Issue 1 2023

ZJUMEDICINE

SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

Cracking Emotional Code

Dialogue with Neuroscientist HU Hailan

Going Beyond Medical Education

How "Medicine+" Talents Cultivated at ZJU

Unlocking the "Code" of Energy Transmission Across Species

A Cross Disciplines Research

Blooming cherry flowers at ZUSM campus in Spring

ZUSM at A Glance

Zhejiang University School of Medicine (ZUSM) founded in 1912, is one of China's top higher medical education institutions, as well as one of its oldest. Located in Hangzhou — one of China's most picturesque cities — ZUSM is organized across 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 health care partnership network composing of 7 affiliated hospitals, 5 non-direct affiliated hospitals and 4 cooperated hospitals. It is home to more than 33,000 faculty members and over 8,700 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 health future for all.

浙江大學 医学院
SCHOOL OF MEDICINE
ZHEJIANG UNIVERSITY

CONTENTS

CONTENTS

Dean's Message

LIU Zhihong, M.D.

Professor of Medicine
Dean, Zhejiang University School of Medicine
Academician, Chinese Academy of Engineering

Dear Readers,

The journal ***ZJU Medicine*** is officially launched!

In 1912, Zhejiang University School of Medicine was founded in Hangzhou, a city known as "Paradise on Earth". Over the past hundred years, the School has composed a splendid chapter in pursuit of truth. Now, it is striding forward with an unprecedentedly high spirit!

Not only a witness, but more importantly a positive participant in the development of modern medical and healthcare in China, the School has always advanced with the times and social trends, sharing the fate of the nation over the last 111 years. It has cultivated a cohort of top medical talents with both patriotism and an international vision, facilitated innovations in a number of world-leading, core medical technologies, and provided a wealth of medical and health-related services to satisfy the needs of society and the people.

Our journal ***ZJU Medicine*** seeks to inherit and carry forward the spirit of ZJU medical scholars who seek truth and pursue innovation. It also strives to be a pioneer on the journey to excellence. We are determined to make it an important platform of exchange between our school and other academic communities both at home and abroad, as well as an indispensable showcase that displays the school's achievements in terms of teaching, research and practice.

Our journal will keep you informed of the lastest teaching modes and curriculums of our school. You are welcome to join us in improving medical education and gathering more respected medical talents.

Our journal will bring the scientific frontiers and achievement transformations of our school to your knowledge. You are also welcome to join us in building the cutting-edge discipline of modern medicine and exploring effective ways to enhance the well-being of humankind.

Our journal will enable you to feel the passion of all of the students and faculty of our school, share with you our life both on and off campus, and record the very moments our dreams come into blossom.

Let us work together, with ambition, mission, and vision, to strengthen the bond of ZJU medical scholars around the world, and to march confidently toward the goal of building the School into the world's first-class medical school with Chinese characteristics!

Cracking Emotional Code

HU Hailan

Professor and Dean, School of Brain Science and Brain Medicine, Zhejiang University School of Medicine

L'Oréal–UNESCO For Women in Science Award (2022)
IBRO–Kemali International Prize (2019)
China's Top 10 Scientific Discoveries (2018)

> ***I hope that one day our understanding of the neurological mechanisms behind psychiatric diseases will be advanced to the level that enables us to create a cure to help people suffering from these illnesses.***

Could you brief us on your research?

My lab studies the brain mechanisms of emotional and social behaviors, with a particular focus on dominance hierarchy and depression. By understanding how these behaviors are encoded in the brain and how they are shaped by experience through plastic changes in the relevant neural circuits, I hope our work will shed light on new treatment strategies for emotional disorders.

What has been the most interesting discovery in your field recently?

We made some advances in understanding the rapid and effective impact of ketamine on a small area of the brain called the habenula, an area that becomes highly activated during depression. It transpires that ketamine is distinctly more efficient than traditional anti–depressants. Identifying this direct connection has therefore shed new light on the etiology of the ill. Along this line of research, we further discovered neural mechanism underlying depressive like state associated with social status loss. This work just came out this year.

What sparks your interest in neuroscience and this specific area?

Psychiatric diseases inflict enormous misery and burden on individuals, families and society. Compared with some other disciplines, neuroscience is still at a relatively infant stage. I hope that our findings in basic science will help the public understand that emotional disorders such as depression are not just psychological problems but have a biological basis. Meanwhile, in the long–term, based on the disease mechanism and brain targets that we discover, we hope to develop new drugs and innovative treatment strategies that can advance the treatments of depression.

How has being at Zhejiang University helped your research?

Zhejiang University boasts a full spectrum of disciplines that are all developing vigorously. The diversity of fields offered here is remarkably beneficial for the birth and development of new cross–disciplinary areas. Also, I have very much enjoyed working with the wonderful researchers and students in the School of Brain Science and Brain Medicine, ZJU, the first school focusing on brain science and brain medicine in China. Together, we hope to create a world–class center for neuroscience research. We are and will be striving to make breakthroughs in dissecting neural mechanisms as well as in discovering novel theories and developing new technologies for the diagnosis and treatment of major neurological and psychiatric diseases.

As a woman scientist, what advice do you have for girls who aspire to pursue an academic career?

In this age with rapid changes, you never know what will be the social favorite three months later, but there are reliables and dependables in science in the many years to come. The self–esteem built upon science is much more reliable than the self–esteem built upon the so–called mainstream images. So if you love science, do not be afraid to become a scientist!

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CAR-T Cell Therapy: from Bench to Bed

HUANG He

Professor and President of the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU)
Director of the Institute of Hematology, Zhejiang University
Member of Executive Committee, Asia–Pacific Bone Marrow Transplantation Group (APBMT)
Member of American Society of Hematology (ASH) and European Society of Blood and Marrow Transplantation (EBMT)

Please describe your research ?

Our team conducts extensive and innovative research on CAR–T cell therapy. By leveraging cutting–edge technologies such as gene editing, single–cell sequencing, and synthetic biology, we have successfully overcome technical bottlenecks in safety, targeted cytotoxic function, and duration. We have developed a series of novel CAR–T cells that achieve significant technological advancement in enhancing CAR–T cell function, precise regulation, and universal application. Our integrated platform has the potential to promote both basic research and clinical applications.

What novel advancements have you achieved recently?

By using non–viral transfection techniques, we have constructed PD1–integrated CAR–T cells, which eliminates the risk of random insertion of virus transfection and ensures clinical feasibility. By incorporating immune–checkpoint knockout, we remove the inhibition of the tumor immune microenvironment on the function of CAR–T cells, resulting in prolonged survival and excellent tumor clearance in patients.

What is the achievement in clinical treatment?

We have achieved remarkable success in CAR–T cell therapy for relapsed/refractory hematological malignancies by focusing on the development of new targets. Our results are outstanding with complete response rates reaching 92%, 87.5%, and 70.3% in patients with acute lymphoblastic leukemia, non–Hodgkin's lymphoma, and multiple myeloma, respectively. Our success has drawn patients from various countries and regions such as Switzerland, Israel, Singapore, Malaysia, Lebanon, among others, to seek CAR–T cell therapy at FAHZU.

How is international collaboration important to your research?

Over the past few decades, CAR–T cell therapy has achieved remarkable success thanks to global efforts. For instance, our team has collaborated with the EBMT for several years, which is one of the largest and most influential international organizations in the field of blood and marrow transplantation. Currently, we are in the process of establishing a peak discipline group in collaboration with leading physicians and scientists from France, Israel, and around the world. This international network will focus on promoting innovation and clinical translation of CAR–T cell therapy, with extensive and in–depth cooperation expected in the future. We anticipate that this joint effort will provide more solutions to alleviate suffering and improve well–being.

With unwavering commitment to human health, we will continue to develop innovative treatment strategy, provide high-quality medical services and bring hope to patients with hematologic malignancies.

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Zhejiang University Leads New National Center for Cancer Research and Treatment in China

With the support of the National Natural Science Foundation of China, Zhejiang University has established a National Basic Science Center with the aim of "mesoscale investigation on tumor metabolism". The center brings together several top national research institutions, including the National Cancer Center, the Cancer Hospital of the Chinese Academy of Medical Sciences, and Peking University. The chief scientist, Prof. Zhimin Lu, Dean of the Institute of Translational Medicine and a Foreign Member of the Academia Europaea, leads the center.

Combining the forefront of tumor research with the major needs of cancer prevention and treatment in China, the center focuses on tumor metabolic remodeling and explores the molecular basis of tumor metabolism from a novel mesoscale perspective in a multi-level and systematic manner. The center aims to reveal a continuous landscape of tumor occurrence and development and provide breakthrough intervention or tools for cancer prevention, diagnosis, and treatment.

The Institute of Translational Medicine (ITM) at Zhejiang University was established in 2014 with the mission to bridge the gap between basic science and clinical practice for accelerated translation of bench-side breakthroughs to bedside diagnostics and therapies, which ultimately benefit patients. ITM is equipped with state-of-the-art facilities supported by resources from the university, School of Medicine, and seven affiliated hospitals to promote interdisciplinary research and collaboration between scientists and clinicians.

The research at ITM covers a wide range of areas, including cancer, metabolism, immunology, cardiovascular diseases and stem cell therapy, as well as medical engineering and new device development. It also houses several research centers, including the Center for Cancer Research, the Center for Metabolic Disease, and the Center for Medical Engineering and Bioinformatics. To date, ITM has about 150 graduate students, 36 principal investigators and 31 post-doctoral fellows. Through research, education, and international collaborations, ITM is playing a crucial role in advancing the field of translational medicine and promoting global health.

