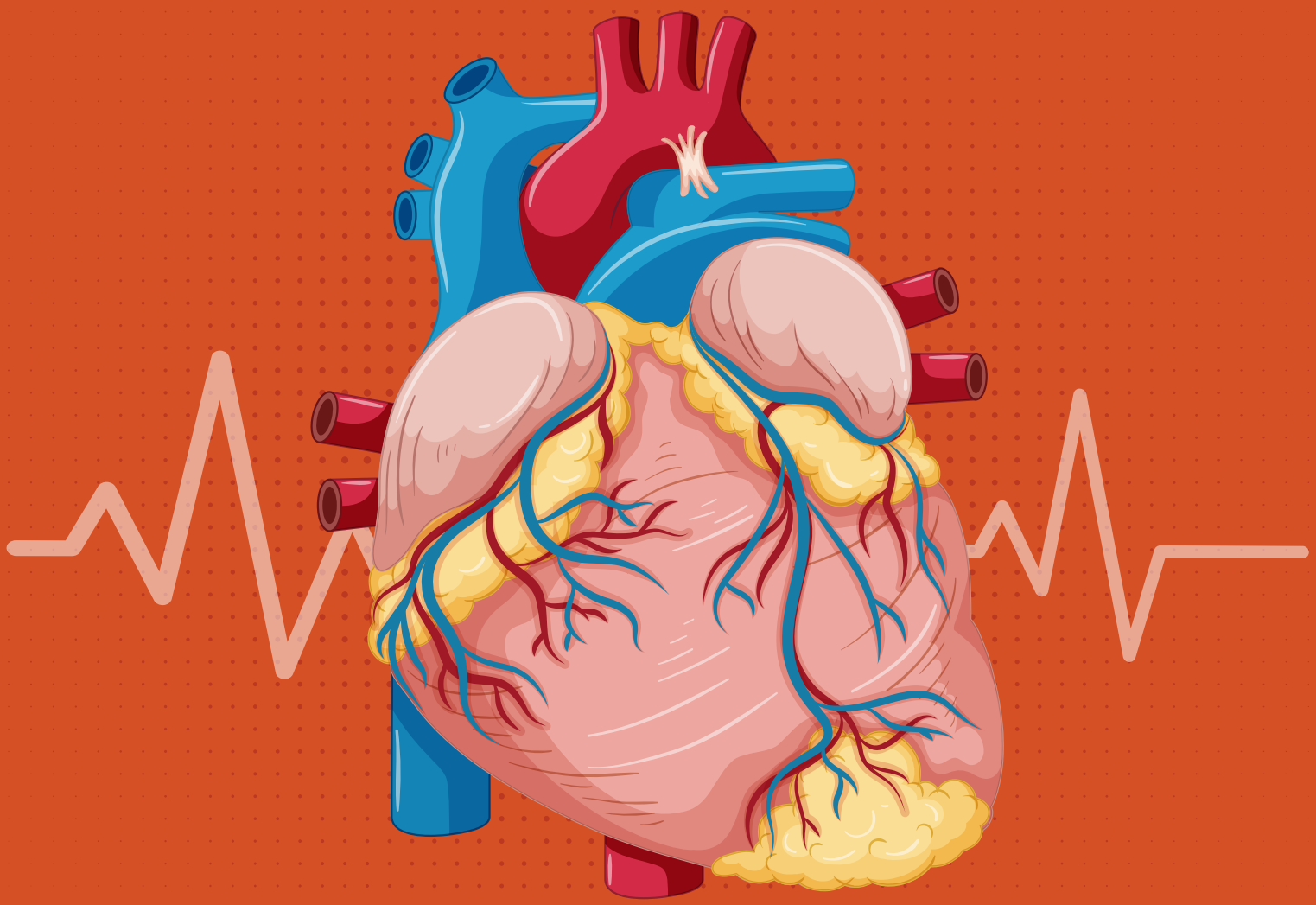
Issue 3 2023

ZJU MEDICINE

SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE



Dedication to the Treatment of the Heart and Beyond

Addressing the Long-standing Cannabis Problem

Youth Volunteers' Contribution to the Asian Games

SNOWY WINTER AT ZUSM CAMPUS

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 composing of 8 affiliated hospitals, numerous non-directly affiliated hospitals and cooperative hospitals. It is home to more than 33,000 faculty members and over 8,800 students.

ZUSM believes that every global partner is unique and each project is irreplaceable. We are together with global partners for a better response to future medical challenges and making effort to build a healthy future for all.

浙江大學 医学院
SCHOOL OF MEDICINE
ZHEJIANG UNIVERSITY

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Dedication to the Treatment of the Heart and Beyond

WANG Jian'an

Academician of the Chinese Academy of Sciences
Director of the National Key Laboratory of Vascular Implantation Devices
Director of the Cardiovascular Research Institute, Zhejiang University
Secretary of the Party Committee and Director of the Heart Center, Second Affiliated Hospital, Zhejiang University School of Medicine
Vice Dean of Zhejiang University School of Medicine

We safeguard people's health, boost patients' confidence, and meet society's expectations.

What sparked your interest in medicine?

My dream since I was young has been to become a doctor. My grandma passed away from lung cancer, and my parents have had long medical histories. These personal experiences have solidified my desire to become a doctor. Being a doctor gives me the chances to directly assist patients, through clinical practice and surgical procedures, and also to help more patients with complex conditions through scientific research. My mission is to reconcile theory and practice while conducting my work with conscience and compassion.

Could you share with us more about your "Hangzhou Solution"?

Compared with patients in the West, nearly half of Chinese patients with severe heart diseases have bicuspid aortic valve stenosis (severe aortic valve stenosis combined with bicuspid aortic valve disease). The implanted valve could easily be popped out or dive into the ventricle due to severe calcification commonly seen in these patients, which significantly reduced treatment's efficacy. Therefore, we decided to develop valve products and intervention methods especially tailored for Chinese patients. Our team developed the first retrievable and navigable transcatheter valve system with independent intellectual property right in China. Moreover, we invented balloon-sizing instead of CT-based measurements to measure the size of the valve. Hence, the surgical process grew safer and more successful, the implantation more precise, with significantly less complications. This is the "Hangzhou Solution".

How do you feel about being elected to the Chinese Academy of Sciences (CAS)?

Many of my old memories came flooding back when I learned about the result of the election, including fatigue from frequent hospital visits in my childhood, hardship from working the night shift in the chilly winter, and office-wide sadness following a botched experiment. Aside from acknowledging my prior efforts, being elected as an CAS Academician entails greater responsibilities. I will keep researching important topics in the field of domestic medicine, and try my hardest to lead the team to advance the growth of the discipline in the industry.

Do you have anything to share with the students and young colleagues?

Being in the medical field allows us to have a profoundly unique influence on people, families, and even entire communities. One needs to be skilled, capable, and visionary in order to take on these challenges. My first piece of advice is to have a caring heart and show it in action; the second is to stay curious and explore unknown areas; and the third is to seek the truth and discern what constitutes true innovation. Scientific research does not always produce results, or proceed as planned. However, the road to the truth is one of unwavering perseverance. Perhaps asking ourselves "why" once more can get us one step closer to our goals.

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More Than Scientific Research

XU Haoxin

Dean, School of Basic Medical Sciences, Zhejiang University
Qiushi Chair Professor of Zhejiang University
Professor of Liangzhu Lab
Visiting Professor, Department of Biology, University of Michigan
Presidential Early Career Award for Scientists and Engineers 2010
Researcher of the New Cornerstone Investigator Program 2023
President of the Zhejiang Society for Neuroscience

What made you decide to come to Zhejiang University?

There are two things I consider frequently: how to create "something different" and to cultivate "what kind of individuals". Zhejiang University has a large scale and various disciplines and has the basic cross-disciplinary advantage. Zhejiang University has a lofty goal in talent training, there is consensus at all levels, there is the motivation for reform, shows a great degree of flexibility, and in order to achieve this goal, everyone is willing to work hard and determined. Because these are in line with my personal development and ambition, they are attractive enough for me, and the future is also worth looking forward to.

Could you brief us on your research area?

My research focuses on ion channels, specifically those on lysosomes. Nearly 15% of the new FDA-approved drugs target ion channels. Lysosomes serve as waste-cleaning factories for cells, and their abnormal function are closely associated with neurodegenerative diseases, metabolic diseases, tumors, and aging. Lysosomal ion channels play an important role in regulating lysosomal functions. In the treatment of disease, finding the direct root cause of the disease is the way to cure the disease, while developing specific interventions to curb disease progression is also beneficial. Only by treating both the symptoms and the root cause of diseases, we can ultimately alleviate patients' suffering. That's why I chose lysosomes as my research object.

What are your plans regarding your future research?

So far, the team has identified a total of 12 unknown ion channel proteins, including 8 lysosomal ion channel proteins, published a series of research results on the lysosomal ion channel TRPML1, established the physiological function of TRPML1, and proposed that TRPML1 channel is a potential target for the treatment of related diseases in a groundbreaking way. At present, the relevant research results have received the attention and investment of many large international pharmaceutical companies, and the conversion company has been established in the United States. In the future, the team will continue to work on lysosomal ion channels, but also expand the study to other organelles, and carry out translational studies on the other seven ion channels that have been discovered. My goal is that each of these ion channels will lead to the development of drugs to treat some of the most difficult diseases that have plagued mankind for a long time.

How will you achieve your dream?

As a scientist, I will always keep introspective, and endeavor to make solid, innovative, and convincing scientific achievements. As an educator, I want to cultivate the young scholars who have certain taste in scientific research, dare to ask critical questions and dare to ask sharp questions and dare to challenge scientific peaks, and build a cross-boundary and diversified platform for them. As the dean of the school, I will encourage innovation and put the innovation in the most important position, to create a tolerant and open growth environment for young people and encourage them to break through and always pursue excellence. and also create an inclusive and open environment for young scientists.

We are confident in making top achievements, training top-notch scholars, exploring world-class innovative projects, and advancing towards becoming a world-class university.

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Leading the Collaborative Development of Minimally Invasive Medicine and Equipment

——National Engineering Research Center of Innovation and Application of Minimally Invasive Instruments

The National Engineering Research Center of Innovation and Application of Minimally Invasive Instruments was established in October 2021 under the leadership of Sir Run Run Shaw Hospital affiliated to Zhejiang University School of Medicine, with Professor CAI Xiujun as the director.

This is the only national research center in the field of minimally invasive surgery in China, which is oriented to clinical scientific problems and national major strategic needs, with major project cooperation as the carrier, uniting with the School of Mechanical Engineering, the College of Biomedical Engineering & Instrument Science, the College of Computer Science and Technology, the School of Materials Science and Engineering of Zhejiang University and a number of domestic enterprises, and possessing multiple platforms for medical research, instruments R & D, achievements transformation, training, and promotion to carry out cross-disciplinary research in the field of medical instruments and diagnostic and therapeutic technological innovations. The center's main research directions include the exploration of new technologies and procedures in minimally invasive medicine, high-end electronic endoscopy and instruments, artificial intelligence technology for medical imaging, multimodal medical imaging combined with surgical navigation system, and surgical robotic systems.

