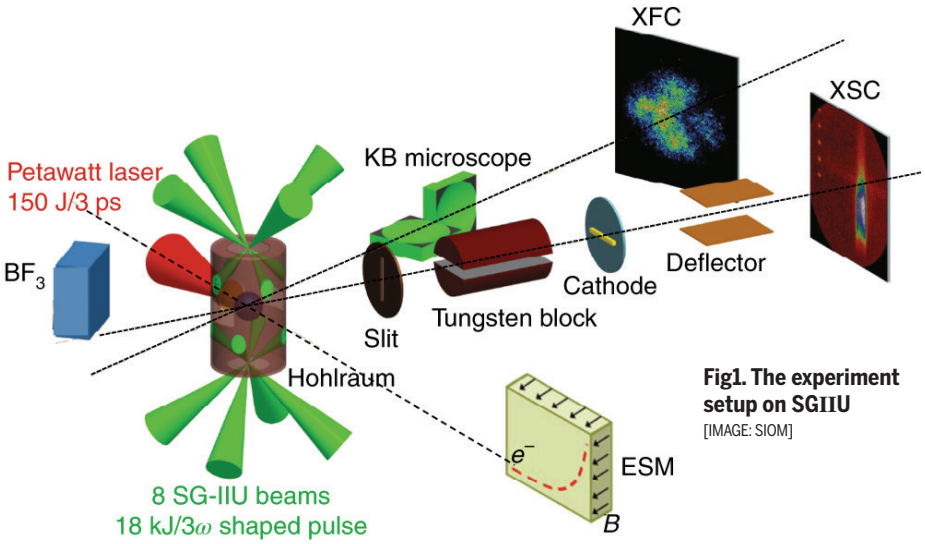

Fig1. The experiment setup on SGIIU
[IMAGE: SIOM]

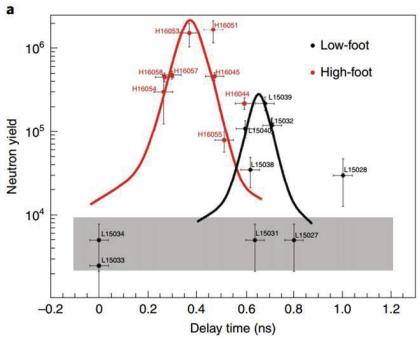

Fig2. The neutron yield obtained from SGIIU
[IMAGE: SIOM]

This work was jointly completed by the Laser Fusion Research Center of the Chinese Academy of Engineering, the Beijing Institute of Applied Physics and Computational Mathematics, the Graduate School of the Chinese Academy of Engineering, the National University of Defense Technology, Peking University, Shenzhen University of Technology, and SIOM.

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General Administrative Office
Shanghai Institute of Optics and Fine Mechanics, Chinese Academy of Sciences

Source: Shanghai Institute of Optics and Fine Mechanics, Chinese Academy of Sciences

Dr. HAN Bin (center) signs the agreement on behalf of CEMPS at Shanghai campus of CEPAMS. [IMAGE: CEPAMS]

China-UK Centre of Excellence expands to tackle global challenges

The successful CAS-JIC Centre of Excellence for Plant and Microbial Science (CEPAMS) was boosted on April 29 by the signing of a new five-year agreement between the three partner institutes in Beijing, Shanghai and Norwich.

CEPAMS was launched in 2015 and has been described as the most advanced Sino-UK collaboration in the life sciences. Its success is based upon a unique model in which virtual bilateral international collaboration is underpinned by a "bricks and mortar" approach involving real laboratories led by world-leading scientists.

The next five years will see an expansion of CEPAMS laboratories in China and a renewed emphasis on harnessing the strengths of Chinese and UK science for global good.

Under the new agreement, signed during a video conference on April 29, the number of world-leading CEPAMS research groups will expand from eight to fifteen; an increase from 110 scientists today to more than 200 by 2025.

CEPAMS' sights are firmly set on global impact. Under the new agreement, areas of research will include climate resilience in food crops, unlocking the anti-cancer potential of traditional Chinese medicine and developing new approaches to the treatment of TB.