ITM is supported by a comprehensive public technology platform, including biochemistry and molecular biology platform, histopathology platform, bioinformatics and big data computing platform, and SPF level experimental animal platform.

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良渚实验室
LIANGZHU LABORATORY

Liangzhu Laboratory Creates Fertile Ground for Gathering Top Talents

Working at the Liangzhu Laboratory of Zhejiang University, WANG Yongcheng is appraised by the MIT Technology Review as a scholar of TR35 China for the year 2022. After receiving his Ph.D. from Harvard University at the end of 2020, he moved to Zhejiang University as a researcher under the "the ZJU100 Global Recruitment Program". Utilizing rich resources of Liangzhu Laboratory, he developed a new pathway single-cell analysis platform, and a year later, established a company.

As one of the first laboratories in Zhejiang Province, Liangzhu Laboratory is located in Hangzhou Future Sci-Tech City, a national base of innovation and entrepreneurship. Supported by public platforms and venture capital funds, the Lab is oriented toward solving clinical problems and targets frontier research. Through innovations in knowledge, technology, and industry, it has gathered multidisciplinary talents in the fields of medicine, engineering, and information technology, and managed to build future-oriented, fertile ground for global life and health sci-tech innovation.

The Lab has gathered a batch of chief scientists who form a multidisciplinary, high-level research team. The three major research fields, namely "Brain Disease", "Undiagnosed Disease"and "Hematology & Immunology Disease", are respectively led by Academician DUAN Shumin, Academician LIU Zhihong, and Professor HUANG He. To create fertile ground for the new era, the Lab makes innovations in talent gathering channels, and integrates administrative, educative, medical, and other social resources. The outcome is satisfying. The Lab not only welcomed leading talents such as XU Haoxin, ZHANG Guojie, and CHEN Jiaming, but also attracted a group of potential scholars, represented by WANG Yongcheng, who is developing new technologies, products, and paradigms for the precise diagnosis and treatment of diseases based on system medicine.

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The Mysterious Evolution of the Germline Mutation Rate Across Species Unraveled

Reproductivity is a crucial factor for explaining the different germline mutation rates between species.

The scientists from China, Denmark, France, Germany and USA discovered the underlying causes and evolutionary patterns of variations in terms of the germline mutation rate across species. Their groundbreaking findings were published in *Nature* on March 2.

As an ultimate source of genetic diversity and a major driver for evolution, DNA mutations are in the spotlight in evolutionary biology and biomedical research. The fundamental reason why offspring develops new traits different from their parents' lies in the fact that the offspring carries the DNA mutations occurred in germ cells from the parents. And the frequency of the DNA mutation occurred cross one generation is called per-generation mutation rate and has been found to be different between species. How this mutation rate varies among species? The question has been baffling biologists for over 80 years.

The researchers quantified germline mutation rates across vertebrates by sequencing and comparing the high-coverage genomes of 151 parent-offspring trios from 68 species of mammals, fishes, birds and reptiles. "The per-generation mutation rate varies among species by a factor of 40, with mutation rates higher for reptiles and birds than for mammals and birds," Dr. Lucie Bergeron, the lead author of the study from the University of Copenhagen, observed. "Given the substantial differences in life-history trait across species, a factor of 40 is not a yawning gap. This suggests that there are resemblances among vertebrates when it comes to the mechanisms underlying mutagenesis."

According to the 'male-driven evolution hypothesis', in mammals and birds, the much larger number of germ cell divisions per generation in the male germ line leads to the expectation of a male mutation rate bias. "In other words, offspring's mutations occur primarily from genomic mutations in parents, but very little is known about the male-to-female contribution ratio," said Prof. ZHANG Guojie, the corresponding author of the study from Centre for Evolutionary & Organismal Biology at Zhejiang University. "Around 48% of all 3,034 de novo mutations (DNMs) could be traced for their parental origin. Our research indicated that approximately 75% of DNMs in bird offspring derive from mutations in paternal germ cells whereas the proportion is roughly 67% in mammals. In contrast, in fish and reptiles, which show a low level of sexual dimorphism, both sexes make literally equal contributions to DNMs."

Moreover, the researchers also found that the earlier a species matures sexually, or the more offspring per generation produces, the lower the per-generation mutation rate will be in germ cells. In addition, they demonstrated that genetic drift also had an impact on the germline mutation rate and found a negative association between the per-generation mutation rate and the effective population size.

Germline mutations are the engine of species evolution, and the mutation rate affects the evolutionary potential of each species and the evolution of new traits in them. "Our study indicates that the mutation rate, like other biological traits, varies from species to species, and that it is also influenced by other biological traits during the macroevolutionary process," ZHANG Guojie stressed.

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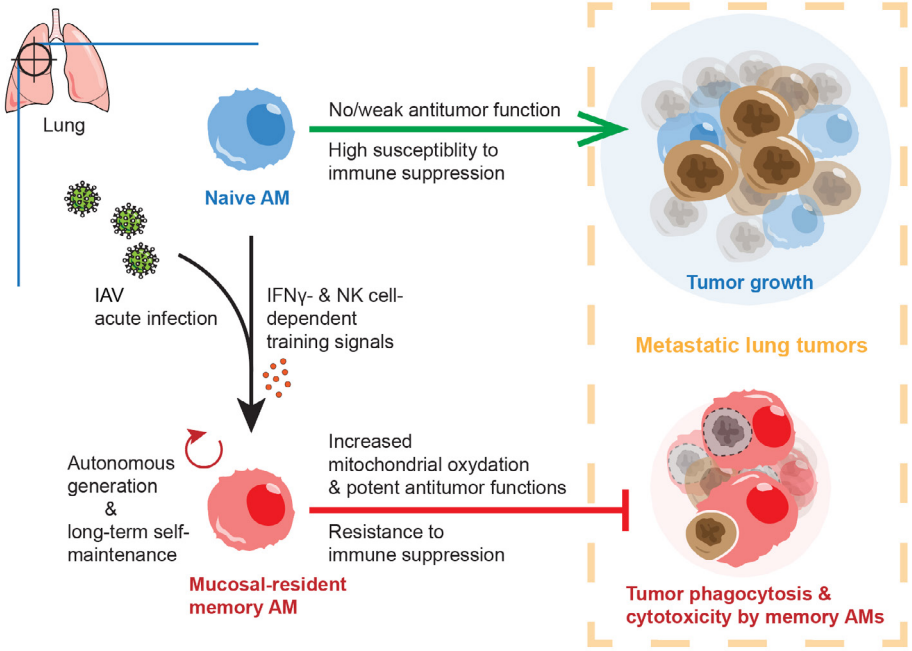
Influenza Trains Alveolar Macrophages to Fight Cancer

The lung is exposed to a variety of respiratory viruses such as influenza, and is also a frequent target organ of both primary and metastatic cancers. Respiratory viral infection was previously shown to induce immunological training of lung tissue–resident alveolar macrophages (AMs) with enhanced anti–bacterial functions. It is however not clear whether previous training experience of AMs by respiratory viral infections is important to anti–tumor immunity in the lung.

On February 20, a group of researchers led by Dr. YAO Yushi from Zhejiang University School of Medicine published a research article entitled "Influenza–trained mucosal–resident alveolar macrophages confer long–term antitumor immunity in the lungs" in Nature Immunology, indicating that acute influenza infection induces long–lasting anti–tumor trained immunity in self–sustaining resident AMs.

In their study, the researchers found that acute influenza infection in mice endows long–lasting anti–metastatic immunity in the lung which is mediated by influenza–trained AMs. Trained AMs exert tissue–specific anti–tumor immunity via enhanced tumor cell phagocytosis and cytotoxic functions, which depend on their enhanced mitochondrial oxidation of fatty acids and glucose. Intriguingly, the researchers identified human AMs with trained immunity traits in non–small cell lung cancer tissues that are associated with a favorable immune microenvironment.



This study sheds light on tissue–resident macrophages as a potential target of trained immunity–based anti–cancer strategy with long–term effects, which is particularly appealing in individuals with extrapulmonary cancers, such as melanoma and breast cancers, with high risks of lung metastasis. "We believe that training tissue–resident macrophages is a promising prophylactic and also possibly therapeutic anti–cancer strategy that deserves further investigation" said WANG Tao, the first author of the paper and a PhD student with Prof. YAO.

