Issue 2 2023

ZJU MEDICINE

SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

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GOLDEN AUTUMN 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.

浙江大学 医学院
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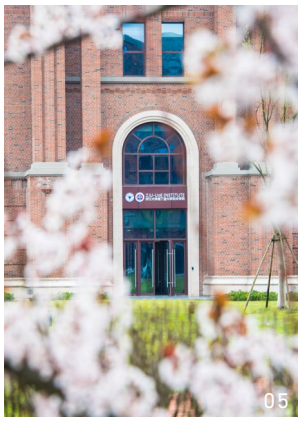

Pioneering Reproductive Medicine

HUANG Hefeng

Academician of the Chinese Academy of Sciences
Honorary Fellow of the Royal College of Obstetricians and Gynaecologists, UK
Academician of the Academy of Sciences for the Developing World
Member of the Chinese Academy of Medical Sciences
Dean, International School of Medicine, Zhejiang University

> ***We are capable of making pioneering contributions to the global medical field, with a commitment to prioritizing the health and well-being of individuals across the globe.***

What sparks your interest in reproductive medicine?

The birth of a new life is sacred and stirring. When I was a student at Zhejiang Medical University (now Zhejiang University School of Medicine), I had the chance of interning at a regional-level hospital, where I encountered many complex cases every day. One day a high-risk puerpera was admitted, and both her life and that of her fetus were hanging in the balance. After an emergency cesarean section was performed, the newborn showed almost no sign of life. Despite our immediate resuscitation efforts, we all thought that the newborn's chance of survival was low. But the newborn's sudden resounding cry made us relieved. That experience let me choose unhesitatingly obstetrics and gynecology as a lifelong career.

Could you brief us on your thoughts about studying and working at Zhejiang University?

Zhejiang University and Women's Hospital, School of Medicine, Zhejiang University (WHZJU) have been allowing me to pursue the work that I love such as providing outpatient care and performing surgeries. Moreover, what makes reproductive medicine truly captivating is not only addressing practical issues for countless patients but also its allure in scientific research. Thanks for the opportunities provided by the university and hospital, I can have an excellent platform to engage in uncharted territories of research in reproductive medicine.

As the only Chinese scientist granted the Fuller W. Bazer SSR International Scientist Award, what advice do you have for students and scholars pursuing a career in reproductive medicine?

I feel deeply honored to have received this award. Human reproduction is an ever-lasting theme, and ensuring mothers welcome healthy newborns is the fundamental mission of obstetricians and gynecologists. I hope that all of my colleagues working in this field will devote themselves to meeting the needs of families worldwide.

As the Dean of the International School of Medicine, Zhejiang University, what is your vision of the future?

I believe we are capable of making pioneering contributions to the global medical field, with a commitment to prioritizing the health and well-being of individuals across the globe. A pivotal aspect of this vision is cultivating excellent international medical students. With the support from the Fourth Affiliated Hospital, Zhejiang University, we are building a comprehensive medical education system encompassing undergraduate and postgraduate cultivation, as well as post-graduation guidance at our medical school. Furthermore, by utilizing the resources of the International Institutes of Medicine, Zhejiang University, we aim to drive innovation and development throughout the entire healthcare sector. We are also forging deeper connections with "Belt and Road" countries in terms of scientific research, medical services, talent cultivation, and promotimg the "Study in China" brand.

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Caring Knows No Boundary

ZHAO Xuehong

Chief Nurse
Deputy Director of the Department of Nursing at the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU)
Director of Disaster Nursing Committee, Zhejiang Nursing Association
Member of Disaster Nursing Committee, Chinese Nursing Association
The 49th Nightingale Medal Recipient

Could you share one thing that has impressed you the most?

I have experienced numerous major global public health events such as SARS, avian influenza, Ebola and the COVID–19 pandemic. In 2015, I worked in Libya as a member of the medical team for Ebola. Late one night, a little boy on the ward was crying, fearing that he would lose his life after he closed his eyes. To calm him down, I told him that we would cure him and that I would lull him to sleep every night until he recovered. When he left the hospital, he called me "Chinese mom", which was a great joy to me.

How do you understand the Nightingale spirit?

I think it is a nursing philosophy featuring humanistic care and professional responsibility. As a health care worker, our mission is to treat every patient with professional skills and a caring attitude and to always put the patient's health first. Meanwhile, we also have the duty to participate in volunteer services and contribute to the development and progress of the nursing profession.

Are there any innovations your team have practiced?

We developed the "Intelligent Emergency Treatment Pre–examination and Triage Information System" in 2011, which is used to screen high–risk patients quickly. The system has completely changed the uncertainty and heterogeneity of the traditional empirical triage and achieved the homogenization and standardization of triage work. In addition, we developed the "Intelligent Fever Clinic Treatment Pre–examination and Triage Information System" and the "Intelligent Risk Warning Model for Infectious Diseases" since the outbreak of COVID–19. The realization of the partitioned management of fever cases reduces the risk of cross–infection among patients.

What kind of support and assistance did you get in your career?

It is on the big platform of Zhejiang University that I gain growth. Its cutting–edge technical information, rich cooperation models, and flexible learning systems enable me to improve greatly in my specialty. Its people–oriented service philosophy and inclusive culture have become my solid spiritual pillars. Every time I fight on the frontline, ZJU and FAHZU are my strongest support.

What would you like to say to the nursing students?

As the saying goes, "Successors excel their predecessors". I hope that young nursing students can stick to their original aspirations and keep their missions in mind, learn more, practice more, think more and communicate more. I believe the sense of fulfillment that arises from helping patients to alleviate their pain and restore their health can overcome all difficulties.

I believe that if I can help patients relieve their pain and regain their health, the sense of achievement I obtain can overcome all difficulties.

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Healthy Zhejiang One Million People Cohort

Large-scale prospective cohort empowered by digital technology is the best source for obtaining standardized, high-quality, multi-scale, and multi-modal health and medical big data, as well as biological samples. The "Healthy Zhejiang One Million People Cohort" project is dedicated to creating a world-leading high-energy-level scientific research and innovation platform for public health and big health, filling the gap in China's million-level cohort and providing core support for clinical medicine, basic medicine, translational medicine, and public health research in the new era.

This large-scale prospective population cohort is led by Zhejiang University and supported by Zhejiang Provincial People's Government in terms of policy and funding, and in collaboration with Zhejiang Provincial Center for Disease Control and Prevention and Zhejiang Provincial Cancer Hospital. The project's chief scientist is Professor WU Xifeng, a globally renowned scientist, national distinguished expert, and top talent in Zhejiang Provincial Kunpeng Plan.

Through various ways, this project will comprehensively collect health and medical big data as well as various types of biological samples from multiple dimensions. It will connect micro-level, e.g., microscopic biomolecular information, meso-level, e.g., personal information, and macro-level, e.g., social factors, integrate multiple dimensions of information and conduct long-term follow-up for health outcome, establishing a cohort of healthy individuals, high-risk individuals, and diseased individuals characterized by digital empowerment.

Based on the cohort, we will break through the challenges of integrating and analyzing multi-scale and multi-modal health and medical big data, and conduct precise prevention, diagnosis, and treatment research covering the continual process of diseases; precision nutrition research and AI nutrition big data research, as well as their translation; environmental health research; aging, cognition and brain health research; multidimensional bioinformatics research, and medical AI-driven big health research. The research results can be transformed into a series of products, including InterGene Kit precision diagnostic kits, AI health prediction tools, intelligent design methods and systems for personalized meal plans, comprehensive health management systems for elderly patients, and intelligent health management platforms for early screening, early diagnosis, and early treatment of elderly patients with chronic diseases.

Through the aforementioned breakthroughs in basic research, we will provide support for residents' health, promote precise population stratification, and adopt targeted three-level preventive strategies for different populations, thereby realizing the integration of prediction, warning, prevention, early diagnosis, early detection, early treatment, precision treatment, and precision health through digital empowerment. This will promote the coordinated development of education, science and technology, and talents, ultimately providing strong support for the construction of a healthy China, a digital China, and a community with a shared future for mankind.

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ZJE 浙江大学爱丁堡大学联合学院 ZJU-UoE INSTITUTE

Pacesetter of Demonstrating Successful Trans-National Education Partnership

Zhejiang University–University of Edinburgh Institute (ZJE) is a trans-national education joint institute between Zhejiang University (ZJU) and University of Edinburgh (UoE) approved by the Ministry of Education in 2016. ZJE currently has a dual-awarded degree programme in the majors of Biomedical Sciences and Biomedical Informatics for undergraduates and a dual-awarded degree programme for PhD candidates. The certificates of both programmes are awarded by ZJU and UoE. In addition, it also has programmes for masters and PhD candidates, the certificates of which are awarded by UoE. ZJE was nominated the Education Institutional Partnership of the Year Award in 2018 sponsored by the British Council. ZJE has been the Chair Institution of the Chinese-foreign Joint Institutes Committee and our Executive Dean Prof. Sue Welburn is the Chair of China-UK Joint Institute Alliance.