A new Chair of CEPAMS' Governing Board was also announced on April 29. Professor Sabeeha Merchant takes the reins at an exciting time in CEPAMS' growth and future prospects. Professor Merchant is Professor of Plant Biology at the University of California, Berkeley and a member of the US National Academy of Sciences.

Dr. Li Yin, Director of the Bureau of International Cooperation, Chinese Academy of Sciences said: "I hope CEPAMS becomes a flagship joint research centre in UK-China collaboration, and the new generation of scientists will make CEPAMS an even greater success."

Professor Dale Sanders of the John Innes Centre (JIC) said: "I am delighted by the success of CEPAMS in the last five years and tremendously excited by its future potential. China and the UK are world-leading in the plant and microbial sciences. I believe that our shared mission to harness this scientific excellence for global good will have great impact in the years to come."

Source: CEPAMS

An honorable and unforgettable experience of life and research at CAS

Being awarded as a CAS-PIFI was a great honor and I was very excited for having the chance and opportunity to work in China in an excellent, high-qualified scientific atmosphere. This award provided a great opportunity for me to extend my scientific work in a broader topic and exchange my experience and expertise with colleagues of the Institute of Subtropical Agriculture of the Chinese Academy of Sciences.

For a long time I have been aware that China promotes science with huge investments and efforts. While a sound financing of science is a prerequisite of excellence, it is not the only requirement. Other requirements are a lean bureaucracy as well as the enthusiasm and high quality of the scientists and students working in academia, such as those of the Chinese Academy of Sciences. During my stay in China and in a CAS institute, everything always went smoothly. The staff and the students at the Institute of Subtropical Agriculture, Chinese Academy of Sciences were very hard working, helpful and friendly. There, the work efforts of our colleagues were always driven by seeking the best progress in science. This concerns both aspects, progress in basic science and development of practical solutions of environmental problems to the benefit of the society. The colleagues at the Institute of Subtropical Agriculture are perfectly addressing both issues. What I like very much is the openness in creating new ideas and in finding ways to realize them. In these discussions, students were always involved in an atmosphere that was characterized by both challenge and encouragement. This provides a very good training for them and is the prerequisite for excellent PhD and PostDoctoral studies.

[IMAGE: INSTITUTE OF SUBTROPICAL AGRICULTURE, CHINESE ACADEMY OF SCIENCES]

I would judge the Institute of Subtropical Agriculture as an excellent group, a hotspot in agricultural science. Besides a very solid number of joint papers, another result of the visiting scientist funding was development of new approaches in the field and at the level of an agroecosystem. I hope that our joint activities will also extend into collaborative projects. With these activities, my colleagues and I are hoping to provide a small contribution to the scientific New Silk Road.

Living in China as a young scientist was an unforgettable experience. People in China are extremely friendly and helpful as were my colleges in the Institute of Subtropical Agriculture. I could learn about China's great history, culture and very amazing food. China has very diverse landscape and natural conditions, which I think make the country very special. I hope that in future I will have the chance to come back to China and work once more within CAS institutes, becoming closer to and more familiar with the marvelous history and culture of China.

Regardless of the massive number of microbes in soil, they occupy only a small

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part of its volume. Most microorganisms form colonies and biofilms and generate aggregate and cluster micro-sites to share nutrients and be sheltered from harmful factors in the environment. Consequently, the main relevant biogeochemical processes take place in these microsites, which are consequently called hotspots. The most impressive and rewarding work that we have done together with the Institute of Subtropical Agriculture of the Chinese Academy of Sciences was to localize, visualize and identify the presence and function of these microbial hotspots in soil. This was an extremely innovative and frontiers study which was performed for the first time. We do believe that our approach and findings will open new directions and shed new light on soil functions in agroecology.

In addition, for the first time, we performed visualization of enzyme activity at the field scale in situ during my stay at CAS.

Overall, I think, all of the work and research that we established and performed was very innovative and successful. Our research results, which were published in highly ranked international journals, strongly improved our understanding of the processes and functions in an agroecosystem.