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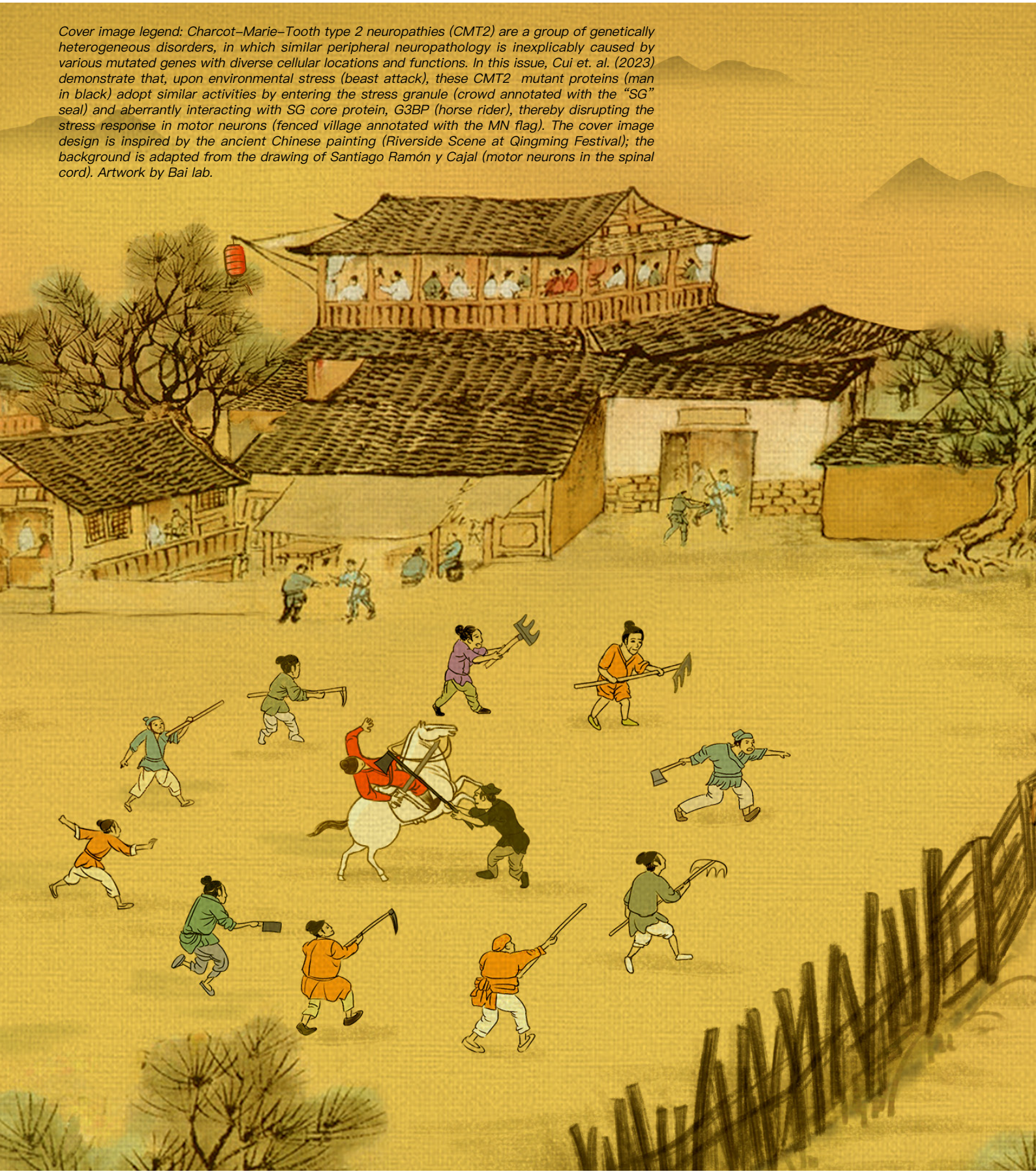
Cover image legend: Charcot–Marie–Tooth type 2 neuropathies (CMT2) are a group of genetically heterogeneous disorders, in which similar peripheral neuropathology is inexplicably caused by various mutated genes with diverse cellular locations and functions. In this issue, Cui et. al. (2023) demonstrate that, upon environmental stress (beast attack), these CMT2 mutant proteins (man in black) adopt similar activities by entering the stress granule (crowd annotated with the "SG" seal) and aberrantly interacting with SG core protein, G3BP (horse rider), thereby disrupting the stress response in motor neurons (fenced village annotated with the MN flag). The cover image design is inspired by the ancient Chinese painting (Riverside Scene at Qingming Festival); the background is adapted from the drawing of Santiago Ramón y Cajal (motor neurons in the spinal cord). Artwork by Bai lab.



Scientists Reveal the Pathogenic Mechanism of Peripheral Neuropathies

Many complex diseases often involve the interplay between genetic and environmental factors. The formation of stress granules (SGs) is an important anti-stress mechanism in response to environmental insults. Charcot-Marie-Tooth diseases (CMT) are a group of inherited peripheral neuropathies with a prevalence of ~1:2500. According to various causal genes, CMT can be classified into many different subtypes. Despite similar clinical presentation among different CMT2 subtypes, their causal mutant proteins are highly varied in their cellular localizations and functions. It remains unclear whether there is a molecular link across different CMT-causal mutant proteins.

On February 3, 2023, Prof. BAI Ge's research group from the School of Brain Science and Brain Medicine, Zhejiang University School of Medicine, and LI Jinsong's research group from the CAS Center for Excellence in Molecular Cell Science, Chinese Academy of Sciences published a cover article in Cell, entitled "Diverse CMT2 Neuropathies are Linked to Aberrant G3BP Interactions in Stress Granules". This study reveals that the stress granules abnormality is the common pathogenic mechanism underlying different subtypes of CMT2 diseases. This finding establishes an important theoretical basis for the development of uniform treatment for multiple CMT subtypes, and provides a new conceptual framework for understanding the genetic heterogeneity in many other diseases.

In this study, researchers started with the glycyl-tRNA synthetase (GlyRS), the causal protein of CMT2D subtype. When motor neurons were exposed to adverse environmental stimuli, the mutant GlyRS proteins translocated from the cytoplasm to the newly formed stress granules, where they aberrantly interacted with the SG core protein, G3BP.

Using techniques including live cell imaging, proximity labeling, quantitative mass spectrometry, and STORM super-resolution imaging, the researchers found that the abnormal interaction between mutant GlyRS and G3BP had no effect on SG dynamics but significantly perturbed the G3BP-centric core SG network, resulting in over-sequestration of many non-SG components. This disrupted SG-mediated stress responses, leading to increased stress vulnerability in motor neurons. The researchers also found that the aberrant interaction between mutant GlyRS and G3BP proteins was mediated by intrinsically disordered region (IDR). Mutations in this region can eliminate the influence of mutant GlyRS upon SGs and alleviate motor deficits in CMT2D mouse model.

Furthermore, the researchers found that this mechanism could be extended to other CMT2 subtypes. By testing more than 20 different CMT2-causal mutant proteins, the researchers found that, upon stress, most of these proteins can enter SGs and aberrantly interact with G3BP. This led to SG abnormalities, and disturbed the stress response in motor neurons. These findings suggested that SG abnormalities may represent a common pathogenic mechanism underlying different subtypes of Charcot-Marie-Tooth diseases.

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ZJU Scientists Unlock the "Code" of Energy Transmission Across Species

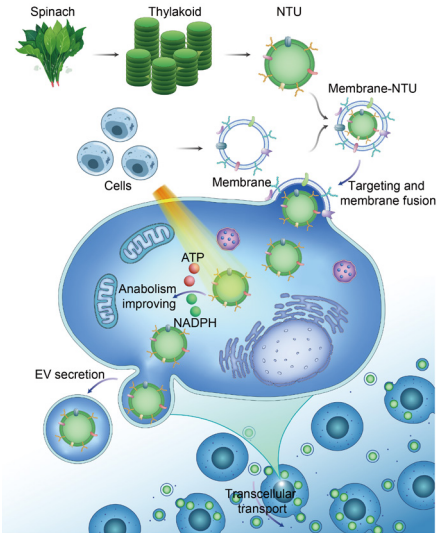
Spinach has left deep childhood memories for many post-70s and post-80s generations because of the cartoon image of Popeye. Apart from appearing on our table as usual, it is truly endowed with the expectation of great power by scientists. The team of Dr. LIN Xianfeng and Prof. FAN Shunwu, from the orthopedics of Sir Run Run Shaw Hospital (SRRSH), Zhejiang University School of Medicine, and the team of Prof. TANG Ruikang from the Zhejiang University Department of Chemistry, successfully extracted the biological battery with photosynthesis – thylakoid from spinach, and through sophisticated preparation technology, delivered the thylakoid across species to the animal's aging cells with lesions for the first time in the world, allowing animal cells to have the energy of photosynthesis like plants, so as to open the Time Gate of reversing cell degeneration and aging. This original research result was published in journal Nature on December 8, 2022.

"Follow the laws of nature, make innovative breakthroughs in the world problem of delivering energy to cells, and open up the possibility of metabolic engineering."

The senior editor of Nature highly praised these latest research results of the team from Zhejiang University. It was reported that the most exciting part of this research was that the team developed the cell membrane nanocoating technology, which covered the mammalian cell membrane in the outer layer of the nanothylakoid, and skillfully transplanted the plant thylakoid into mammalian cells through the way of camouflage and encapsulation of the cell membrane, successfully unlocked the code of energy transmission across species and achieved energy supply specifically, which was verified in the treatment of degenerative osteoarthritis.

