

### CASNewsletter

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# THE EARTH AND THE UNIVERSE: FAST TELESCOPE OPEN TO INTERNATIONAL SCIENTISTS

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### 2 | Lead Article



Photo taken on January 11, 2020 shows China's Five-hundred-meter Aperture Spherical Radio Telescope (FAST) under maintenance in Southwest China's Guizhou Province. China's FAST, the world's largest single-dish radio telescope, will be available for global service from April 1. The National Astronomical Observatories of China (NAOC), part of the Chinese Academy of Sciences, the operator of the telescope, confirmed on January 4 that scientists from across the world can make online appointments to use the device for observation from April 1. An allotted timetable will be available by August 1. [IMAGE:XINHUA]

# China's FAST telescope will be available to foreign scientists

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Jiang Peng, chief engineer of FAST with NAOC, said that in the first year of the telescope's opening up to the global scientific community, about 10 percent of the observation time will be allocated to foreign scientists. "Chinese scientists also need to comply with the online application formality," Jiang said.

Located in a deep and round karst depression in Southwest China's Guizhou Province, FAST is believed to be the world's most sensitive radio telescope. It started formal operations on January 11, 2020.



# USHERING IN THE FUTURE OF COMMUNICATION

### 4 | Hot Issue

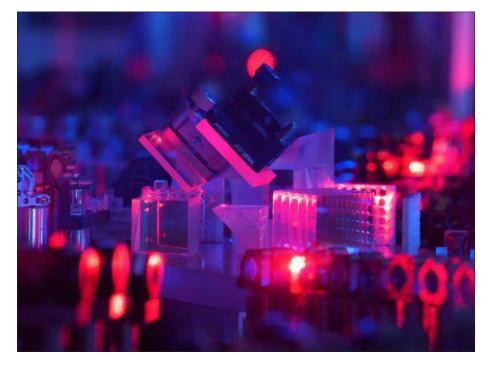
# World's first integrated quantum communication network

hinese scientists have established the world's first integrated quantum communication network, combining over 700 optical fibers on the ground with two ground-to-satellite links to achieve quantum key distribution over a total distance of 4,600 kilometers for users across the country.

The team, led by Professors Pan Jianwei, Chen Yuao, Peng Chengzhi from the University of Science and Technology of China (USTC) of the Chinese Academy of Sciences in Hefei, reported their latest advances towards the global, practical application of such a network for future communications in the journal *Nature*.

Unlike conventional encryption, quantum communication is considered unhackable and is therefore the future of secure information transfer for banks, power grids and other sectors. The core of quantum communication is quantum key distribution (QKD), which uses the quantum states of particles - e.g. photons — to form a string of zeros and ones. Any eavesdropping between the sender and the receiver changes this string or key and is noticed immediately. So far, the most common QKD technology uses optical fibers for transmissions over several hundred kilometers, with high stability but considerable channel loss.

Another major QKD technology uses the free space between satellites and ground stations for thousand-kilometer-level transmissions. In 2016, China launched the world's first quantum communication satellite (QUESS, or Mozi/Micius) and achieved QKD with two ground stations which are 2,600 km apart. In 2017, an over 2,000-kmlong optical fiber network was com-



pleted for QKD between Beijing and Shanghai.

Using trusted relays, the groundbased fiber network and the satellite-toground links were integrated to serve more than 150 industrial users across China, including state and local banks, municipal power grids, and e-government websites. "Our work shows that quantum communication technology is sufficiently mature for large-scale practical applications," said Professor Pan.

"Similarly, a global quantum communication network can be established if national quantum networks from different countries are combined, and if universities, institutions and companies come together to standardize related protocols, hardware, etc.," he added.

In the last couple of years, the team extensively tested and improved the performance of different parts of the integrated network. For instance, with an increased clock rate and more efficient QKD protocol, the satellite-toground QKD now has an average key generation rate of 47.8 kilobits per second, which is 40 times higher than the previous rate. The researchers have also pushed the record for ground-based QKD to beyond 500 km using a new technology called twin-field QKD (TF-QKD).