Building on the multidisciplinary comprehensive advantages of the university and integrating the education philosophy from the eastern and western culture, the fundamental mission of ZJE is to educate innovative talents in Biomedical Sciences with the core idea of "comprehensive quality cultivation, global access, and social practice". The biomedical sciences undergraduate programme has been selected into one of the national-level first-class undergraduate programmes. In 2021, the trans-national education model was awarded the second prize of Zhejiang Provincial Teaching Achievement. The external examiners nominated by UoE evaluated our programme "Second to None" in the annual report. Our undergraduate students published research articles as the first author in international journals and won the golden prize in the national "Internet +" innovation competition. 89.7% of total 155 graduates continue pursuing their postgraduate study, with 43.9% recruited by top 20 universities.

ZJE aims to carry out cutting-edge basic research in the field of life and health, and implement sophisticated research and development of disease diagnosis and treatment. Among 26 talented young scientists from all over the world who choose to join ZJE, 40% are international faculty. The research theme of the institute mainly focuses on the domains such as cellular signaling, regenerative medicine, biomedical system, infection and immunity and cancer.

In the near future, ZJE will always maintain its original vision and mission of cultivating innovative leaders in biomedical sciences, keep integrating into the "New Medicine" strategy, serving the university's ultimate goal of being world-class universities, and completing the three-year actional schedule to be a pacesetter of international educational partnership.

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Why Can Eating Fish Make Us Smarter?

When we speak of fat in food, we will easily associate it with its negative effect of "gaining weight". However, one type of fat has a "weight-losing" effect — it is omega-3 fatty acids. Not only can omega-3 fatty acids reduce fat, but also they can strengthen the brain, regulate the blood pressure, and ease inflammation. Therefore, they can be found in many health products and infant formula powder.

What has led to these substantial differences? Recently, Prof. ZHANG Yan from Zhejiang University School of Medicine and Liangzhu Laboratory teamed up with Prof. SUN Jinpeng, Prof. FENG Shiqing and Prof. YU Xiao from Shandong University to unravel this enigma. Their research findings were published in the journal *Science* on March 2.

Scientists have been intrigued by the magical function of omega-3 fatty acids. Previous studies reveal that the chemical signals that omega-3 fatty acids send should first be encoded by a G protein-coupled receptor (GPCR) called GPR120. Nevertheless, GPR120 can activate both saturate and unsaturated long-chain fatty acids.

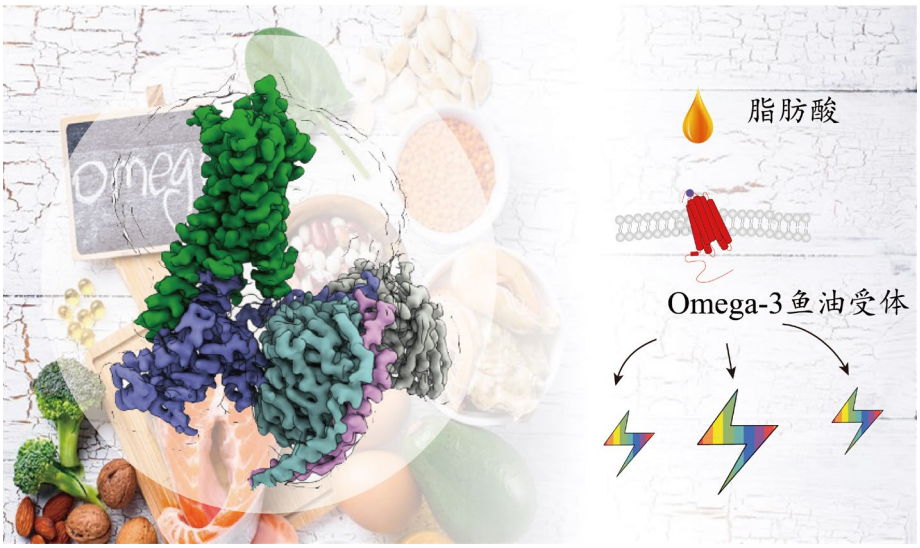
Therefore, it is essential to understand the physiological responses triggered by different long-chain fatty acids after the activation of GPR120 if we want to know why some fatty acids are beneficial while others are not.

"This is an extremely tough task," said Professor ZHANG, "Long-chain fatty acids are remarkably similar to each other in chemical structure, and there may be a subtle difference only in double-bond position. Moreover, the encoding of fatty acid signals is also a dynamic process, during which various configurations and states may emerge, thus making it difficult for researchers to make some stable observation of the samples."

The introduction of cryo-electron microscopy has made it possible to observe the 3D structure of cells in a quick, efficient and meticulous manner. Professor ZHANG has been committed to research into the mechanisms for cellular transmembrane signal transduction and relevant precise regulation approaches. As early as 2017, Professor ZHANG led his team to obtain the high-resolution structure of GPCR using cryo-electron microscopy, which was hailed as a milestone study in the field of structural biology by the journal *Nature*.

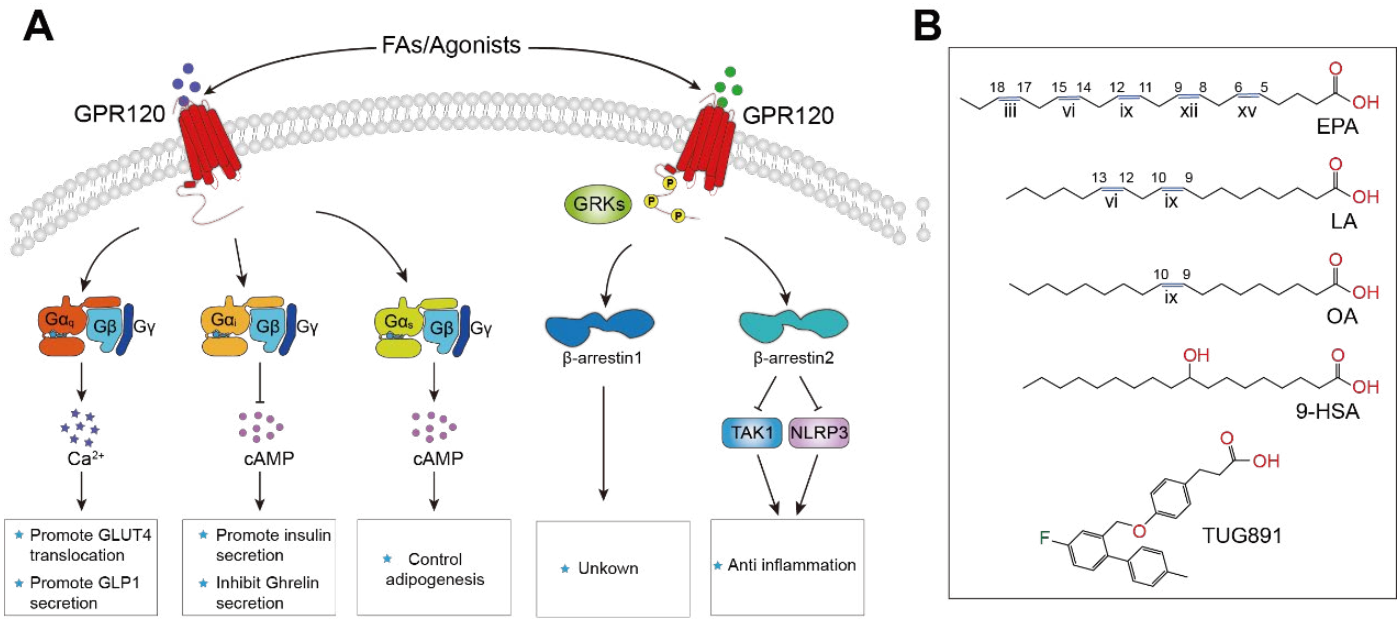
"Thanks to the cutting-edge cryo-electron microscopy facility in Liangzhu Laboratory, we were able to put the samples in a stable state activated by a certain signaling molecule and observe how the receptor regulates cellular signals at the atomic resolution level," said Professor ZHANG "It reached a precision of 0.3 nanometers, 10 times higher than photolithography."

In the study, the researchers selected five different types of long-chain fatty acids and synthetic compounds as ligands to send signals to GPR120.



"We found that in response to signaling stimuli from different ligands, GPR120 could mediate the signaling pathways of multiple downstream effectors and that different G proteins could play a crucial role in mediating different physiological functions," said Dr. MAO Chunyou, the lead author of the study from Sir Run Run Shaw Hospital, Zhejiang University School of Medicine.

Through structural determination, molecular dynamics simulations, and mutant screening, the researchers discovered the transmission ties connecting ligand pockets with



(A) Schematic overview of G protein and arrestin mediated GPR120 signaling and related functions.
(B) Chemical structures of fatty acid ligands and synthetic ligand TUG891.

downstream physiological responses. They demonstrated that omega–3 fatty acids were beneficial because they added an instruction to their receptor, allowing the signals that might otherwise go in other directions to "turn around" and take a pathway beneficial for metabolism.