The Chinese Academy of Sciences is very strong in fostering not only national research but also scientific networking with partner countries. I would like to strongly encourage the Chinese Academy of Sciences to continue this way. Quite a lot of the joint research of China and Germany is coordinated by the Sino-German center in Beijing. From my point of view, it would be very beneficial, if this center could get a bigger budget for funding joint research activities. Of course, this would include both partner countries.

Personally, I would be very grateful if the collaboration with the Institute of Subtropical Agriculture of the Chinese Academy of Sciences could be continued and expanded. One idea of my Chinese collaborators and me is the establishment of joint projects and workshops in plant-soil microbiome interaction of agroecosystems. Perhaps there will be an opportunity to discuss this further in the framework of the Sino-German Center or directly between the Chinese Academy of Sciences and the German Science Foundation.

Finally, I would like to express my sincere gratitude to the Chinese Academy of Sciences for funding my stays as a visiting scientist at the Institute of Subtropical Agriculture of the Chinese Academy of Sciences.

Source: Bahar S. Razavi,
Institute of Subtropical Agriculture,
Chinese Academy of Sciences

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In this study, serum proteins were first separated into low-abundant and high-abundant proteins by acetonitrile precipitation. After digestion, the N-linked intact glycopeptides were enriched by hydrophilic interaction liquid chromatography (HILIC) and a portion of the enriched N-linked intact glycopeptides was processed by N-Glycosidase F (PNGase F) to generate N-linked de-glycopeptides. Both N-linked intact glycopeptides and de-glycopeptides were analyzed by LC-MS/MS.

N-linked de-glycopeptides were first identified by searching their MS/MS spectra against human protein sequences, considering four types of N-linked glycosylation sequence motifs (NXS/T/C/V, X≠P) to recognize the N-linked de-glycopeptides. Then, the spectra of the N-linked de-glycopeptides identified were utilized to construct the spectral library of N-linked de-glycopeptides with the addition of a series of Y ions (Y1,Y2…Y5) in each spectrum. A database of 739 N-glycan masses was also constructed.

The identification of N-linked intact glycopeptides was performed with a spectral library search strategy using pMatchGlyco software, a library of N-linked de-glycopeptides and an N-glycan mass database. Compared with the sequence search method, the spectral library search method is faster and more sensitive. Moreover, by precursor mass optimization and taking into account semi-specific digestion and abundant chemical modifications, identification sensitivity was further improved.

In total, 526 N-linked glycoproteins, 1,036 N-linkedglycosites, 22,677 N-linked intact glycopeptides and 738 N-glycan masses were identified under 1 percent FDR, representing the most in-depth N-glycoproteome of human serum identified by LC-MS/MS at N-linked intact glycopeptide level. Transferrin is a well recognized glycoprotein in serum. Four N-linked glycosites (N432, N523, N630 and N637) with 371, 2, 364 and 34 N-glycans at each site respectively have been identified in serum transferrin. Five N-linked glycosites (N432, N491, N523, N630 and N637) with 559, 5, 6, 547 and 117 kinds of N-glycans at each site respectively have been identified from the commercial serum transferrin standard. The results show the microheterogeneity of glycosylation modification in serum transferrin.

This is the second collaboration between Yang's group and Fu's group, and follows their development in 2018 of pMatchGlyco, which is software for the analysis of N-linked intact glycopeptides.

For more information, please contact:
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Email: fqyang@ibp.ac.cn
Institute of Biophysics, Chinese Academy of Sciences

Source: *Dr. Yang Fuquan's group*
Institute of Biophysics,
Chinese Academy of Sciences

Big data platforms for a global pandemic

In response to the global COVID-19 pandemic, a Chinese Academy of Sciences program known as Big Earth Data Science Engineering (CASEarth) began to organize data and information that could help curb the outbreak. CASEarth coordinated a national effort to develop a global big data platform for coronavirus. This platform has been publishing and disseminating timely, authoritative scientific data and information concerning COVID-19, including detection methods, electron micrographs, genomes, scientific literature, results from ongoing scientific research, and a collection of virus strains from the National Pathogen Microbial Resource Bank. These resources are valuable for scientific studies on COVID-19 and for experts active in prevention and control of COVID-19 infections. In addition to COVID-19 genome data, the system has so far integrated 3,135 coronavirus genomes and 32,865 nucleic acid sequences from 20,241 strains, extracted from 496 different host types and 568 collection sites.