According to the "Administrative Measures of National Engineering Research Center", the center relies on Sir Run Run Shaw Hospital affiliated to Zhejiang University School of Medicine, and operates relatively independently. The center has invested the first batch of construction funds of 50 million yuan, has a construction area of 6,000 square meters, has set up a management office, and has completed minimally invasive surgery laboratory, GMP laboratory, animal laboratory, minimally invasive surgery training center, biospecimen repository, research wards, and China-Israel Innovation Center, with 45 full-time scientific researchers and administrative personnel. The center is in the process of constructing a joint laboratory of medicine, engineering and information technology, a joint laboratory of the academy and enterprises, and a training center of robotic surgery, which is expected to be completed in 2024. The center and the leading domestic minimally invasive instrument companies will jointly build a research institute with an independent legal person. The first phase is expected to invest 100 million yuan.

Since its establishment, the center has obtained 6 medical instrument registration certificates, 6 authorized invention patents, and 4 pieces of software, and conducted 19 clinical studies, completed the development of a prototype of multimodal medical imaging combined with a surgical navigation system, and carried out clinical studies of four-armed surgical robots.

The center will adhere to the concept of leading the coordinated development of minimally invasive medicine and equipment, and will spend 5–10 years in building a new "minimally invasive precision" diagnosis and treatment system, building a fullchain world-class innovation platform integrating academic research, technology development, achievement transformation, and clinical application, promoting China's "minimally invasive medicine" to the internationally leading level, and establishing a complete, high-end minimally invasive medical instruments industry chain to lead the overall development of the industry.

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Building a Model Area for Local International Medical Education

Built on Zhejiang University's hundred-year history, International School of Medicine of Zhejiang University (ZJU-ISM) has aimed high since its inception. With its Medicine listed as national First-class discipline, the University is confident and capable of extending medical education into the central region of Zhejiang Province. Huang Hefeng, academician of the Chinese Academy of Sciences and well-renowned scientist in reproductive medicine, is the inaugural dean of ZJU-ISM. With the combined support of the University and Yiwu government, ZJU-ISM will better serve the national "Double First-class" Initiative and deliver the top-quality care the region needs, and transform health professional education in an interconnected world.

Adhere to cultivating virtue and nurturing talents, ZJU-ISM builds a medical education system that covers the entire process of international undergraduate, graduate and post-graduation education. Its brand-new campus was opened in September 2023. Enjoying advanced facilities and excellent learning environment, nearly one hundred MBBS students from 25 countries have embarked on their academic journey here. Meanwhile, the school has also recruited nearly five hundred postgraduates since 2020.

Focusing on cutting-edge science and technology, and major strategic needs, ZJU-ISM has established a public technology platform, experimental animal center and standardized PI laboratory. At present, there are 1 academician and over 100 outstanding experts working in six research centers, including reproductive medicine, oncology medicine, regeneration and aging medicine, RNA medicine, metabolic medicine, and genetic medicine. The School is committed to exploring new models for clinical and basic integration and interdisciplinary system development, benchmarking on national high-energy life and health platforms.

Gathering global talents, ZJU-ISM will breed up the best medical professionals and research achievements. It will also promote innovation in medical education, establish its role as a global leader in science and technology, unleash the vitality in the healthcare industry, and address global health challenges.

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CB1
Gi
bar

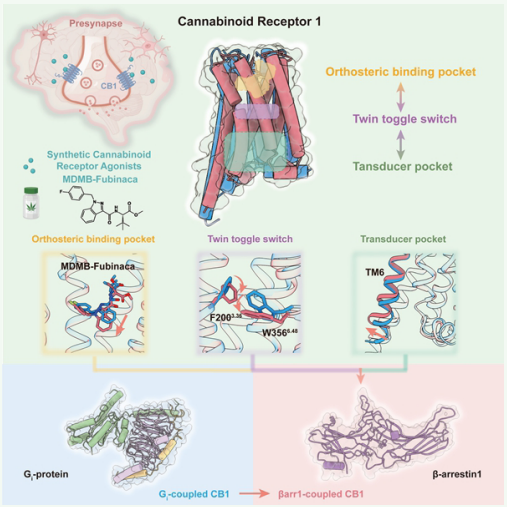
ZJU Scientists Decipher the Biased Signaling Mechanisms toward Cannabinoid Receptor 1

Addressing the long-standing Cannabis problem, an oddity that has vexed scientists for decades, joint research by Professor LI Xiao-Ming and Professor ZHANG Yan from Zhejiang University School of Medicine achieved a breakthrough by unraveling the signaling bias mechanism toward cannabinoid receptor 1 (CB1), facilitating safer synthetic cannabinoid targeting CB1. The findings were published in ***Cell*** under the title "Snapshot of the cannabinoid receptor 1—arrestin complex unravels the biased signaling mechanism" on Dec 14th, 2023.

Over the last ten years, the research team led by Prof. LI Xiao-Ming has been dedicated to identifying key target molecules CB1 in nervous system diseases and developing corresponding treatment strategies, thereby rendering CB1 a promising therapeutic target for pain relief, anti-anxiety, and anti-depression treatment. Cannabis activates CB1, which elicits analgesic and emotion regulation benefits, along with adverse effects, via Gi and β-arrestin signaling pathways. However, the lack of understanding of the mechanism of β-arrestin1 (βarr1) coupling and signaling bias has hindered drug development targeting CB1.

Prof. ZHANG Yan and his team have been devoted to studying the signaling transduction mechanisms of GPCR in major diseases and have also made substantial contributions to the advancement and establishment of cryo-electron microscopy (cryo-EM)-based GPCR pharmacology.

Prof. LI Xiao-Ming, Prof. ZHANG Yan and their colleagues have cooperated to determine the 3.1 Å cryo-EM structure of the CB1—βarr1 complex. The availability of a high-resolution map facilitates the accurate determination of the binding features of ligands in the CB1—βarr1 structure and reveals notable differences in



the transducer pocket and ligand-binding site compared with the Gi-protein complex, a task that has been unachieved in most GPCR—βarr1 complexes characterized at lower resolutions. βarr1 occupies a wider transducer pocket promoting substantial outward movement of the TM6 and distinctive twin toggle switch rearrangements, whereas FUB adopts a different pose inserting more deeply than the Gi-coupled state, suggesting the allosteric correlation between the orthosteric binding pocket and the partner protein site.

Taken together, the joint labs led by Professors Li and Zhang have pioneered studies of cannabinoid receptors. Furthermore, this research not only proposes a comprehensive model for the molecular mechanism of signaling bias, but also builds a solid foundation for the development of safer synthetic cannabinoids and the clinical application for the CB1 compounds in treating neurological and psychiatric disorders.

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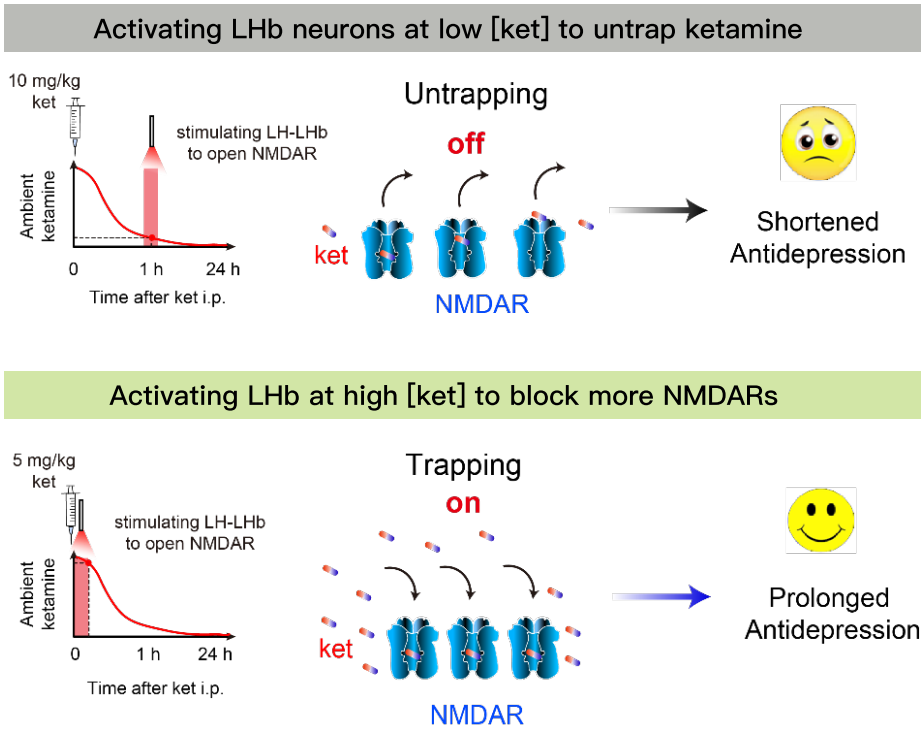
HU Hailan's Group Published in *Nature* on Ketamine

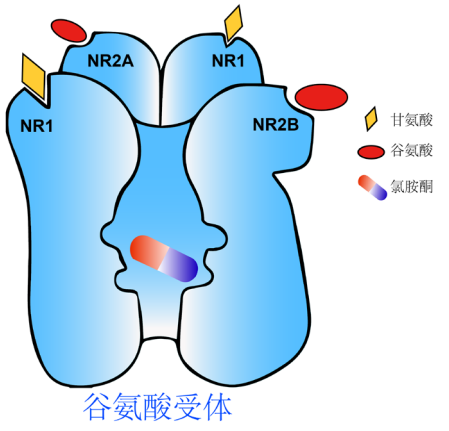
The research team led by Prof. HU Hailan has recently published an article titled "Sustained Antidepressant Effect of Ketamine through NMDAR Trapping in the LHb" on ***Nature*** online on Oct 18th, 2023. This research revealed ketamine trapped in NMDAR to mediate the mechanism of the sustained antidepressant effects of ketamine.

The use-dependent trapping properties of ketamine for NMDAR are the essence of its sustained antidepressant effects.

Ketamine, an N-methyl-d-aspartate receptor (NMDAR) antagonist, has revolutionized the treatment of depression because of its potent, rapid and sustained antidepressant effects. Although the elimination half-life of ketamine is only 13min in mice, its antidepressant activities can last for at least 24h. This large discrepancy poses an interesting basic biological question and has strong clinical implications. Here we demonstrate that after a single systemic injection, ketamine continues to suppress burst firing and block NMDARs in the lateral habenula (LHb) for up to 24h. This long inhibition of NMDARs is not due to endocytosis but depends on the use-dependent trapping of ketamine in NMDARs. The rate of untrapping is regulated by neural activity. Harnessing the dynamic equilibrium of ketamine—NMDAR interactions by activating the LHb and opening local



NMDARs at different plasma ketamine concentrations, we were able to either shorten or prolong the antidepressant effects of ketamine in vivo. These results provide new insights into the causal mechanisms of the sustained antidepressant effects of ketamine. The ability to modulate the duration of ketamine action based on the biophysical properties of ketamine—NMDAR interactions opens up new opportunities for the therapeutic use of ketamine.