"GPR120 is like a lock cylinder, and the single bonds and multiple bonds on fatty acids are like the teeth of different keys. The way to open the lock cylinder varies. Although the same lock is turned, it may lead to different words," Professor ZHANG explained with a vivid analogy.

The understanding of the mechanisms for fatty acids can pave the way for scientists to engage in precise molecular design and develop fatty acid supplements or drugs that are beneficial to human health.

To Professor ZHANG, the inspiration for this research is very simple, but it will open up promising vistas. "In my childhood, my elders would always say that eating fish could make one smart.

Professor ZHANG Yan (right) and his colleagues in the lab

This word holds true, for fish is rich in omega–3 fatty acids. As a researcher, I have been driven by my insatiable curiosity about the story behind their positive effects on human health."

"Our vision is that everyone can live to the age of 120 healthily and happily," Professor ZHANG said. "In the future, we will continue to decipher the 'key' that regulates life functions and help humanity open the door to a long and healthy life."

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GPRC5D-Targeted CAR T Cells Show Efficacy in Phase 1 Trial of Relapsed/Refractory Multiple Myeloma

Multiple myeloma is a malignant disease characterized by the proliferation of clonal plasma cells in the bone marrow. While numerous advances in treatment, such as proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies, have significantly improved patient survival over the years, the disease remains incurable. Novel immunotherapies, particularly chimeric antigen receptor (CAR) T-cell therapy, show promise for treating relapsed or refractory multiple myeloma. B-cell maturation antigen (BCMA), which is widely and almost exclusively expressed on plasma cells and B cells, is a promising target for multiple myeloma drug therapy. However, low-to-negative BCMA-expressing myeloma cells can evade BCMA-targeted CAR T-cell therapy and lead to relapse, necessitating the identification of complementary new targets.

On January 31, 2023, Prof. HUANG He, president of the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU) published an article entitled "GPRC5D CAR T Cells (OriCAR-017) in Patients with Relapsed or Refractory Multiple Myeloma (POLARIS): A First-in-Human, Single-Centre, Single-Arm, Phase 1 Trial" in the journal *Lancet Haematology*. The study demonstrated the safety and preliminary efficacy of GPRC5D CAR T cells in patients with relapsed or refractory multiple myeloma, including those who relapsed after BCMA CAR-T cell therapy.

GPRC5D is a G protein-coupled receptor that is highly expressed in malignant plasma cells. GPRC5D expression does not depend on BCMA. Moreover, GPRC5D is minimally expressed in bone marrow samples of other hematological malignancies, such as acute leukemia and diffuse large B-cell lymphoma, making it a promising immunotherapy target for treating patients with multiple myeloma. Professor HUANG He's team developed CAR T cells targeting GPRC5D (OriCAR-017) and conducted a phase I clinical study in patients with relapsed or refractory multiple myeloma. Early data from this study was presented orally at the 2022 ASCO annual meeting and attracted considerable attention. A summary of the latest data from the study is now published in *Lancet Haematology*, showing exciting clinical benefits.

The study included 10 patients with relapsed or refractory multiple myeloma, including five patients who had relapsed after BCMA CAR-T cell therapy. Six of the ten patients had a high-risk cytogenetic profile, four had extramedullary lesions, and eight had stage II or III disease. The median number of previous lines of therapy was 5.5. In terms of safety, the study had no dose-limiting toxicity and no serious adverse events were reported in any of the 3 dose groups. Common grade 3 or higher adverse events were hematological toxicities, but recovery was rapid. Low grade cytokine release syndrome occurred in all patients, including 9 cases of grade 1 and 1 case of grade 2, and no neurotoxicity was reported. The overall response rate in the 10 patients was 100%, with 6 (60%) achieving strictly complete remission and 4 (40%) achieving very good partial remission. These results demonstrate the excellent safety and preliminary efficacy of OriCAR-017 in relapsed or refractory multiple myeloma, as well as the great promise of future clinical applications.

"Data from our study showed that with extraordinary clinical efficacy, OriCAR-017 has been proved to be a novel, safe and effective therapy for patients with relapsed/refractory multiple myeloma, especially for those who experienced a relapse after receiving BCMA-targeted therapy." Prof. HUANG He commented that the study results highlight GPRC5D as a new immunotherapeutic target for multiple myeloma, in addition to BCMA. Future research is needed to explore the sequencing of BCMA and GPRC5D targets for immunotherapy and investigate whether the combination of these two targets will result in a stronger effect and induce more durable responses.

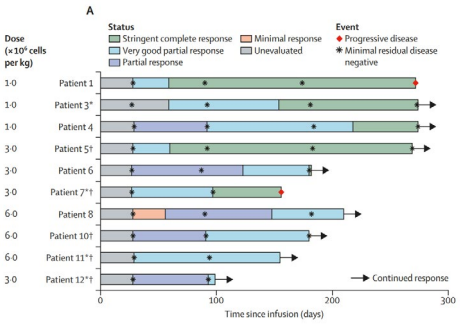

Figure: Clinical response to GPRC5D-targeted CAR T cells

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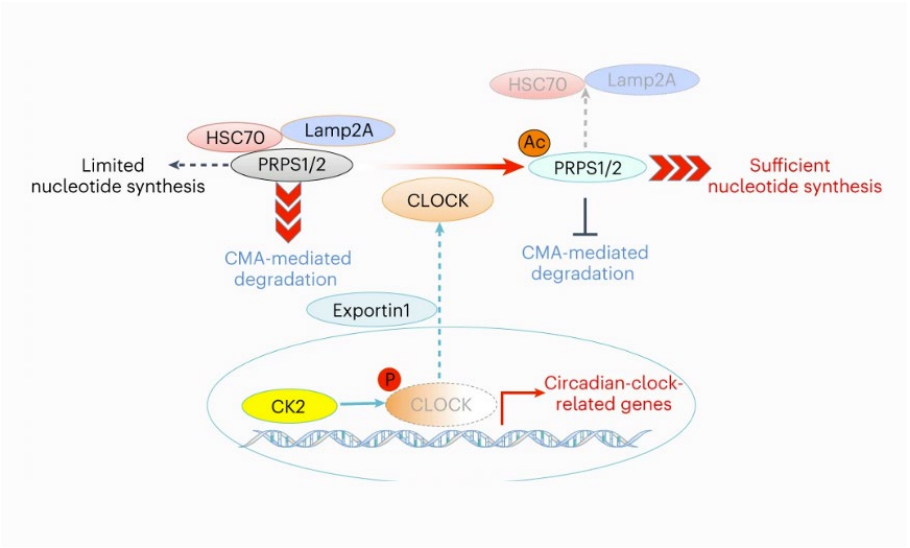
CLOCK Acetylates PRPS to Promote De Novo Nucleotide Synthesis and Tumor Growth

The biological clock is the timing controller of life activities, maintaining the orderly coordination of life activities at the organ, tissue, and cell levels, and presenting a clear circadian rhythm. The disturbance of the biological clock is closely related to the occurrence and development of various diseases including cancer. In 2017, Jeffrey C. Hall, Michael Rosbash and Michael W. Young won the Nobel Prize in Physiology or Medicine for discovering the important role of circadian rhythms in physiology and disease.



The mammalian circadian clock is composed of a time–delayed transcription–translation feedback loop at the molecular level: in normal cells, CLOCK binds to BMAL1 to form a heterodimer during the day, acting as a positive regulatory element to bind to E–BOX for promoting the transcription of downstream target genes (including PER and CRY); at night, PER and CRY accumulate in the cytoplasm to form PER/CRY heterodimers, which are transferred to the nucleus and inversely inhibit the activity of CLOCK/BMAL1, thereby forming the functional regulation of circadian rhythm gene transcription.

Increasing evidence has shown that compared with normal tissues, there are significant differences in the function of the biological clock and the expression of the downstream genes regulated by the biological clock in tumor tissues. However, whether cancer–promoting signals elicited by growth factor receptor activation are directly involved in the regulation of the circadian clock remains unclear.

Drs. XU daqian's and LU zhimin's groups recently reported in *Nature Cell Biology* (2023, PMID: 36646788) that the activation of growth factor receptors blocked the circadian clock regulation function of the transcription factor CLOCK and endowed it with an important role in regulating nucleic acid synthesis. Upon the activation of insulin–like growth factor 1 receptor (IGF1R) in liver cancer cells, CK2 phosphorylates CLOCK S106, alters CLOCK conformation, and disrupts the CLOCK/BMAL1 complex, thereby inhibiting the transcription of the downstream target genes and consequently interrupting the circadian regulation of the biological clock. CLOCK S106 phosphorylation with altered structure exposes its nuclear export signal sequence (NES), leading to its translocation from the nucleus to the cytoplasm. Cytosolic CLOCK exerts the non–canonical function and functions as a protein acetyltransferase to acetylate K29 of PRPS1/2, the rate–limiting enzyme in de novo nucleic acid synthesis. PRPS1/2 K29 acetylation inhibits degradation of PRPS1/2 by blocking the HSC70 chaperon–mediated autophagy. The stabilized PRPS1/2 accelerates the de novo nucleic acid synthesis and promotes the progression of liver cancer.