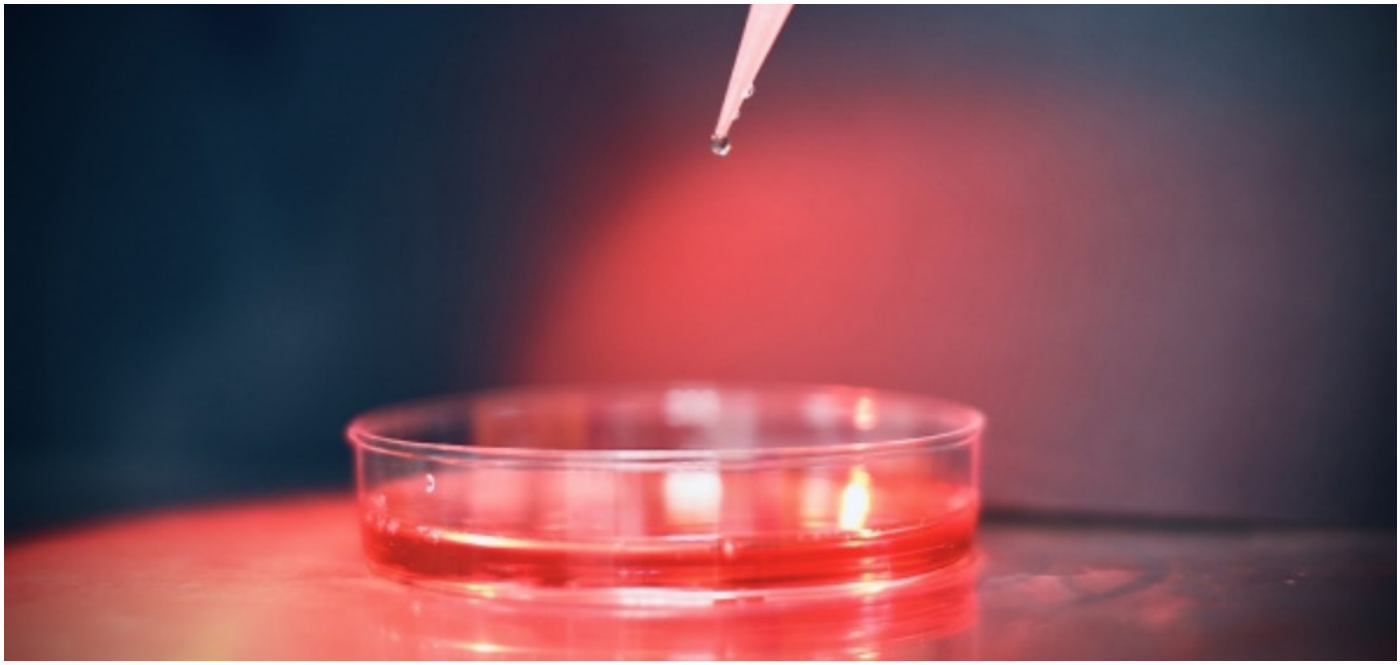
With the progress of disease research, more and more studies had found that the lack of energy in animal cells was the key reason for the occurrence of tissue aging and the development of degenerative diseases. Just as human beings need nutrition three times a day, cell renewal and metabolism also need energy and supplies. Exactly, ATP and NADPH are indispensable energy currency and material currency for cell regeneration and repair. However, it was a huge scientific problem to provide direct energy and materials to degenerative cells.

An idea burst into LIN Xianfeng's mind, Can we design a 'charging' device to controllably generate ATP and NADPH in cells? The brainstorming triggered by the cross discussion between the two groups of medicine and chemistry opened up a new world of research. Based on the long-term exploration in the field of biomaterials from the orthopedic research team of SRRSH, the chemical biology research idea of materials regulate biology provided by the TANG Ruikang's team and the concept of artificial organelle, the whole team keenly turned their eyes to the magical nature. In the natural world, plants and animals form a perfect complementary relationship. As you can see, plants produce oxygen and sugar by absorbing carbon dioxide, while animals do the opposite. Can we realize this complementary relationship at cellular level and make the plant energy supply system become the biological battery for animal cells to supply energy by implanting photosynthetic organelles?



Schematic diagram of membrane-coated nanothylakoid units

For billions of years, plants have evolved an almost perfect organelle used for energy supply —thylakoid, which is exactly an energy factory that can generate ATP and NADPH in a controllable and stable way. The researchers selected spinach as the raw material, which is the greenest in the vegetable market and widely used in the field of plant metabolism, and through great efforts, successfully extracted and purified thylakoid from spinach green leaves.



Schematic diagram of light stimulated chondrocytes

The battery for energy supply was prepared and next problem was the interface. How to deliver thylakoids safely and accurately to the aging and degenerative cells of animals has become a huge problem that limited their medical application. For a long time, the research on cross species delivery of bioactive components had progressed slowly. Especially the human body has a complex immune system. Various immune cells, mainly macrophages, will actively recognize and phagocytosis invaders, and then digest them through lysosome degradation.

How can we overcome the barriers between species? The team successfully disguised the nanothylakoids with the cell membrane and achieved the intracellular delivery of nanothylakoids with bold assumptions and careful verification. The escape of exogenous biomaterials from lysosomes is an important link to achieve successful delivery. The team had repeatedly verified that animal cells no longer removed nanothylakoids as 'foreign bodies' through a variety of endocytosis inhibition tests, so that the thylakoid became a part of it.

After one year or even more of experiments and analyses, the team verified that the nanothylakoid can retain the protein and other functional monomers required for photosynthesis on the thylakoid, maintain sufficient action time and degradation stability, and ensure the sufficient production of ATP and NADPH, so as to systematically reverse the metabolic state of pathological cells through a variety of interdisciplinary technologies. In order to test whether this kind of biological battery can reverse the metabolic state of diseased cells, the team first selected the disease model of osteoarthritis to carry out conceptual verification. Osteoarthritis is one of the most important causes of deformity and disability in clinical practice. It is precisely because of the imbalance of energy metabolism of chondrocytes and the depletion of ATP and NADPH that destroys the articular cartilage. At present, the clinical prognosis of osteoarthritis is still poor since the biological treatment can't systematically correct the metabolic imbalance of injured and degenerated chondrocytes.
Led by FAN Shunwu, the team continuously sought various interdisciplinary technologies for more than one year and systematically verified that the nanothylakoid encapsulated by the membrane of cartilage cells can not only effectively escape the elimination of the immune system, but also be selectively taken by degenerated cartilage cells. Through non-invasive light therapy in vitro, the level of ATP and NADPH in degenerated chondrocytes can be precisely enhanced and sufficient endurance can be maintained, which reshaped the anabolism of chondrocytes and achieve the treatment of degenerative osteoarthritis.

This research shows a biomedical application, namely, a cross-species transplantation of thylakoids from natural plants to mammalian cells. The key raw materials of this research are from natural plants with high biosafety. At the same time, the cell membrane nanocoating technology has the potential for large-scale production, which is expected to be applied in medicine, energy, materials and other fields in the future.

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Metabolic Enzyme Moonlights as Protein Phosphatase

Cancer cells can overcome energy stress via 'moonlighting' functions of a gluconeogenesis enzyme

Metabolic reprogramming induced by oncogenic signals elicits uncontrolled tumor cell proliferation and metastasis. Critical regulation of metabolic enzymes results not only from modulation of their canonical activity, but also from their noncanonical, or non–metabolic (moonlighting) functions. Emerging evidence demonstrates that metabolic enzymes can function as protein kinases and regulate gene expression, DNA repair, cell–cycle progression, cell proliferation, survival, apoptosis, as well as tumor microenvironment remodeling. Protein kinase–mediated protein phosphorylation is counter–regulated by protein phosphatase. However, whether a metabolic enzyme possesses protein phosphatase activity is unknown.

Cancer cells prefer to produce energy through aerobic glycolysis even in the presence of abundant oxygen. Gluconeogenesis is the reversal of glycolysis. Fructose–1,6–bisphosphatase (FBP) is a conserved metabolic phosphatase that catalyzes the rate–limiting hydrolysis of fructose–1,6–bisphosphate (F–1,6–BP) to fructose–6–phosphate (F–6–P) during gluconeogenesis.

"We found that cancer cells can overcome energy stress via non–canonical 'moonlighting' functions of gluconeogenesis enzyme FBP1," said LU Zhimin, professor of Institute of Translational Medicine, Zhejiang University. "It is the first time to report that metabolic enzyme can function as protein phosphatase, uncovered a new moonlighting function of FBP1 to dephosphorylate histone H3 and differentially modulate chromatin in normal and tumor cells, conferring tumor–cell–specific survival and growth ability in a nutrient–fluctuating microenvironment." The groundbreaking findings were published in Nature Cell Biology on October 20, 2022.

The team found that upon energy stress, PERK phosphorylates FBP1 S170 in normal hepatocytes, which converted the FBP1 tetramer to monomers for FBP1–nuclear translocation. In the nucleus, S170–phosphorylated FBP1 interacted with transcription factor PPARα. Importantly, FBP1 functioned as a protein phosphatase to dephosphorylate histone H3 pT11, thus suppressing PPARα–mediated β–oxidation gene expression and promoting energy–stress–induced apoptosis.

However, in contrast to normal hepatic hepatocytes, liver tumor cells exhibited much elevated glycosyltransferase OGT expression, leading to FBP1 S124 O–GlcNAcylation, which blocked PERK–mediated FBP1 S170 phosphorylation and its nuclear translocation. This inhibition abrogated the inhibitory effect of FBP1 on PPARα and resulted in greatly enhanced β–oxidation, leading to the increased energy production that supports tumor cell survival and liver tumor growth under energy stress conditions.

"This study elucidated that energy stress induced coordinated regulation of glucose and lipid catabolism in tumors and underscored the potential to modulate the protein phosphatase activity and nuclear functions of FBP1 for human cancer treatment," says LU.