In the future, the team will further expand the network in China and with their international partners from Austria, Italy, Russia and Canada. They also aim to develop small-scale, cost-efficient QKD satellites and ground-based receivers, as well as medium and high earth orbit satellites to achieve all-time, ten-thousand-km-level QKD.

> Source: University of Science and Technology of China, Chinese Academy of Sciences

#### January 2021

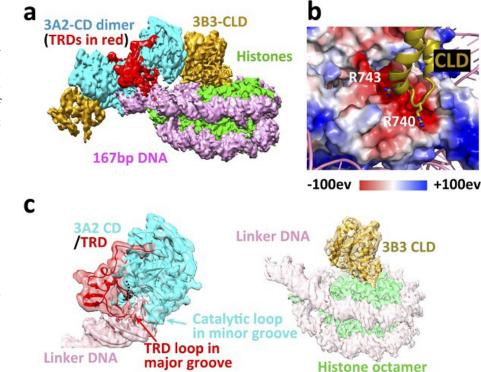
# Structure of de novo DNA methyltransferase and nucleosome analyzed in high resolution

n September 23, 2020, GMT, the Xu Huaqiang group from the Shanghai Institute of Materia Medica (SIMM), Chinese Academy of Sciences, together with the Karsten Melcher group and the Peter Jones group from the Van Andel Institute (VAI) of the United States published important research on de novo DNA methyltransferase (DNMT) entitled "Structure of nucleosome-bound DNA methyltransferases DNMT3A and DNMT3B" in *Nature*.

The teams used advanced Cryo-EM technology to determine the high-resolution structure of de novo DNMT3A2/ DNMT3B3 with nucleosome substrate, elucidated the binding mode of DN-MT3A2/DNMT3B3 with a nucleosome core particle, and proposed a genomewide DNA methylation model.

DNA methylation can change chromatin structure, DNA stability, and DNAprotein interactions, which can control gene expression. DNA methylation can be inherited by the offspring DNA along with the DNA replication process which makes it an important epigenetic mechanism. The DNA methylation in a chromatin context is far more complex than in solution, particularly because the DNA wrapped by a nucleosome is refractory to cytosine modification by either prokaryotic or mammalian enzymes. Also, most of the de novo DNMT3s bound to nucleosomes are not actively engaged in catalysis. CpG methylation by the de novo DNMT3A and DNMT3B is essential for mammalian development and differentiation and is frequently dysregulated in cancer.

By analyzing the expression pat-



a. Cryo-EM density map of the human DNMT3A2-DNMT3B3-NCP complex b. Acidic patch interaction c. Binding of the DNMT3A2 catalytic domain (3A2 CD) to linker DNA and binding of the DN-MT3B3 catalytic-like domain (3B3 CLD) to the histone core

terns of different subtypes of DNMTs in thousands of normal tissues (GTEx database) and cancerous tissues (TCGA database), this study focused on determining the interaction of DNMT3A2 and DNMT3B3 with a nucleosome core particle (NCP), because these are the two main subtypes expressed in human cancers. The crystal structures of isolated DNMT3A catalytic domain and DNMT3L catalytic like domain with or without free DNA have been analyzed. However, due to its limitations, the in-

[IMAGE: XU TINGHAI]

teraction mechanism between DNMT and its natural substrate nucleosome has not been illustrated.

To reveal the interaction between DNMT3A2/3B3 and nucleosomes, and to understand the DNA methylation on chromatin, the joint group successfully determined in near-atomic resolution the cryo-EM structure of nucleosome-bound DNMT3A and DNMT3B complexes.