This study elucidates the molecular mechanism by which oncogenic signals in tumor cells interrupt the circadian clock by the disruption of the CLOCK–BMAL1 dimer. Importantly, oncogenic signals confer CLOCK a vital function as protein acetyltransferase to directly control DNA/RNA synthesis. These findings have laid a foundation for the development of anti–cancer drugs by targeting the aberrantly regulated CLOCK.

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Are People with High Social Status More Prone to Depression?

Alpha is the "king" of a horde of mice. While meeting another mouse in the pipeline, Alpha can scare it away with merely a glance. But one day the situation changes. With unexpected courage, the little "mouse brother" pushes Alpha out of the way directly after confronting the "king" for several seconds. After experiencing the Waterloo for several successive days, Alpha becomes depressed and loses his previous dominance.

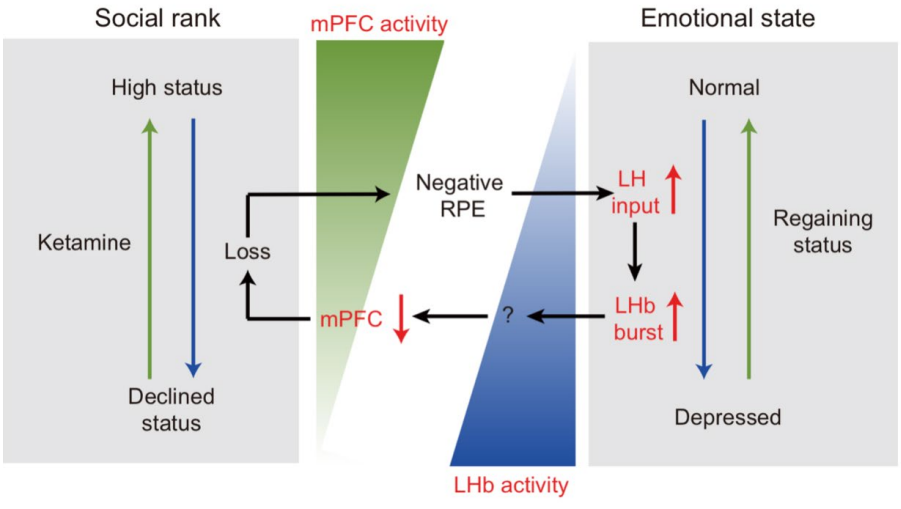
This reversal was orchestrated by a cohort of brain scientists who witnessed the whole process of Alpha's 'crown loss' and recorded its neural activity in the brain. After six years of experiments, the team led by Prof. HU Hailan has established a mouse model of depression to explore the key neural mechanism behind this process.

Their findings were published in an article titled "Neural mechanism underlying depressive–like state associated with social status loss" in the journal *Cell* on January 23.

Social hierarchy is pervasive in humans and animals. To measure social hierarchy in mice, HU's team developed the tube test by which the social rank of each mouse could be determined by the number of wins it gained when competing against other mice.

In both humans and animals, social status has a significant impact on their physical and mental health. A study of immigrants in the United States reveals that immigrants with status decline are nearly three times as prone to depression as other people.

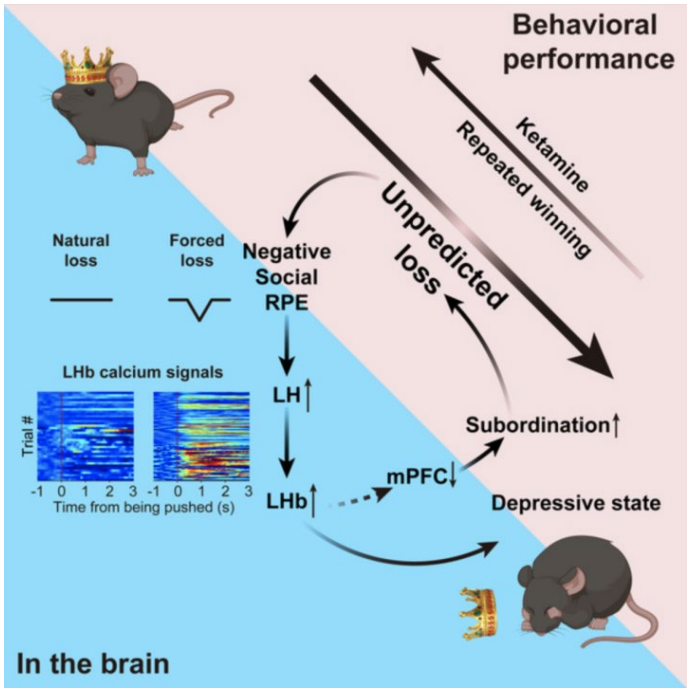
Prof. HU Hailan was intrigued by the neural mechanism behind these phenomena. "90% of the human depression cases are triggered by social factors." For scientists, the first step is to build animal models that could simulate the process in the lab. Thus, Alpha becomes the "chosen" mouse because it is the "king" of the tube test.



A new day comes. The little "mouse brother" is about to go through a new round of competition in the tube. This time, the researchers quietly block the passage behind the little "mouse brother". Soon, it finds that the only way out is to charge forward. It thus braces itself to push Alpha hard. After several back–and–forth shoves, Alpha is pushed out of the way.

After several consecutive days of "forced defeat", Alpha loses its dominance. Even in the absence of human intervention, the "king" begins to yield to the little "mouse brother" spontaneously. "This shows that it has lost its dominant position," says FAN Zhengxiao, the leading author of the study.

Subsequent forced swimming tests or sucrose preference tests suggest that Alpha shows conspicuous depressive–like behaviors. "Alpha's experience, to some extent, mimics depression induced by the decline in dominance in the human world," says FAN Zhengxiao. The researchers can perform a series of experiments on this new animal model to explore the neural mechanism behind it.



Graphical abstract

According to FAN Zhengxiao, they rule out the effect of loss per se. The lower-ranking mice won't get depressed even if they suffer from continuous losses to those higher-ranking mice. Depressive-like behaviors are triggered only in those higher-ranking mice which experience a rapid decline in social status. This suggests that depression may be related to the discrepancy between the expectation of winning and the reality of losing.

Through a series of experiments, HU's team hypothesizes that the negative reward prediction error may act as a catalyst for neural changes, which mediate depressive-like behaviors induced by social status loss. "In a forced loss scenario, the higher-ranking mouse tends to have a higher expectation of winning. The forced loss will generate a negative prediction error. In contrast, the lower-ranking mouse, more often than not, has a lower expectation of winning. Therefore, their loss won't bring any psychological disparity," says FAN Zhengxiao.

In the study, HU's team repeatedly "replays" the "crown loss" scenario and tracks calcium activity and neuroelectric activity signals in specific brain areas via fiber photometry. After a series of experiments, the underlying neural mechanism gradually becomes clear. The lateral habenula (LHb) functions as an anti-reward center and it can be activated by a variety of aversive stimuli.

When the high-ranking mouse suffers from a "forced loss", the reward prediction error signal will activate the LHb, thereby inducing depressive-like behaviors. Meanwhile, in the medial prefrontal cortex (mPFC) where social competition is encoded, the activity of excitatory neurons will also be reduced, leading the high-ranking mouse to "retreating" and "self-degrading" behavior. "The activation of the LHb mediated by the negative reward prediction error is the neural mechanism behind the depressive-like state associated with social status loss," says FAN Zhengxiao.

Interestingly enough, if neuronal activity in the LHb is inhibited by optogenetics, the higher-ranking mouse displays less depressive-like behaviors after a "forced loss".

The tube test is a non-violent social competition. Alpha's experience to some extent simulates the dynamics of competition in human society, thus promising to help understand and intervene this type of socially-induced depression.

Moreover, HU's team discovers the close interaction between the "social brain" and the "emotional brain". The activation of the mPFC can rekindle the "fighting spirit" of the mouse. With this spirit, it can reverse the situation. After several successive victories like this, the mouse will show less depression-like behaviors. In the end, Alpha—the mouse that has gone through several "forced losses"—regains its past glory. "This discovery provides insights into interventive therapy for depression," FAN Zhengxiao says.

Compared with low-ranking mice, high-ranking mice, which are accustomed to winning, can be more fragile and vulnerable to losses. Prof. HU Hailan thinks that this phenomenon may illustrate the necessity of "frustration education".

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ZJU Scientists Reveal the Treatment Prospect of Key Immune Cell Subsets of Septic Heart Dysfunction

Sepsis is a life-threatening organ dysfunction driven by a dysregulated host response, which affects approximately 50 million individuals and causes over 11 million fatalities worldwide annually. Sepsis-induced cardiomyopathy (SICM) is a common and important cause of death in patients with sepsis. Patients usually display the reduced ejection fraction, abnormal ventricular dilatation, poor response to fluid therapy and cardiovascular active agents. Notably, patients with SICM have a transient and significant improvement in cardiac function, suggesting that cardiac homeostasis can be restored after the septic stress. However, the underlying mechanisms facilitating the heart rehabilitation during sepsis have not been fully elucidated.

