Issue 6 2024

ZJUMEDICINE

SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

Driving The Development of Oral Medicine

Dialogue with DUAN Shengzhong

The Mystery of Wound Healing

Acceleratin Regeneration Process

A Meaningful Medical Lesson

Three Academicians Unveil the Path for Students

ZUSM at A Glance

Zhejiang University School of Medicine (ZUSM), founded in 1912, is one of China's best and oldest higher medical education institutions. Located in Hangzhou – one of China's most picturesque cities – ZUSM is organized across the School of Basic Medical Sciences, School of Brain Science & Brain Medicine, School of Public Health, School of Nursing, 7 clinical medical schools (School of Clinical Medicine, School of Obstetrics and Gynecology, School of Pediatrics, School of Stomatology) and a healthcare partnership network composed of 8 affiliated hospitals, numerous non-directly affiliated hospitals and cooperative hospitals.

It is home to more than 35,000 faculty members and over 8,300 students.

ZUSM believes that every global partner is unique and each project is irreplaceable. We collaborate with global partners for a better response to future medical challenges and strive to build a healthier future for all.

浙江大學 医学院
SCHOOL OF MEDICINE
ZHEJIANG UNIVERSITY

CONTENTS

Towards a Healthy Future: Promoting Public Health with Intelligence

WU Xifeng

Dean, School of Public Health, Zhejiang University
Vice President, The Second Affiliated Hospital of Zhejiang University School of Medicine
Executive Dean, The D. H. Chen School of Universal Health, Zhejiang University
Director, National Institute for Data Science in Health and Medicine, Zhejiang University
Dean, Center for Big-Data Research in Medical Insurance and Health Policy, Zhejiang University

You are an outstanding Chinese scholar in the field of public health. What attracted you to join the Zhejiang University School of Medicine?

I once pursued my master's degree at Zhejiang University, a place that holds cherished memories of my youth. The academic environment and teaching philosophy here had a profound impact on me. In recent years, Zhejiang University has achieved remarkable accomplishments. I hope to combine the experience and insights I have gained overseas with the university's outstanding resources to achieve new heights in the field of public health. This effort is my way of contributing to the Healthy China Initiative and the vision of a shared future for humanity.

You are taking the lead in developing the Healthy Zhejiang One Million People Cohort Project. Could you please give a brief introduction to this project?

My drive to advance this project is deeply-rooted in my recognition of and support for these national strategies—Healthy China and Digital China. This project is a large-scale, prospective population cohort study, whitch was initiated by Zhejiang University with strong support from the Zhejiang Provincial Party Committee and Provincial Government. It also involves collaboration with Zhejiang Provincial Center for Disease Control and Prevention and the Zhejiang Cancer Hospital. Our goal is to establish a cohort of one million participants, encompassing general populations, high-risk groups, and individuals with specific diseases. Currently, the project has been rolled out across 49 sites in both rural and urban areas of Zhejiang Province, with nearly 300,000 participants already enrolled. By integrating bio-molecular, personal, and societal data at micro, meso, and macro levels, our vision is to establish a globally leading, high-impact innovation platform for public health and the health industry. In the future, through the collection, integration, analysis, and application of mass cross-scale, multi-modal data, we seek not only to achieve groundbreaking advancements in fundamental research, but also to provide precise, robust health solutions for individuals, contributing China's wisdom and solutions to the building of a global community for health and well-being.

How should public health education and research adapt to the needs of future society, especially in terms of addressing the global public health crises?

I believe that the current priority is to strengthen interdisciplinary integration and collaboration as well as continuously promote the "Public Health + X" education model. This approach should break down the traditional academic barriers, deepen both the domestic and international partnerships, and focus on public health competencies. The goal is to cultivate professionals with multidisciplinary backgrounds. Simultaneously, key global public health challenges should be addressed through in-depth research that bridges laboratory work and clinical practice in an iterative, bidirectional process. Moreover, we must leverage emerging technologies such as big data, artificial intelligence and cloud computing to build a stronger global cooperation network, comprehensively enhance our capacity and efficiency for responding to public health crises.

Public health is not achieved in a single day, it is a responsibility passed down through generations. With the commitment of this lifetime, I pledge to safeguard every inch of the health defense line.

For more information
Contact us: ***xifengw@zju.edu.cn***

Driving the Development of Oral Medicine Through Scientific and Technological Innovations

DUAN Shengzhong

Dean of The Stomatology Hospital, Zhejiang University School of Medicine
Zhejiang University Qiushi Distinguished Professor

Building an innovation base for the integration of medicine, engineering, and information technology, focusing on clinically relevant cutting-edge scientific and technological questions, and striving to enhance the ability to innovate and translate, with the aim of driving the discipline development of oral medicine through scientific and technological innovations.

What is your current primary research area? And what significant research achievements have you made in these fields?

My current primary research area is the interdisciplinary study of oral diseases and systemic diseases. Funded by National Natural Science Foundation major projects, key projects, major research plans, and national key R&D programs, we have established a novel paradigm for the intertwined research between oral diseases and systemic diseases such as cardiovascular disease, metabolic disease and neurological disease, elucidated the direct relationships and associated mechanisms between them, and provided a basis for the joint prevention and control of oral diseases and systemic diseases.

What are the main challenges that the field of oral medicine is currently facing, and how do you think we should effectively respond to these challenges?

Oral medicine has developed rapidly in recent years, but we still face several challenges. For instance, there is insufficient public awareness of oral health, unbalanced oral health services and a shortage of oral medical resources, including a lack of medical professionals, medical facilities, and research funding.

To respond to these challenges, we can strengthen oral health education through various channels such as media, schools, and communities. We should implement oral health promotion projects to enhance the public's self-care awareness and capabilities. and increase support for grassroots oral medical institutions to improve their service capabilities.

Interdisciplinary collaboration is an important trend in the current development of scientific research development. In this respect, what initiatives and successful cases does Zhejiang University School of Stomatology have?

Zhejiang University School of Stomatology (ZJUSS) has made many attempts at interdisciplinary collaborations and yielded some positive results. Focusing on cutting-edge scientific research issues, we have achieved breakthrough in publishing papers in top international journals such as Cell through basic research, interdisciplinary integration and international collaborations. Domestically, we have pioneered the development of a biomimetic repair fluid for enamel, receiving over 10 million yuan in industry-academia collaboration support, and translational products have served more than 100,000 patients in over 3,000 medical institutions.

Looking into the future, what are your goals or visions in the field of oral medicine?

Our vision is "Creating a first-class discipline of stomatology, building an outstanding stomatology hospital, and climbing the peak of international stomatology." To achieve these grand goals, we will always adhere to the people-oriented philosophy and the pursuit of excellence, focus on improving patient satisfaction, comprehensively enhancing the quality of medical services. Keeping up with international trends in oral medicine, we will strengthen discipline development and enhance scientific research innovation and the ability to translate. I firmly believe that under the concerted efforts of all, we will become the benchmark in the field of oral medicine in China and contribute more to the development of international stomatology.

For more information
Contact us: ***duansz@zju.edu.cn***

Leading Global Research in Medical Genetics and Developmental Biology

The Zhejiang University Institute of Medical Genetics and Development was officially established in June 2024, located on the Qianjiang Campus of the Women's Hospital, Zhejiang University School of Medicine. adjacent to the Qiantang River. Covering approximately 5,000 m^2, the institute is equipped with state-of-the-art research facilities and serves as a modern hub for research, teaching, and translational medicine within the university. It is led by Professor HUANG Hefeng, an academician of the Chinese Academy of Sciences, Honorary Fellow of the Royal College of Obstetricians and Gynaecologists in the United Kingdom, and academician of the Academy of Sciences for the Developing World.

Leveraging the exceptional resources of its affiliated hospital and Zhejiang University, the institute integrates research across life sciences, public health, and clinical medicine. By focusing on innovative technological development and translational application, the institute aims to advance medical genetics and reproductive medicine. Under Professor HUANG's leadership, the institute's research is centered on three core areas: elucidating the mechanisms of reproductive and developmental disorders, developing early intervention strategies, and pioneering technologies for genetic birth defect prevention.

The Zhejiang University Institute of Medical Genetics and Development is dedicated to advancing the field of medical genetics and developmental science. The institute focuses on technological innovation while promoting research in basic science. It aims to establish a leading national research platform, cultivate top-tier researchers, and translate scientific discoveries into practical applications to improve public health.

The institute strives to make significant breakthroughs in the understanding of developmental and hereditary diseases, with the goal of preventing birth defects. By conducting cutting-edge research and fostering international collaborations, the institute seeks to establish itself as a global leader in the field of medical genetics and developmental science.

For more information
Contact us: ***jinglanzhang@foxmail.com***

To Create a World-Class Journal of Pediatrics

World Journal of Pediatrics (WJP) (ISSN 1708-8569), founded in 2005, is the first international pediatric journal in English in the Chinese mainland. Co-published by Children's Hospital, Zhejiang University School of Medicine and Springer Nature, WJP was also the first pediatric academic journal in Chinese mainland to be indexed by authoritative international databases such as SCIE and PubMed/Medline.

WJP is dedicated to reporting cutting-edge developments in pediatric medicine, promoting new technologies, achievements and experiences, disseminating pediatric medical knowledge, and fostering academic communication in pediatrics globally. Over the past two decades, WJP has become a prominent platform for international academic exchanges in the field of pediatrics.

Achievements and Impact

Global Rankings and Honors:
· In 2023, WJP ranked 4th among pediatric academic journals worldwide based on impact factor, maintaining its position as the top journal in Asia for 13 consecutive years.
· It was included in the "China Science and Technology Journals International Impact Enhancement Project" (D-level in 2014 and C-level in 2016).
· In 2019, it was selected as a T2 journal under the "Excellence Action Plan for China Science and Technology Journals" and upgraded to a leading journal in the second phase of the program in 2024.
· It is the only leading journal of Zhejiang University and was recognized as an Outstanding Science and Technology Journal in the 2024 China University Sci-Tech Journal Construction Demonstration Case Library.

Editorial Board:
The journal is co-edited by Professors ZHAO Zhengyan and SHU Qiang. Its editorial board comprises experts from 11 countries, with international members accounting for 58%. Among its 14 associate editors, all of whom are top pediatric specialists globally, five were listed in the "2024 Global Top 2% Scientists."

Submission and Citations:
· Submissions come from 110 countries and regions worldwide, with international contributions accounting for approximately 60%.
· From 2020 to 2024, the journal received over 1300 submissions annually.
· Cited articles come from over 100 countries, with international citations making up 62%.

Dissemination and Brand Development

WJP keeps pace with international trends by building a multidimensional communication matrix to enhance the visibility and impact of its publications. Its dissemination platforms include

Bilibili, WeChat (official accounts and video channels), Twitter (X), Bluesky, Medium, and others. Through diverse forms and approaches, WJP aims to promote high-quality academic achievements effectively.

Supported by its high-quality content and international vision, WJP has a high reputation in the global pediatric academic community, focusing on significant global pediatric health needs and addressing key clinical challenges.

