Issue 5 2024

ZJUMEDICINE

SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

New Quality Productive Forces Drive the Development of Minimally Invasive Medicine

Dialogue with CAI Xiujun, President of SRRSH

"All-in-One"

Promising Treatment for Aggressive Blood Cancers

The Potential of Gut Bacteria

New Findings in Cancer Therapies

ZUSM at A Glance

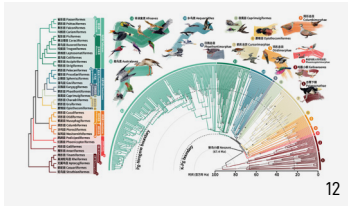
Zhejiang University School of Medicine (ZUSM), founded in 1912, is one of China's best and oldest higher medical education institutions. Located in Hangzhou – one of China's most picturesque cities – ZUSM is organized across the School of Basic Medical Sciences, School of Brain Science & Brain Medicine,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

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

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

浙江大学 医学院
SCHOOL OF MEDICINE
ZHEJIANG UNIVERSITY

CONTENTS



New Quality Productive Forces Drive the Development of Minimally Invasive Medicine

CAI Xiujun

Vice Dean of Zhejiang University School of Medicine
President of Affiliated Sir Run Run Shaw Hospital (SRRSH)
Standing Committee Member of the 14th National Committee of the Chinese People's Political Consultative Conference (CPPCC)
Vice Chairman of Zhejiang Provincial Committee of the CPPCC
Director of National Engineering Research Center for Minimally Invasive Devices Innovation and Application

Minimally invasive medicine is the mainstream direction of medical development in the 21st century. What are the advantages of minimally invasive medicine?

In the 1980s, laparoscopy began to be introduced to China as an emerging surgical technology. This technology, characterized by less trauma, fast recovery, reduced pain, and shortened hospital stays, has been well-received by patients and their families, who have put forward higher requirements for disease diagnosis and treatment under today's high-quality development. It has stimulated the enthusiasm of medical workers to explore and expand the application scope of minimally invasive technology, improve its accuracy and safety, in order to better meet the health needs of the people.

As one of the leading figures in the field of minimally invasive medicine in China, how do you continuously innovate in the area and maintain a leading position?

Discovering and solving problems from clinical practice and ultimately serving patients is an optimal path for medical innovation. For example, we invented a laparoscopic multifunctional surgical dissector and created a laparoscopic scraping and aspiration dissection method for liver resection (included in the American College of Surgeons' surgical atlas textbook); created a completely laparoscopic "two-step" liver resection with a round-the-liver ligature; invented a degradable anastomosis stent and a degradable bypass stent, created the stent assisted anastomosis and the stent assisted bypass, which have greatly improved medical efficiency, the quality of life of patients. The stent assisted bypass technique broke the traditional surgical method used internationally for 168 years, avoiding enterostomy, artificial anus retention, and a second-stage operation, shortening the treatment cycle from 3-6 months to 3 weeks.

There is still great potential for the development of minimally invasive medicine in China. How do you view the role of new quality productive forces in promoting minimally invasive medicine?

New quality productive forces align with the development path of minimally invasive medicine. the emergence of new instruments, new technologies, and new procedures is promoting minimally invasive medicine to be more intelligent, precise, and humane. However, many electronic components for laparoscopy and endoscopy, as well as surgical materials, cannot be fully domestically produced so far. Meanwhile, the nature of minimally invasive medicine has gone beyond a simple medical technology to become an integration of multidisciplinary collaboration and advanced technologies such as communication, artificial intelligence, and big data. SRRSH is leading the construction of the National Engineering Research Center for Minimally Invasive Devices Innovation and Application. We expect to create a full-chain open and shared service platform to integrate academic research, technology development, achievement transformation, and clinical application, to promote the sustainable development of minimally invasive medicine in China with new quality productive forces.

Developing new quality productive forces is the only route to promote medical discipline innovation and high-quality development of public hospitals, as well as an inevitable choice to solidify the health foundation of Chinese-style modernization.

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

The Continual Promotion of the Translation of Scientific Research into Clinical Applications

LU Zhimin

Member of Academia Europaea
Vice Dean of the School of Medicine, Zhejiang University
Dean of the Institute of Translational Medicine, Zhejiang University

Aiming at national strategic needs, we are committed to enhancing our capabilities in technological innovation and service. Our goal is to promote the translation of more research outcomes, striving to establish ourselves as a leading translational medicine research institute in China, with distinctive features and international excellence.

What factors attracted you to join the faculty at Zhejiang University School of Medicine full-time?

ZJU School of Medicine has the best hospitals in the country, providing a unique platform for advanced translational and clinical research. As a leading comprehensive university in China, ZJU covers diverse research fields, offering a rich scientific environment that facilitates interdisciplinary collaboration. Equally importantly, researchers at ZJU have the freedom to pursue their personal, interest-driven research and also to organize or to participate in large projects involving multiple teams from different fields. ZJU School of Medicine is a hub where "bench to bedside" research can thrive.