On January 12, 2023, Prof. FANG Xiangming's team from the First Affiliated Hospital, Zhejiang University School of Medicine published an article entitled "TREM2hi resident macrophages protect the septic heart by maintaining cardiomyocyte homeostasis" in the journal *Nature Metabolism*. This study shows that bacterial sepsis induces marked but transient changes in the immune compartment of the mouse heart, including the disappearance of a type of tissue-resident macrophages that protects the heart by scavenging defective mitochondria released by cardiomyocytes.

Which immune cell subset is critical for SICM?

Cardiac immune cells are the key regulator of heart microenvironment and closely related to cardiac homeostasis and diseases. So, two questions are coming up: how do cardiac immune cells change in SICM? And which is the SICM-associated essential cell subset? To address these questions, using flow cytometry and single cell RNA-sequencing (scRNA-seq), the team analyzed 29537 cardiac immune cells from the hearts of 14 wild-type (WT) mice at steady state (SS), and 3, 7 and 21 days post-CLP, respectively. They observed that macrophages were the most abundant immune cells in both WT and septic hearts, and displayed a dynamic change following sepsis. Intriguingly, one macrophage subset (Mac1) reduced first and recovered later on following sepsis. Mac1 subset is characterized by the expression of Trem2, Retnla, Lyve1, Cd163 and Folr2, and resembled the transcriptomic signatures of cardiac tissue-resident macrophages. The finding that Mac1 subset associated with the recovery of cardiac function in sepsis prompts us to explore whether Mac1 is the Angels or the Demons in SICM.

Which gene is the key regulator of SICM-associated macrophage (Mac1)?

The RNA-seq data analysis revealed that genes upregulated in Mac1 were related with phagocytosis and endocytosis in biological terms, including the triggering receptor expressed on myeloid cells 2 (Trem2). Trem2, which is mainly expressed on the surface of macrophages, regulates the function of macrophages, and involves in pathogen phagocytosis, anti-

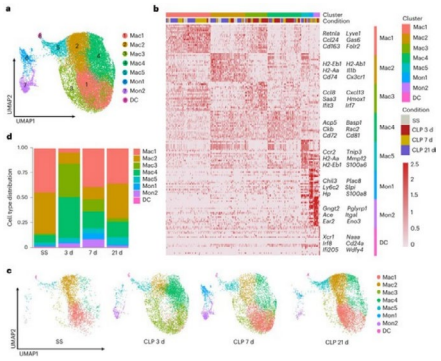


Fig. 1: A distinct cardiac macrophage subset (Mac1) is associated with the recovery of SICM.

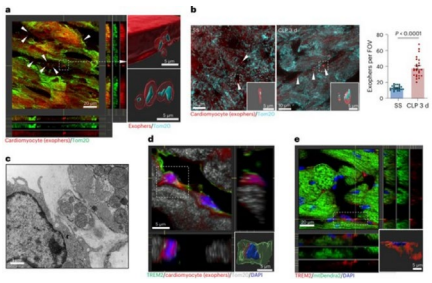
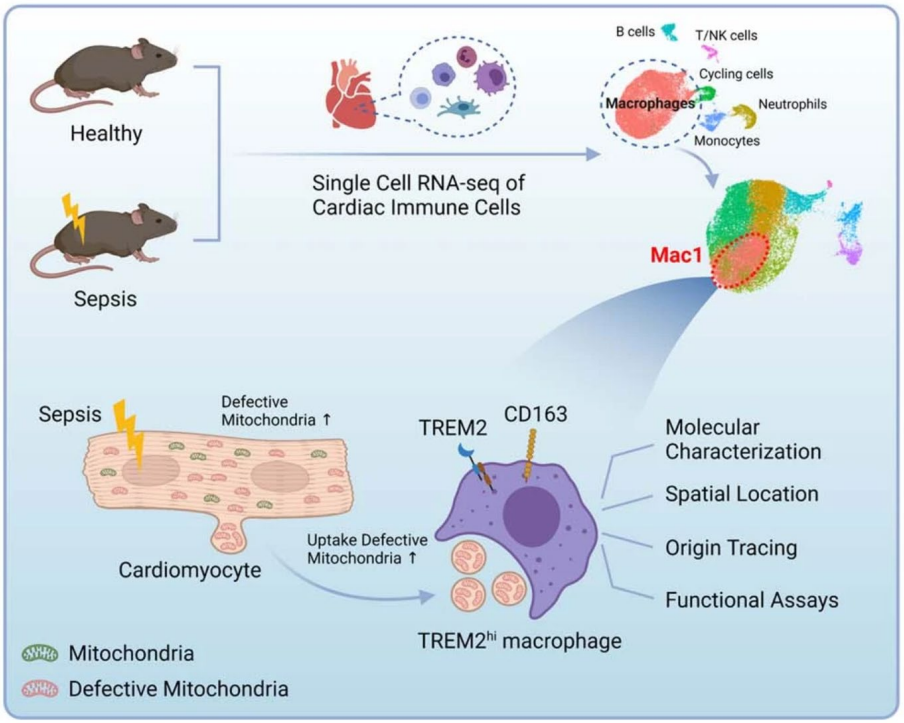


Fig. 2: TREM2 promotes the uptake of cardiomyocyte-derived mitochondria by Mac1 in septic heart.

inflammatory mediators' production, and lipid and energy metabolism 10–13. Importantly, the team observed Trem2 is highly expressed in Mac1 cells and essential for Mac1 remodeling during SICM. The proportion of Mac1 cells both significantly decreases in WT and Trem2−/− mice 3 days post−CLP. 7 days post CLP, Mac1 cells recover to normal levels in WT mice, but Trem2−/− mice could not restore the proportion of Mac1 cells, suggesting a key role of Trem2 in Mac1 cells. The study further showed that Trem2 deficiency impairs the proliferative capability of Mac1 cells.



What's the function of TREM2^{hi} Mac1?

The fate mapping data strongly support that Mac1 cells are self−renewing resident macrophages. Nicola´s−A´ vila et al. has implied that cardiac resident macrophages could engulf a type of extracellular particles (known as exophers) which contain defective mitochondria, and preserve mitochondrial function in the heart. The research team wondered whether TREM2^{hi} Mac1 could protect heart function in sepsis. To address it, they constructed αMHC^{Cre}:Rosa26^{TdTom} mouse line to track cardiomyocyte−derived exophers, as well as αMHC^{Cre}:mtD2$^{Flox/Flox}$ mouse line and AAV−Tnnt2−mtKeima to track cardiomyocyte−derived mitochondria. 3D reconstruction and video showed that TREM2^{hi} Mac1 scavenged exophers and defective mitochondria released from cardiomyocytes. Furthermore, Trem2 deficiency led to the failure of removing these defective mitochondria and consequently accelerated heart injury.

How to understand the value of SICM−associated macrophage subset?

The study illustrates immune cells of heart under steady state, sepsis progression, and recovery using single cell RNA−seq and reveals that a subset of macrophages are positively related to cardiac function. It then shows that the high expression of TREM2 is the key feature of these SICM−associated macrophages and clarifies their roles in septic heart. In addition, the transplantation of Mac1 subset can ameliorate the cardiac dysfunction. Investigating the SICM−associated macrophage subset can not only help to better understand the pathogenesis of septic heart, but also accelerate the transformation of macrophage immunotherapy. Identification of the specific markers and function of disease−associated macrophages will provide the direction for cell therapy, including designing the specific cell−killer CAR−T or transplantation of functional cells. The method−reveals of manipulating macrophage subsets both of tissue resident macrophages or monocyte−derived macrophages in vivo and in vitro reveals the origins and plasticity of macrophages. iPSCs derived specific macrophage subsets could play important roles in popularizing macrophage immunotherapy in sepsis. Medicines targeting macrophage activity to destroy/enhance their function are relied on detailed characterization of macrophage subsets.

In summary, Prof. FANG's team find TREM2hi Mac1 removes exophers released from myocardium to maintain homeostasis of septic heart and improves the outcome of SICM murine model. The study lightens the future way in the application of cellular targeted therapy including SICM−associated Mac1 subpopulations. Although there is a long way to go, it's worthy to overcome these impediments to realize it in sepsis precise treatment.

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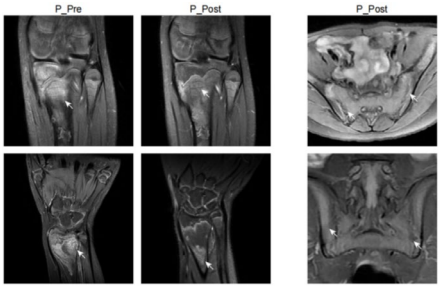
Zhejiang University Liangzhu Laboratory Team Overcomes Rare Disease

On June 13, 2023, a groundbreaking research paper titled "Identification of an IL–1 Receptor Mutation Driving Autoinflammation Directs IL–1–Targeted Drug Design" was published in *Immunity*, authored through the collaborative efforts of Professor YU Xiaomin's and Professor ZHOU Qing's research group from Liangzhu Laboratory of Zhejiang University.