For more information
Contact us: **wjpch@zju.edu.cn**

The Mystery of Wound Healing-Accelerating Regeneration Process

Common types of tissue damage, such as external injuries from bumps and bruises, surgical wounds, and muscle degeneration due to aging, are an inevitable part of life. The speed at which wounds heal and tissues regenerate has a direct impact on overall health. Inflammation plays a vital role in this repair process, with some clinical studies suggesting that using anti-inflammatory drugs too soon after surgery may actually slow down wound healing. This underscores the importance of understanding how early inflammation contributes to later stages of tissue rebuilding.

A breakthrough study by Professor WANG Di's team at Zhejiang University School of Medicine sheds new light on this process. The researchers found that when human tissue is damaged, macrophages—critical immune cells—will be activated into a hyperactive state. In this state, the cells create pores on their membranes using a protein called GSDMD, allowing them to release specific lipid molecules that promote tissue repair. The findings, published on September 11 in ***Nature*** in an article titled "Gasdermin D-mediated metabolic crosstalk promotes tissue repair", offer new insights into how the body heals itself.

The potential of "hyperactivation"

Macrophages, which play a central role in the body's inflammatory response, are present throughout the human body. A critical player within these cells is the protein GSDMD, which has long been recognized for its role in defending against pathogens and inflammatory diseases by triggering inflammation. Previous studies suggested that when the body is under threat, GSDMD is activated to form pores in cell membranes, leading to a type of cell death known as pyroptosis.

However, a breakthrough discovery by the research team revealed that during tissue repair, these GSDMD pores in macrophages don't necessarily result in cell death. Instead, the macrophages enter a "hyperactive" state, retaining critical functions that help the body heal.

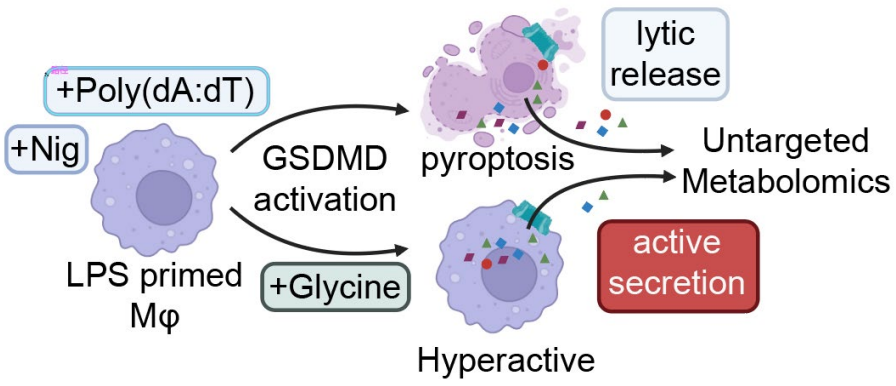
The big question: how do these hyperactive macrophages contribute to tissue repair?

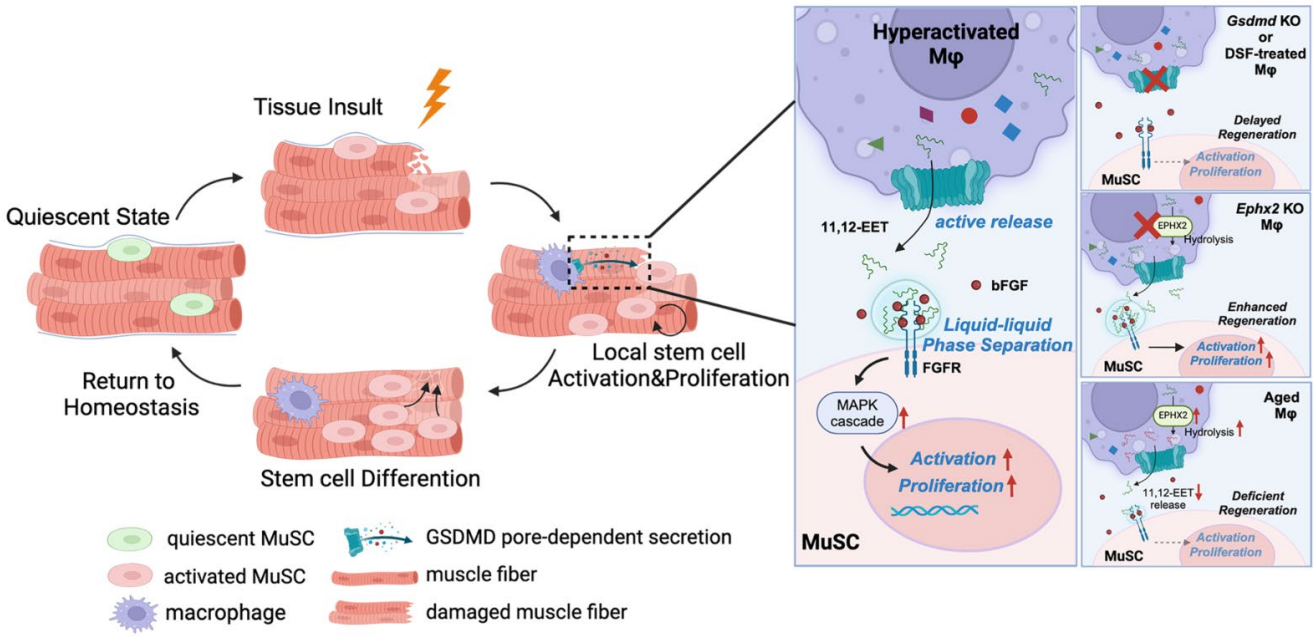
The researchers postulated that these macrophages might secrete bioactive metabolites and other factors through GSDMD pores to influence adjacent cells or shape the surrounding tissue environment.

To their surprise, they found that in addition to releasing inflammatory signals, hyperactive macrophages also secrete a specific lipid metabolite called 11,12-EET through GSDMD pores. This molecule, found in both lab-grown macrophages and injured muscle tissue, plays a crucial role in the healing process, actively boosting the repair of damaged tissue.

The miraculous "repair agent"

Tissue repair hinges on the ability of stem cells to proliferate and differentiate. However, stem cells don't work alone; they need the help of surrounding cells to thrive. Imagine stem cells as seeds with unlimited potential. For these seeds to sprout and grow, they need nourishments from the "soil," or the microenvironment of the damaged tissue.





As essential players in this microenvironment, macrophages fulfill multiple roles by releasing pro- and anti-inflammatory mediators, growth factors, and other bioactive molecules. However, the metabolic communication between macrophages and other types of cells—and how these exchanges help coordinate tissue repair—have largely remained enigmatic.

To address this, the researchers zeroed in on a key factor: 11,12-EET. They employed a two-pronged approach, supplementing 11,12-EET externally and knocking out its degrading enzyme in macrophages of mice to boost its endogenous level. Both approaches provided compelling evidence that 11,12-EET is crucial for activating and proliferating muscle stem cells.

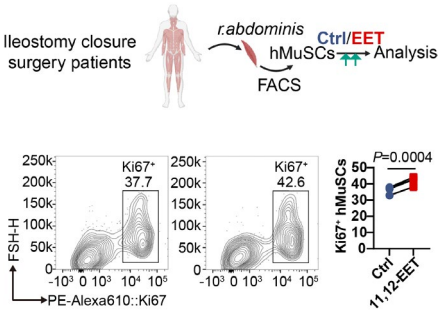
More importantly, the team found that the regenerative potential of 11,12-EET depends on GSDMD creating effective metabolic communication channels between macrophages and muscle stem cells. This discovery opens the door to a new understanding of how macrophages and stem cells interact, and sheds fresh light on the critical function of membrane pores in tissue repair.

The versatile role of 11,12-EET

One of the biggest challenges in tissue repair is the low concentration of regenerative factors in the damaged areas, making it difficult for the body to trigger a swift and efficient healing process. This is where the lipid molecule 11,12-EET comes in, playing a critical role in amplifying the body's repair signals. By studying the behavior of primary muscle stem cells, both with and without exposure to 11,12-EET, the researchers discovered that the molecule helps gather growth factors in the damaged tissue. This leads to a more favorable environment for healing, accelerating the regeneration process.

Given 11,12-EET's ability to activate stem cells, could this function have broader applications?

The team tested its therapeutic



potential on models of muscle, corneal, and skin injuries. The results were impressive—11,12-EET exhibited broad tissue-repair capabilities. What's more, it even helped aging mice regain muscle vitality by increasing their muscle stem cell reserves and stimulating the proliferation of human muscle stem cells.

"This offers strong support for the clinical use of 11,12-EET," said CHI Zhexu, the first author of the paper. "It opens up new vistas for treating wounds, tissue damage, and muscle degeneration in aging patients."

For more information
Contact us: ***diwang@zju.edu.cn***

Ketamine Targets Specific Brain Region to "Fire First Shot" to Depression

For decades, ketamine was primarily recognized as an anesthetic and a recreational drug known as "Special K." Its remarkable capacity to rapidly alleviate depression, however, has transformed its reputation, turning it into a pivotal tool in mental health treatment. This transformation has been driven by advancements in understanding the mechanisms underlying ketamine's antidepressant effects.

Professor HU Hailan's team at Zhejiang University has identified the lateral habenula (LHb), often referred to as the brain's "anti-reward center," as a critical brain region for ketamine's action. Their research demonstrates that ketamine's initial interaction occurs at NMDA receptors on LHb neurons, revealing the drug's precise brain-region-specific effects and mapping neural pathways from the LHb to the hippocampus.

In studies published in ***Nature*** in 2018 and 2023, HU's team revealed ketamine's rapid and long-term antidepressant effects. Additionally, their latest study, published in ***Science*** on August 9, 2024, further elucidates these mechanisms, emphasizing the role of LHb NMDA receptors. Together, these findings construct a comprehensive framework that not only informs ketamine's clinical application but also guides the development of new antidepressant therapies.

Is it parallel or sequential?

While ketamine's primary target is known to be NMDA receptors, which are broadly distributed across the brain, it remains unclear whether its effects are synchronous across regions or sequential. Answering this question is critical for deciphering ketamine's action mechanism.

In 2018, HU's team demonstrated that ketamine suppresses the burst firing of LHb neurons to alleviate depression. Other studies, however, highlighted ketamine's impact on the hippocampus and cortex, suggesting positive effects on neural plasticity. Whether these processes are sequential or simultaneous was unresolved until HU's latest study.

Using electrophysiological and in vivo recording techniques, HU's team administered ketamine to depressive-like mice and tracked neural responses. Within minutes, neuronal activity in the LHb significantly decreased, while no immediate changes were observed in the hippocampus. This indicates that the LHb is the first brain region to respond to ketamine, underscoring the region-specific nature of its action.

How does ketamine anchor to a specific brain region?