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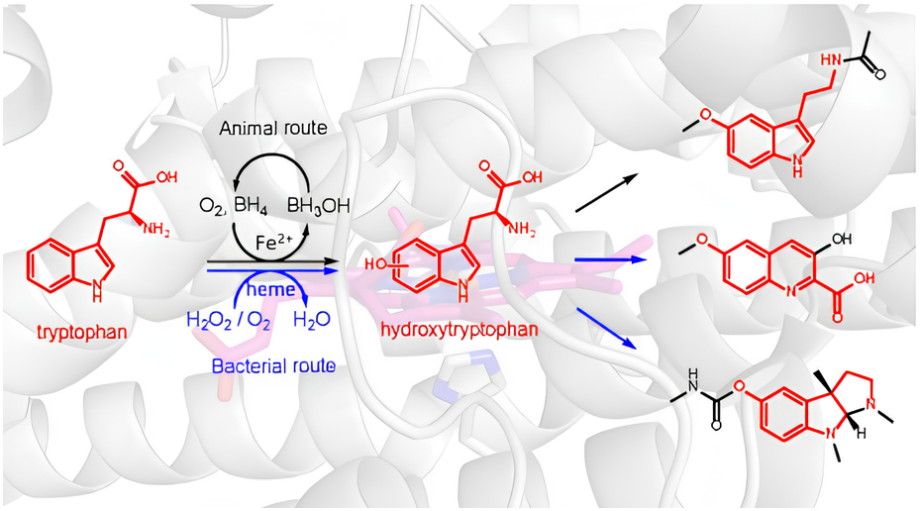
Discovery of a Novel Bacterial Route to 5-hydroxytryptophan

Tryptophan is one of the essential proteinogenic amino acids for the human body. In addition to its role as a building block for protein synthesis, tryptophan is also a metabolic precursor to a variety of important signaling molecules, including the important human neurotransmitter serotonin (5–hydroxytryptamine, 5–HT), the plant growth hormone indoleacetic acid and the bacterial signaling molecule indole.

In the biosynthesis pathway of 5–HT in humans, tryptophan hydroxylase (TPH1 or TPH2) catalyzes the initial hydroxylation reaction at the C5 position of tryptophan's indole ring, forming 5–hydroxytryptophan (5–HTP), which then undergoes decarboxylation to yield 5–HT. The neurotransmitter 5–HT widely participates in regulating human emotions, cognition, memory, and other physiological processes. 5–HT can be further converted into the hormone melatonin, which is a hormone that regulates circadian rhythm. Eukaryotic tryptophan hydroxylases, including the human's, belong to the family of aromatic amino acid hydroxylases. These enzymes use molecular oxygen and tetrahydrobiopterin as co–substrates and insert one oxygen atom from O2 into tryptophan. Although bacteria are also known to utilize 5–HTP as a building block for several specialized metabolites, how bacteria synthesize hydroxytryptophan remains a mystery.



On August 31, 2023, an article titled "Hydroxytryptophan biosynthesis by a family of heme–dependent enzymes in bacteria," from Du Yi–Ling's group at Zhejiang University School of Medicine, was published in ***Nature Chemical Biology***. In this study, researchers report a class of tryptophan hydroxylases that are involved in various bacterial metabolic pathways. These enzymes utilize a histidine–ligated heme cofactor and molecular oxygen or hydrogen peroxide to catalyze regioselective hydroxylation on the tryptophan indole moiety, which is mechanistically distinct from their eukaryotic counterparts from the nonheme iron enzyme family. Through genome mining, researchers also identify members that can hydroxylate the tryptophan indole ring at alternative positions. These results thus reveal a conserved way to synthesize hydroxytryptophans in bacteria.

Compared to the eukaryotic pathway, the reaction catalyzed by the bacterial tryptophan hydroxylase family is more streamlined. Considering that hydroxytryptophans hold great potential as building blocks for pharmaceutically important molecules, the newly discovered bacterial tryptophan hydroxylases could be valuable biocatalysts in the field of synthetic biology. Melatonin has various uses such as improving sleep, regulating immunity, and anti–aging, and boasts a global market scale in billions. As a proof of concept, the researchers designed a novel artificial pathway for efficient biosynthesis of melatonin in engineered bacteria.

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PML B-Box 2 Trimerization Yields a Cysteine Triad for Arsenic Binding in APL Therapy

ProMyelocytic Leukemia (PML) protein controls various biological functions, such as apoptosis, senescence or stem cell self-renewal. PML may elicit these functions by scaffolding the spherical shells of PML Nuclear Bodies (NBs), which subsequently act as hubs of post-translational modifications, in particular sumoylation, for the broad range of proteins trafficking through their inner cores. PML NBs are disrupted in Acute Promyelocytic Leukemia (APL) driven by the PML-RARA oncogenic fusion protein. Arsenic trioxide (ATO) cures 70% APL patients through driving PML-RARA degradation and NB reformation. In non-APL cells, arsenic binding onto PML also amplifies NB formation. Yet, the actual molecular mechanism involved remains elusive.

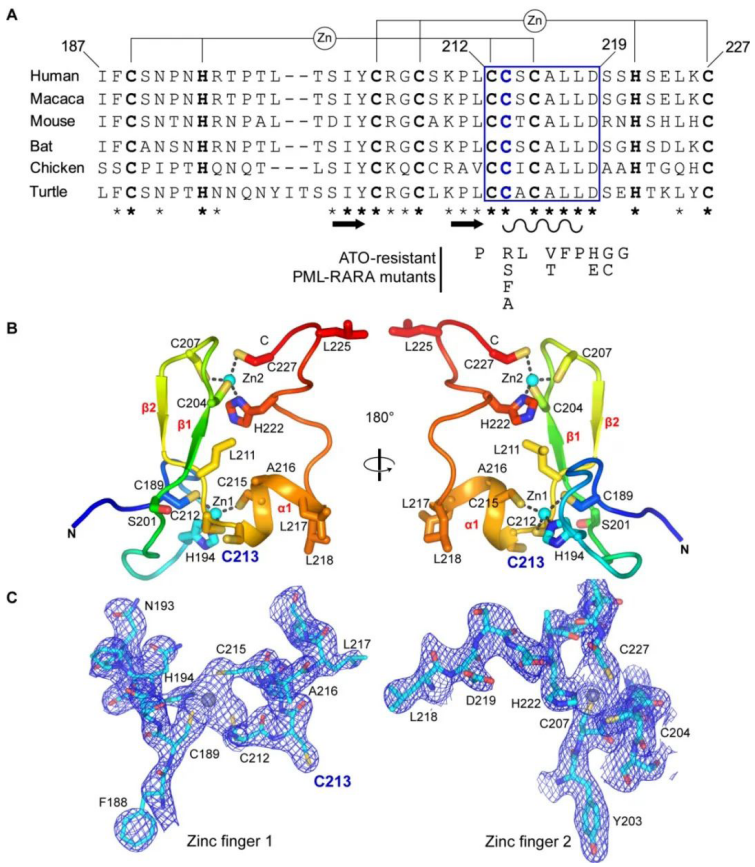

Figure 1. Crystal structure of PML B2 monomer.

The research team led by Professors HUA Naranmandura, ZHOU Chun from Zhejiang University School of Medicine and Hugues De The, Valerie Lallemand-Breitenbach from France, has made a significant breakthrough in understanding how arsenic targets the PML protein. The research team has successfully elucidated the crystal structure of PML B-box 2 (B2) and identified an α-helix that mediates B2 trimerization through hydrophobic interactions. Importantly, the α-helix-mediated trimer organizes a triad of free C213 cysteines to which trivalent arsenic covalently docks. This triggers ATO-induced PML-RARA-degradation, which is the first step in ATO's anti-leukemia cure. Their findings are detailed in an article titled "Structural Basis of PML/RARA Oncoprotein Targeting by Arsenic Unravels a Cysteine Rheostat Controlling PML Body Assembly and Function", published in ***Cancer Discovery***.

B-box domains are frequently present in Tripartite Motif (TRIM) proteins. TRIM5α B2 was proposed to trimerize through a specific α-helix around a tryptophan core in vitro. We thus looked at whether PML B2 monomers could self-assemble into a trimer through Alphafold2 molecular modeling. In the model, the trimer is predicted to be driven by α1-helix mediated interactions, involving hydrophobic interfaces and in particular, I202,

C213, A216, L217 and L218. Supporting this notion, point mutations of these potentially interfacing residues (I202A, L218G, L217G, A216V) disrupted NB assembly and exhibited highly dynamic exchange with liquid–like behaviors, as analyzed by immunofluorescence and FRAP. Furthermore, SEC–MALS analysis revealed three forms of purified MBP–B2 with molecular weights corresponding to monomer, dimer, and critically, abundant trimer.

ATO and other therapeutic arsenic derivatives provide trivalent arsenic (As(III) oxidation state) at physiological pH and in vivo. As(III) can form stable complexes with thiol groups through covalent binding to sulfur and may form a complex with three glutathiones in solution. Critically, the key C213 residues are organized in a triad positioned at the center of the PML B2 helix trimer, fitting with an ideal arsenic docking. We thus hypothesized that ATO could target PML NBs by interacting with this triad of C213 residues within the B2 trimer. To interrogate the relevance of this model in cellulo, we generated several point mutations. While mutations of C213 removing thiol group (C213S or C213A) and increasing steric hindrance (C213L or C213F) all disrupted basal PML NB assembly, replacing C213 by valine unexpectedly fully rescued the basal NB formation and normal dynamics. Strikingly, both PML C213V localization and dynamics were insensitive to ATO, implying that the sensor function was lost. Accordingly, alkylation by NEM, which disrupted WT NBs, had no effect on PMLC213V NBs, stressing the unique features of this cysteine residue. Altogether, this suggests that, within the B2 domain, C213 may directly contribute to arsenic binding.