### 6 | Research Progress

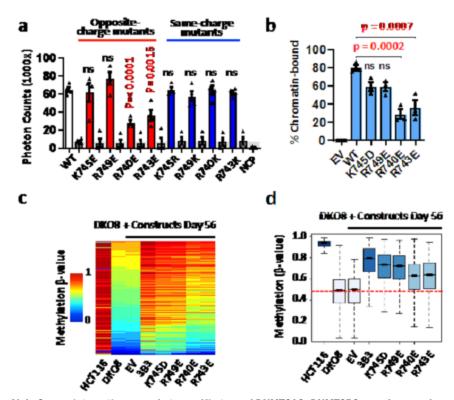
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The structure shows that a heterotetrameric 3B3-3A2-3A2-3B3 complex is very similar to that formed by the isolated catalytic domains and catalytic-like domains of DNMT3A and DNMT3L. This complex interacts asymmetrically with the NCP, with one of the two DN-MT3B3 catalytic-like domains anchored to the acidic patch region of the nucleosome core. Central to this interaction are the DNMT3B3 arginine finger residues R740 and R743. This acidic patch is a key structural element that also has crucial interactions with many other NCP-binding proteins. The DNMT3A2 catalytic domains do not contact the nucleosome core but rather follow the path of the linker DNA, interact with the linker DNA and methylate the linker DNA. Despite the conserved catalytic domains in the DNMT3 family, structural alignment of DNA-bound DNMT3A2 and nucleosome core-bound DNMT3B3 revealed a switch function for the TRD. The TRD found in all catalytically active DNMT3A and 3B subtypes makes key contributions to DNA binding, yet sterically blocks the binding of the catalytic domains to the nucleosome core.

To test the importance of the acidic patch interaction for nucleosome recruitment, mutation analysis at the center positions of 740 and 743 of 3B3, and amino acids 745 and 749, which are away from the acid patch region of nucleosomes as controls, was performed.

In vitro interaction experiments (AL-PHA Screen) showed that the opposite charge mutations near the acidic patch (K745E or R749E) had little influence, while R740E and R743E at the acidic patch strongly reduced the ability of the DNMT3A2/DNMT3B3 heterotetramer to bind the NCP. As expected, the four same-charge mutations showed no significant changes in binding ability.

In cell chromatin association assay also confirmed that acidic patch interaction residues 740 and 743 arginine mutations



a. AlphaScreen interaction assay between His-tagged DNMT3A2–DNMT3B3 complexes and biotinylated NCP

b. Graphical representation from three independent biological replicates of DNMT3 chromatin association assays

c. Methylation heatmap of CpG sites in wild-type (HCT116) cells and DKO8 cells expressing DNMT3B3 WT or CLD mutants

d. Box plot of 109,998 probes, showing the distribution of DNA methylation levels for each cell line [IMAGE: XU TINGHAI]

lead to significantly reduced binding to chromatin. To test whether the acidic patch interaction is important for reestablishing DNA methylation patterns in vivo, DNA methylation (Infinium MethylationEPIC BeadChip) was analyzed.

The analysis revealed that the ability of mutant DNMT3B3 to restore DNA methylation is related to chromatin binding capacity. The K745 and R749 mutant methylation, as controls, showed similar methylation recovery patterns as wild-type DNMT3B3. The limited micrococcal nuclease (MNase) digestion assay confirmed the strong increase in protection from nuclease digestion of about 10 bp on either side of the NCP in the presence of the DNMT complex. These data strongly indicate the importance of the interaction of the catalyticlike domain of DNMT3B3 with the acidic patch for nucleosome recruitment and DNA methylation, and that the binding to DNA does not require a CpG at the active site of the enzyme.

By separating core nucleosome targeting and CpG methylation through catalytically inactive and active DNMTs, the DNMT3 complex can be recruited to core nucleosomes with its poorly accessible DNA while targeting CpG methylation to accessible linker DNA. This suggests that remodeling of the nucleosome core is required for spreading DNA methylation to nucleosomal DNA in vivo, e.g., through DNA replication, transcription, or other nucleosome remodeling events.

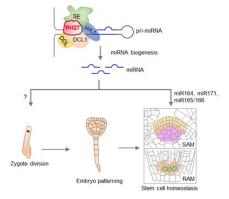
# Role of RNA helicase in zygote activation and stem cell homeostasis in plants

fter double fertilization, zygotic activation occurs to initiate a new life cycle, followed by cell division, cell differentiation and organogenesis. During post-embryonic development, stem cells located in shoot apical meristem (SAM) and root apical meristem (RAM) allow plants to continuously generate new tissues and organs. Therefore, understanding the role of zygote activation and stem cell homeostasis has been of longstanding interest to scientists.