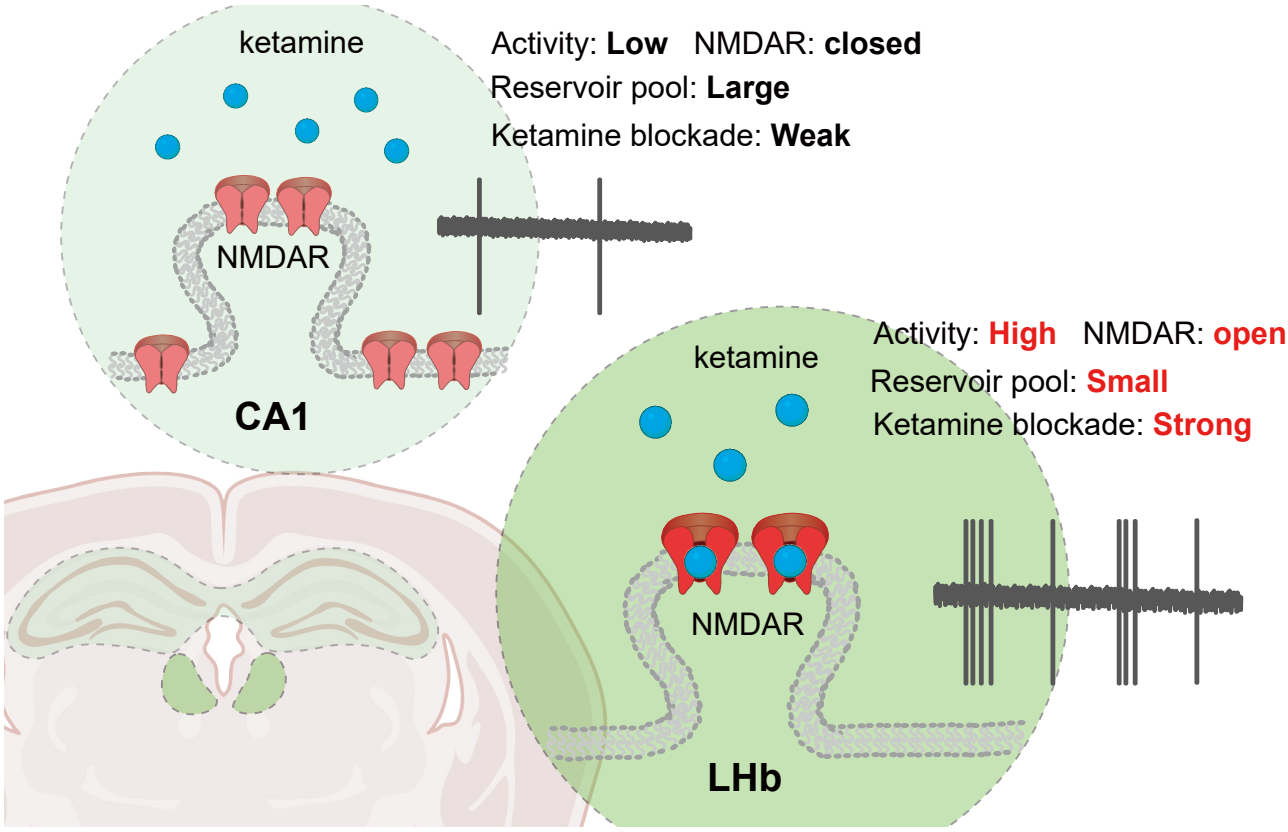
The specificity of ketamine's action in the LHb is attributed to the activity-dependent nature of NMDA receptors. As ion channels, NMDA receptors only open during neuronal activity, allowing ketamine to bind and block them. The team found that neuronal activity levels in the LHb are significantly higher than in hippocampal pyramidal neurons, providing ketamine with more opportunities to act in this region.

Further analysis revealed that LHb neurons have a lower synaptic reserve of NMDA receptors compared to hippocampal neurons. This limited reserve allows even small doses of ketamine to efficiently block NMDA receptors in the LHb, enhancing its antidepressant efficacy. By modulating neuronal activity in these regions, the team reversed their sensitivity to ketamine, providing experimental evidence for the drug's brain-region-specific action.

Unraveling Upstream and Downstream Interactions

While the LHb plays a pivotal role in ketamine's antidepressant effects, understanding its upstream and downstream neural interactions is essential. Ketamine has been shown to increase serotonin and brain-derived neurotrophic factor (BDNF) levels in the hippocampus, yet these changes appear to be secondary to its action in the LHb.

To investigate this, HU's team selectively knocked out the NR1 subunit of NMDA receptors in LHb neurons. Following ketamine administration, the rapid antidepressant effects were



abolished, and no significant increase in serotonin or BDNF was observed in the hippocampus. These findings confirm the LHb as the initial site of ketamine's action, with downstream regions contributing to its broader effects.

Bridging Theoretical Frameworks

Ketamine's antidepressant mechanisms have been explained through two main hypotheses. The "disinhibition" hypothesis posits that ketamine alleviates depression by suppressing overactive inhibitory signals in the brain, while the "neuroplasticity" hypothesis highlights its role in enhancing synaptic connectivity and neural growth. HU's latest findings bridge these perspectives, demonstrating that ketamine's effects on the LHb initiate a cascade of downstream neuroplastic changes, integrating both mechanisms into a unified framework.

Clinical Implications

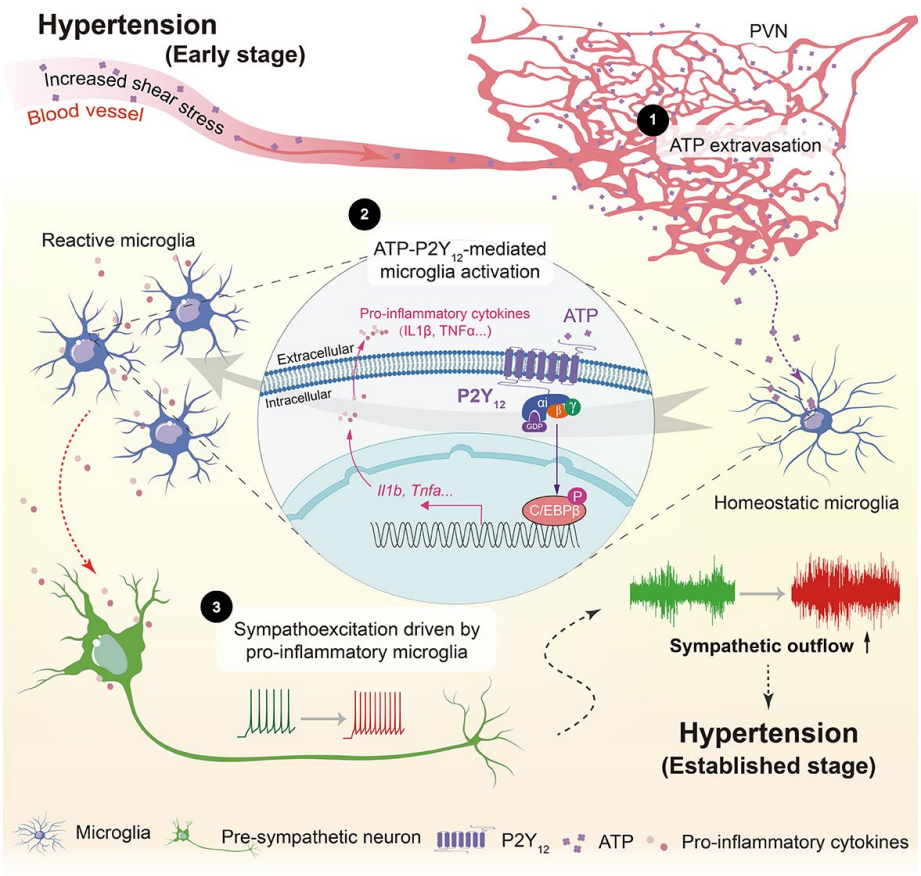
The LHb-centered framework developed by HU's team has significant clinical implications. Traditional treatments for depression, such as deep brain stimulation (DBS), rarely targeted the habenula. However, inspired by the team's 2018 findings, larger-scale DBS studies focusing on the habenula have shown promising results. At hospitals in Shanghai and Beijing, DBS targeting the LHb has achieved notable efficacy in treating treatment-resistant depression. "This clinical feedback validates our theoretical framework and motivates us to further explore the core mechanisms of depression," says HU. By unraveling the intricacies of ketamine's action, HU's research not only advances scientific understanding but also offers hope for novel therapeutic strategies to combat depression.

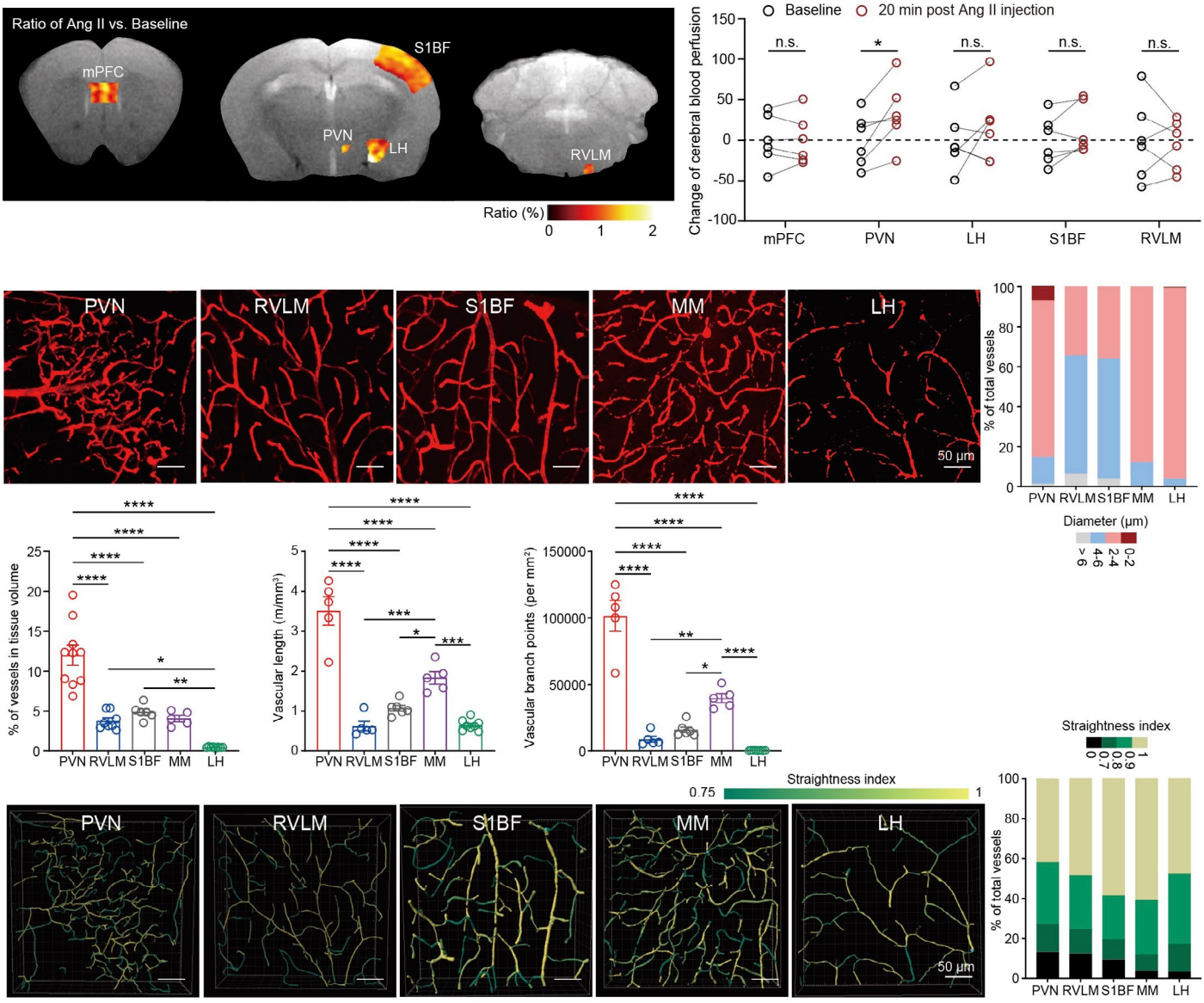
For more information
Contact us: ***huhailan@zju.edu.cn***

Butterfly Effect: Brain Immune Cells Bridge Hemodynamic Chaos to Sympathetic Neurons

High arterial blood pressure (*A.K.A.* hypertension) attacks over 1/3 of adult population worldwide. As a "silent killer", hypertension exacerbates lethal outcome of cardiovascular diseases such as heart attack, heart failure, stroke and kidney failure. Despite its etiological obscurity, a pronounced elevation of sympathetic nerve activity (SNA) has been well recognized in propelling hypertension progression. Renal sympathetic denervation has been successfully used to treat resistant hypertension patients in clinic, underscoring the pivotal role of sympathoexcitation in hypertension. However, the ultimate question, i.e., how SNA is unleashed during hypertension remains unresolved.