This study establishes that the PML B2 structure reveals an alpha helix that drives B2 trimerization and positions a cysteine trio to form an ideal arsenic–binding pocket. Altering either of

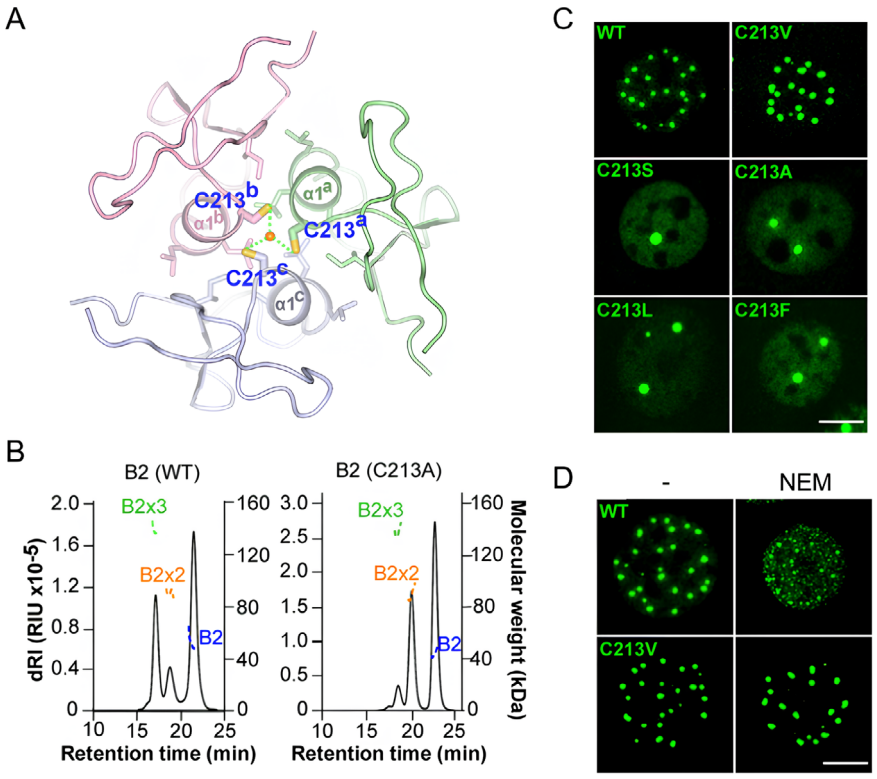

Figure 2. Arsenic docks on a C213 tri–cysteine pocket of B2 trimers

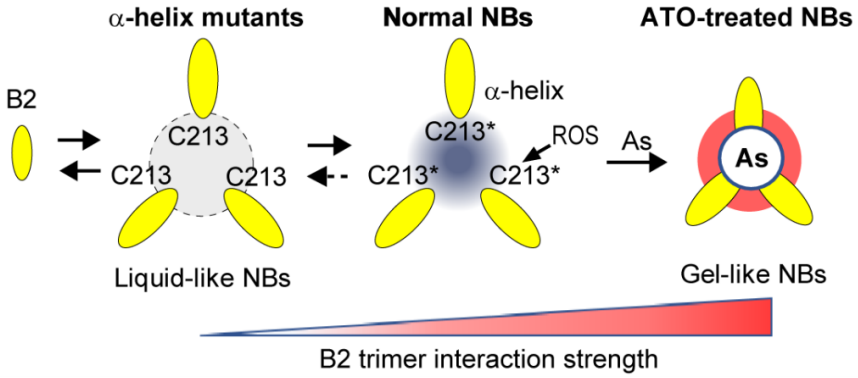

Figure 3. Model of PML NB liquid to gel–like transition controlled by the C213–containing B2 α1 helix hijacked by ATO

the latter impedes ATO–driven NB–assembly, PML sumoylation, and PML–RARA degradation, providing a mechanistic explanation for clinical ATO–resistance. The B2 trimer and the C213 trio create an oxidation–sensitive rheostat that controls PML NB assembly dynamics and downstream signaling in both the basal state and during stress response. These findings identify the structural basis for arsenic targeting of PML, which could pave the way for novel cancer drugs.

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Seeking and Targeting the Root Cause of Human Leukemia Complexity

Leukemia stem cells (LSC) are the root cause of acute myeloid leukemia (AML), a devastating form of blood cancer characterized by hyper–proliferation of aberrantly differentiated cancerous blood cells of the myeloid lineage. Conventional theory holds that LSCs are primarily cell cycle quiescent, and thus are capable of evading cell cycle targeting chemotherapy agents, leading to life–threatening relapse responses. Thus, LSC targeting represents an important strategy in the development of new therapies for a better cure of AML.

Recent studies in the AML field began to illustrate the complex inter — and intra–patient heterogeneity of human acute myeloid leukemia, posing immediate and unformidable challenges to the development of targeted therapies such as small molecule BCL–2 inhibitor Venetoclax and immunotherapies such as the Chimeric Antigen Receptor — T (CAR–T) cell therapy. The root cause of "heterogeneity" as well as the intervention of therapeutic strategies to target the "heterogeneity", however, are significantly lacking.

On August 17th, 2023, Dr. PEI Shanshan's group at Liangzhu Laboratory and Bone Marrow Transplantation Center of the First Affiliated Hospital of Zhejiang University School of Medicine along with Dr. Craig Jordan's group from the Division of Hematology, University of Colorado School of Medicine published a paper titled "A novel type of monocytic leukemia stem cell revealed by the clinical use of venetoclax–based therapy" in the journal ***Cancer Discovery***. The paper reports a new type of LSCs is responsible for the root cause of monocytic AML and confers relapse/refractory responses to venetoclax–based therapy in AML patients and reveals biological mechanisms underlying the "cladribine/Venetoclax" combination therapy, showing effective targeting of AML heterogeneity and better cure of AML.

Dr. PEI Shanshan, the co–first and co–corresponding author of this paper, joined Liangzhu Laboratory as a principal investigator in early 2022. His team is focusing on basic and clinical translational research of human acute myeloid leukemia. Dr. PEI's lab members Wang Yanan, Dr. Liu Lina, and Dr. Liu Jun jointly contributed to this research.

Venetoclax is a newly FDA–approved drug to treat AML through targeting the antiapoptotic protein BCL–2. Due to its remarkable efficacy, venetoclax–based therapies are revolutionizing the AML clinic. It is important to note that after almost fifty years of the "conventional chemotherapy era", the AML field is rapidly evolving into the "new venetoclax era" in the past few years. However, a significant proportion of AML patients treated with a venetoclax therapy are still experiencing relapse/refractory responses. Thus, it is urgent to reveal their resistance mechanisms and develop targeted solutions.

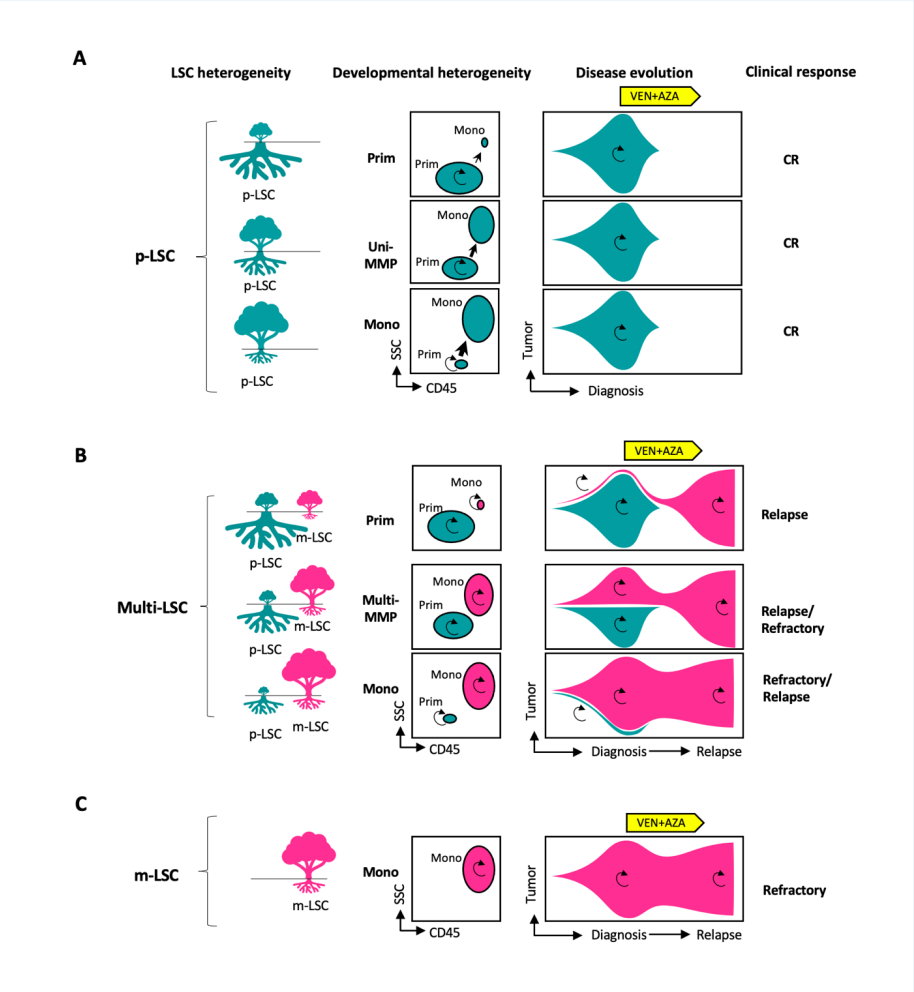
This study is designed to meet the above challenge by focusing on AML patients treated with venetoclax–based therapies. By analyzing longitudinal tumor samples obtained from AML patients who relapsed from the venetoclax–based therapy, applying experimental approaches such as patient–derived xenograft mouse models (PDX), single–cell multi–omic analysis (CITE–seq), whole exome sequencing (WES) and others, the study found that the use of venetoclax–based therapy has revealed a previously unrecognized form of pathogenesis characterized by monocytic disease progression. The study demonstrated that this form of disease arised from a fundamentally different type of LSC, designated as monocytic LSC

(m–LSC), that is developmentally and clinically distinct from the more well–described primitive LSC (p–LSC). The m–LSC is distinguished by a unique immunophenotype, distinct transcriptional state, preferential reliance on purine metabolism, and selective sensitivity to a well–known drug—cladribine.

Importantly, the study found in a subgroup of AML patients, m–LSC and p–LSC subtypes can co–reside in the same patient and simultaneously contribute to the patient's tumor complexity —shedding light on the root cause of AML heterogeneity at the stem cell level. By combining Cladribine with Venetoclax–based therapies in PDX models, leukemia subpopulations initiated by p–LSC and m–LSC can be eliminated simultaneously, effectively targeting the heterogeneity of AML and achieving a deeper cure.

It is worth mentioning that this study not only explores the relationship between LSC heterogeneity and the development and clinical evolution of AML, but also provides important mechanistic insights that may explain results from several recent clinical trials reporting superior treatment outcomes when venetoclax is combined with chemotherapy regimens containing cladribine or its close analogue fludarabine. These regimens have produced unprecedented overall response rates up to 95%, significantly above the rate of 65–70% achieved by conventional chemotherapy. The opposing spectrum of venetoclax resistance and cladribine sensitivity along the myeloid differentiation axis revealed in this study indicates that treatment regimens combining cladribine and venetoclax can be an important future direction in the AML clinic.

Based on the work, the research team provided a model of how LSC heterogeneity determines the development and clinical evolution of AML disease.



As shown above, the authors use the tree as an analogy to describe the developmental hierarchy of AML where the underground roots represent LSCs and the branches above the ground symbolize more differentiated leukemia disease, aka, blasts. In panel A, a single class of more primitive LSCs (p–LSCs) may be present in newly diagnosed AML patients, with varying degrees of monocytic differentiation potential. In this scenario, no m–LSCs are present, and venetoclax–based therapies would be predicted to confer relatively high CR rates and longer remissions. In contrast, as shown in panel B, some AML patients present with at least two distinct subtypes of LSC with primitive vs. monocytic characteristics (p–LSC and m–LSC). Depending on the size of the m–LSC population, these patients would be expected to experience brief responses followed by relapse, or to be refractory to venetoclax–based therapies. Finally, as shown in panel C, in more extreme cases, m–LSCs are the dominant population, which would likely result in disease that is upfront refractory to venetoclax.