In this study, Professor YU Xiaomin and Professor ZHOU Qing and their colleagues identified a new autoinflammatory disorder caused by a novel de novo missense variant p.Lys131Glu in IL–1R1. The substitution occurred on the critical the positively charged amino acid, which disrupted IL–1 receptor antagonist (IL–1Ra) binding site and resulted in mutant IL–1R1 resisting to IL–1Ra inhibition. The gain–of–function mutation led to the constitutive IL–1RAP and MyD88 association with IL–1R1 upon IL–1β stimulation, and unopposed activation of the IL–1 pathway. The patient exhibited strong activation of NF–κB and MAPK pathways and overproduction of proinflammatory cytokines such as IL–1β, IL–6 and IL–8, especially in monocytes and neutrophils. Knock–in mice with $Il1r1^{R134E/R134E}$ presented unresponsive to IL–1Ra with upregulation of inflammatory cytokine under IL–1β stimulation and showed greater susceptibility to collagen antibody induced arthritis. They showed that dysregulated IL–1 signaling could drive pathological osteoclastogenesis, which is responsible for the pronounced defect of bone homeostasis in the development of erosive arthritis or osteomyelitis observed in patients and Il1r1 mutant mice. Based on the diagnosis, patients manifested with chronic recurrent multifocal osteomyelitis were treated with canakinumab (anti–IL–1β) and responded quickly with ameliorated inflammation indicated by normalized inflammatory markers CRP, ESR, and SAA, decreased proinflammatory cytokines and downregulated NF–κB signaling pathway, as well as improvement of bone lesions. Moreover, this study provided a good example of new drug design of a more specific IL–1 Trap inspired by the identified mutation in patients. Based on the mechanism of the mutation, the modification on rilonacept with the K131E mutation could generate a much more effective IL–1 inhibitor as it only traps IL–1β and IL–1α but not IL–1Ra.

Together, based on data derived from patient cells, in vitro biochemical analysis, mutant mouse models and definitive clinical responses to IL–1 targeted therapy, this study not only identified a new autoinflammatory disease caused by a novel disease causal gene IL1R1, but also clarified the disease mechanisms and provided effective treatment to patients. In addition, this designed a new IL–1 Trap which is a more potent IL–1 inhibitor for the treatment of IL–1–driven disorders based on the mechanism of the mutation. The authors designated this disease as Loss of IL–1R1 Sensitivity to IL–1Ra (LIRSA) and the new drug as rilabnacept.

"While currently there are just a few cases, with increased awareness, more LIRSA cases will be accurately diagnosed," stated YU Xiaomin. "Identifying the novel disease–causing gene allows precise diagnosis and targeted treatment, offering hope to countless patients with rare disease, who have been seeking medical help in vain. Additionally, we hope that the new drug, rilabnacept, can swiftly enter clinical practice to provide more accurate treatment options for a broader range of autoinflammatory disease patients."



Magnetic Resonance Imaging of Yaya's Left Knee, Right Wrist, and Sacroiliac Joints before Treatment and Four Months after Treatment

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The World's First 5G Ultra-long-distance Domestic Robotic Resection Surgery

On June 18, 2023, good news came simultaneously from the remote robot surgery center of Sir Run Run Shaw Hospital (SRRSH) and the operating room of Xinjiang Corps Alar Hospital (Alar Hospital): the world's first 5G ultra-long-distance domestic robotic liver resection surgery was successful!

The left liver lobectomy took only 40 minutes to successfully remove an 8 cm tumor from the patient. The operating surgeon was Prof. LIANG Xiao, the chief physician of the Department of General Surgery at SRRSH in Prof. CAI Xiujun's team. The assistant doctor in Xinjiang, Dr. LI Zheyong, vice president of Alar Hospital and the associate chief physician of the Department of General Surgery at SRRSH, is also a member of the team.

In February this year, Prof. CAI Xiujun's team completed China's first 5G ultra-long-distance domestic robotic cholecystectomy.

Three cases of 5G ultra-long-distance robotic liver and gallbladder surgery

As a new banner leading minimally invasive surgery in China and the world, SRRSH has taken the lead in introducing two surgical robots in China, and its single-machine surgery cases rank among the top three in this country. In February of this year, SRRSH Alar Campus (National Regional Medical Center in Xinjiang) was officially unveiled. The continuous delivery of high-quality medical resources from Zhejiang makes Alar Hospital the only hospital in Xinjiang that can perform robotic surgery.

"We hope to use the 5G ultra-long-distance robotic surgery model to serve more local patients in mountainous areas, islands, and border areas with high-quality medical resources." Prof. CAI Xiujun says that 5G remote robotic surgery can break through resource allocation's temporal and spatial limitations, save time for doctors and patients, reduce economic costs, improve treatment efficiency, and greatly expand the application boundaries of remote diagnosis and treatment.

So far, teams in Hangzhou and Xinjiang have jointly carried out three cases of 5G ultra-long-distance robot-assisted surgery, including two cases of cholecystectomy and one case of left liver lobectomy. They have also trained local robot-assisted surgeons in general surgery and urology.

Domestic technology guarantees high-quality medical services to expand and sink

"I can hardly feel any delay in the 5G ultra-long-distance robotic surgery. The surgical field and the operation are clear," says Prof. LIANG Xiao. "The consecutive 'firsts' are not only a breakthrough in China's medical field but also a powerful proof that China's 5G technology and domestic medical equipment technology have taken the lead in the world."

As a leading unit of the National Engineering Research Center for Minimally Invasive Instruments Innovation and Application, SRRSH is committed to working with universities, research institutes, enterprises, and other research and development entities to jointly promote the leapfrog development of minimally invasive medicine in China and the independent innovation of medical devices, achieving a transformation from being an importer of minimally invasive equipment to an exporter in this field.

Not long ago, SRRSH appeared as the only 5G + smart medical project display unit at the "5G Development Achievement Exhibition" of the 31st China International Information and Communication Exhibition, demonstrating on-site its 5G ultra-long-distance domestic robotic surgery and 5G + AR remote emergency rescue system.

For more information
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The Highest National Teaching Award! How the Ophthalmology Medical Students Trained

The National Teaching Achievement Award is the highest award in the field of education. It is presented every four years, and is a national award representing the highest level of education in our country. Recently, the Exploration and Practice of Dry–to–Wet Lab Teaching Reform for Ophthalmology Professional Degree Postgraduates completed by the team of Professor YAO Ke from the Eye Center of the Second Affiliated Hospital, Zhejiang University School of Medicine won the second prize in the 2022 National Teaching Achievement Award for Higher Education.
The team has been persistently exploring and practicing the teaching reform of postgraduate students majoring in ophthalmology in China for 14 years. The results have formed an influential new model of ophthalmology teaching with Chinese characteristics, which is a breakthrough in the reform of ophthalmology professional degree postgraduate teaching, and has a very high leading role and application value (appraisal opinion).

Gradual Dry–to–Wet Lab teaching reform

The team leads the reform of ophthalmology teaching with the new concept of from theory to practice. A three–year practice training link is added in the cognitive period, system training period, and advanced training period. The new layered system implements a step–by–step basic, specialist, and comprehensive practical teaching content.

As a result, the team has established a full interaction practical teaching mode, and realized the in–depth integration of the Dry–to–Wet Lab teaching system to the three–stage training. It also has portrayed a clinical problem–oriented teaching blueprint, which not only fills the gap in domestic ophthalmology education but also effectively improves the quality of personnel training. The teaching model has been used for reference by 10 domestic universities, and numerous internationally renowned universities such as Columbia University, Johns Hopkins University have come to communicate. The team has successively won 21 important teaching honors, including the Zhejiang Province Teaching Achievement Special Award, the first batch of national university Huang Danian–style teacher teams from the Ministry of Education, the MARKTSO Golden Apple Award,

and the highest education award of the International Council of Ophthalmology.

Progressive Dry-to-Wet Lab multi-dimensional practical teaching program

The team introduced a D-D-D diversified teaching method. They use computer simulation, online learning platforms, and digital resources to implement theoretical teaching. They use visual virtual simulators, simulation experimental models, and simulation platforms of Dry Lab to train students to develop a sense of depth and three-dimensionality under microscopes. They use three-dimensional teaching methods such as 3D surgical teaching, so that students can obtain an immersive experience of surgical observation and take the role of an ophthalmologist. Based on the Wet Lab platform, they build a progressive training system of basic operations, specialist training, and comprehensive strengthening, to realize the goal of gradual focus on the breadth of practice.