On August 7, 2024, ***Immunity*** published a study entitled "Microglia in the hypothalamic paraventricular nucleus sense hemodynamic disturbance and promote sympathetic excitation in hypertension" by Dr. SHI Peng from Zhejiang University Institute of Translational Medicine. In this study, it shows that a subtle but significant increase of plasma ATP triggers microglia, the resident immune cells in the brain, switching from a surveillant towards a reactive state. ATP is an intracellular "cash" to supply energy for biochemical reactions. An increase of extracellular ATP is considered as a danger signal to immune cells. Nearly all immune cells express various purinergic receptors, which render the "police cells" remarkably alert to cell or tissue damages. When blood cells such as red blood cells experience increased sheer stress due to blood pressure increase, intracellular ATP would be released via transiently opened pannexin channels, leading to an ATP elevation in blood plasma. This blood-borne ATP is detected by purinergic receptors $P2Y_{12}$ of microglia. By using a series of loss-of-function approaches, the researchers finally validated that ATP-$P2Y_{12}$ ligation is required for microglial activation, which subsequently promotes the electronic activity of sympathetic neurons by secreting proinflammatory mediators. Consequentially, it leads to a massive and sustained elevation in SNA and blood pressure. More importantly, this study unravels a precedently unappreciated microanatomic structure in the brain which predisposes the paraventricular nucleus (PVN), a hub of sympathetic regulation, susceptible to hemodynamic alteration. The research group found that the PVN possesses the highest microvessel density, the thinnest lumen diameter, the least straightness, and the most ramification





compared with the other examined brain regions (Figure 1). As such, the cerebral blood flow would be slower and leave sufficient time window for small molecules, e.g., ATP (507 Da) to undergo extravasation. With the aid of magnetic resonance imaging (MRI), this study found that transient increase of arterial blood pressure resulted in an exclusive increase of blood perfusion in the PVN rather than other brain regions (Figure 2). Altogether, the data strongly indicate that a unique vascular topology renders the PVN receiving more blood-borne ATP in blood pressure increase, which drives a sympathetic overflow in hypertension.

Blood pressure is a vital factor warranting organs and tissues to receive sufficient blood perfusion, which is tightly regulated by a series of neuronal circuitry including evolutionally conserved negative feedback. Vasoconstriction of arteries or arterioles caused by persistently increased SNA is highly associated with hypertension. How SNA is raised despite the existing negative brakes in hypertension is a long-lasting mystery. Current study provides a novel answer to that. Local microglia would sense blood chemicals and initiate a cross-talk with neurons, which relies on a featured vasculature topology in the PVN. Breaking central ATP-$P2Y_{12}$ signal pathway could be a potential therapeutical intervention for hypertension and other relevant diseases.

For more information
Contact us: ***ship@zju.edu.cn***

"TriLoS" Framework for Gene Networks Design

The cells in our body function like "miniature computers," incessantly receiving, processing, and transmitting information, and promptly reacting to these signals. Could we control these cells and empower them to conduct complex calculations and logical operations, like computers?

On July 31st (CST), a research team led by Dr. SHAO Jiawei from the Fourth Affiliated Hospital, Zhejiang University School of Medicine, International School of Medicine, Zhejiang University, and the Regeneration and Aging Center of International Institutes of Medicine, Zhejiang University published their latest research findings in ***Cell***. Their research paper, titled "Multi-layered computational gene networks by engineered tristate logics," introduces a tristate-based logic synthesis (TriLoS) framework, which "programs" human cells to perform intelligent biocomputation and cell-based therapies.

Designing a "Programming Language" for Cells

Computers carry out complex calculations through applying logical operations based on two voltage states: "0" and "1". Similarly, the gene expression system within cells has two states—active gene expression (ON-state) or inactive gene expression (OFF-state). Researchers have been working to introduce the "0/1" logic from the field of electronic engineering to enable cells to perform similar logical operations.

For instance, by designing gene circuits that can function as "biological logic gates," we can enable human cells to process biological signals and perform complex digital operations, such as addition and subtraction. This is akin to "implanting" computational capacity into cells, allowing them to execute commands like computers.

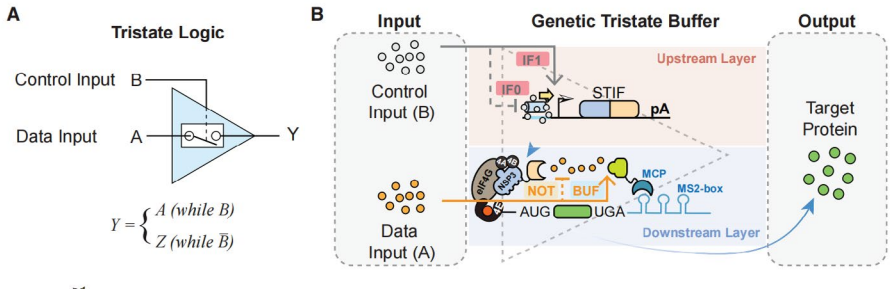
However, progress in mammalian cell biocomputing has been difficult due to the intricacy of gene regulation in mammalian cells, the immaturity of the available artificial gene circuits, and the lack of a comprehensive theoretical framework. Therefore, multi-layered computational gene networks within single cells ground to a halt at half-adders and half-subtractors in 2012.

To overcome these technical challenges and establish a comprehensive theoretical framework for designing complex gene networks and biocomputing, the team introduced TriLoS, a programming strategy for gene networks based on the principle of "tristate circuits," thus providing a "language" for cell programming.

Expanding the Potential of Cell Computing

"Tristate circuits", as the term suggests, possess three output states. In addition to the high voltage state (1) and low voltage state (0) in general logic circuits, there is a high-impedance (Z) state, which is controlled by the upstream input signal (B). For instance, when the upstream control signal is activated, the downstream will produce an output of 0 or 1, based on the input signal A. However, when the control signal is inactivated, the output will become a high-impedance state Z, equivalent to a "silent" state. Thus, using TriLoS to construct multi-layered gene networks ensures a smooth connection between the modules while maintaining fast, efficient signal transmission.

Researchers have discovered that gene



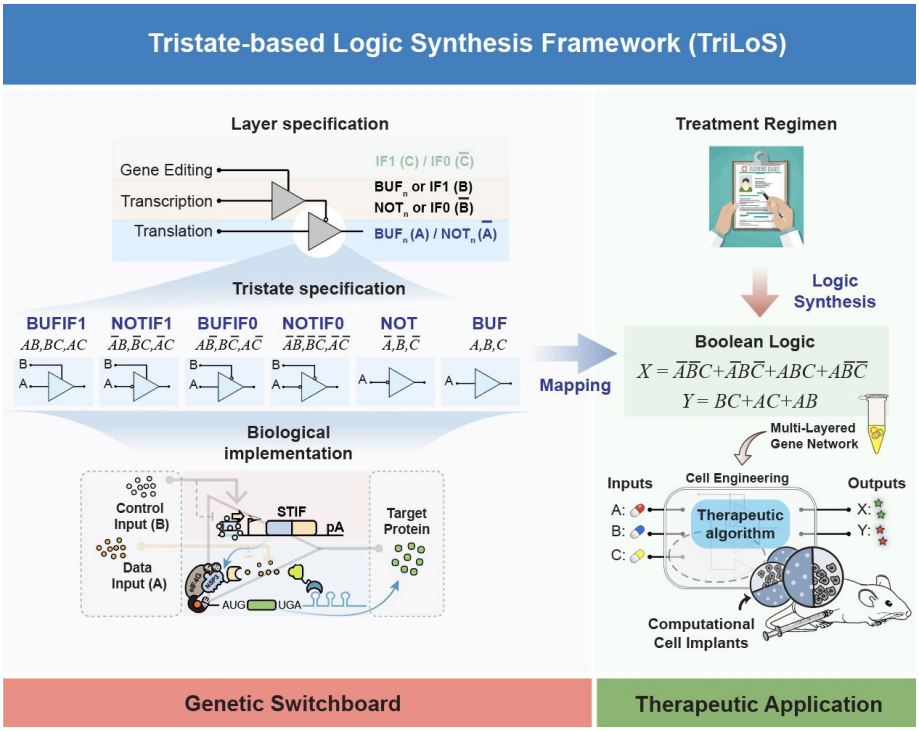
expression regulation within cells can also be abstracted into a tristate buffer model. For instance, transcriptional regulation from DNA to the eventual protein serves as the upstream control signal, while translational regulation acts as the downstream input and output. By designing these "biological tristate buffers," researchers have successfully constructed complex gene regulatory networks, thereby endowing cells with significant computational capabilities.

Utilizing the "biological programming language," researchers can design tailored "applications" for cells, thus equipping them with computational functions. This approach addresses the current research paradigm, which relies heavily on empirical methods involving blind design and repetitious trial-and-error. For instance, cells can be engineered to possess the computational capabilities of an adder or subtractor, and even to perform more complex logical operations. This advancement expands the computational potential of cells and holds promise for the refinement of precision medicine in the future.

Making Cells "Smart Doctors"

After endowing cells with new computational capabilities, researchers further applied them to the precise treatment of diseases.

Metabolic diseases exhibit unique progression patterns. While successfully breaking through the limits of computation within single cells, the team has also advanced the conceptualization of disease treatment from a biocomputational perspective, by simplifying the treatment plans for metabolic diseases into mathematical formulae. After that, following signals matched by the TriLoS theoretical framework, cells can act accordingly to develop therapeutic algorithms (APPs) and tailor intelligent cellular treatment plans related to a range of metabolic diseases.



In essence, the future holds the potential to transform cells into "smart doctors," capable of autonomously identifying disease types and guiding the production of therapeutic proteins, thereby achieving more precise phased, hierarchical, and personalized treatments.

For instance, researchers have categorized diabetes into three types, based on its severity and etiology: obesity, type 2 diabetes, and type 1 diabetes, and have also formulated corresponding treatment plans employing glucagon-like peptide 1 (GLP-1) or insulin (INS). Unlike the previous methods, which allowed an intelligent cell to address only one type of diabetes at a time, the complex cell computation enabled by TriLoS can monitor different disease types without changing the implanted intelligent cells and adjust the therapeutic protein production, thus identifying more precise treatment.