In summary, this study provides a new perspective to understand the root cause of AML heterogeneity and how they affect the development and clinical evolution of AML. It also serves as the proof–of–principle for the design of treatment strategies such as the Cladribine/Venetoclax combination therapy that are tailored to target AML heterogeneity and deliver a better cure.

For more information
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How Gut Microbes Manipulate the Immune System to Trigger Fat Absorption

Microorganisms are often in battle with the immune system. But research in mice has shown that gut microbes work in tandem with it to determine how much fat the gut absorbs.

Microbes have been found to harness the immune system to suppress the production in the gut of genetic material — called long non–coding RNA (lncRNA) — which increases fat absorption from food. The finding may hint at new ways to treat obesity and type 2 diabetes.

Gut microbes are known to influence metabolism, but the details have been unclear until now, says WANG Yuhao, a biochemist at Zhejiang University, who led the study. "The relationships between gut microbiota and host metabolism are intricate and complex," he says.

The experiments were performed on mice, but humans carry the same lncRNA, says Wang. "Our findings reveal intriguing therapeutic targets and raise the prospect of novel therapies for metabolic diseases, such as obesity and type 2 diabetes."

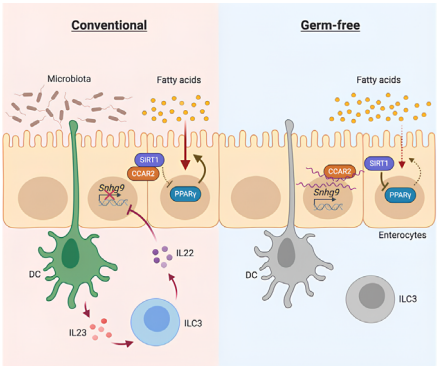
Fat control

Wang's team had already identified the mouse circadian clock as one factor in the relationship between gut microbiota and mice metabolism. lncRNAs were another factor shown to influence metabolism, but whether the microbes could direct lncRNA production remained unclear.

For their study, published in ***Science***, the team first analysed all the lncRNAs produced by cells lining the intestines of mice that were devoid of gut microbes, and compared them to those of normal mice. The gut microbe–free mice contained many more copies of one lncRNA called *Snhg9*, suggesting that microbes may suppress levels of it.

The researchers found that *Snhg9* is bound tightly to CCAR2 in the intestinal cells, a protein called which inhibits an enzyme that decreases fat absorption from food. They hypothesized that when *Snhg9* blocked the action of CCAR2 in this way, it unleashed the fat–regulating enzyme, resulting in less fat being absorbed by the intestine.

To test their idea, the researchers edited mice the genes of mice so that they produced more *Snhg9* and then fed them a high–fat diet. Compared to the unaltered mice, also on a high–fat diet, the edited mice had less fat in their intestines and excreted more fat. Once they reached 10 weeks of age, the gene–edited mice had less body fat and less liver fat compared to the unaltered mice. Unaltered mice that had their gut microbiota eradicated with antibiotics also had less body and liver fat, suggesting that without the gut microbes, they were less efficient at absorbing fat.



Immune mechanisms

Further testing by the Zhejiang team revealed that the gut microbiota achieves control of the production of *Snhg9* via the mouse immune system. Microbial signals are first recognised by immune cells called myeloid cells which secrete an immune signaling protein called interleukin–23. This triggers a cascade of different immune proteins, until one, called interleukin–22, is secreted. This triggers cells lining the intestine to stop producing *Snhg9*. The researchers are now confirming the type of gut microbe that induces this immune cascade, and working on ways to control the production of *Snhg9* by adjusting microbial communities in mouse intestines. "Controlling *Snhg9* with targeted compounds, or developing other therapies through microbiome alterations with probiotics or prebiotics, could be novel avenues for treating metabolic disorders," says Wang.

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Zhejiang Pioneers Robot-Assisted Surgery to Alleviate Children's Pain

In April 2020, the Children's Hospital of Zhejiang University School of Medicine, hereinafter referred to as Children's Hospital, took the lead in introducing the first Da Vinci surgical robot to children's hospitals in China. This cutting-edge technology found its home in the hospital's 15th operating room. Since the arrival of this machine, the 15th operating room has been operating almost 24/7. Over the past 43 months, it has been involved in more than 2,300 surgeries with a success rate exceeding 99%.

Under the doctors' adept operation, the cold instruments have been turned into magical tools, thus alleviating the suffering of thousands of children plagued by diseases.

Xinxin is a 5-year-old boy from Jiaxing City, Zhejiang Province. Two years ago, he underwent "heart repair" surgery at Affiliated Children's Hospital due to patent ductus arteriosus (PDA). He was the first child in the country to undergo daytime PDA ligation surgery with the assistance of the Da Vinci surgical robot.

"The child is now in kindergarten, with his height and weight exceeding the class average. He rarely experiences colds or fevers." Two years have passed, and his good health has even allowed his parents to forget that he was once a child with congenital heart disease.

His parents mentioned that before the surgery, they had also contemplated other treatments. They opted for PDA ligation surgery with the assistance of the Da Vinci robot because they wanted to have their child treated in a thorough yet minimally invasive way, which worked out just as they'd hoped.

Xinxin's surgery was performed by the team led by Professor SHU Qiang, a pioneer in pediatric surgery. His team is also the world's first to attempt Da Vinci surgical robot-aided PDA ligation surgery. SHU Qiang acknowledged that PDA is not a complex condition and the surgery could have been performed efficiently without the Da Vinci robot, which would involve less risk and pressure for the doctors. However, it is hard to achieve technological progress without exploration and innovation. The surgical outcomes justified the value and merit of the attempt.

Similarly, Mei Mei, a 12-year-old patient, also benefited from Da Vinci robot surgery. Having been diagnosed with a liver tumor measuring the size of a goose egg (7.6*6.4cm) over a year ago, Mei Mei underwent Da Vinci robot-assisted liver tumor removal surgery and was discharged in less than ten days. Professor GAO Zhigang, Director of the Laparoscopy Center, led the surgical team. Mei Mei is now able to attend school every day, showing no signs of being a former liver tumor patient.

"Advancements led by the surgical team in the fields of cardiology, thoracic surgery, urology, general surgery, neonatology, and oncology have expanded the applications of surgery. Even newborns weighing 1.5kg can now undergo such surgery, and an increasing number of children are benefiting from modern medical advances."

Children's Hospital has been designated as the National Teaching Demonstration Center for Da Vinci robotic surgery, the Chinese Pediatric Thoracic Surgery Teaching Center for Da Vinci robotic surgery, and the Artificial Intelligence-Assisted Treatment Technology Training Base. The hospital will continue to spearhead domestic exploration into the integration of medical education and practices, disseminating advanced experiences and technologies not only within the country but also internationally. Pediatric Robotic Surgery, co-edited by SHU Qiang and others, was recently published by Springer and distributed globally.

"Our multifaceted exploration and innovation, such as the innovative layout for reducing Trocar spacing and depth for newborn patients, and lowering intraabdominal pressure to a minimum, have significance for our international counterparts as well." noted GAO Zhigang.

For more information
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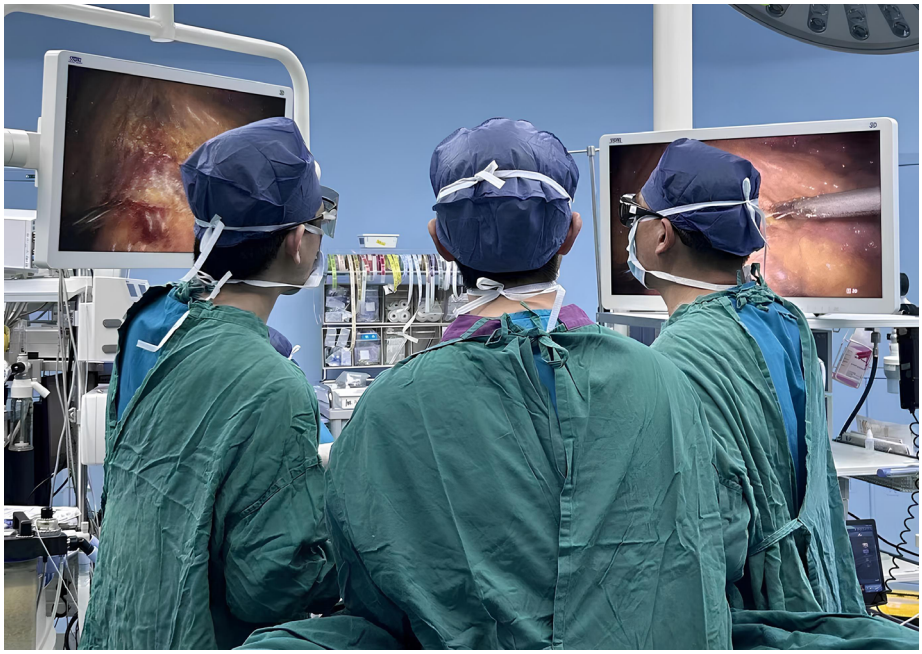
The World's First 3D Laparoscopic-Assisted Living-Donor Small Bowel Transplantation in China

The First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU) recently performed the world's first 3D laparoscopic–assisted living–donor small bowel transplantation. A critically ill two–year–old girl received 1.8 meters of the small intestine from her 29–year–old mother. Both the mother and daughter have currently been doing well and the little girl is about to be discharged from the hospital soon.

The patient, nicknamed as Nini from Henan province, China, was diagnosed with acute intestinal volvulus in early 2022. Because of subsequent necrosis, most of her bowels were removed. Despite parenteral nutrition support, her condition continued to deteriorate along with hepatic impairment and catheter–related sepsis. The Nini's mother, who had been pregnant with her second child, came to the Intestinal Transplant Center for help.

Dr. WU Guosheng, Professor and Chief of the Intestinal Transplant Center, is a leading expert in intestinal transplantation. After carefully evaluating Nini and her mother, he suggested living donor transplantation and proposed using 3D laparoscopic surgery to procure a segmental bowel for grafting. Compared with decreased donation, this approach has advantages including shorter cold ischemia times, better HLA matching, easier application of desensitization therapy, and elective nature.



In June 2023, the transplant team procured a segmental small bowel using 3D laparoscopy from Nini's mother and successfully grafted into this little poor girl. The total operation time was approximately five hours and was uneventful.

After a short stay in the intensive care unit, Nini was transferred to a regular ward and the precious bowel gift from her mother has been functioning well. She started to take oral food and would be discharged soon.

Dr. WU said that the intestinal transplant program has performed more than one hundred cases of small bowel transplantation since its establishment in October 2019.