Recently, researchers led by Professor Liu Chunming from the Institute of Botany, Chinese Academy of Sciences (CAS), found that DEAD-box RNA helicase 27 (RH27) plays critical roles in miRNA biogenesis, zygote activation, and stem cell homeostasis.

The Arabidopsis genome has 58 genes encoding DEAD-box RNA helicases, some of which are implicated in RNArelated events including mRNA export, mRNA splicing and rRNA processing.

However, the role of DEAD-box RNA helicases in miRNA biogenesis has not been reported in plants. In this study, a zygote-lethal mutant *zyg4-1* was identified, and map-based cloning showed



RH27 regulates zygote division and stem cell homeostasis through miRNA biogenesis [IMAGE: KEY LABORATORY OF MOLECULAR PHYSIOLOGY, CHINESE ACADEMY OF SCIENCES]

that the mutation was caused by a point mutation in the *RH27* gene.

Interestingly a weak allele of rh27-2 exhibited compromised stem cell homeostasis in both the SAM and RAM. In rh27-2 plants, the expression of stem cell homeostasis-related genes was upregulated, alongside reduced levels of their regulatory miRNAs. Small RNA sequencing and RT-qPCR analyses showed reduced accumulations of a large subset of miRNAs and their primiRNAs in rh27-2.

Further biochemical studies revealed

that RH27 is associated with pri-miR-NAs in vivo and directly interacts with miRNA biogenesis components, DCL1, DDL, HYL1 and SE. These data together demonstrate that RH27 is a new component of the microprocessor complex, and is required for zygote division and stem cell homeostasis. This work indicates a potential role of miRNA in zygote activation and stem cell homeostasis.

This work was published online in *The Plant Cell* on November 17, 2020. It was performed by Liu Chunming's group at the Institute of Botany, CAS, in collaboration with Professor Cao Xiaofeng's group at the Institute of Genetics and Developmental Biology, CAS.

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> Source: Key Laboratory of Plant Molecular Physiology, Chinese Academy of Sciences

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This work was initiated by Xu Tinghai, who is the first author of this article. Xu Tinghai got doctorate degree in 2017 from SIMM, and currently is a postdoctoral fellow jointly supervised by Dr. Peter Jones and Dr. Karsten Melcher at VAI. Dr. Liu Minmin, Dr. X. Edward Zhou, Dr. Zhao Gongpu, and Professor Liang Gangning from the University of Southern California involved also in this work. Dr. Xu Huangqiang from SIMM, and Dr. Peter Jones, Dr. Karsten Melcher from VAI are the cocorresponding authors.

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*Source: Shanghai Institute of Materia Medica, Chinese Academy of Sciences* 

# CHINA STRUGGLES AGAINST PANDEMIC WITH ALL OF THE WORLD

# Clinical histone deacetylase inhibitors are effective against COVID-19

he Coronavirus Disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed serious health threats to humanity and jeopardized the global economy.

However, no effective drugs are currently available to treat COVID-19 despite the great demand to fight against it.

By combining computational screening and an efficient cellular pseudotyped virus system, a research team led by Professor Yuan Shuguang from the Shenzhen Institutes of Advanced Technology (SIAT) of the Chinese Academy of Sciences has confirmed that clinical histone deacetylase (HDAC) inhibitors can efficiently prevent SARS-CoV-2 and potentially be effective against COVID-19.

The researchers found that several HDAC inhibitors can bind to human angiotensin I converting enzyme 2 (ACE2) on the cell surface which in turn results in overall structural changes of ACE2. Since SARS-CoV-2 recognizes the human ACE2 receptor by its Spike protein during viral infection, such alterations inhibit ACE2-S protein binding and prevent host cell entry by SARS-CoV-2.