"We hope that, through this research, we will be able to apply the principles of biocomputing to precise treatment by intelligent cells and utilize human cells with programming capabilities in order to create digital, logic-based treatments for complex diseases, thereby rendering treatments more intelligent, precise, and personalized," stated Dr. SHAO Jiawei.

For more information
Contact us: ***jiaweishao@zju.edu.cn***

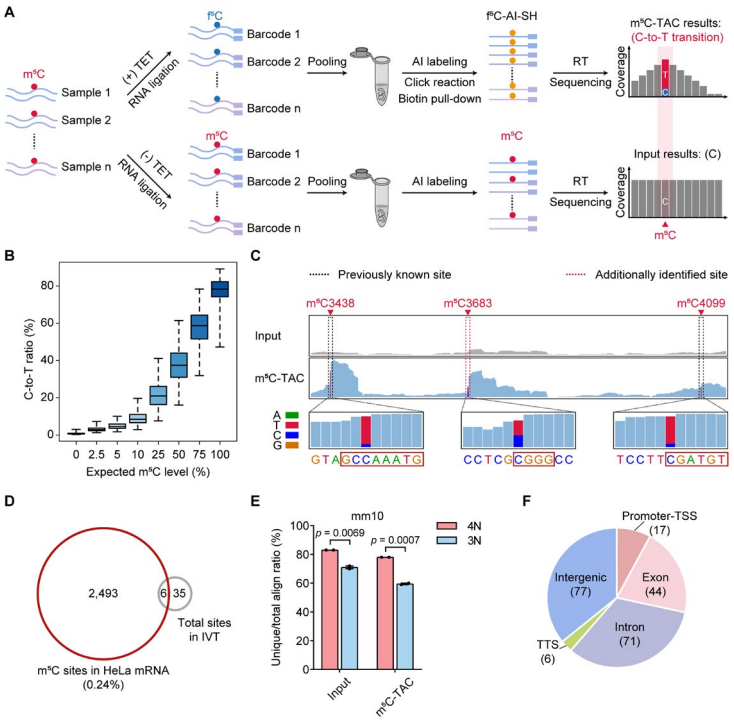
A Bisulfite-free Sequencing Technology for Base-resolution m^{5}C Profiling across the Mammalian Transcriptomes

RNA 5-methylcytosine (m^{5}C) modification is a conserved post-transcriptional modification widely distributed in rRNA, tRNA, and mRNA. The m^{5}C methylation on mRNA is mainly catalyzed by methyltransferases, including NSUN family proteins and DNMT2, and can be further oxidized to hm^{5}C and f^{5}C by TET family proteins and ALKBH1. RNA m^{5}C methylation could be recognized by specific binding proteins and thus participate in regulating various aspects of RNA metabolism, including export, stability, splicing, and translation.

The exploration of the function of RNA m^{5}C methylation requires sensitive and accurate detection technologies. Currently, bisulfite sequencing (BS-seq), in which unmodified cytosine (C) is converted to uracil (U) and m^{5}C remains intact, has been widely used to identify m^{5}C methylations by detecting the unconverted Cs. Although BS-seq is simple, convenient, and can achieve m^{5}C methylation detection at base resolution, its application in mRNA is hindered by three main challenges: 1) Indirect detection of m^{5}C, relying on the efficient conversion of unmodified C, with incomplete conversion potentially leading to false positives; 2) Harsh reaction conditions that result in RNA degradation, limiting the detection of low-input samples and low-abundance RNAs; 3) A reduction in sequence complexity after C is converted to U, which affects alignment accuracy and limits the detection of m^{5}C in low-sequence-complexity RNAs. Although several bisulfite-free RNA m^{5}C detection methods have been developed, each has its limitations and cannot achieve unbiased detection of RNA m^{5}C methylation at base-resolution across the transcriptome.

On July 12th, 2024, Prof. LI Xiaoyu's group from Zhejiang University School of Medicine, in collaboration with Prof. YI Chengqi's group from Peking University School of Life Sciences published an article entitled "Base-resolution m^{5}C profiling across the mammalian transcriptome by bisulfite-free enzyme-assisted chemical labeling approach" in the journal ***Molecular Cell***. This study developed a novel bisulfite-free detection technology, m^{5}C-TAC-seq (m^{5}C detection strategy enabled by TET-assisted chemical labeling). This technology combines TET-assisted m^{5}C-to-f^{5}C oxidation with selective chemical labeling, enabling direct base-resolution m^{5}C detection through pre-enrichment and C-to-T transitions at m^{5}C sites in the transcriptome-wide manner.

The technology optimizes the TET

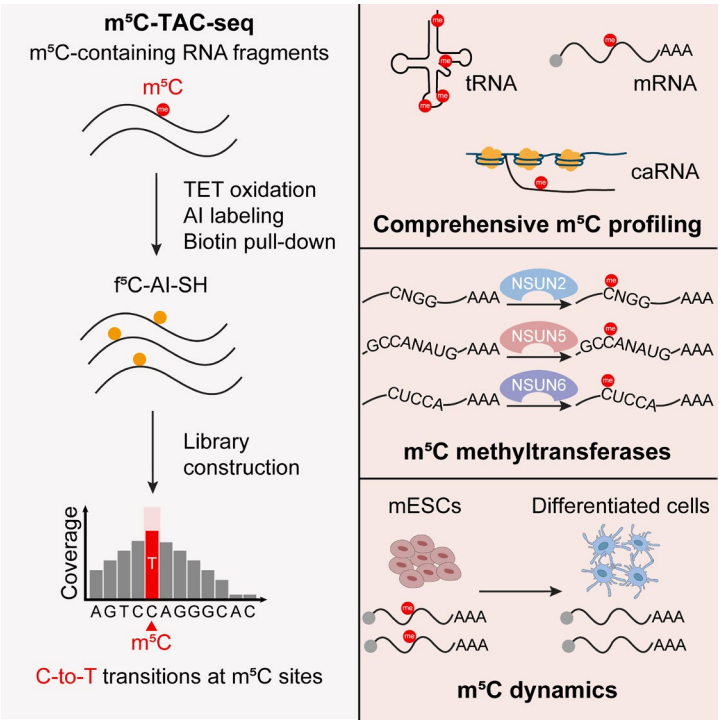


reaction to oxidize RNA m^5C to f^5C, and further utilizes the azido derivative of 1,3-indandione (AI) to specifically label f^5C. The labeled product not only induces a C-to-T transition, but also allows for enrichment through click-reaction and biotin pull-down, enabling direct detection of m^5C methylations at base- resolution. This direct detection feature enables sensitive detection of m^5C sites with methylations levels as low as 2.5%. Furthermore, the reaction conditions of this method are mild and do not affect the nucleotide composition of the transcriptome, making it applicable to low-abundance and low-sequence-complexity transcripts. Additionally, by using a multiplexing library construction strategy, this technology reduces batch effects between samples and more importantly, achieves semi-quantitative detection of m^5C methylation.

To evaluate the sensitivity and accuracy of m^5C-TAC-seq, researchers first applied it to rRNA and tRNA with known m^5C sites. In rRNA, m^5C-TAC-seq not only accurately detected the known m^5C sites but also identified an new site, m^5C3683, along with its corresponding methyltransferase, thereby demonstrating the sensitivity of this technology. For tRNA, which has strong secondary structures and low sequence complexity, m^5C-TAC-seq identified all reported m^5C sites and their corresponding methyltransferases. Furthermore, by preserving the quaternary nucleotide composition, it enabled accurate detection of different tRNA isodecoders, further highlighting the robustness of this technology.

Using m^5C-TAC-seq, researchers profiled the base-resolution m^5C methylomes of HeLa, HEK293T, and mESC, identifying 2,499, 765, and 664 m^5C sites, respectively. The reliability of these sites were further validated through the modification-free transcriptomes. More importantly, the methyltransferases for most m^5C sites were identified, further confirming the accuracy of these sites. In addition to the known NSUN2 and NSUN6, the rRNA methyltransferase NSUN5 can also act on mRNA. Further comparison with BS-seq revealed that m^5C-TAC-seq showed high accuracy and sensitivity in detecting low-stoichiometry sites, emphasizing the robustness of its direct detection strategy.

In addition, using m^5C-TAC-seq, researchers found that the methylation levels of most mRNA m^5C sites were downregulated during mESC differentiation, and were enriched in transcripts associated with the cell cycle and cell division, suggesting that m^5C methylation may play a role in mESC differentiation. Facilitated by the mild reaction conditions and preservation of the nucleotide composition, m^5C-TAC-seq allowed the identification of m^5C sites on chromatin-associated RNA (caRNA), which contains a large number of low-complexity sequences, demonstrating the importance of the preserving quaternary nucleotide for detecting m^5C methylation on low-complexity sequences.

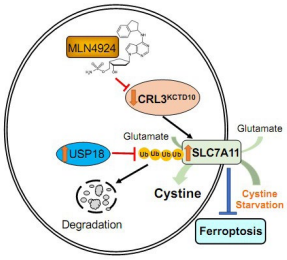


Conclusion

In summary, this study has developed a new technology, m^5C-TAC-seq, for the direct detection of m^5C methylation, demonstrating its sensitivity and accuracy. m^5C-TAC-seq can be applied to various RNA species, including low-abundance and low-sequence-complexity RNAs, as well as sites with low m^5C levels. Additionally, it enables detection of m^5C dynamics across various biological processes, which contributes to a deeper understanding and facilitates the exploration of the biological functions of RNA m^5C methylation.

For more information
Contact us: ***xiaoyu_li@zju.edu.cn***

The CRL3^{KCTD10} Ubiquitin Ligase-USP18 Axis Coordinately Regulates Cystine Uptake and Ferroptosis by Modulating SLC7A11



Cell death is essential for normal development and homeostasis maintenance, which is often dysregulated in a plethora of human diseases, including cancer. A hallmark of cancer cells is their ability to evade cell death, which contributes to tumor development and therapeutic resistance. Among various types of cell death defined, ferroptosis, which is driven by iron-dependent lipid peroxidation, is of particular interest because is morphologically, genetically and biochemically unique. Its induction can selectively kills certain types of cancer cells, offering the potential to overcome the resistance of cancer therapies.

Cystine, an oxidative cysteine dimer, was transported into cells via system Xc^-, a heterodimeric plasma membrane cystine/glutamate antiporter consisting of the transporter subunit solute carrier family 7 member 11 (SLC7A11) and the transmembrane regulatory subunit SLC3A2. System Xc^-, especially SLC7A11, is regarded as a cardinal regulator of ferroptotic cell death. Although SLC7A11 plays an important role in cystine transport, and acts as a crucial determinant of ferroptosis, how SLC7A11 stability is coordinately regulated by pairs of E3-deubiquitylase, and under what physiological and pathological conditions this regulation occurs, remains elusive.

Neddylation, an ubiquitylation-like posttranslational modification, is a biochemical reaction to attach NEDD8 onto the lysine residue of a substrate. Cullin family proteins, the scaffold component of Cullin-RING ligase (CRL), are the best-characterized physiological substrates of neddylation. Cullin neddylation activates CRLs, the largest family of E3 ubiquitin ligases that control many biological processes through ubiquitylation and degradation of many key signaling proteins. Recently, the authors found that neddylation inactivation remarkably alters global metabolic profiling via inhibiting mitochondrial function and promoting glycolysis, and also induces glutamine uptake and metabolism by targeting CRL3^{SPOP} E3 ligase. Given that cystine metabolism via Xc^- system orchestrates glutamine metabolism and sustains tumor cell growth, it is likely that an undefined neddylation-CRL(s) system controls the levels and function of Xc^- system to regulate ferroptosis.