The patient and graft survival have steadily been improving. The recent publications from his team show that LDITx is a valuable treatment option for patients with end–stage intestinal failure. Improved immunosuppression, better HLA matching, and shorter cold ischemia times are associated with reduced rates of rejection, viral–mediated infection, and improved graft survival. In addition, living donor graft resection is associated with minimal short — and long–term morbidity and remains an attractive alternative for potential recipients when suitable deceased donors are unavailable.

For more information
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The Lung Transplantation Team at SAHZU

Perhaps no one understands the value of breathing more profoundly than patients awaiting lung transplants. With their lungs extensively damaged and breathing with great difficulty, they depend entirely on oxygen, ventilators, and ECMO for survival. For them, lung transplantation represents the last and only hope for life.

Recently, Professor CHEN Jingyu's team at the Second Affiliated Hospital of Zhejiang University School of Medicine (SAHZU) successfully performed a double lung transplantation on a patient who had been maintained on ECMO for 131 days, thereby setting a new record for successful lung replacement in ECMO bridge patients.

Recalling the patient's harrowing battle against death, CHEN Jingyu described it as "thrilling". "When we saw the patient, everyone was extremely anxious for him! He had severe pneumonia, lung fibrosis, severe pulmonary hypertension, septicaemia, post-cardiac arrest CPR... Plus, he had been on ECMO for over four months. His whole body's coagulation function was almost completely disordered, with his platelets in single digits. This posed a tremendous challenge for us," said CHEN Jingyu.

During the procedure, CHEN Jingyu modified the usual anterolateral thoracotomy to a Clamshell trans-sternal incision, significantly improving the surgical field of view. The ECMO setup was altered from peripheral VV-ECMO to central VAV-ECMO, further reducing the strain on the heart. To address bleeding throughout the thoracic cavity, transfusions of prothrombin, fibrinogen, and platelets were administered. In response to sudden intraoperative ventricular fibrillation, emergency intrathoracic defibrillation was performed... After more than seven hours, the surgery concluded successfully, with the newly transplanted lungs beginning their vital functions within the patient's body. However, the surgery was just the first step. The lengthy postoperative recovery period was overseen by Director HUANG Man's ICU lung transplantation team. Fortunately, under the meticulous care of the intensive care team, the patient successfully navigated this phase, was discharged as planned, and returned to a normal life.

Prior to this, the lung transplantation team led by CHEN Jingyu had achieved several medical breakthroughs. These included the world's first ECMO-assisted double lung transplant for lung fibrosis resulting from H1N1, with ECMO support lasting 45 days before the transplant, the world's first bilateral lobectomy ectopic lung transplantation, and a successful double lung transplantation for a COVID-19 patient who had been maintained on ECMO for 73 days.

"Lung transplantation cannot succeed based solely on the efforts of the surgeon alone; it requires the comprehensive strength of the hospital and the collaboration of a multidisciplinary team," CHEN Jingyu explained. The rapid advancement in lung transplant procedures at SAHZU is attributed not just to mature surgical techniques, but also to the robust support of a diverse team, including experts from the departments of lung transplant, critical care medicine, anesthesiology, thoracic surgery, cardiology, nursing, and medical technology, all providing strong backing and ensuring patient safety.

Since the first lung transplantation performed on September 28, 2002, CHEN Jingyu has performed over 1,500 surgical procedures. The early survival rate of Chen's patients remains at an impressive 90%, and CHEN Jingyu has earned the title "China's Best Doctor for Lung Transplantation."

In 2021, CHEN Jingyu spearheaded the establishment of the Lung Transplantation Center at SAHZU. The Center now has one ward with 32 beds. Over the past three years, in addition to routine lung transplantation, the center has also pioneered several world firsts and national firsts related to lung transplantation procedures. They have also developed unique standardized procedures for perioperative management and rapid recovery.

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Medical Educators Giving Marvelous Lectures

Giving an exemplary lecture is, in itself, an art. In the Zhejiang University School of Medicine (ZUSM), a cohort of devoted educators, well-versed in their respective fields and driven by a passion for teaching, are taking the lead in shaping the future generation. They dedicate their time and energy to each class and lesson, epitomizing an unwavering commitment to education.

YU Peilin
Associate Professor, Department of Toxicology, Zhejiang University School of Public Health
First Prize Winner, Medical Group, 6th National University Teaching Competition for Youth Teachers

Putting students at the center is the key to delivering an excellent lecture for Yu. In the teaching design of the segment on "Ionizing Radiation" within the course on "Environmental Toxicology", she initiates the course content by delving into a case that is widely known among the students—the Chernobyl disaster. Following an extensive literature review and online research, she narrows her focus to the population who were involved in the post-accident radiation cleanup efforts. Through a role-playing interactive activity, she introduces the ionizing radiation-induced toxic effects and harm that people suffered. Building on this foundation, she integrates research findings from the field of science to focus on the key mechanisms, further analyzing the protective measures for combatting ionizing radiation. She elevates the discussion from the selfless dedication of those involved to a scientific approach to dealing with nuclear radiation, connecting it to a sense of patriotism and scientific spirit in the course's ideological and political education, and thereby transforming the entire lecture into a well-structured, progressively layered, logically coherent entity.

> ***In university classrooms, the teaching objectives of any outstanding course must encompass comprehensive guidance for students at different levels of knowledge, thinking, and ideology. This aligns the imparting of knowledge, the cultivation of scientific thinking, and ideological education under the core principle of content supremacy.***

JIANG Hongjie
Deputy Chief Physician, Department of Neurosurgery, Second Affiliated Hospital, Zhejiang University School of Medicine
Special Prize Winner, Medical Group, 13th Zhejiang Province Teaching Competition for Youth Teachers

In Jiang's classroom, establishing a good doctor-patient relationship is one of the essential components. "In practical terms, medical treatments and diagnoses pose no inherent issues; however, when relayed to patients, they often seem to carry a different tone. The crux of the matter lies in doctor-patient communication. It demands the skill to convey highly specialized knowledge in a straightforward manner that resonates with patients and their families. This, indeed, is a nuanced skill."

Therefore, in the teaching process, Jiang particularly emphasizes the close integration of medical knowledge outlined in the curriculum with practical clinical work. Additionally, he strives to reasonably incorporate medical knowledge, diagnostic and treatment skills, doctor-patient humanities, and cutting-edge advancements into the teaching sessions, hoping that students can fundamentally understand and master the seemingly tedious and voluminous medical theories in the textbooks through these authentic clinical practices.

> ***Medical education is a crucial part of the growth process for medical students. As a clinical physician, my deepest insight is that clinical teaching should focus on the students, flexibly apply theoretical knowledge, and transform textbook knowledge into clinical practice.***

Education is not about instilling, but igniting. The exploration of teaching innovation should always revolve around how to effectively promote the practice of teaching and learning. Only when students are engaged in the process of constructing knowledge does their learning truly attain depth and significance.

SHEN Jing

Associate Director, Department of Pathology and Pathophysiology, Zhejiang University School of Medicine

Third Prize Winner of the Third National University Innovative Teaching Competition

"Utilize online and offline resources, digitize, and multidimensionally focus on the entire process of inquiry — based learning." This is the answer provided by SHEN Jing, the teacher for the "Physiological Science Experiment" course.

Shen has implemented a series of innovative reforms, driving the comprehensive digitization of the course. In the online realm, she has constructed virtual patient experiments based on "physiological data-driven" approaches, ranging from local organ systems to overall disease models. This enables students to apply their basic medical knowledge in early-stage virtual clinical practices, shifting from passive teaching, where the emphasis is on instructing, to a mode where the primary focus is on application through active learning. In the classroom, by modularizing the key teaching segments and standardizing the guiding strategies, Shen Jing, along with the teaching team, has created various student-centered active learning methods, including discussion-based flipped classrooms, a combination of virtual and real Team-Based Learning (TBL), case-driven integrated TBL (iTBL), and project-based team collaboration.

Shen also employs digital evaluation methods throughout the teaching process. Seamlessly integrating teaching and research, she actively transforms the latest research findings into educational content to ignite the students' interest in both learning and research.

CEN Dong

Attending Physician, Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine

First Prize Winner, Medical Group, 13th Zhejiang Province Teaching Competition for Youth Teachers

Cen's classroom is characterized by a teaching model that seamlessly integrates theoretical knowledge with clinical cases, aligning teaching content with the development of the discipline. This approach, which closely intertwines classroom instruction with collaborative exploration, has garnered widespread acclaim among students. Cen has meticulously crafted a problem-oriented, case-based, easily comprehensible, and progressively structured teaching methodology.

Taking acute pancreatitis in surgical science as an example, Cen uses clinical cases as an introduction, leading into the topic and posing questions. Throughout the lecture, he incorporates etiology, pathogenesis, and clinical manifestations in the initial section, while addressing diagnosis and treatment in the subsequent parts. The prevention of recurrence and follow-up are assigned as post-class reflection questions, completing the clinical practice loop for acute pancreatitis. Incorporating real clinical cases, Cen, by employing methods such as teacher-student Q&A and group discussions, applies and practices theoretical knowledge in clinical cases. He also integrates communication skills between doctors and patients with clinical cases, thus cultivating the students' humanistic spirit. Furthermore, he integrates prospective research from esteemed journals, such as ***the New England Journal of Medicine***, amalgamates team research accomplishments, introduces treatment principles, and develops an innovative teaching model, that is centered on patients and guided by clinical problems. This realization underscores the integration of ideology and education within the curriculum.

As a young teacher, my greatest belief is the importance of empathetic thinking. Sometimes, considering issues from the students' perspective can achieve results with half the effort.

Youth Volunteers' Contribution to the Asian Games

On October 8, 2023, the 19th Hangzhou Asian Games successfully concluded. The Chinese delegation won a total of 383 medals, marking its best ever performance. Volunteers from the Zhejiang University School of Medicine, known as the "Little Green Lotus," have served and supported the Asian Games in various ways.

"If you have any problem, turn to the volunteers." As the leader of our volunteer team, I felt immensely proud every time I heard that comment. It was these simple, plain words that inspired all of us teachers and students to make concerted efforts regarding the Asian Games. Thank you, dear "Little Green Lotus". Through your sincerity and enthusiasm, you have shown the world the "warmth and mien of China", allowing the "strength of Zhejiang University's Green Lotus" to shine even more brightly!

YUAN Weiqi, counselor, School of Medicine

"Little Green Lotus blossoms, fragrant for miles; volunteers on duty, spirited for days." I was keen to be a volunteer, contributing to the Games and shouldering my responsibilities. I was keen, with a strong, resilient heart, to display the spirit of Zhejiang University students to the world.

HUANG Jinhao, Class 2103, Clinical Medicine (5+3 program)

As a volunteer at the Main Media Center, my job is to guide and provide assistance to visitors. Through my position, I have experienced the joy of interacting with others and the satisfaction of genuinely helping people. Rain or shine, I am always fully committed to my duties and serve every journalist to the best of my ability.