Inspired by this result, the team then screened 18 commercially available HDAC inhibitors and studied their efficacy in inhibiting the entry of SARS-CoV-2 into cells. They found that the four inhibitors panobinostat, givinostat hydrochloride monohydrate, CAY10603 and sirtinol are noticeably effective.

The lowest half maximal effective concentration (EC50) of viral transduction inhibition achieved by these four HDAC drugs is about 3  $\mu$ M, which is far less than the EC50 obtained from other non-effective drugs (all more than 100  $\mu$ M).

The possible mechanism of these HDAC inhibitors that makes them effective against SARS-CoV-2 was revealed by cellular signaling network analysis.

This work was published as a cover story in ACS Pharmacology & Translational Science.

> Source: Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

### Sino-French cryogenic-based joint venture set up on Science Island

joint venture intending to independently develop, manufacture and sell integrated and cost-competitive helium cryogenic systems and offer related services was set up on Science Island, Hefei, East China's Anhui Province, on January 8 by the Hefei Institutes of Physical science (HFIPS) of the Chinese Academy of Sciences and Air Liquide Advanced Technologies (ALAT).

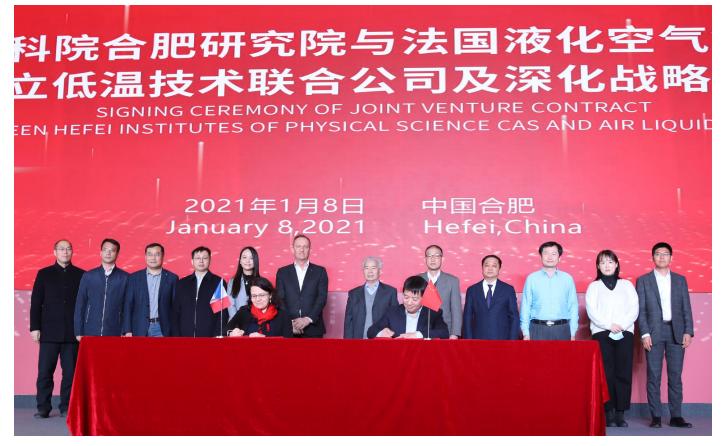
According to the contract HFIPS and ALAT agreed to collaborate on technology research, technology transfer, technology consulting and technical services in the field of new energy, as well as construction of helium cryogenic plants and sales of ancillary equipment.



Petra Pechoval, General Manager of Air Liquide Advanced Technologies (China), shakes hands with Song Yuntao, Vice President of HFIPS. [IMAGE: HFIPS]

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### 10 | International Cooperation



A cryogenic-based joint venture was set up on Science Island, Hefei, Anhui Province. [IMAGE: HFIPS]

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The efforts can be traced back three years to when the Institute of Plasma Physics (ASIPP) of HFIPS, encouraged by the French Atomic and Alternative Energy Commission (CEA), started talks with ALAT on cryogenics and magnetism in fusion.

"These two pillars of world scientists and technology could only eventually meet each other," said Alain Becoulet, head of the ITER engineering domain who joined the signing ceremony online as a long-term ASIPP partner. "The new joint venture will surely be a win-win for both ASIPP and Air Liquid."

The joint venture is not only a product of long-lived "deep and diverse cooperation between the two countries", but also a reflection that "science and technology cooperation can boost economic growth", according to Song Yuntao, Vice President of HFIPS.

"We are delighted to cooperate with the Hefei Institutes of Physical Science to promote the localized production and application of helium refrigeration systems and jointly contribute to the evolution of Big Science," said Nicolas Poirot, President and CEO of Air Liquide China. "Air Liquide will continue to integrate global resources and technologies, strengthen exchanges and cooperation with local enterprises and research institutions, and actively participate in the open innovation and economic and social development of Anhui Province and Hefei."