"We found that the stability of SLC7A11, a key determinant for cystine transport and ferroptosis, is regulated negatively by CRL3^{KCTD10} E3 ligase, and positively by USP18 deubiquitylase" said Dr. SUN Yi, a professor at Cancer Institute of the 2nd Affiliated Hospital and Institute of Translational Medicine, Zhejiang University School of Medicine. The findings were published in ***PNAS*** on July 9, 2024.

The team found that MLN4924, a small molecule inhibitor of neddylation modification, promotes cystine uptake by inactivating CRL3 to cause accumulation of SLC7A11. Mechanistically, CRL3^{KCTD10} act as an E3 ligase, whereas USP18 acts as a DUB for SLC7A11, and the levels of the KCTD10–USP18 axis are coordinately regulated in response to environmental cystine for precise control of the SLC7A11 stability. Biologically, KCTD10 and USP18 confer the sensitivity or resistance to ferroptosis of breast cancer cells, respectively, via targeting SLC7A11. In breast cancer tissues with reduced cystine abundance, a negative correlation between KCTD10 and SLC7A11 and a positive correlation between USP18 and SLC7A11 were observed, respectively. Therapeutically, the combination of MLN4924 with SLC7A11 inhibitor Erastin or its derivative IKE markedly enhanced the killing of breast cancer cells both in vitro and in vivo.

"The study highlights a novel regulatory axis (CRL3^{KCTD10}-USP18/E3-DUB) crucial for SLC7A11 stability and ferroptosis, offering insights into potential anti-cancer strategies" said Dr. SUN Yi.

A scheme to show a mechanistic insight into how the CRL3^{KCTD10}/E3-USP18/DUB axis regulates ferroptosis by modulating SLC7A11 stability.

For more information
Contact us: ***yisun@zju.edu.cn***

World's First Expert Consensus on the Diagnosis and Treatment of Macrolide-Resistant Mycoplasma Pneumonia in Children

On August 14, 2024, the Expert Consensus on the Diagnosis and Treatment of Macrolide-Resistant Mycoplasma Pneumoniae Pneumonia in Children was published online in the ***World Journal of Pediatrics***. The consensus was led by Professor CHEN Zhiming from the National Clinical Research Center for Child Health (NCRCCH) at the Children's Hospital, Zhejiang University School of Medicine. This is the world's first consensus on the diagnosis and treatment of pediatric macrolide-resistant Mycoplasma pneumoniae (MRMP) pneumonia.

Since the first report on MRMP in children was published by Japanese scholars in 2001, MRMP has become more prevalent worldwide, especially in East Asia, where the isolation rate of MRMP has reached as high as 70-90%. This poses a serious challenge to the treatment of Mycoplasma pneumoniae infections in children. In recent years, MRMP has become an epidemic on the Chinese mainland, with the isolation rate of MRMP in clinical strains exceeding 90% in most cases. This has resulted in major challenges for Chinese patients, society, and pediatricians. However, due to various factors, there has been a lack of global consensus on the diagnosis and treatment of MRMP in children, particularly regarding antimicrobial therapy for MRMP, which remains highly controversial.

Against this backdrop, the Children's Hospital, Zhejiang University School of Medicine invited 29 Chinese experts majoring in pediatric pulmonology and epidemiology to conduct evidence collection using electronic databases, such as PubMed, Embase, Web of Science, CNKI, Medline, and the Cochrane Library. They summarized and studied MRMP data from various countries and regions, with a specific focus on the Chinese context. This culminated in the development of the Expert Consensus on the Diagnosis and Treatment of Macrolide-Resistant Mycoplasma Pneumoniae Pneumonia in Children. The release of this consensus aims to guide and standardize pediatricians' approaches to the diagnosis and treatment of MRMP, reduce the irrational use of antimicrobial drugs, decrease the occurrence of sequelae, lower the mortality rates, and alleviate the medical burden.

For more information
Contact us: ***chxczx@zju.edu.cn***

The First in China to Use a Leadless Pacemaker+ Pulsed Ablation to Solve Complex Arrhythmia

The Fourth Affiliated Hospital of Zhejiang University School of Medicine has achieved a significant milestone by performing China's first interventional operation combining a leadless pacemaker with pulsed ablation to treat complex arrhythmia. The patient, a 72-year-old woman, had suffered from sudden blackouts and dizziness due to severe sick sinus syndrome with paroxysmal rapid atrial fibrillation.

Cardiologist FENG Chao identified the condition, which was challenging to treat due to the uneven heartbeats. XIA Shudong, the department director, opted for a two-step treatment: first, implanting a leadless pacemaker to address cardiac arrest, and then tackling rapid atrial fibrillation.

On June 5th, XIA Shudong successfully implanted the pacemaker, which is less invasive and ideal for elderly patients. Post-operation, the patient's cardiac arrest was resolved, but she still experienced rapid atrial tachycardia and atrial fibrillation.

To address the persistent arrhythmia, XIA Shudong and FENG Chao decided to use Pulsed Field Ablation (PFA), a novel technique. The procedure required precision to minimize impact on the pacemaker, which was in close proximity to the ablation site. FENG Chao emphasized the importance of accuracy and speed in the operation for better patient outcomes.

On June 28th, with a collaborative effort, FENG Chao conducted the pulsed ablation under local anesthesia. The operation successfully isolated the sources of atrial fibrillation, marking a significant advancement in arrhythmia treatment.

For more information
Contact us: ***shystone@126.com***

Targeting the "King of Cancers"

Pancreatic cancer often presents insidiously, making early diagnosis challenging. The disease typically progresses rapidly, with a short survival time for patients and poor prognosis, earning it the title of "king of cancers".

Recently, a special patient visited the Department of Hepatobiliary and Pancreatic Surgery at the Second Affiliated Hospital of Zhejiang University School of Medicine. Seventy-four-year-old Ms. CHEN (a pseudonym) walked in without difficulty, accompanied by her daughter-in-law. Her smile conveyed her inner joy as she repeatedly expressed her gratitude.

In the first six months of last year, Ms. CHEN was diagnosed with locally-advanced pancreatic cancer. Professor YAN Sheng's team carefully evaluated Ms. CHEN's condition and, based on her examination and test results, developed a treatment plan that included neoadjuvant therapy followed by surgery. Six months later, Ms. CHEN finally had the opportunity to undergo a curative surgical resection.

On September 12, 2023, Professor YAN's surgical team performed a total pancreatectomy on Ms. CHEN. Additionally, autologous islet isolation and reinfusion were carried out using the negative-margin pancreatic body and tail tissue. After her surgery, Ms. CHEN recovered well, and her fasting C-peptide level had returned to 0.18 U/L at discharge, indicating that her islets were starting to survive and function.

During the year-long follow-up after her discharge, Ms. CHEN continued with routine chemotherapy but didn't really suffer from hypoglycemia. Enjoying her daily meals and engaging in light physical activities, and was well-nourished and in a good physical condition.

Similarly, 53-year-old Ms. MAO (a pseudonym) was also diagnosed with locally-advanced pancreatic cancer, which invaded and encased the superior mesenteric artery and vein, making surgery highly challenging. After six months of neoadjuvant treatment at her local hospital, Ms. MAO visited Professor YAN's clinic for a surgical evaluation.

Following a thorough preoperative assessment, on November 1, 2023, Professor YAN performed a total pancreatectomy with resection and reconstruction of the portal vein, along with autologous islet transplantation for Ms. MAO. Remarkably, during her hospitalization and after being discharged, Ms. MAO managed to maintain stable blood glucose levels without requiring insulin or any other hypoglycemic medications. Her blood glucose fluctuations remained minimal, and consistently within a relatively normal range. At the follow-up on the 321st postoperative day, Ms. MAO's fasting blood glucose was 4.74 mmol/L, her fasting C-peptide was 0.19

nmol/L, and her 2-hour postprandial C-peptide was 1.6 nmol/L. Her glycated hemoglobin (HbA1c) was 5.8%, and her tumor marker CA 19-9 lay within the normal range. By this point, she had been living tumor-free for nearly a year while enjoying an excellent quality of life.

WANG Weilin, chairman of the Second Affiliated Hospital and the head of the Department of Hepatobiliary and Pancreatic Surgery, noted that the total pancreatectomy with autologous islet transplantation performed by Professor YAN's team has significantly improved the life quality of pancreatic cancer patients with better nutrition and a stronger physical condition. This approach can even lead to insulin independence, extend tumor-free survival, reduce surgical complications, and increase the postoperative survival rates, thus laying a solid foundation for prolonging patients' survival time, and significantly improving the treatment outcomes for pancreatic cancer surgeries.

For more information
Contact us: ***hx_fu79@zju.edu.cn***

A Meaningful First Lesson-Three Academicians Unveil the New Journey for Medical Students

Academician HUANG Hefeng delivered the first lecture on Histology and Embryology.

"Dear students, the clinical therapies you will one day employ have their roots in basic scientific principles. Breakthroughs in basic science study pave the way for novel treatments and revolutionary clinical approaches. Many areas remain uncharted in today's medical landscape, presenting you with various opportunities for discovery and innovation," announced HUANG Hefeng at the start of her lecture. At 8 am, on September 9, in classroom B405, Medicine School Building of Zhejiang University's Zijingang Campus, a packed classroom listened intently as HUANG, an academician of the Chinese Academy of Sciences, a renowned reproductive medicine specialist, and dean of the Zhejiang University School of Medicine, introduced sophomore students to their first course on Histology and Embryology.

Academician HUANG combined fundamental medical theories with clinical case studies, illustrated the complex journey from fertilization to the early stages of embryonic development, examined the structure of fetal membranes and placentas, and shed light on disease mechanisms from life's inception and the spatiotemporal omics analysis of body development and the regeneration process. What's more, her lecture also underscored the vast unknowns still prevalent in medicine, hoping that the students would learn from the basic science to reveal the mysteries of human physiology and pathology, thereby equipping them to safeguard public health in the future.

On the same day, WANG Jian'an, an academician of the Chinese Academy of Sciences, cardiovascular expert and Secretary of the Party Committee at the Second Affiliated Hospital of Zhejiang University School of Medicine, delivered a lecture on the first class of Basic Theories of Pathology and Pharmacology. Additionally, DUAN Shumin, an academician of the Chinese Academy of Sciences, neurobiologist and prominent figure, dean of the Faculty of Medicine and Pharmaceutical Sciences, at Zhejiang University, also taught a course on Human Physiology to the sophomore students.

This initiative marks the first time that Zhejiang University School of Medicine has involved three academicians in introducing the core curriculum in basic medical science to undergraduate clinical medicine students. This also reflects the commitment of the School of Medicine to implementing a profound reform, designed to nurture exceptional, innovative talents.

High-quality medical talents are the cornerstone and an essential component for building a healthier China. For several years, the School of Medicine has aligned with the national strategic needs, accelerating educational innovation and prioritizing a student-centered approach. This system, rooted in clinical competence, continues to evolve, exploring fresh avenues for advanced curriculum development and faculty enhancement.