As a result, the team has constructed a two-dimensional combined with the three-dimensional full-scenario training method, and created a real clinical environment for students. Since 2008, the Eye Center has trained more than 2,000 graduate students with professional degrees in ophthalmology. In the past three years, the proportion of graduate students who can independently perform cataract surgery has increased from 10% to more than 90%. The employment rate has remained 100% year after year. The team trained 1/6 of cataract surgeons in the country, directly benefiting nearly 300,000 ophthalmologists at all levels.

Teaching achievements actively serve the society

Through knowledge services such as popular science lectures on Eye Care Day, presentations on myopia prevention and control, etc., the practical teaching classroom has been moved from on-campus to off-campus. Practical services such as Han Hong's Charity Restoration Action, Africa Mali Brightness Walk, etc., convey the public welfare concept of supporting borders with science and technology and strengthen graduate students' sense of professional mission.

As a result, the results actively moved the second classroom of teaching from school to society, and transformed people's livelihood issues into teaching propositions. At the same time, this practical service model provides vivid and real scenes for socialist medical ethics education, endows talent training with more vitality, and sublimates the overall value of talent training. LIU Xin, a professional degree graduate student trained by the team, participated in the Brightness Project Cataract Restoration of Sight project during the poverty alleviation period of the People's Hospital of Taijiang County, Guizhou Province. HE Jingliang, a trainee trained by the team, participated in the Mali Brightness Tour in Africa organized by the Zhejiang Provincial Health Commission. Some of the trainees trained by the team took root in the west, leaving a medical team that cannot be taken away. The 2nd Affiliated Hospital Automobile Eye Hospital, which cultivates postgraduates' sense of professional mission and practical skills, won the gold medal in the Chinese Youth Volunteer Service Project Competition of the Central Committee of the Communist Youth League. Medical public welfare activities have spread all over the country.

Looking back 14 years, we move forward with love. The 2nd Affiliated Hospital Eye Center Team innovates in practice, educates people in innovation, and sticks to the original intention of educating people. Facing the future, it will closely follow the urgent needs of the national health strategy, accelerate the construction of new medical departments, and cultivate a group of ophthalmologists with excellent practical skills and a high sense of professional mission.

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Encounters with the World, Journeys to New Horizons

In the summer of 2023, the Zhejiang University School of Medicine (ZUSM) launched on-site international exchange programs, sending more than 80 participants to cities such as London, and Manchester in the UK, and Vancouver in Canada. The students participated in a feast of intellectual exchanges, expanding their international perspectives and enhancing their overall competence.

The University of British Columbia, Canada

The University of British Columbia offered a total of 13 course packages, covering topics such as An Introduction to Clinical Medicine and Scientific Research in Hospitals, An Introduction to Population and Public Health, Anatomy, etc. These courses aimed to provide students with a profound understanding of the similarities and differences between domestic and international medical education, fostering a stronger sense of professional responsibility and values.

"This exchange program has been incredibly enriching for me. Not only did I gain in-depth insights into Canada's healthcare system and culture, but I also learned about their healthcare policies and practices. I had the opportunity to engage with local medical students and professionals, which expanded my global perspective. "
—— **HUANG Sicheng, Clinical Medicine**

"At UBC, we delved into the Canadian healthcare system, experiencing a dual immersion in academia and practice. In Vancouver, we pondered the exotic wisdom, trying to figure out how to better fulfill our mission as youths. We are medical students from a university based on belief in truth. Guided by our ideals, we innovate and explore."
—— **SHAO Luqiao, Clinical Medicine**

Yale University, USA

The Yale School of Public Health offered the program in Environmental Health Sciences (SIPEHS), an online course consisting of lectures and training camps. The program covered subjects such as biostatistics, chronic disease epidemiology, environmental health sciences, microbiology epidemiology, and global health. It allowed the students to recognize the severity and urgency of environmental health issues on a global scale and the significance of public health for the well-being of humanity.

"What Yale University has given us is not only the enlightenment of scientific research and cutting-edge knowledge and technology but also a broadening of my horizons."
—— **FANG Shenghao, Preventive Medicine**

"SIPEHS, with its lectures and training camps, offered us an opportunity to delve deeply into the disciplines of public health and environmental health sciences. It gave us a clearer understanding of the research directions in various fields, greatly fueling our interest in public health."
—— **TU Yinuo, Chemical Engineering**

King's College London, UK

King's College London organized a 10-day program, providing students from all around the world with an interactive learning environment and genuine international experience. This allowed students to explore various disciplines and make friends from all corners of the globe. Through completing the course of Healthcare & Technology, they gained insights into topics related to the nervous system and digital systems. Through studying the London Cityscape & London Life course, they learned about the evolution of London's urban landscape, its historical origins, and the cultural characteristics that it embodies.

"As a student from ZUSM, participating in King's College London summer exchange program has been an unforgettable experience in my life. This program not only allowed me to gain a deep understanding of cutting-edge international medical education, but also broadened my horizons and enriched my knowledge."

—— SHEN Xinyi, Stomatology

"My awareness of the global medical challenges has ignited my interest in global cooperation and medical development. I participated in various SOCIETY activities and explored the city of London with many outstanding peers, forging deep friendships. This precious experience has not only assisted me academically but has also made me appreciate the value of international friendships."

—— HE Chuchu, Basic Medical Sciences

The University of Manchester, UK

The University of Manchester has excelled in the fields of bioscience, medicine, and integrated health. This summer, the university offered a 4-week summer school program, aiming to provide an immersive experience of Manchester's cultural landscape alongside academic exchanges at this prestigious institution.

"The University of Manchester's teaching approach encourages independent thinking through problem-based learning. The utilization of small group discussions fosters intellectual collisions, while innovative methods like role-playing and scenario simulations breathe life into otherwise dry academic concepts, subtly making them internalized."

—— LIU Xinyi, Stomatology

"The UoM's supportive teaching model has consistently motivated me to explore the unknown. The curriculum is diverse, and the autonomy it offers is empowering. The professors always present their materials in an engaging and accessible manner, sparking our enthusiasm for learning. In just one month of the exchange study, I gained a deeper understanding of the UK's teaching methods and its cultural nuances."

—— GAN Maji, Preventive Medicine

Seeking the truth of science, cultivating a global perspective, embracing the virtues of humanity, appreciating the beauty of art, and finding the essence of life—these are the exceptional pursuits of every Zhejiang University medical student. On the long path of medicine, with unwavering dedication and a thirst for knowledge, ZUSM students explore the world based on a belief in truth and innovation. They strive to become well-rounded, exceptional medical professionals with an international perspective, leaving their mark on the global stage.

2023 White Coat Ceremony

Donning the white coats and taking the oath of a medical student, over 600 students from the class of 2022, including those in the eight-year program, have started a momentous chapter in their medical voyage. Wearing the emblematic white coats, they are embarking on a demanding path, yet Zhejiang University School of Medicine stands as the nurturing ground where these students will cultivate their aspirations and set forth toward the realization of their medical dreams.

> *Health related, life entrusted. The moment I step into the hallowed medical institution, I pledge solemnly...*

In the solemn setting of the Lakeside Plaza at Zijingang Campus, Zhejiang University, the students made their pledge

Collaboration with Harvard

In recent years, the Affiliated Hospitals of Zhejiang University School of Medicine have actively promoted cooperation with Harvard University in the fields of physician training, medical services and scientific research.

Intensive Clinical Research Training Course

Thirty physicians from the Second Affiliated Hospital, Zhejiang University School of Medicine (SAHZU) attended the first intensive clinical research training course offered by Harvard T.H. Chan School of Public Health (HSPH) in July 2023.

The five-day course is structured around clinical epidemiology, biostatistics and scientific writing, with a focus on the principles and methods for quantitative clinical research and the demonstration of their applicability in research in clinical medicine and their relations with biomedical and public health research.

The course is a vital part of SAHZU–HSPH collaboration since 2021.

"I would often keep Prof. Albert Hofman's words in mind: When making a research decision, keep asking yourself, which 'Hippocratic questions' are you targeting? Etiology, diagnosis, treatment, or prognosis? Think big, start small. I was encouraged by this course to return to the essence of clinical medicine in order to solve clinical problems and provide better services for patients."
—— GE Ziyu (SAHZU General Dentistry)

In-depth Cooperation with Boston Children's Hospital

In June, a delegation from the Affiliated Children's Hospital of Zhejiang University School of Medicine (ZCH), led by SHU Qiang, the Secretary of the CPC ZCH, paid a visit to Boston Children's Hospital. Both sides engaged in discussion and shared perspectives on various aspects of clinical treatment, research transformation, education and teaching from different dimensions.

ZCH and Boston Children's Hospital, since a cooperation agreement was signed in 2020, have achieved fruitful collaboration on MDT international consulting, excellence specialist training and exchanges, etc. During the visit, through talks on disciplinary development, ZCH and Boston Children's Hospital planned to enhance cooperation on leading disciplines, start exchange programs for pediatric personnel and deepen curriculum reform and postgraduate training, collectively cultivating talents.