Guo Huadong, Chairman of Academic Committee, Institute of Remote Sensing and Digital Earth, Chinese Academy of Sciences [IMAGE: CHINESE ACADEMY OF SCIENCES]

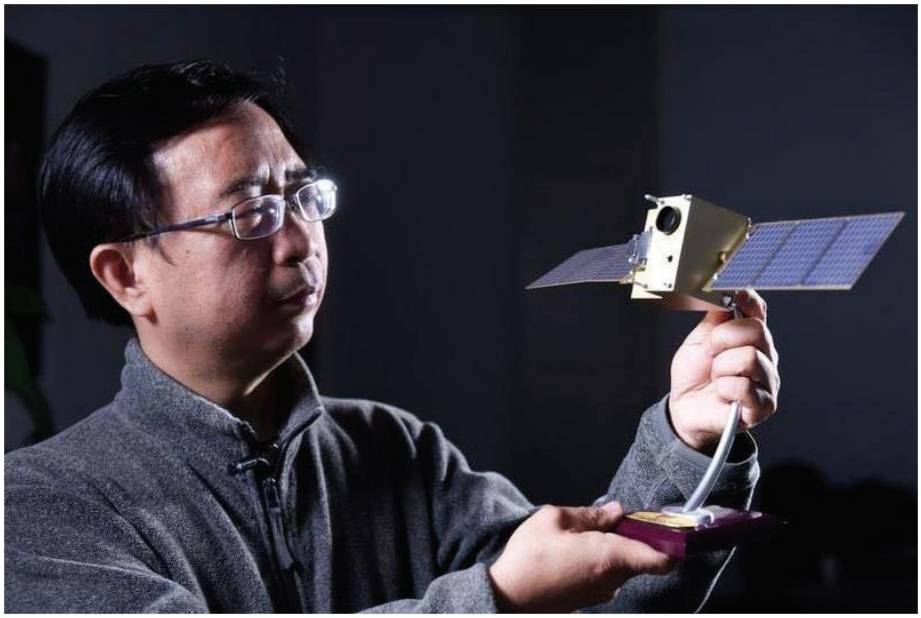
Source: Guo Huadong, Institute of Remote Sensing and Digital Earth, Chinese Academy of Sciences

Chinese quantum physicist receives ZEISS Research Award

Renowned Chinese quantum physicist Pan Jianwei is this year's ZEISS Research Award for his contributions to the field of optical quantum information, according to the University of Science and Technology of China, where he is a faculty member.

One of the most remarkable results of Professor Pan's research is the distribution of entangled photons over a distance of 1,200 km, by far the longest distance ever reached, ZEISS said in an announcement on its website, noting that he has also contributed significantly to the development of optical quantum computing.

ZEISS is a technology enterprise in the fields of optics and optoelectronics. It presents the award every two years to those who have demonstrated outstanding achievements in the field of optics or photonics.



Chinese quantum physicist Pan Jianwei and a model of quantum experiments satellite 'Micius' in University of Science and Technology of China [IMAGE: XINHUA]

The award will be presented to Pan in 2021 due to the worldwide coronavirus pandemic, ZEISS said.