XU Zihang, Class 2102, Preventive Medicine

It was an honor to serve as a volunteer at the awards ceremonies of the Asian Games. In July, we received targeted strength training—lifting bottles of water. We were asked to lift between one and five bottles steadily, while maintaining a graceful, natural posture. The training was tough, but when I stood next to the award podium, sharing the joy and pride at the victory with the athletes, there were only two words in my mind: worth it.

QI Ziyi, 2022 graduate student of Nursing

My experience of serving at the Asian Games was filled with joy and opportunities. I not only celebrated victories with my colleagues, but also had the privilege of catching a glimpse of the athletes who attended press conferences. By contributing to the Asian Games, I was able to become integrated into the cultural wave of Asia and the world.

TAO Yaoyun, Class 2101, Preventive Medicine

My office was right next to the press hall, where I could hear the latest news about the Asian Games and see the athletes attending press conferences, with a tangible feeling that great events were unfolding. It was truly fulfilling to see the smooth operation of the Games, with contributions from myself and my fellow volunteers.

LIN Xiantian, 2021 PhD student of Internal Medicine

Father and Son Learning at ZJU: The Story of Two International Students from Thailand

The International School of Medicine of Zhejiang University (ZJU-ISM) welcomes nearly 100 international students from 25 countries to its brand-new campus. Among the freshmen studying the Clinical Medicine Major at ZJU-ISM is 19-year-old LI Sunwu from Thailand.

On Sept. 10, LI Sunwu arrived at ZJU-ISM in Yiwu County, Zhejiang Province, to register as a student, accompanied by his father, LI Xiongying, who commented, "The new campus is gorgeous! It reminds me of my own student days at ZJU."

LI Xiongying, professor at the College of Arts, Media and Technology (CAMT) of Chiang Mai University (CMU), pursued his doctoral degree in the School of Management of Zhejiang University from 2006 to 2012. During the six memorable years, LI Sunwu spent 18 months in a kindergarten in China, where he began to learn Chinese.

Since then, the Li family has developed a strong bond with China, and now they continue their connection with China in Yiwu, Zhejiang, known as the "World Supermarket".

"I want to study in China like my father and graduate from the same university," said LI Sunwu.

A month later, LI Sunwu was fully immersed in campus life. His courses, all taught in English, highlight fundamental skills, interdisciplinary research, and clinical practice. To review and better digest the content of his classes, he accessed it on the Zhiyun App, an online learning system of ZJU which is recognized as the most advanced in the province. During his leisure time, he goes to the stadium to take exercise, which offers first-class sports facilities: a spacious gym, dance rooms, martial arts halls, table tennis rooms, a swimming pool, tennis courts, etc.

LI Sunwu aspires to become an excellent clinician through six years of learning and bring back brilliant medical knowledge to Thailand. Also, he hopes to build a bridge of mutual understanding between people in China and Thailand.

In recent years, LI Xiongying, committed to cultivating talents in trade between China and Thailand, has started courses on cross-border e-commerce in CMU. Earlier, he paid several visits to Yiwu to conduct investigations. "Thailand is a co-contributor to the Belt and Road Initiative, and China has become its largest trading partner and market for agricultural exports. A remarkable part of the initiative, I believe, is seeking common development," commented LI Xiongying. He also expressed a desire to learn from Yiwu's experience of cross-border e-commerce, supply chains, and logistics systems, then introducing Yiwu products and experience to Thailand while bringing more Thai products to China. Following the registration, the father and the son headed immediately to the Yiwu International Trade City, the renowned small commodity market. "We are continuously adding new chapters to our story with China," commented LI Xiongying.

Saving a Life for the First Time after Receiving His Medical License! Thank You, Tao!

Tao, a postgraduate from the Zhejiang University School of Medicine (ZUSM), became the 965th hematopoietic stem cell donor in Zhejiang Province, successfully saving the life of a patient with a hematologic disease. He is also a resident physician at the Orthopedic Standardized Training Base of the affiliated hospital of ZUSM. This patient was his first since obtaining his medical license. From being a medical student to becoming a doctor, Tao exemplifies the compassionate spirit of the medical profession, demonstrating a "benevolent heart" in action.

A Single Act of Voluntary Blood Donation Spreads Love and Hope

This June, Tao received a call from the Red Cross, informing him that his registered blood sample had initially matched successfully with a patient. He was filled with a mix of astonishment and joy, having waited for this call for six whole years.

In 2016, he was admitted to ZUSM. Deepening his knowledge in medical studies, he discovered that hematopoietic stem cell transplantation is one of the effective treatments for patients with hematologic diseases, which motivated him to become a hematopoietic stem cell donor. In 2017, when a mobile blood donation unit visited the campus, Tao participated in his first voluntary blood donation. There, after learning about the procedure for hematopoietic stem cell donation, he contributed 10ml of blood and joined the Chinese Hematopoietic Stem Cell Donor Database.

After six years, when the awaited call finally came, Tao firmly replied, "I agree to donate".

Practicing the "Benevolent Heart" of A Doctor in His Own Way

Tao successfully donated 190ml of hematopoietic stem cell suspension. This 190ml of 'spark of life' helped a stranger with a hematologic disease start anew.

"This was my first patient after I obtained my medical license. Now, as a trained orthopedic doctor, I never anticipated that my first patient would be someone with a hematologic disease. I hope that my stem cells will assist the patient in defeating the illness, and I wish him a swift recovery and strength," he said.

Coloring His Youth with Selflessness

In 2019, while on route to a hospital internship, Tao encountered an elderly man suffering from cardiac arrest. At this critical moment, he swiftly moved to assess the situation and resolutely administered cardiopulmonary resuscitation.

In college, Tao devoted himself to public welfare activities, lending the vigor of his youth to noble causes. He organized his fellow students to conduct voluntary teaching activities in Qinghai, participated in activities aiming at raising public awareness of voluntary blood donation, stem cell donation, and organ donation, and served as a volunteer regarding anti–fraud and epidemic control activities.

Upon sharing his donation experience on the campus forum, he said, "I hope that what I share will enhance my classmates' understanding of hematopoietic stem cell donation. I hope everyone can help others and pass on warmth and strength in whatever way they can."

The 3rd Joint Lecture Series on Cancer Biology between Zhejiang University and University of Oxford

The 3rd Joint Lecture Series on Cancer Biology between Zhejiang University and University of Oxford was successfully held on November 8, 2023, at the Liangzhu Laboratory in Hangzhou. The event attracted over 400 attendees, both online and offline, from Zhejiang, Shanghai, as well as Hong Kong and Macau.

Professor Ouyang Hongwei, Deputy Director of the Liangzhu Laboratory, delivered the opening remarks. The conference chairperson, Professor Wang Qingqing, presented a certificate of Guest Professor from Zhejiang University to Professor Mark Middleton, who is Head of the Department of Oncology at University of Oxford.

The joint lecture series centered around the theme of "Translational Oncology: Bridging Innovations to Clinical Applications in Cancer Immunology Research." Professor Mark Middleton delivered the keynote address. Seven professors from University of Oxford and six from Zhejiang University shared their latest advancements in fields such as tumors, immunity, and lysosomes. Their presentations provided fresh insights and perspectives regarding the use of precision and personalized medicine (PPM) in oncology, making the event an academic feast within the field.

In addition, University of Oxford and Zhejiang University jointly conducted a recruitment seminar for the "4+1" Joint Degree Program. This program offers students the opportunity to pursue a Master's degree at the Department of Oncology at University of Oxford following their undergraduate studies at the School of Basic Medical Sciences at Zhejiang University. The seminar aimed to inform the students at Zhejiang University of the Qiushi Class in Basic Medical Sciences about the Department of Oncology at Oxford, thereby providing a platform for students who are interested in furthering their studies at University of Oxford.

About the Program

The collaboration between the School of Basic Medical Sciences at Zhejiang University and the Department of Oncology at University of Oxford began in 2018. Later, the inaugural joint lecture series on cancer biology was held in 2019 at Zhejiang University, followed by the second series in 2021, held in a hybrid format. The current event represents the third series.

Over the course of this collaboration, significant strides have been made regarding scientific research, student exchange programs, and faculty training. Notably, in October 2023, three students from the Qiushi Class in Basic Medical Sciences joined the "4+1" Joint Degree Program, allowing them to embark on further studies at University of Oxford.

Belt and Road Physician Training Center

As a vice-chair member of the Belt and Road Health Professional Development Alliance, this year, the Second Affiliated Hospital Zhejiang University School of Medicine (SAHZU) has welcomed several young doctors and medical students from countries of the Belt and Road Initiative (BRI).

Dr. Sujai Nikhil
Cardiovascular Physician from India

"The willingness to teach."

Dr. Sujai Nikhil graduated from Mahatma Gandhi Medical College in India and assumed the role of cardiovascular physician-in-charge in 2018.

Dr. Nikhil completed a three-month fellowship in cardiology (from April to June 2023). This fellowship was divided into two main parts: the first focused on coronary intervention treatments, including procedures like Percutaneous Coronary Intervention (PCI), while the second addressed the treatment of structural heart disease, such as Transcatheter Aortic Valve Replacement (TAVR) and MitraClip. Following his fellowship, Dr. Nikhil gave the Cardiology Department top marks in the survey, expressing admiration for its high standards of surgery and excellent teaching atmosphere.

Dr. Zamir Shah and Dr. Asif Dar
Colorectal Surgeons from India

"I am impressed by the professionalism of SAHZU in particular."

Dr. Shah Zamir Ahmad and Dr. Asif Mehraj Dar, both from India, are the inaugural trainees in the International Colorectal Surgery Training Academy (ICSTA), a program initiated by the SAHZU in association with the Colorectal Cancer Committee of the Chinese Anti-Cancer Association.

Both graduated from the Sher-i-Kashmir Institute of Medical Sciences and were endorsed by the Indian Association of Colorectal Surgeons to acquire expertise in laparoscopic surgery for colorectal cancer.

Over the two-month course, they actively observed and participated in various surgical procedures, including laparoscopic colorectal surgery, CRS+HIPEC, LISH, and taTME, among others. Additionally, they engaged in multidisciplinary team (MDT) discussions, and gained hands-on experience with the Da Vinci surgical system under guidance.

Dr. Michele Cricrì and Dr. Federico Maria Mongardini
Colorectal Surgeons from Italy

"The knowledge I am getting, the skills I am improving and the people I am meeting will be forever part of my development, as a young surgeon and as a man."

Dr. Michele Cricrìand and Dr. Federico Maria Mongardini are colorectal surgeons, who graduated from the University of Naples Federico II and the University of Campania Luigi Vanvitelli, respectively. They constitute the second cohort of trainees at the ICSTA. They mainly focus on the techniques and experiences related to colorectal tumor surgery, inflammatory bowel disease treatment, and colorectal trauma surgery, as well as the methodologies and concepts associated with robotic colorectal surgery.