Established in 1994, the Cryogenic Technical Division of HFIPS is based on the Cryogenic Team of the Technique Centre and is mainly responsible for the design, construction, operation and maintenance of the 2kW@4.5K large-scale helium cryogenic system for EAST (Experimental Advanced Superconducting Tokamak). It focuses on cryogenic engineering and technology and is now undertaking the design and construction of the cryogenic system for the Comprehensive Research Facility for Fusion Technology (CRAFT).

Technologies and services for industry and health involving oxygen, nitrogen and hydrogen embody the scientific territory of ALAT, a world leader in gases, and have been at the core of the company's activities since its creation in 1902. Over the past decades ALAT has strengthened its expertise in extreme cryogenics.

> Source: Hefei Institutes of Physical science, Chinese Academy of Sciences

# Astronomy in the city

he first time I came to China was in 2013, at the beginning of my PhD, for the International Astronomical Union meeting in Lijiang. During that same trip I also had the opportunity to visit the Shanghai Astronomical Observatory (SHAO, CAS) and the group in which I am now working.

SHAO is located in a tall building in the city centre, an awesome site for an astronomical observatory. Because I love both astronomy and big cities, I knew Shanghai would offer me the perfect work-life balance experience, so I applied for a post-doctoral position here in 2015.

The research of the Shanghai group was very related to my PhD research and I already knew two faculty members and three postdocs in the group, therefore moving to China felt like the obvious choice for my career path. I was already in Shanghai in 2016 when I received the PIFI and was of course very glad I had the opportunity to extend my stay here, and with a much better salary.

My work focuses on the study of our home galaxy, the Milky Way. At the center of our galaxy there is a large population of stars which form "the Bulge". Together with the Galactic Dynamics group in SHAO, we have worked on studying the distribution and motion of stars in the Bulge. It has been a privilege to work in this group because of the expertise of my SHAO host and the hard work of a few very dedicated PhD students.

For me perhaps one of the biggest rewards was seeing the PhD students grow, become independent and start taking initiative. But the rewards have been numerous:

• having articles published in prestigious astronomical journals

• making new contacts both inside China and abroad while traveling for



conferences

• establishing new collaborations with visitors, who love to visit our institute

• collecting new data from world-class telescopes using the Chinese TAP services

• reaching out to the wider Chinese public through science competitions and the Astronomy Open Day at the Shanghai History Museum And, personally, I have made many local friends who work in other fields, some of whom are now my best friends. And in my first week in 2016 I adopted a cat called Kinu, who has been living with me since.

> Iulia Simion Shanghai Astronomical Observatory, Chinese Academy of Sciences

### 12 | News in Brief



Fishing boats amidst Arctic "sea smoke" near Qingdao, China on January 7. A result of frigid air passing over relatively warm water; the phenomenon is rare, even in the Arctic. [IMAGE: WANG SHAOQING]

### Upper ocean temperatures hit record high in 2020

Even with the small COVID-19-related dip in global carbon emissions due to limitations on travel and other activities, global ocean temperatures continued to break records in 2020. A new study by 20 scientists from 13 institutes around the world reported the highest ocean temperatures since 1955, from surface level to a depth of 2,000 meters.

The study was published in *Advances in Atmospheric Sciences* on January 13. It concluded with a plea to policymakers and others to consider the lasting damage that can be caused by warming oceans, and to redouble efforts to mitigate the effects of climate change.

Using a method developed by the Institute of Atmospheric Physics (IAP) of the Chinese Academy of Sciences (CAS), the researchers calculated the temperature and salinity of the oceans down to a depth of 2,000 meters, with data taken of all available observations from various measurement devices in the World Ocean Database.

They found that, in 2020, the upper 2,000 meters of the world's oceans absorbed 20 more zettajoules than in 2019.

That amount of heat could boil 1.3 billion kettles, each containing 1.5 liters of water.

This work was supported by the National Key Research & Development Program of China, the Strategic Priority Research Program of the Chinese Academy of Sciences, the Key Deployment Project of Centre for Ocean Mega-Research of Science, the U.S. National Science Foundation and the U.S. National Aeronautics and Space Administration.

Source: Institute of Atmospheric Physics, Chinese Academy of Sciences