Since 2005, the School of Medicine has upheld the tradition of academicians delivering the inaugural lecture to fresh

medical students. This year, they have expanded this tradition by appointing academicians as the chief professors for the foundational clinical medicine courses, setting an academic standard and offering mentorship from the very beginning of the students' medical journey.

"This semester, we've appointed numerous highly-esteemed clinicians to teach the foundational medical sciences and integrated classic theory with actual clinical cases. This vivid approach, including the true stories and examples of saving lives, transforms passive learning into a dynamic quest and solidifies the groundwork for their future roles in clinics and research," commented HUANG.

Academician Wang Jian'an gave the first class on the Fundamentals of Pathology and Pharmacology.

In Academician WANG Jian'an's lecture, titled "Reflecting on the importance of an integrated education in basic medical sciences from the perspective of an aspiring doctor," he stated that "The more extensive the interaction with the patients, the deeper the understanding of their afflictions and consequent recognition of the inherent limitations within medicine. Young students need to foster a spirit of courage in relation to practical application and innovation. They must engage deeply with pivotal medical issues and seek solutions through undertaking pioneering research."

Academician DUAN Shumin delivered foundational knowledge on Human Physiology. He pointed out that innovations, such as brain-machine interfaces and big data, are expanding the potential for medical advancements. DUAN expressed his hope that students will transcend the traditional academic boundaries, merge different knowledge fields, and innovate across multiple disciplines. This approach aims to cultivate high-caliber, composite, inventive talents, who are poised to advance China's health initiatives.

To date, Zhejiang University School of Medicine has established foundational clinical teaching teams across seven pivotal courses, including Systematic Anatomy, Histology and Embryology, Human Physiology, Basics of Pathology and Pharmacology, Neuroscience, Psychomotor Systems I, Cardiovascular, Respiratory, Hematological, and Urinary Systems I, and Digestive and Endocrine Systems I.

Academician Duan Shumin presented the opening lecture on Human Physiology.

Showing the World ZUSM Young Talents!

In the summer of 2024, Zhejiang University School of Medicine (ZUSM) organized six offline overseas exchange programs, through which more than 140 undergraduates visited Hong Kong (China), London (UK), Manchester (UK), Perth (Australia), Vancouver (Canada) and Alberta (Canada) for overseas exchange and practice. With the desire for knowledge and the ideal of "practicing medicine to help the public", the medical students of ZJU stepped through a door of wisdom leading to the frontier of international medicine this summer. Different medical concepts collide with each other, just like the stars shining in the vast sky, interweaving to create a colorful and beautiful picture.

The University of Hong Kong, Hong Kong, China

The University of Hong Kong hosts the "Leadership in Public Health" summer program, which exposes students to changes in the health of the world's populations, where they are heading and why, as well as how to influence these changes. The students are equipped with the skills and knowledge to evaluate and assess critically the relevant evidence so that they can become effective policy makers and problem solvers.

The summer program at the University of Hong Kong was a valuable learning opportunity. It has not only enabled me to gain knowledge and skills, but also given me a deeper understanding of and love for the field of public health. —— YAN Xinyu

King's College London, UK

King's College London (UK) is running an exchange program this summer to provide an interactive learning environment and a truly international experience for students from all over the world, allowing them to explore a wide range of academic disciplines and make friends from across the globe.

During the two-week study period, I not only learned about cutting-edge medical technology, but also further consolidated my theoretical knowledge through practical activities. In addition, the interaction with students from different cultural backgrounds enabled me to better understand and respect cultural differences. ——YAN Jiaxuan

University of Manchester, UK

The University of Manchester summer exchange program offers basic medicine, clinical medicine and public health courses, including both lectures and seminars, as well as poster studies, social practices, etc. The personalized learning themes are tailored for different classes, and students are exposed to cutting-edge knowledge about genetics, biochemistry and biochemical analysis, cellular imaging, neuroscience, as well as the cultural atmosphere of the English coast.

The University of Manchester has provided me with an invaluable platform for enhancing my professional knowledge, practical experience and interpersonal skills. This experience represents an important cornerstone in my future medical path and will inspire me to keep moving forward in the pursuit of excellence. —— QIU Junming

University of British Columbia, Canada

The summer programs offered by the University of British Columbia in Canada are varied, ranging from working in small groups to collaborate on innovative and scientifically sound research ideas; writing novel research proposals and critically assessing research evidence on biological aging through oral presentations and peer evaluation; to researching and presenting one's findings on musculoskeletal injuries/conditions and the corresponding treatments.

This experience has not only given me a deeper understanding of the medical field, but also helped me to realize how, as a future medical practitioner, I can contribute to global health issues through collaboration and communication. I believe that this valuable learning experience will be an important cornerstone in my future career, pushing me to move forward in the medical field. —— SU Bei

Faculty of Medicine and Dentistry, University of Alberta, Canada

The University of Alberta hosts an international medical student training program, with multiple lectures covering a wide range of areas, including medical education, research methods and clinical practice, providing a glimpse into the teaching of medicine in Canada. At the same time, the students visited the university's Mechanical Center, Astronomical Observatory, Ophthalmology Center, Cancer Treatment Center, Children's Eye Hospital, etc., absorbing many details about medicine and this university.

This exchange program was a valuable learning experience, which not only allowed me to increase my knowledge, but also enabled me to make friends from all over the world. I will bring the experience and insights from this exchange back to my home country and hope to contribute to China's medical education. —— LI Linhan

The University of Western Australia, Australia

The University of Western Australia's summer course program aims to provide an opportunity for international medical students to experience the Australian healthcare system by offering courses in medical research methods, research ethics and scientific writing skills. These courses and practices not only broaden the students' horizons, but also give them a deeper understanding of the healthcare systems in both China and Australia.

Through this exchange program, I have not only improved my professional knowledge and research ability, but also gained a deep understanding of the cross-cultural communication skills and diversified ways of thinking that medical students need to possess in the context of globalization. This valuable experience will inspire me to maintain my thirst for knowledge and passion for medicine in my future study and career. —— ZENG Huixuan

With the ending of the summer, this year's overseas exchange programs have reached a successful conclusion. These programs not only provide students with valuable opportunities for international exchanges, but also open up their global vision regarding their medical path. These seeds will surely flourish in the future and contribute the wisdom and strength of ZJU School of Medicine to the development of the global medical field. The students of ZJU School of Medicine will move forward and shine more brightly in the international medical arena, continuing to write a brand new chapter of international exchange and cooperation in the field of medicine.

Saving People Like Me——
A Medical Student Helping Defeat Leukaemia

Twelve years ago, CHEN Ge was diagnosed with acute lymphoblastic leukaemia, and all of a sudden, his life turned gray. During his treatment at the First Affiliated Hospital, Zhejiang University School of Medicine, he took a break from school, underwent chemotherapy, experienced a relapse, and finally received a hematopoietic stem cell transplant to get his life back on track. Now, having overcome leukaemia, he is pursuing a master's degree in haematology at the School of Medicine of Zhejiang University and wants to help more people facing similar challenges.

"The disease has made me more determined to do what I want."

'In fact, before I got sick, I had longed to be a doctor and found it very fulfilling to be able to treat the sick and save people.' CHEN Ge said with a smile, 'After my illness, this dream has become even more specific that I want to be a doctor specializing in treating blood diseases.' Back in 2012, the then 16-year-old CHEN noticed in maths class that the middle part of a straight line on the blackboard was blurred, and curiously asked his deskmate if he could see that clearly. The latter was surprised by his question and gave an affirmative answer.

When CHEN Ge returned home on Saturday, he mentioned his sight problem to his mother, who immediately took him to the ophthalmology department of the local hospital to be examined. It was found that there were symptoms of haemorrhage in the lower part of his right eye. Based on a comprehensive evaluation of other test results, the local hospital recommended that he undergo a bone marrow puncture. The result identified acute lymphoblastic leukaemia. CHEN Ge's blurred vision was due to the severe reduction of platelets and extramedullary leukemic infiltration. 'At first, my parents didn't dare to tell me what the disease was. They just said that I should go to a big hospital for a check-up.' Accompanied by his parents, CHEN Ge came to the First Affiliated Hospital, Zhejiang University School of Medicine to receive treatment by the team of Professor HUANG He, a hematologist. Despite a significant improvement after chemotherapy, the leukemia relapsed subsequently, and finally CHEN received a bone marrow transplant.

CHEN Ge's transplantation was successful and he returned to his campus two years later. He took the college entrance exam and, when the time came to apply for colleges and majors, his attention was constantly drawn to medical colleges and related majors. Eventually, he was admitted to a medical school in Zhejiang, majoring in clinical medicine.

Seeing more possibilities here

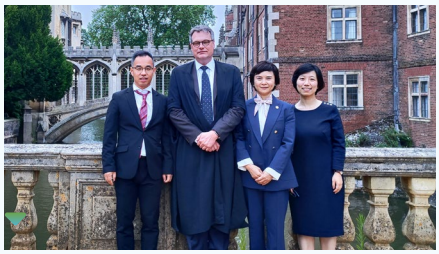
'Dr HUANG, can I become a hematologist?' CHEN Ge asked Professor HUANG He very sincerely during a regular review, when he was approaching the end of his undergraduate studies and needed to make a decision about his future.

'I think you're more qualified to study haematology than other students, because you've overcome the blood disease yourself!' Professor HUANG, as a doctor who had witnessed CHEN Ge "grow up" along the way, firmly told CHEN that he could do it.

So when CHEN Ge took the entrance exam for postgraduate school, he chose haematology without hesitation and applied for Zhejiang University School of Medicine. 'I can not only help haematology patients from a medical point of view, but also encourage them with my own experience, and it's my dream to study in the place that gave me a new life!' said CHEN Ge.

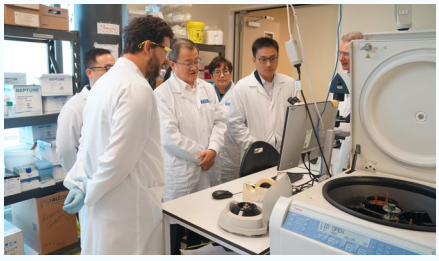
Thanks to his excellent academic capability and outstanding performance, CHEN Ge has fulfilled his dream! Drawing on his personal experience and interests, CHEN is now focusing on research about the prognosis of bone marrow transplantation. 'Studying at Zhejiang University School of Medicine, I've seen more possibilities, such as becoming an excellent clinician who can help many patients; or becoming a medical researcher and making breakthroughs in basic research, which can also help more people in terms of treatments and medicines.'

Zhejiang University School of Medicine Engages with World-Class Universities



From July 10 to 17, a delegation from Zhejiang University School of Medicine visited the United Kingdom, engaging in in-depth discussions with the University of Cambridge, the University of Oxford, University College London, Imperial College London, and the University of Edinburgh. The discussions focused on topics such as student development, talent training, and clinical research collaboration, further strengthening the partnerships with these outstanding British universities. During the visit, the delegation also met with local Zhejiang University alumni in the UK and representatives of the Zhejiang Federation of Returned Overseas Chinese in London, to foster connections and promote a sense of camaraderie.