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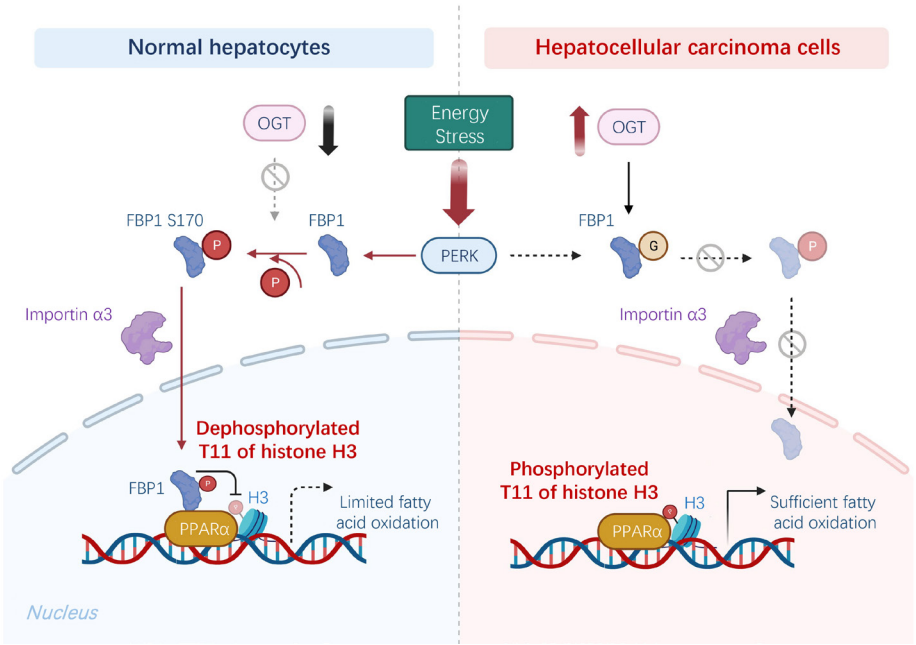
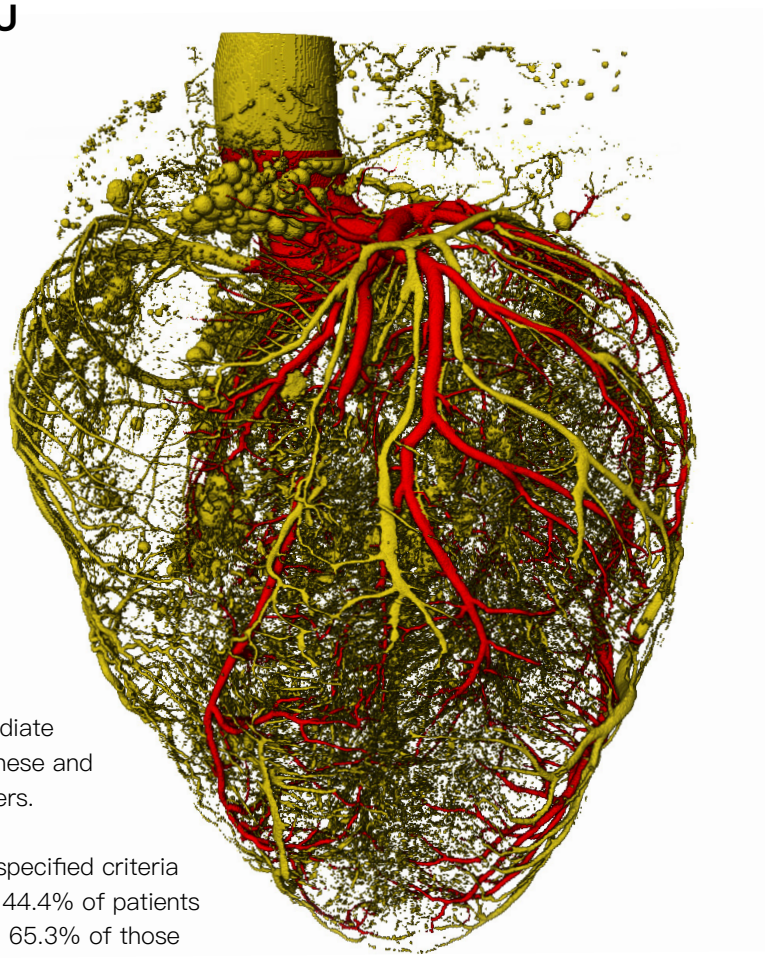


A scheme of molecular mechanism of FBP1 as a protein phosphatase to differentially regulate gene expression in normal and tumor cells.

Fractional Flow Reserve (FFR) vs. Intravascular Ultrasonography (IVUS): Which to Guide Percutaneous Coronary Intervention? ZJU Cardiologists Unveil the Result on NEJM



FLAVOUR Study, a multi-center international clinical trial, showed that in patients with intermediate stenosis, fractional flow reserve (FFR) guidance was noninferior to intravascular ultrasonography (IVUS) guidance in terms of the composite of death, myocardial infarction, or revascularization (8.1% vs. 8.5%, P=0.01 for noninferiority) at 24 months.

The study was led by Prof. WANG Jian'an, chair of SAHZU Heart Center and Head of the Second Affiliated Hospital, Zhejiang University School of Medicine (SAHZU), The results were published on the *New England Journal of Medicine* (NEJM) on Sep. 1, 2022.

For patients with intermediate coronary stenosis, cardiologists often use FFR to evaluate the potential of an ischemia-induced stenosis and whether percutaneous coronary intervention (PCI) is needed.

Meanwhile, they also use IVUS to select the appropriate stent size and to evaluate whether the vessel is optimally stented after procedure.

Therefore, combining FFR to make PCI decision and IVUS to improve stent implantation is considered as the best strategy.

However, many cardiac catheterization laboratories are equipped with only one of them. Given the lacking data regarding the difference between FFR- or IVUS-guided strategies, a head-to-head comparison between the two strategies was investigated in the study.

FLAVOUR Study is a prospective, randomized, open-label trial that is conducted on 1,682 patients with intermediate stenosis from 18 Chinese and Korean medical centers.

According to the prespecified criteria for revascularization, 44.4% of patients in the FFR group and 65.3% of those in the IVUS group underwent PCI. At 24 months, a primary-outcome event had occurred in 8.1% of the patients in the FFR group and in 8.5% of those in the IVUS group with non-inferiority p=0.01.

Accordingly, Prof. WANG Jian'an, and his research team conclude that, in patients with intermediate stenosis, FFR guidance was noninferior to IVUS guidance with respect to the primary outcome, which was defined as a composite of death, myocardial infarction, or revascularization at 24 months.

Jane Leopold, deputy editor of NEJM and associate professor of Medicine at Harvard Medical School, wrote an editorial for the paper and spoke highly of the trial as of immediate relevance to cardiologists and cardiac catheterization laboratories with only one of the two devices, either FFR or IVUS, and she looked forward to future studies that assess either the use of FFR or IVUS alone vs. the combination strategy, or the applicability of these results to patients with higher risks.

Rocco Vergallo wrote an editorial for FLAVOUR trial in European Society of Cardiology and call it can be used to guide and optimize PCI of intermediate coronary stenoses in a low-risk, mostly stable, population of patients with CAD.

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Prevention and Treatment of Liver Failure after Large-scale Hepatectomy: Bioartificial Liver with Transdifferentiated Hepatocytes

China is a country with a high incidence of liver disease, and more than 60% of hepatic carcinoma patients each year are in the medium or terminal stage when discovered. Because of the large excessive volume of the liver cancer, the large resection scope will easily lead to postoperative liver failure. How to provide these patients with an opportunity of surgical resection, improve the resection rate of liver tumor, and reduce the occurrence of post-hepatectomy liver failure, is a new direction to improve the prognosis of patients with hepatic carcinoma.

Bioartificial liver therapy in vitro is one of the potential therapeutic methods for the treatment of postoperative liver failure in the future. Based on transdifferentiation human fibroblasts into proliferative functional hepatocytes (hiHep) (Cell Stem Cell, 2014) by expressing liver transcription factors, the team solved the problem of seeding cells for bioartificial liver. Furthermore, hiHep cells were used as seed cells to construct a new type of bioartificial liver (hepaCure).

Xiujun Cai et al. established a porcine model of extended liver resection and completed the precilincal experiment to prove the safety and efficacy of the bioartificial liver therapy on the model. Now, Affiliated Sir Run Run Shaw Hospital has successfully performed bioartificial liver therapy on 7 patients with hepatic insufficiency after large-scale hepatectomy. All patients recovered after the treatment and were discharged from hospital.

The first patient was a teacher with severe cirrhosis and large right hepatocellular carcinoma. Preoperatively, the liver volume was reconstructed in three dimensions and only 40% of the liver was predicted to remain after surgical resection. There was a significant increase in liver enzymes from the second postoperative day. Then she was treated with a 6-hour bioartificial liver of replacement therapy at 48 hours after the surgery. All liver indicators stabilized after the treatment. On the 7th day after the surgery, the liver volume had recovered to 60%.