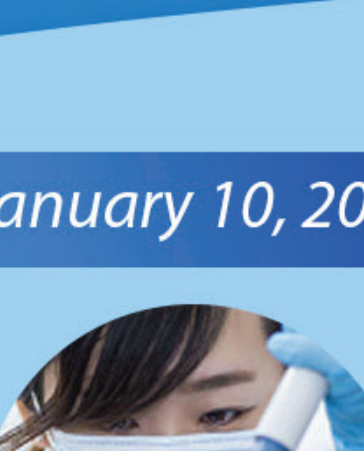
Source: Xinhua

As part of its efforts to jointly fight the pandemic with the rest of the world, the Chinese Academy of Sciences (CAS) lost no time in setting up databases of novel coronavirus information. It updates these databases with the latest developments in virus research and shares all relevant data with the world, in order to contribute to international exchanges and cooperation in COVID-19 prevention and control. Now let's follow the timeline to take stock of what we've done.

CAS helps marshal global science community's COVID-19 fight

The Chinese Academy of Sciences (CAS) has built global data sharing platforms to contribute to international research on COVID-19 prevention and control.

January 10, 2020



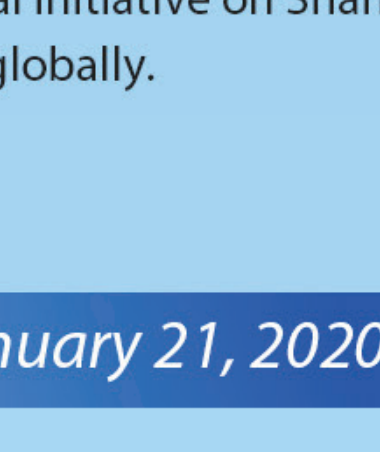
Research institutions including the Wuhan Institute of Virology (WIV) under CAS develop testing kits.

January 12, 2020

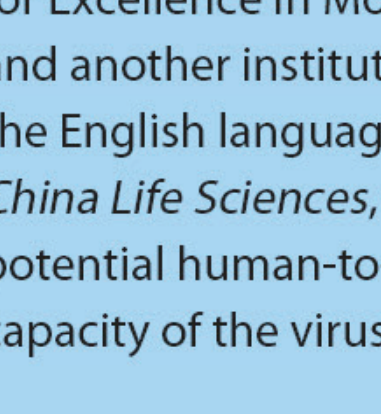
China CDC, the Chinese Academy of Medical Sciences and WIV under CAS submit the genome sequence of SARS-CoV-2 to the WHO. It is published by the Global Initiative on Sharing All Influenza Data (GISAID) and shared globally.

January 21, 2020

Researchers from the Institut Pasteur of Shanghai under CAS, the CAS Center for Excellence in Molecular Plant Sciences and another institute publish a paper in the English language version of *Science China Life Sciences*, evaluating the potential human-to-human transmission capacity of the virus.

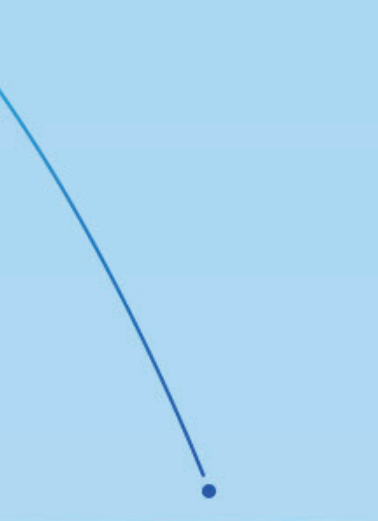


January 22, 2020



The 2019 Novel Coronavirus Resource (2019nCoVR), a database developed by the China National Center for Bioinformation, is launched.

January 23, 2020



Researchers from WIV under CAS and other institutes find that the full-length genome sequence of SARS-CoV-2 shares 79.5 percent of the SARS-CoV sequence, and publish those findings on the bioRxiv preprint platform.

January 24, 2020

The National Microbiology Data Center and the National Pathogen Resources Collection Center establish the Novel Coronavirus National Science and Technology Resource Service System, releasing the first electron microscope picture of the virus as well as strain information.