Dr. Mitre Reyes
Colorectal Surgeon from Mexico

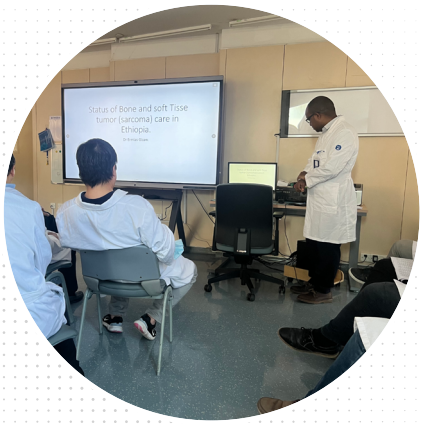
"The basis of success is to create work and friendship ties."

Dr. Mitre Reyes, representing the largest and oldest institution in Mexico, the National Autonomous University of Mexico (UNAM), joins the second cohort of trainees in the ICSTA. Dr. Mitre Reyes, well-qualified due to his surgical residency training and fellowship training in colorectal surgery in Mexico, is licensed to practice independently. He has also served as a mentor for surgical residency training. For this training stint, Dr. Mitre Reyes has a clear objective: within three months, he aims to fully grasp the surgical techniques and experiences of the SAHZU in Total Anorectal Mesorectal Excision (TATME), Natural Orifice Transluminal Endoscopic Surgery (NOTES), and Transanal Minimally Invasive Surgery (TAMIS). He intends to gain exposure to robotic colorectal surgery as well.

During the initial month of their program, Dr. Mitre Reyes, Dr. Michele Cricrì, and Dr. Federico Maria Mongardini each actively participated in an average of 60 colorectal surgical procedures.

Dr. Ermias Gizaw
Orthopedic Surgeon from Ethiopia

"Hope we in Ethiopia will be able to adapt that."



Dr. Ermias Gizaw is an orthopedic surgeon from Ethiopia who holds a position at the Addis Ababa University, the largest and top-ranked university in the country. Dr. Gizaw underwent a three-year fellowship training at the Royal College of Physicians and Surgeons of Glasgow in the UK, making him the only doctor in Ethiopia who has received formal fellowship training in bone and soft tissue tumors.

At SAHZU, Dr. Gizaw followed his mentor to further his skills in orthopedic tumor surgery, learn prosthetics utilization and installation, and observe minimally invasive tumor resection procedures. In addition to learning surgical techniques, Dr. Gizaw also shared insights into orthopedic tumor diagnosis and treatment in Ethiopia with the bone tumor team at the SAHZU.

Dr. Lim Shin Hoei
Anesthesiologist from Malaysia

"(This program) will be of great help in my future career."

Upon learning about the leading position of the Anesthesiology Department of the SAHZU in perioperative ultrasound technology, as well as the department's extensive experience in ultrasound applications in cardiology, pulmonology, gastroenterology, neurology, vascular medicine, and pain management, Dr. Lim Shin Hoei traveled all the way from Malaysia to pursue further studies in transesophageal echocardiography (TEE) and cardiac anesthesia at the SAHZU.

She participated in the training program about perioperative echocardiography organized by the Anesthesiology Department, where she engaged in theoretical studies on cardiac anatomy and pathophysiology. Additionally, under the guidance of her mentors, she received instruction during operations and participated in case discussions. Simultaneously, she observed and learnt during daily anesthesia sessions with the attending anesthesiologist.

Application details: **en.z2hospital.com**

Outstanding Moments of International Communication

1 ZUSM delegation visits Massachusetts General Hospital

2 ZUSM and UCLA sign an agreement on student exchange program

3 ZUSM participates in the Third Sino-German Sustainable Development Forum in Berlin, Germany

4 Silvio Brusaferro, the former President of Italian National Institute of Health, visits ZJU School of Public Health

5 School of Nursing, ZUSM and University of Toronto ink an MoU

6 Affiliated Sir Run Run Shaw Hospital, ZUSM and Arab Association of Urology ink an MoU

7 Affiliated Women's Hospital, ZUSM visits Hospital da Luz Lisboa in Portugal

8 Affiliated Children's Hospital, ZUSM and Indonesia's National Cardiovascular Center ink an MoU

ZHU Shenghe: Seventy Years of Dedication and Duty

ZHU Shenghe, who was born on August 8, 1922, has been affiliated with both Zhejiang University School of Medicine and Zhejiang Medical University. She held several prominent positions, including Head of the Department of Microbiology and Immunology, Vice President of the Zhejiang Microbiology Society, and Vice President of the Zhejiang Society for Immunology. Since the 1950s, her primary focus has been on virus immunology, where she has made significant contributions to understanding the pathogenesis, prevention, diagnosis, and treatment of diseases such as measles and poliomyelitis. ZHU Shenghe is the chief editor of numerous medical publications, including *Clinical Diseases and Immunity, Medical Microbiology,* and *The 21st Century Textbook of Excellence for Medical Schools and Colleges — Microbiology*. She has also led over 20 national–level continuing education projects in the field of medicine. Even in her eighties, she remains actively engaged at the forefront of medical education, delivering over a hundred academic lectures at medical societies, hospitals, and higher education institutions across more than 50 cities.

ZHU Shenghe (centre), leading the research on the live measles vaccine in the early 1970s

Association with Zhejiang University

In 1948, ZHU Shenghe graduated from the Central University (now known as Nanjing University), becoming a teaching assistant in the Department of Bacteriology at the University's Medical School. Towards the end of 1948, following her grandparents' relocation to Hangzhou, Zhu moved to Zhejiang University to engage in medical laboratory work. Since the Medical School was still at the planning stage, she initially worked in the laboratory of Zhejiang No.1 Hospital.

About one year later, Zhejiang University planned to set up a Medical School in Longquan Hall on Daxue Road. ZHU Shenghe, along with her technician colleagues, was among the first to join this new institution. In her role as assistant professor, she began her research in immunology. A few years later, the School moved to the Red House on Yan'an Road, which marked the origin of the Zhejiang University School of Medicine.

Scientific Research

ZHU Shenghe employed microscopes to study diseases that are transmitted by bacteria carried by flies, and used mosquitoes as model organisms to investigate their pathogenic mechanisms. In 1953, she conducted extensive research on fungi in the dermatology department of a Shanghai hospital. Upon her return, she introduced the mycological studies to Zhejiang University. In the early 1950s, she also pioneered the use of domestic antifungal agents. In 1960, Zhu travelled to Changchun, where she first delved into virology. The knowledge she acquired there laid the groundwork for initiating virology research at Zhejiang University. ZHU Shenghe's efforts were

Lecturing at university and encouraging young students and teachers at the age of 97

pivotal in introducing these new scientific disciplines to the university.

Subsequently, ZHU Shenghe made several noteworthy contributions that significantly advanced China's medical field. In the 1970s, following the Cultural Revolution, there ensued a period of rejuvenation. The Zhejiang University School of Medicine, Shanghai Epidemiological Station, and several other institutions focused on research on neonatal vaccinations. This work aimed to determine the appropriate vaccines for newborns within their first few days or months of life, including the optimum timing of these vaccinations. The research successfully addressed a gap in China's neonatal vaccination practices. Additionally, during a time when measles was prevalent, Beijing led a collaborative effort with Zhejiang and Pujiang, resulting in a decade of progressive breakthroughs in measles prevention. The goal was to discover how the measles vaccine could confer lifelong immunity. In 1984, ZHU Shenghe's participation in the "National Research on the Durability of Measles Live Vaccine Immunity" earned the Ministry of Health's Grade A Science and Technology Prize. Furthermore, she was involved in research on various types of poliomyelitis with Kunming. Biennial visits to Kunming were made to summarize the progress and eventually report the findings nationally. Concurrently, ZHU Shenghe actively participated in educational reform initiatives undertaken by Zhejiang Medical University, Shanghai Second Medical College, and Jiangsu Medical College, achieving significant outcomes.

Her Activities

Professor Zhu was also passionate about culture and arts. WANG Qidong, the then president of the university, proposed to establish a place for teachers' activities in Hangzhou, so eight professors (four men and four women) went to Dengxin Alley to prepare for the performances. They rehearsed several times a week, preparing eight shows, including catwalks, ballroom dancing, plays, etc., which lasted for about an hour, and were finally staged in the Hangzhou Theatre on Yan'an Road.

In 1998, when the four universities merged to form the new Zhejiang University, ZHU Shenghe took charge of medical education. She compiled an insightful manuscript on educational reforms, emphasizing the "three basics", namely basic knowledge, basic theories, and basic skills, and also published many articles on teaching reforms in the Zhejiang Medical University newspaper. Zhu mentioned that, when she was a student, her teachers had not relied on textbooks, but had internalized their knowledge thoroughly and could explain complex topics vividly and cohesively on a chalkboard. Now as the leader of the university's supervisory team, Zhu observes that contemporary courses rely heavily on multimedia, displaying a series of slides in succession, so students may miss a lot of information in the classroom. She believes that chalkboards remain indispensable. A qualified teacher needs to embed the knowledge into their brain rather than simply relying on multimedia teaching. Of course, she acknowledges that multimedia makes it easier to present academic reports in a vivid, fast format.

ZHU Shenghe has been engaged in various kinds of education, such as continuing education, adult education, distance education, and senior university education. She believes that the legacy of Zhejiang University also requires young people to cultivate themselves and make further progress while remaining prudent and bearing in mind the fundamentals, so as to build a truth–seeking, pragmatic, and renowned university with a galaxy of talents.


蛋白质检测技术之
最美实验图


原创学术奖


技术达人奖

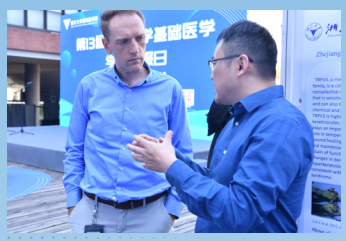

学术新人奖

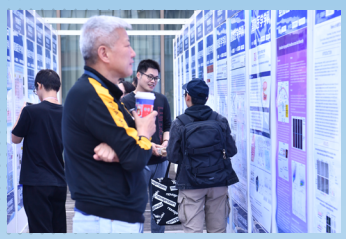

创意设计奖

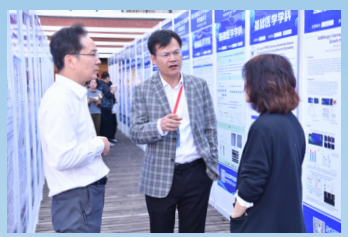

科研新星奖

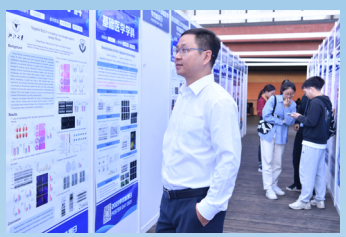

十佳墙报奖

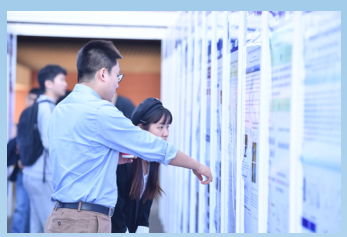

第13届浙江大学基础医学
学术墙报日











Poster Day

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ZJU MEDICINE
SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

Seeking Truth and Innovation with
Benevolence and Humane Proficiency

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