This is the first clinical transformation of human transdifferentiation derived cells, and also the first step towards clinical treatment of liver failure with hiHep-BAL. No treatment-related adverse reactions, hematological toxicity, or liver and kidney function impairment occurred in those 7 patients, which proved the safety and feasibility of clinical treatment of hiHep-BAL and reached the primary clinical endpoint. In addition, hepacare is important for the decrease of liver injury indicators ALT, AST and TBIL, the improvement of coagulation indicators INR, etc., the decrease of blood ammonia level (the cause of hepatic encephalopathy), the decrease of inflammation indicators IL6, etc., and the increase of liver volume (an indicator of liver regeneration).

It is a great breakthrough in the field of bioartificial liver therapy in China, and it makes up for the deficiency of non-bioartificial liver treatment extensively. HiHep-BAL has the potential to treat postoperative liver failure and, in the future, the potential for surgical treatment for individuals who, in the absence of hepatectomy, would otherwise be at danger of liver failure. Currently, the Center for Drug Evaluation (CDE) of the National Medical Products Administration has approved the application for Investigational New Drug (IND) of hiHep-BAL.

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ZJU Team Pioneers a Holistic Approach to Pancreatic Cancer

Pancreatic cancer is becoming an increasingly common cause of cancer mortality. The survival rate of pancreatic cancer has long been dismal. Because symptoms and signs of pancreatic cancer are mostly nonspecific, early diagnosis remains a major challenge. Only 15% of all cases are deemed resectable at diagnosis, while the remaining are already at more advanced stages. For locally advanced pancreatic cancer, radical resection is usually impossible because of significant tumor infiltration and vascular invasion. Although the application of neoadjuvant therapy may downstage the tumor and make radical resection possible, the conversion rate is far from satisfactory.

In order to tackle this issue, Prof. LIANG Tingbo and his multidisciplinary team, from the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU), have pioneered a holistic approach — radical resection combined with intestinal autotransplantation (RRCIA). In brief, the organ transplantation technique is integrated into the traditional surgical approach for pancreatic cancer. The RRCIA procedure is proven to be efficient in achieving an "en-bloc" and "non-touch" R0 resection for locally advanced pancreatic cancer with longitudinal encasement of SMA and SMV by Prof. LIANG's team. The primary results indicate that the RRCIA procedure has significantly improved the R0 rate of locally advanced pancreatic cancer. More than forty cases of RRCIA have been performed successfully since 2018.

Recently, the book entitled "Radical Resection Combined with Intestinal Autotransplantation for Pancreatic Cancer" was published by the People's Medical Publishing House. As the first book globally describing this novel RRCIA technique, it has drawn worldwide attention. And the primary results of the RRCIA procedure were recently published in the journal of Annals of Surgery.

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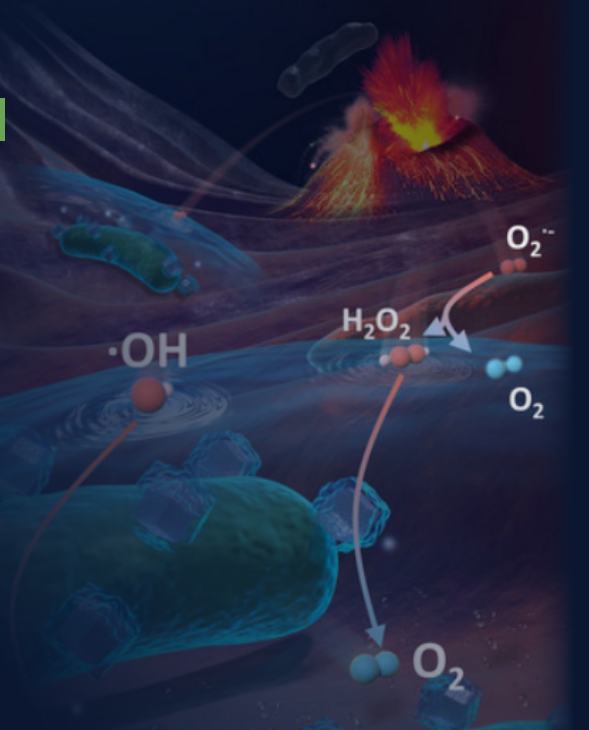
Scientists Open Door for Curing Intestinal Inflammation



Probiotics in the human body are known as the "guardians" of the intestinal tract. They play a crucial role in regulating the immune system and balancing the gut microbiota, thus able to promote nutrient ingestion and maintain the health of the intestinal tract.

Taking probiotics orally has long been the most direct and convenient way of supplementation. However, the effect of probiotics is often reduced in the unique microenvironment of the inflammatory intestine.

To this end, Prof. WANG Weilin at the Second Affiliated Hospital of the Zhejiang University School of Medicine collaborated with Prof. MAO Zhengwei at the Zhejiang University Department of Polymer Science and Engineering and Prof. CHEN Xiaoyuan at the National University of Singapore in pioneering the development of artificial-enzyme-armed Bifidobacterium longum (BL) probiotics for reshaping a healthy immune system in inflammatory bowel disease. Their findings were published in Nature Nanotechnology.

Probiotics are oxygen-intolerant. The researchers at Zhejiang University analyzed BL, a common type of probiotics, and found that it couldn't autonomously scavenge reactive oxygen species (ROS) for lack of a series of antioxidant enzymes, such as superoxide dismutase (SOD) and catalase (CAT).

"We took a bold move in combining these antioxidant enzymes with probiotics in an artificial fashion so that probiotics could autonomously metabolize toxic substances into non-toxic products," MAO Zhengwei introduced. "This strategy can effectively improve the survival of probiotics in the inflamed intestine and fulfill the functions of maintaining the balance of the gut microbiota and repairing the intestinal mucosal tissue".

To achieve this goal, MAO Zhengwei's group and CHEN Xiaoyuan's group employed the Fe/C-based single-atom nanozyme (B-SA) and designed the first probiotics / nanozyme composite. This novel "armor" empowers probiotics to defend better against the "bullets (ROS)" in the immune response.

The researchers modified the phenylboronic acid functional group on B-SA and took advantage of the supramolecular interaction between boronic acid and exopolysaccharides on the surface of bacteria to achieve the combination of B-SA and BL in mild conditions, thereby maximally preserving the activity of probiotics and artificial enzymes.

Structure and function diagram of the probiotics / artificial enzyme composite In the follow-up study, MAO Zhengwei's group and WANG Weilin's group carried out validation experiments on both small-animal and large-animal models. They found that the probiotic / artificial enzyme composite performed better than the mixture of probiotics and artificial enzymes and drug combinations in clinical settings in treating inflammation and promoting the balance of the gut microbiota.

"To cure inflammatory bowel disease, including ulcerative colitis and Crohn's disease, it is of supreme importance to eliminate inflammation and restore the balance of the gut microbiota," said WANG Weilin. "Our treatment strategy can serve dual purposes in this regard."

Probiotic therapy has been adopted in clinical settings in China, the industrialization of probiotics has a solid foundation, and its safety has been verified. Featured by their remarkable safety, catalytic efficiency, stability and cost-effectiveness, nanozymes can also be mass-produced.

MAO Zhengwei is quite confident about the future of this study. "On the strength of the enormous potential of industrialization and the perfect safety of application, our team will strive to push the probiotics / artificial enzyme composite to clinical applications," he said.

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Going Beyond Medical Education: How "Medicine+" Talents Cultivated at ZJU?

WANG Qiwen is a postdoc who graduated from Zhejiang University under an eight–year clinical medicine program. As the first author, he has published several articles in top journals in the field of biological materials; one of his projects has received support from the National Natural Science Foundation, and a Second Prize Award for Science and Technology Progress from the Ministry of Education. What may be surprising is that this medical scholar was once an undergraduate majoring in applied chemistry. Last year, he adopted a chemical approach in an attempt to improve the conventional therapy for cardiovascular disease. The outcome, a new montmorillonite material achieved through chemical modification, was published in a leading international journal, with him as the first author.

> *Interdisciplinary education has exerted a great influence on me. Before moving to clinical medicine, I spent four years studying in another field. For scholars, the encounter with different disciplines makes scientific innovation possible and successful.*

“Striving towards New Medicine that is characterized by interdisciplinarity, we aim to cultivate ‘medicine+’ talents, whose innovation is fueled by their integrated knowledge from various backgrounds. To that end, the Zhejiang University School of Medicine provides potential interdisciplinary talents with two portals: X+Medicine and Medicine+X,” commented ZHOU Tianhua, Vice President of Zhejiang University.

Arising from China’s first eight–year doctoral program in clinical medicine initiated in 2005, and China’s first postdoc program in clinical medicine that commenced in 2015, the School of Medicine has devised the “X+Medicine” portal for excellent clinical medical doctors. It comprises four years of undergraduate study outside the field of medicine, four years of doctoral study in the field of medicine, and a three–year postdoc program in the field of clinical medicine.

On the other hand, the “Medicine+X” portal targets medical undergraduates who wish to pursue a doctoral diploma immediately. Under an interdisciplinary system that transcends the boundaries of disciplines, programs, supervisors, teachers, and peer students, students receive individualized instruction and are exposed to innovative practices on their journey to becoming medical scientists who are concerned about health–related issues, deal with scientific problems, and benefit from interdisciplinary coordination.

Over the last five years, the feasibility of “Medicine+X” has been well proven: more than 200 articles have been published by relevant students as the first author in internationally prestigious academic journals, and a total of 34 prizes have been won at national competitions, such as the China International College Students’ “Internet+” Innovation and Entrepreneurship Competition, and the “Challenge Cup” National College Student Competition of Extracurricular Academic and Scientific Works.