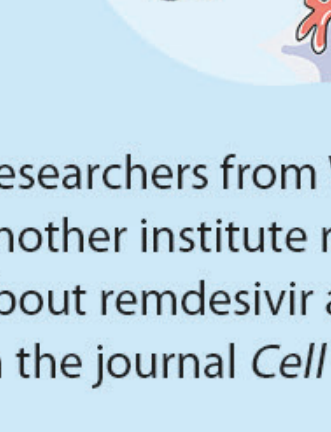
January 29, 2020

A thesis on the genome sequence of SARS-CoV-2 by a research team from WIV under CAS is accepted by the journal *Nature*.

Researchers from WIV under CAS and other institutes publish in *The Lancet* an article regarding clinical features and treatment of COVID-19 patients.

A research team of the Shanghai Institute of Materia Medica (SIMM) under CAS publishes an article on the bioRxiv preprint platform that reveals research findings about drugs which have resulted from computer-simulated screening.

February 4, 2020

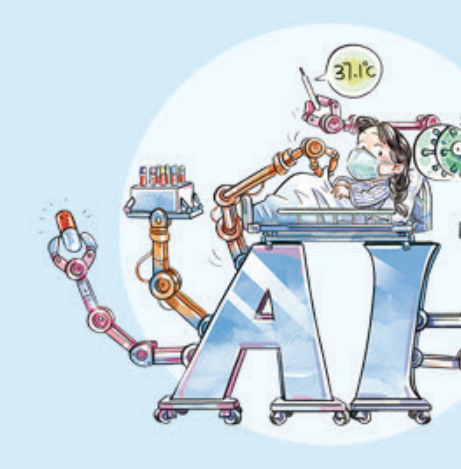


Researchers from WIV under CAS and another institute release a paper about remdesivir and chloroquine in the journal *Cell Research*.

February 18, 2020

The Institute of Microbiology under CAS releases the Global Coronavirus Data Sharing and Analysis System.

February 25, 2020



The Intelligent Diagnosis System for COVID-19 is launched.

March 13, 2020

Experts from the University of Science and Technology of China (USTC) and its first affiliated hospital publish an article, titled "Pathogenic T cells and inflammatory storm in severe COVID-19 patients".

March 30, 2020

The COVID-19 Pneumonia Scientific Literature Sharing Platform is launched in both Chinese and English.

OPEN DATA PLATFORMS

for international scientists

2019 NOVEL CORONAVIRUS RESOURCE (2019nCoVR)

Offering free and open access to all researchers and health workers around the world to download the information they need

Since it began operating in late January, it has served more than **114,000** users from **165** countries and regions and has had data downloaded more than **18.3** million times.

Top 10 foreign countries with the most downloads

Country	Downloads
USA	2,238,788
Egypt	1,153,270
India	494,268
Canada	304,598
France	272,266
Japan	253,318
Turkey	172,314
Botswana	137,628
Italy	136,801
South Korea	136,666

Source: China National Center for Bioinformation / National Genomics Data Center
By April 21, 2020

NOVEL CORONAVIRUS NATIONAL SCIENCE AND TECHNOLOGY RESOURCE SERVICE SYSTEM

Collecting data garnered from independent domestic research, such as information about virus strains and protein structure

A total of **203,323** users from **140** countries and regions worldwide made **8.4** million visits, **660** thousand of which were by **18,260** overseas users in **137** countries.

Top 10 foreign countries with the most visits

Country	Visits
USA	237,942
Japan	38,441
Canada	35,777
Britain	31,160
Australia	20,905
Russia	19,651
Germany	18,801
Italy	17,540
India	16,420
Singapore	15,532

Source: Institute of Microbiology, CAS
By April 22, 2020

COVID-19 PNEUMONIA SCIENTIFIC LITERATURE SHARING PLATFORM

Collecting papers written by CAS researchers and providing an important reference for coronavirus research

A total of **4,582** users from **69** countries and regions worldwide made **238,823** visits, **25,831** of which were made by **1,194** overseas users from **66** countries.

Top 10 foreign countries with the most visits

Country	Visits
USA	5,526
Canada	950
France	360
Japan	337
Britain	335
Indonesia	297
Germany	228
Thailand	178
Russia	142
Ukraine	58

Source: Institute of Microbiology, CAS
By April 22, 2020