During the visit, the delegation earnestly promoted the *World Journals of Pediatrics* and *World Journal of Pediatric Surgery*, two English magazines sponsored by ZCH.

Promoting All-round Cooperation with the National University of Singapore

Zhejiang University and the National University of Singapore (NUS) have recently promoted a series of cooperation and exchange in medicine, which is supported by the Sino–Singapore Innovation Program at NUS that was set up by entrepreneur Mr. OUYANG Xiuzhang.

NUS Medicine Delegation visited ZUSM

The 4th Joint Seminar in Biomedicine

ZUSM Affiliated Stomatology Hospital Delegation Visited NUS School of Dentistry

Medical Education

In July, Lau Tang Ching, Vice Dean of the NUS Yong Loo Lin School of Medicine and his delegation visited Zhejiang University School of Medicine, its Second Affiliated Hospital, and the International School of Medicine. The two sides reached further agreement to cooperate regarding medical education, the exchange of clinical internships for medical students and faculty training.

Academic Exchange

In August, the fourth bilateral joint seminar between the Yong Loo Lin School of Medicine of the National University of Singapore and the School of Basic Medical Sciences of Zhejiang University was successfully held in Singapore. The theme was "Regulation of Cellular Activities in Human Diseases and Therapies". At this two–day joint seminar, 30 scholars from the two universities fully shared their ideas and presented the latest scientific research achievements in the field of biomedical science.

Stomatology Collaboration

In August, CHEN Qianming, Secretary of the CPC Committee of the Affiliated Stomatology Hospital of Zhejiang University School of Medicine and Dean of the School of Stomatology, led a delegation to visit the School of Dentistry of the National University of Singapore, and jointly explored innovative practices, such as deepening the collaboration between medical education, broadening students' international vision and cultivating highly skilled and internationally competitive medical talents.

Since 2012, the Affiliated Hospital of Stomatology has maintained a close cooperative relationship with the Faculty of Dentistry of the National University of Singapore, actively promoting teacher–student exchanges and resource sharing.

Make It a Beacon of International Collaboration

The Loma Linda University Health delegation visited SRRSH

In June 2023, the delegation of Loma Linda University Health (LLUH) led by Dr. Richard HART, President of LLUH, visited Affiliated Sir Run Run Shaw Hospital (SRRSH), stretching over their deep friendship that lasts nearly 30 years. The two sides carried out a series of activities regarding clinical medical education.

In SRRSH's infancy, LLUH was invited to participate in the comprehensive management of the hospital. To this day, LLUH has sent more than 1,000 experts in total to support SRRSH on site and has received 350 staff members of the hospital for medical training. In 2016, Dr. Hart was awarded "the Chinese Government Friendship Award", the highest national prize given by the Chinese Government to foreign experts working in China.

Seeking In-depth Cooperation: the Founding of SALITAH

On June 23, SRRSH and LLUH International Training Academy for Healthcare was founded. The first Clinical Competency Medical Education Seminar was then held with in-depth discussions on key topics of medical education.

Graduation of the First Dental Hygiene Class and Inauguration of the Periodontal Center of SRRSH

The close cooperation in oral hygiene between SRRSH and LLUH is time-honored. Early in 2009, the first batch of full-time "oral hygienists" in China trained by the two parties graduated, thus building a periodontal specialty development pattern with unique SRRSH characteristics.

In 2019, the International Institute for Health Sciences was established and the parties jointly organized the nursing oral hygiene class. The program broke new ground in the training of oral hygiene bachelors in China with its first batch of students graduating on June 21st, 2023 after 4 years of studying.

Meanwhile, the Periodontal Center of SRRSH was inaugurated. The center will further concentrate superior resources and expert strength, build a multidisciplinary joint diagnosis and treatment model for periodontal diseases, and provide more standardized, diversified and professional oral health care services for a wide range of patients.

LU Qi: The Coloproctologist with "Magic Hands"

LU Qi, hailed as the "Master of Hemorrhoids", is a pioneer in the field of hemorrhoids and colorectal surgery in China. In the 1960s, he was invited to Beijing to treat Premier ZHOU Enlai. LU Qi established the Department of Colorectal Surgery at Zhejiang University School of Medicine. He pioneered the "Suppository Therapy for Internal Hemorrhoids", led the establishment of the Coloproctology Branch of the China Association of Chinese Medicine, and founded the *Chinese Journal of Coloproctology*.

Professor LU Qi and his wife at Tian'anmen Square

Devoting Himself to Medicine and Establishing the Department of Colorectal Surgery

LU Qi was born in 1921 in Ouhai, Wenzhou. His grandfather and great-grandfather were renowned local practitioners of Traditional Chinese Medicine (TCM). In his youth, LU Qi worked part-time during his studies at the Ouhai Hospital. He specialized in researching common diseases of the rectum and anus. He continuously improved the hemorrhoid treatments available based on his clinical practice, and accumulated over 1,000 medical records. Through engaging in

constant exploration, he improved his medical skills and became renowned as a specialist in the treatment of hemorrhoids in his hometown. As there were no highly effective treatments for internal hemorrhoids available at that time, patients often suffered intense pain. Therefore, LU Qi began to study more effective drug treatments for internal hemorrhoids in order to reduce their recovery time.

LU Qi was dedicated to incorporating TCM into the treatment of hemorrhoids while combining Western therapies. He collected folk records and prescriptions and experimented repeatedly, finally developing the Suppository Therapy for Internal Hemorrhoids. Under this therapy, medication could directly act on internal hemorrhoids and cause the prolapse of necrotic hemorrhoid mucosa. In order to benefit more patients, he conducted clinical trials. Over the course of more than a year, he treated over 100 cases and conducted various examinations, thereby accumulating a wealth of valuable data. With positive clinical therapeutic effects, LU Qi summarized the research findings and submitted them for publication. He also wrote a paper on the groundbreaking Suppository Therapy for Internal Hemorrhoids in order to exchange ideas with his peers. Subsequently, he published over 20 further papers with the aim of providing detailed explanations and responding to questions, thus allowing more of his peers to understand, master, and apply this therapy in their own clinical practice.

In the 1950s, LU Qi established the Department of Colorectal Surgery. Based on foreign rubber band ligature, he successfully developed a suction ligator in 1974, which won an award at the 1978 National Medical and Health Science Conference.

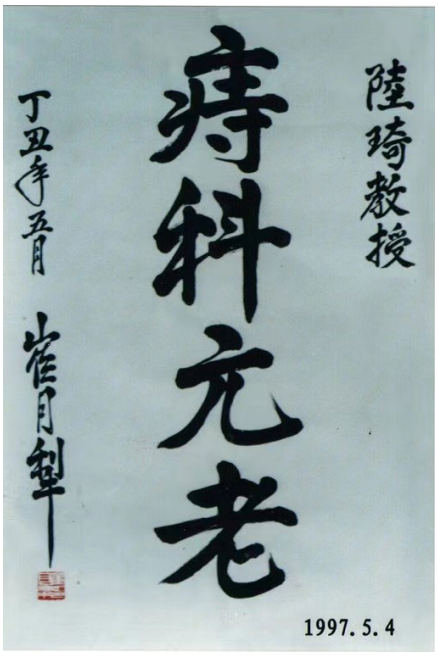
Devoting Great Efforts to Promoting Discipline Development

In order to cultivate more talents in the field of coloproctology, LU Qi organized coloproctology classes in 1964, which educated over 200 students from various hospitals. Upholding a rigorous and realistic spirit, he delivered each lesson carefully and shared his research findings and cutting-edge techniques with his students without reservation. These students applied what they had learned in clinical practice after graduating, with many of them becoming key experts in the field of coloproctology.

By offering classes to train talents, LU Qi envisioned the formation of a nationwide coloproctology organization to facilitate in-depth exchanges and discussions among researchers from different regions and promote further development of the proctology discipline. Thus, the Coloproctology Branch of the China Association of Chinese Medicine was established.

In 1981, Professor LU Qi, along with Professor SHI Zhaoqi and Professor DING Zemin, founded the *Chinese Journal of Coloproctology* and served as its first editor-in-chief. The journal aimed to enhance the academic progress and achievements of the combined therapy of traditional Chinese medicine and Western medicine in the field of coloproctology in China. To counteract the lack of funding, LU Qi used his own salary to subsidize the journal initially. He also devoted his personal breaks to organizing and selecting the manuscripts despite his heavy workload of clinical treatment, sparing no effort to promote the academic quality of the journal.

When discussing his lifelong dedication to the medical profession, the 100-year-old professor LU Qi remains full of enthusiasm. He believes that medical practitioners will drive the vigorous development of the medical field generation after generation. To support the work of his successors, Professor LU donated to the First Affiliated Hospital of Zhejiang University School of Medicine his collection of two large boxes of professional books in various languages, such as Chinese, English, Japanese, and Russian. Professor LU earnestly stated, "I hope everyone can read more, learn more, think more, and contribute their own strength to the development of medicine."



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Seeking Truth and Innovation with
Benevolence and Humane Proficiency

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