“Under the interdisciplinary program, my supervising team matched me with other students and project teams, and encouraged me to collaborate and communicate with others in the fields of medicine, chemistry, material science, and pharmacy. These extensive exchanges empowered me to study major scientific issues from a broader, deeper, and more diversified perspective,” commented ZHONG Danni, a doctoral candidate of the “Medicine+X” program.

Interested in biological material and translational medicine, ZHONG Danni is devoted to designing and developing medical materials with a better prospect of clinical translation. No stranger to the National Scholarship for Graduate Students, she has published 26 articles in international journals, and her research outcome was listed as one of the Top Ten Students’ Academic Achievements of Zhejiang University in 2021.

A Journey: Trained to be a Doctor in China

Planting a Seed in the Heart

Frozan Khoshbakht, a medical student at the Fourth Affiliated Hospital, Zhejiang University School of Medicine (ZJU4H), is currently interning in the Department of Obstetrics. Originally from Afghanistan, Frozan encountered a heartwarming moment with a patient from the Middle East.

Maya, a pregnant woman from Middle East, had been experiencing severe pregnancy reactions, losing 10 kilograms of weight and struggling to walk. Frozan provided counseling and care under the instruction of her mentor whenever Maya was uncomfortable with the specter of a possible miscarriage. After a week of treatment, Maya fully recovered and expressed her gratitude, saying, "The medical technology and services here are professional and international. Thank you all very much."

This experience has further solidified Frozan's desire to become a doctor in China and help women across the country. She is determined to pursue her dream and make a difference in the lives of her patients. She said, "I want to stay in China and become a doctor. I really want to help my female friends throughout China."

The Journey of Chasing A Dream

After graduating from medical school in Afghanistan in 2015, Frozan continued her pursuit of a master's degree. However, her studies were interrupted due to her own pregnancy and relocation to Yiwu. "When I learned that Zhejiang University (ZJU) had an affiliated hospital in Yiwu, I was excited about the possibility of resuming my studies in medicine," she said.

In September 2022, Frozan's dream came true. Professor Xu Jian, Secretary of the CPC at ZJU4H and International School of Medicine, Zhejiang University (ZJU–ISM) as well as the Director of the Reproductive Medicine Center, became her supervisor.

Frozan now aims to learn Chinese, excel in her medical studies, and stay in China as an obstetrician and gynecologist. Many foreign women come to Yiwu to join their spouses or families, and some may not be able to communicate fluently in English. These patients have unique customs and religious beliefs, and the unfamiliar environment may make them hesitant to seek medical treatment. "I want to provide as much assistance as possible to make them feel at home here," she said.

International Medical Center: A Dream Destination for International Students

The International School of Medicine, Zhejiang University (ZJU–ISM) is located in Yiwu, the world's largest wholesale market of consumer goods, recognized by the United Nations, World Bank, and other authoritative organizations. Since 2020, the school has admitted 369 full–time students, committed to training future doctors with international perspectives.

Listening to the Mountains

CHEN Ruixue is a doctoral student who joined Zhejiang University School of Medicine (ZUSM) in 2020. She is the president of the Graduate Student Association, College of Obstetrics and Gynecology of ZUSM, former president of the Federation of Student Associations of Zhejiang University, former vice president of the University Student Union, and former director of the Student Street Dance Club.

In 2017, CHEN Ruixue responded to the national policy of poverty alleviation by joining the 19th graduate group of volunteer teachers. For a year, she served as a voluntary teacher at Taijiang Ethnic Middle School in Taijiang County, Qiandongnan Prefecture, Guizhou Province.

There, she initiated a project called "listen to the mountains", which matches local middle-school students with nation-wide college students through letters. Over 3,000 letters were written by more than 400 pairs of students during that year. It was her belief that even the simplest medium could greatly help children to understand the world beyond the mountains.

"What Taijiang students lack most is the very motive for learning. That's why we provided inspirational education, such as the project of 'listen to the mountains'. We wanted to help them to understand the importance of learning and catch a glimpse of the world beyond the mountains."

During her year of voluntary teaching, CHEN Ruixue stayed close to over 200 children there. Together, they performed exercises, did PE classes, and participated in extracurricular activities. As a result, Ms. CHEN gradually became Moma CHEN among the students, who would give her surprise gifts from time to time.

Obstetrics and gynecology are a choice that CHEN Ruixue attributes to her internship. "I always feel infinite hope in every beautiful birth of a new life." She happily devotes herself to reproductive medicine, explaining that "there are many infertile families faced with the distress caused by long-term fertility problems. By working in the field of reproductive medicine, I hope to solve their problems."

In spite of her seemingly dedicated medical career, CHEN Ruixue leads a colorful life, switching between multiple identities. She is called President or Director of student clubs and associations. "I love these 'part-time jobs'. They improve my decision-making skills, team leadership, and social skills, which are so different from my medical professional skills. In the future, I hope to visit remote, poor areas again as a doctor to contribute my youthful strength".

Silent Mentors: Reverence and Remembrance

On the morning of March 22, more than 300 teachers and students from Zhejiang University School of Medicine stood in commemoration before the monument of "silent mentors" on Zijingang Campus, Zhejiang University. Dressed in white, the representatives presented flower baskets with respect to the monument and made three bows to convey their reverence and remembrance regarding their "silent mentors".

It has been a common practice since 2012 that the School of Medicine holds such an annual event in commemoration of those selfless donors during the Qingming Day period – an occasion for Chinese people to honor their ancestors. Now it has been the largest memorial site for the "silent mentors" among China's medical schools. Besides, to its professional curriculums, the School has added courses related to the outlook on life and death, breaking bad news, and hospice care, in relation to areas such as anthropology, doctor–patient communication, and the philosophy of nursing. It has also bolstered the students' medical humanistic quality through lectures, on–campus exercises, social practices, and overseas training. For example, the course that integrates human anatomy with life education not only imparts professional medical knowledge to students but also enhances their understanding and reverence for life.

At the ceremony, eight medical students extended their deep–felt respect and gratitude to these "silent mentors". It is their selfless donation that builds the bridge between medical theory and practice, and it is their twilight that lightens the dreams of numerous medical students. Their life has been continued and their spirit will last forever.

WHZJU and Center for Cancer Biology of VIB ink MoU for Science and Technology Cooperation

On April 24, the Affiliated Women's Hospital, Zhejiang University School of Medicine (WHZJU) and Center for Cancer Biology (CCB) of Vlaams Instituut voor Biotechnologie (VIB) signed a memorandum of understanding to promote the establishment of the Single-cell Multi-omics Joint Center, high-calibre talent cultivation and academic cooperation. Prof. WANG Hui, president of WHZJU, and Prof. Diether Lambrechts, Director of CCB represented each party to sign the MoU.

Vlaams Instituut voor Biotechnologie (VIB) is an internationally-renowned entrepreneurial non-profit research institute, with a clear focus on groundbreaking strategic basic research in life sciences, including on the molecular mechanisms that regulate the functions of the human body and translating scientific results into pharmaceutical and industrial applications. VIB's Center for Cancer Biology (CCB) aims to identify novel biomarkers for the early detection, monitoring of cancer progression and therapy response and, ultimately, develop more effective anticancer therapies.

Relaunch of the SAHZU International Joint Training Rrogram

This spring saw the return after three years of international students and physicians to the campuses of the Second Affiliated Hospital Zhejiang University School of Medicine (SAHZU).

Louie Wang, a medical student at UCLA (University of California, Los Angeles), was the first medical student that registered for a medical elective at SAHZU. He swiftly booked a flight to Hangzhou.

The Department of Emergency Medicine at SAHZU, which is ranked fourth in emergency medicine in China, is where Louie Wang decided to complete his elective. Louie dealt with a lot of instances when he was here that are uncommon for an emergency room in a U.S. hospital. He gained knowledge of emergency tracheal intubation, mechanical ventilation, the management of severe trauma and acute upper gastrointestinal bleeding, and even had the chance to perform under supervision actual procedures like central venous line placement, lumbar puncture, and bedside ultrasound. He witnessed the use of 5G technology for the first time in pre-hospital settings, hospital emergency rescue and intensive care, and drone blood delivery. The creation of a pre-hospital emergency care network between the United States and Mexico is Louie's desire, and his experiences at SAHZU have left him feeling inspired and motivated.

Louie provided an unexpected response when asked why he selected SAHZU for his medical elective out of all of UCLA's international exchange programs: I decided to enroll in the UCLA School of Medicine when I learned that they have an exchange program with SAHZU since I'd already received medical care from SAHZU doctors. Louie grew up in Hangzhou, and his mother would take him to SAHZU to visit a doctor whenever he was ill, it turns out. He was able to go home for a visit because of the medical student exchange program between UCLA and SAHZU.

Together with Louie, Victoria Chen, a fellow UCLA medical student, also joined the program. Victoria, a medical student and an oral surgery resident, was interested in the work that her coworkers at the SAHZU department of oral and maxillofacial surgery were doing.

Victoria had the opportunity to take part in numerous operations during her stay, including the radical resection of oral cancer, free flap reconstruction, and complex maxillofacial fractures. She also helped with the design and creation of KISS flaps, which she had never seen before. Victoria cited one of her most impressive experiences as the fact that more than 20 radical oral cancer surgeries were conducted at SAHZU Oral and Maxillofacial Surgery in just a few weeks, as opposed to just two such surgeries each week at UCLA. She also saw a number of cases of oral tumor and maxillofacial fascia space infections that she had only read about in textbooks.