Between August 30 and September 4, the delegation traveled to leading universities and institutions in New Zealand and Japan, including the University of Auckland, the University of Tokyo, Kyoto University, Kobe University's School of Medicine and Graduate School of Medicine, RIKEN (the Institute of Physical and Chemical Research), and the Kobe Biomedical Innovation Cluster. They also visited the Embassy of the People's Republic of China in Japan. The discussions focused on advancing collaboration regarding student education, scientific research, and clinical translation, thereby further solidifying Zhejiang University School of Medicine's partnerships with the leading universities and research institutions in both New Zealand and Japan.



From October 10 to 20, a delegation led by Zhejiang University Vice President LI Xiaoming visited the University Hospital Zurich in Switzerland, the Faculty of Medicine at Ludwig Maximilian University of Munich in Germany, the European Molecular Biology Laboratory (EMBL), and the Cordeliers Research Center of the French National Institute of Health and Medical Research (INSERM).

During this visit, Zhejiang University School of Medicine renewed its student exchange agreement with the Faculty of Medicine at Ludwig Maximilian University of Munich. The visit further deepened the cooperation between Zhejiang University and the leading European medical institutions.

International Academic Exchange

To deepen the cooperation and exchanges with European countries in the fields of sustainable development and medical research, Zhejiang University successfully hosted the First Sino-French Forum on Health and Medical Research in France and the 4th Sino-German Sustainable Development Forum in Germany in mid-October. These forums focused on encouraging in-depth discussions on the latest advancements in medical science.

The First Sino-French Forum on Health and Medical Research, held in Paris, France, focused on the latest developments in cancer research. Against the backdrop of the 60th anniversary of the establishment of diplomatic relations between China and France, the forum adhered to the vision of a global community of health for all. Co-organized by Zhejiang University School of Medicine and the Cordeliers Research Center of the French National Institute of Health and Medical Research (INSERM), this forum attracted scholars from both China and France to explore innovative approaches and future directions within the field of cancer research.

The 4th Sino-German Sustainable Development Forum, held in Berlin, Germany, took place under the auspices of the 16th World Health Summit (WHS 2024). With the theme of exploring new frontiers in clinical medical research, the forum was co-organized by Zhejiang University, the World Health Summit, and the Charité – Berlin University Medicine. Over 20 experts and scholars from both China and Germany gathered to share the latest research findings and emerging trends in various fields, including neuroscience and mental health, new advancements in cancer and immunotherapy, women and children's health research, and the transformative role of artificial intelligence in medicine.

The Comprehensive Launch of the Clinical Research Methodology Special Training

With the intention of "taking clinical problems as the guide, transforming them into scientific problems, and ultimately finding solutions through innovative research," the Second Affiliated Hospital, partnering with the Harvard T.H. Chan School of Public Health in the United States and the George Institute for Global Health in Australia, designed a multi-phase clinical research methodology training program from June to September, 2024. Aiming to transform clinical problems into scientific ones and find innovative solutions, the program intended to foster scientific thinking and research skills among clinicians.

Two courses for department heads were co-organized with Harvard, with 30 participants from the hospital. The training focused on the theme of clinical research methodology, covering the meticulous considerations related to clinical research design, an in-depth analysis of the effectiveness of medical research, as well as the frontier trends in epidemiological and statistical clinical research methods, and the key elements of statistical analysis and quality assessment.

Additionally, a total of 120 doctors from 50 clinical departments were involved in the scientific research training course co-organized with the George Institute, covering almost every clinical department in the hospital. The training was divided into four sessions, each lasting one month, and it's centered on themes such as the fundamentals

of clinical research and randomized controlled studies. This training analyzed and demonstrated clinical research methods and the application and design of clinical trials through theoretical lectures, case analyses, and group discussions.

The 2nd UK-China Healthcare Workforce Development Annual Conference

"Accelerate the cultivation of innovative medical talents and empower the development of new quality productive forces". On October 21, 2024, the 2nd UK-China Healthcare Workforce Development Annual Conference was held in Hangzhou. The meeting was organized by the Health Human Resources Development Center of the China's National Health Commission and the UK Department for Business and Trade, hosted by Affiliated Sir Run Run Shaw Hospital.

The event brought together 50 experts, scholars, and elites in the healthcare sector from 18 Chinese and British institutions. The two sides discussed the latest developments and trends in the building of the healthcare talent training system, international cooperation, scientific research innovation, etc. Going forward, it is expected that with the cooperation enthusiasm and innovative thinking stimulated by this platform, we can achieve more fruitful and substantial results in healthcare talent

development in the joint endeavors of experts from China and the UK, making positive contributions to global health.

WANG Man: " Treat Patients as Family Members."

WANG Man, born in October 1927, is a professor and chief physician who previously served as the deputy director of Women's Hospital, Zhejiang Medical University, the predecessor of Women's Hospital, School of Medicine, Zhejiang University, hereinafter referred to as "Women's Hospital". After graduating from the six-year medical program at Guizhou Medical College in 1950, she began her career at Zhejiang University School of Medicine. She was also dispatched to Mali as part of a Chinese medical aid team to Africa. Throughout her career, she participated in exchange visits to the United States, Mexico, and several Nordic countries. In 1956, WANG Man was recognized as an advanced worker in Hangzhou and was honored for her efforts at the Fourth International Women's Conference for her efforts. In 1990, she received a certificate of honor from the National Education Commission for 40 years of work in science and technology in higher education. Since 1992, she has been a recipient of the Special government allowances of the State Council. WANG Man was awarded a Lifetime Achievement Award by Zhejiang Medical Association in 2013 . In 2021, she was honored with the "Lifetime Achievement Award" by the Health Commission of Zhejiang Province.

A Connection with Women's Hospital : Balancing Treatment and Education

In the summer of 1950, WANG Man graduated from university. At that time, her former teachers, WANG Jiwu and YAN Shuzhao, had established a medical school at Zhejiang University in Hangzhou. Inspired by their work, she wrote to Professor YAN Shuzhao, requesting a recommendation to enter the obstetrics and gynecology department at Zhejiang University School of Medicine.

Thus, filled with nostalgia, WANG Man returned to Hangzhou and joined the Affiliated Hospital of Zhejiang University School of Medicine, the predecessor of the First Affiliated Hospital of Zhejiang University School of Medicine, as a teaching assistant and assistant resident physician. Since then, she embarked on a path that integrated medicine, education, and research.

In 1956, WANG Man delivered her first large lecture in obstetrics and gynecology. Under the mentorship of her predecessors, including YAN Shuzhao, LIU Tianxiang, and LU Wenbo, she served as the deputy director of the obstetrics and gynecology teaching and research office for many years. During this period, she played a crucial role in establishing and refining regulations, systems, and training programs for the education and teaching of obstetrics and gynecology, as well as the training programs for physicians at all levels, ensuring a structured promotion system for medical professionals.

While excelling in clinical medical work, WANG Man also placed great importance on teaching and talent cultivation. Integrating clinical practice with teaching, she cultivated a large number of specialized obstetricians and gynecologists for the country. In the 1980s, she supervised six graduate

WANG Man (first from the right, front row) and her students in 1982

students, one of whom, HUANG Hefeng, is now an academician of the Chinese Academy of Sciences. This group of graduate students went on to mentor over 100 doctoral candidates.

Medical Aid to Africa: Establishing a Foundational Data Framework for Obstetrics and Gynecology in Mali

In 1974, WANG Man was dispatched to Mali for medical assistance. At that time, there was little understanding of the prevalent diseases among the Malian population, with no systematic reference materials available. Therefore, WANG Man conducted some investigative research on local diseases and wrote her first article titled "Investigation Report on Pelvic Measurements and Reproductive Conditions of Women in Mali".

In her obstetrics and gynecology practice in Mali, she frequently encountered cases of difficult labor. Due to a lack of knowledge about the basic anatomical characteristics of the pelvis of Malian, there was often a degree of uncertainty in diagnosis and treatment.

WANG Man conducted measurements on 500 women at Sikasso Regional Hospital's outpatient and obstetric wards, gathering data on the average values and ranges for the interspinous distance, intercristal distance, bitrochanteric diameter, external conjugate, and ischial tuberosity distance. This became the first set of data in this field in Mali's history.

Additionally, WANG Man summarized the reproductive and neonatal survival conditions of Malian women, providing foundational information for subsequent diagnoses of women's diseases.

Later, WANG Man continued to write articles, including "Preliminary Understanding of Dystocia among Malian Women (A Summary of 100 Cases)," "Discussion on 30 Cases of Uterine Rupture, a Severe Complication of Dystocia, in Mali", "Incidence and Treatment of Uterine Prolapse in Malian Women", "A Preliminary Summary of Surgical Treatment for Urinary Fistula (With 23 Cases)", and "A Summary of Surgical Treatment for 23 Cases of Urinary Fistula".

Moreover, WANG Man compiled a list of common drug names, medical terms, and laboratory terms in English, French, and Chinese to aid subsequent medical teams in diagnosis, ward rounds, and communication with patients.

Seventy Years of Clinical Practice: Committed to Research and Achieving Continuous Breakthroughs

After further studies in Shanghai in 1960, WANG Man began performing extensive radical surgeries for cervical cancer and lymphadenectomy at the hospital and established a follow-up system. From 1979 to 1980, to promote traditional Chinese medicine and address some difficult and intractable clinical issues in obstetrics and gynecology, WANG Man led practitioners from her hospital and the province to research and explore the integration of traditional Chinese and Western medicine in the clinical field. In 1980, after receiving a laparoscope from the delegation of The Society of Laparoendoscopic Surgeons, WANG Man and her colleagues led new diagnostic and therapeutic techniques such as laparoscopy and hysteroscopy, significantly enhancing the level of clinical medical treatment in obstetrics and gynecology in Zhejiang Province.

As a leading figure in clinical research on the common and prevalent disease "endometriosis" in China, WANG Man began serving as the head of the national research collaboration group on this topic in 1982. She compiled data from 1,553 cases of endometriosis across eight regions in the country and published the article "Research and Treatment of Pelvic Endometriosis" in *China Journal of Modern Medicine* after in-depth analysis and research in 1986. Additionally, she led project team members and graduate students in addressing clinical issues, conducting research on computer-aided diagnosis of endometriosis, the ultrastructure of ectopic endometrium, estrogen and progesterone receptors, histochemistry, and the effects of drugs on the DNA synthesis of endometrial cells. She also integrated clinical practice with research on endometriosis, using both traditional Chinese and Western medicine, experimental research on the use of traditional Chinese medicine such as acetylated cotton phenol, research on the relationship between prolactin secretion from ectopic and normal endometrium and the prolactin secretion function of patients, research on immunological aspects of infertility in patients with endometriosis, and research on the effects of the pelvic environment on infertility. Related results were published in nationally recognized, authoritative professional journals. Her series of studies titled "Characteristics of Ectopic Endometrium in Endometriosis and Clinical Implications" won the Second Prize of Scientific and Technological Progress Award in Zhejiang Province.

"When I practiced medicine, I always thought that it was the working people who raised me to attend university and become a doctor, so I should give back to them. Patients are vulnerable and thus seek help from us doctors. We should do our best to care for them and their family. We must strive for excellence in our skills and treat our patients as if they were our own family members." This is also WANG Man's message to the younger generation of medical professionals.

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Editorial office
Zhejiang University School of Medicine
866 Yuhangtang Road, Hangzhou 310058
P.R. China.
T: +86-571-88208100
F: +86-571-88208022
E: global_zusm@zju.edu.cn
www.cmm.zju.edu.cn/cmmenglish