Apart from Louie and Victoria, the Malaysian anesthesiologist Dr. Lim Shin Hoei and the Indian cardiologist Dr. Sujai Nikhil are enrolled in training programs at SAHZU concurrently. Dr. Lim Shin Hoei will spend 6 months at SAHZU Anesthesiology honing her skills in cardiac anesthesia and Trans-esophageal Echocardiography while Dr. Sujai Nikhil will spend 3 months at SAHZU Cardiology concentrating on interventional cardiology procedures and structural heart problems.

Opening Ceremony of FAHZU on November 1st, 1947, ZHU Kezhen couple (front row, middle right) and WANG Jiwu couple (front row, middle left)

Lineage in Medicine:

A Family of Four Generations that Witness the Development of Zhejiang University School of Medicine

WANG Kaiming's family has a rich lineage in the field of medicine. After graduating from Zhejiang University School of Medicine (ZUSM) in 1960, she worked at the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU). She has been Director of the Department of Gastroenterology, Director at the Teaching and Researching Section of Internal Medicine. Her son and daughter also graduated from ZUSM. Last year, her granddaughter, JIAO Ruilin, successfully enrolled in the undergraduate program of clinical medicine at the same School; and her father, Prof. WANG Jiwu, was the first Dean of the ZUSM, and the first President of FAHZU.

The first generation at ZUSM: The pathfinder of ZUSM and FAHZU

At the invitation of Prof. ZHU Kezhen, who was the President of Zhejiang University at that time in 1945, Prof. WANG Jiwu took charge of establishing ZUSM and served as its first Dean. Later, in 1947, he inaugurated the First Affiliated Hospital of the University, now known as FAHZU. As one of the pioneers in the field of infectious disease research in China, he edited Infectious Diseases as China's first medical textbook for higher education.

> ***A solid foundation of knowledge is prerequisite to drawing parallels from inference, and essential for a better understanding and integration of all learning.***

As the first Dean of the ZUSM and first President of FAHZU, Prof. WANG maintained a rigorous, down-to-earth attitude to his work.

The second generation of ZUSM: Solid knowledge and a meticulous attitude

As the second daughter of Prof. WANG Jiwu, Prof. WANG Kaiming found her way, wittingly or unwittingly, to study medicine at ZUSM in 1955, and followed her father's path by working at FAHZU after graduation.

WANG Kaiming was deeply impressed by an event that occurred during the early 1960s, shortly after she joined the hospital. During one of her father's ward rounds, a patient was admitted to the hospital, suspected of suffering from septic shock. During his preliminary examination and interrogation of the patient, however, her father failed to find any signs of infectious disease, and so judged that the shock was not septic but hemorrhagic in nature, caused by gastrointestinal bleeding. His diagnosis was later verified by a detailed examination.

"The case keeps telling me that solid knowledge and a meticulous attitude make a good doctor," WANG Kaiming commented. Since then, she had been upholding this standard whenever she provided treatment.

The third generation of ZUSM: A down-to-earth philosophy regarding life and work

Just like their mother, the two children of WANG Kaiming seem to share an unbreakable bond with medicine.

Her son, CHEN Xiangdong, who graduated from ZUSM in 1989, is a prestigious expert in the field of cosmetic medicine, and once served Director of the Dermatology Department at Shanghai Ninth People's Hospital. As for her daughter, CHEN Xiaoming is Deputy-Chief Technician of the State Key Laboratory of Infectious Disease Diagnosis and Treatment at FAHZU, working on clinical virus detection and related research.

"Our doctor parents made us familiar with medicine and hospitals since our childhood. Plus, our grandfather WANG Jiwu had a huge influence on me. His rigorous attitude and down-to-earth philosophy are invaluable assets for us."

The fourth generation of ZUSM: Following the lead toward a rigorous, down-to-earth attitude

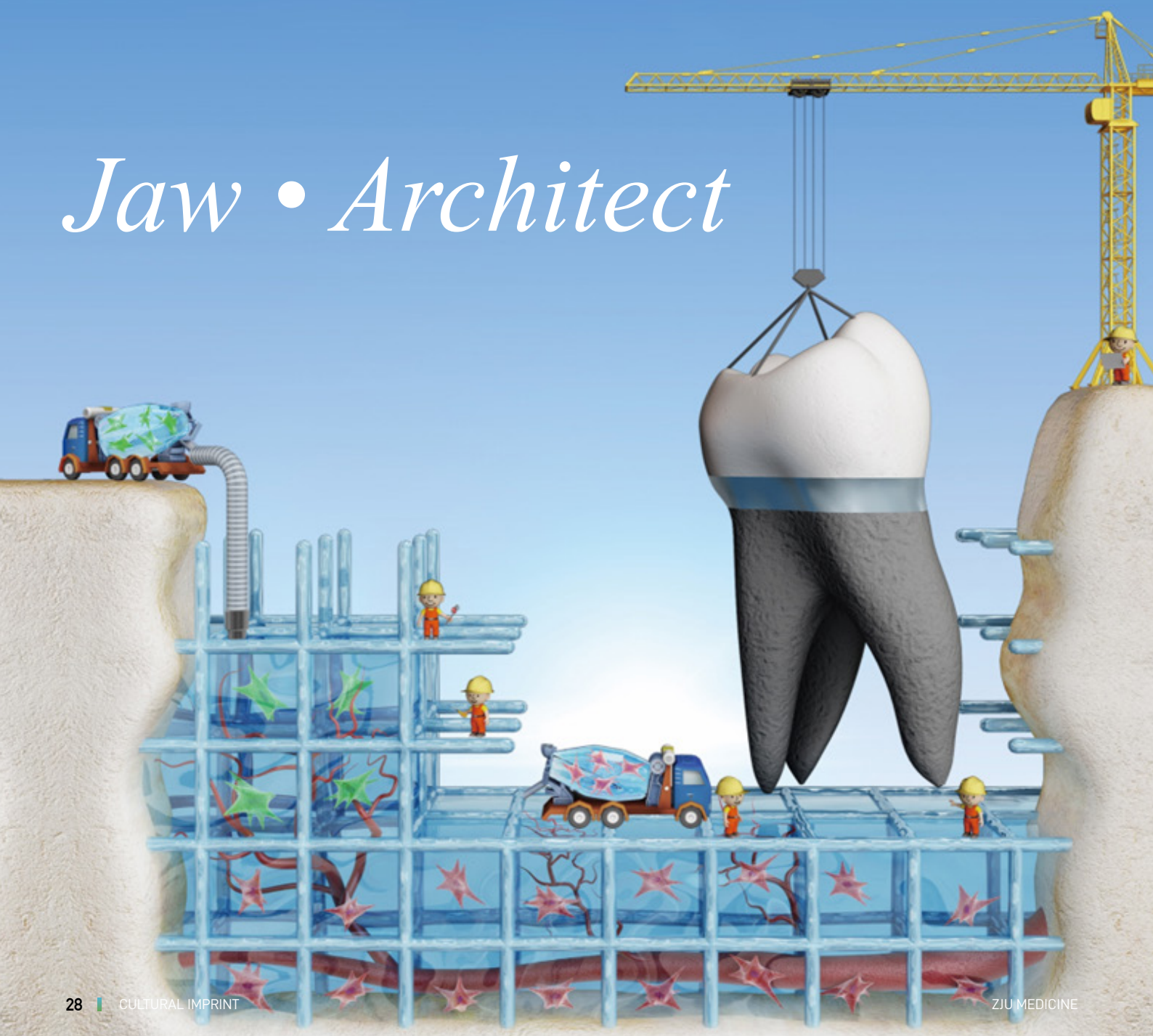
JIAO Ruilin is WANG Kaiming's granddaughter, and now a freshman at ZUSM. Her choice of medicine seems to have been made as early as 2012. "That was the year when our family visited ZUSM and attended the unveiling ceremony of the bronze statue of Prof. WANG Jiwu. Perhaps that was the moment when a medical seed was planted in her soul," recounted her mother, CHEN Xiaoming.

"I have the greatest admiration for the persistence and meticulousness of my grand-grandfather as a doctor and professor of medicine. When I become a doctor in the future, I will model myself on his rigorous, down-to-earth attitude, and contribute as much as I can to China's medical causes!" stated JIAO Ruilin.

A family photo of WANG Kaiming

Jaw • Architect

The poster "Jaw Architect" presents a joint reconstruction technology for tooth and jaw tissue by synchronously designing and sequentially manufacturing three–dimensional vascularized tissue engineering bone and integrated biomimetic dental implants. The resulting biomimetic tooth and jaw tissue can reduce surgical time and cost, improve surgical outcomes, and successfully enable minimally invasive and efficient mandibular reconstruction. This work won the Grand prize of the 17th Challenge Cup National College Students Extracurricular Academic Science and Technology Works Competition, guided by the supervisor from the Affiliated Stomatology Hospital, Zhejiang University School of Medicine.



The little girl in the painting is WU Mei, a former uremic patient who had been under treatment for nine months in the Affiliated Children's Hospital, Zhejiang University School of Medicine before receiving a kidney finally. The two medical staff by her side is the head nurse LI Dongyan and the nurse QIAN Lidan who used to take care of her.

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