What do you think are the future trends in the field of tumor metabolism? Are there any cutting-edge technologies or research directions that are particularly noteworthy?

Advances in cancer metabolism research will enhance our critical understanding of metabolic enzymes and metabolites, both in their canonical and noncanonical capabilities. Studies on the moonlighting functions of these enzymes and metabolites will shed light on their broader impact on various essential cellular activities, independent of their conventional functions. Basing on these studies and advances, effort will be taken to develop medicines to inhibit the cancer-specific metabolic and moonlighting functions of metabolic enzymes and metabolites in tumors to archive improved cancer therapy with limited advanced effect. Based on these studies and advances, efforts will be made to develop medicines to inhibit the cancer-specific metabolic and moonlighting functions of metabolic enzymes and metabolites in tumors to achieve improved cancer therapy with limited adverse effects. In addition, developing clinically validated and innovative non-glucose-based tumor imaging techniques to complement 18F-FDG PET/CT and enhance tumor detection and metabolic classification will provide additional tools for cancer care.

As a leading figure in the field of tumor metabolism, what recent research discoveries have you made, and what new insights and approaches do these offer regarding tumor diagnosis and treatment?

For the past two decades, my lab has published more than 50 papers in the ***Cell***, ***Nature***, and ***Science*** series journals, demonstrating that the moonlighting functions of metabolic enzymes and metabolites not only promote tumor cell proliferation but also govern the tumor cell-intrinsic immune response and the activities of immune cells. Based on these findings, approaches to modulate the composition and availability of metabolic enzymes and metabolites in tumor microenvironments, as well as their functions in tumor and immune cells, through targeted approaches and specific dietary nutrient interventions, can enhance the efficacy of current therapies, including chemotherapy, radiation, and immune and targeted treatments.

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

Reproductive Medicine Center

Reproductive Medicine Center of the Fourth Affiliated Hospital of Zhejiang University School of Medicine focuses on the cutting-edger of science and technology and people's life and health. At present, the Center for Reproductive Medicine has formed a basic scientific research and clinical team, led by Academician Huang Hefeng of the Chinese Academy of Sciences as the chief scientist, with Professor Xu Jian serving as the director and a group of young professionals as major contributors. Relying on the construction of the Fourth Affiliated Hospital of Zhejiang University School of Medicine and the International Institutes of Medicine, Zhejiang University, the center is a highly integrated entity of medical education and research. Located in Yiwu City, Zhejiang Province, it covers an area of nearly 10,000 square meters, including a seven-story independent medical center, mainly composed of reproductive clinic, IVF laboratory, reproductive research room, etc. There is a shared animal experiment center, a biobank and an advanced technology equipment platform.The clinical staff includes 1 chief physician, 4 deputy chief physicians, 2 attending physicians and 5 resident physicians; 1 deputy chief technician and 3 technicians; There are 6 reproductive nurses. In the past 3 years, we has presided over 4 projects of the National Natural Science Foundation of China, 3 major outstanding young and key projects of the Natural Science Foundation of Zhejiang Province, participated in 3 national key R&D projects as a backbone, and published more than 60 high-level SCI papers in journals such as ***LANCET***, ***Nature***, and ***Nature Medicine***.

The center actively responds to the national reproductive health strategy, conforms to the development trend of reproductive medicine, faces the new challenges and bottlenecks of

reproductive health and aims to serve the reproductive health of regional people and build a world-class reproductive medicine basic research, clinical transformation, medical service and talent cultivation center, and strives to provide important technical support for the national reproductive medicine scientific research and make important contributions to serving the national healthy strategy. Welcome outstanding talents at home and abroad to join us!

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

National Clinical Research Center for Child Health and the National Children's Regional Medical Center

Children's Hospital Zhejiang University School of Medicine (ZCH) has actively aligned with national policies and strategic needs. With the support of Zhejiang University, ZCH has been approved to establish Dual Centers, namely the National Clinical Research Center for Child Health and the National Children's Regional Medical Center. Thus, as part of the first batch in China, it became the first children's hospital that operates two national centers in the Yangtze River Delta.

Since launching the Dual Centers, ZCH has focused on pediatric science and technology innovation while enhancing medical service capacity. It prioritizes innovation as the core driving force and promotes the synergistic development of treatment, teaching, research, prevention, and management.

First, it implements the plan of "one hospital with four campuses" and nurtures a dynamic of collaboration and complementarity, aiming at high-quality development. Based in Zhejiang but extending nationwide, ZCH integrates over 200 medical institutions into a collaborative network, enhancing inter-provincial resource sharing and elevating pediatric medical services across the region and the country.

Second, ZCH leads the building of Children's Large Organ Transplant Center in China, and performing nearly 40 cases of transplants of large organs. It pioneers artificial heart implantation, setting a record for the youngest age and the lowest body weight of patient, and initiating China's first department of Heart Failure & Mechanically Assisted Circulation. Leading in da Vinci robotic-assisted surgeries in China, ZCH revolutionizes minimally invasive pediatric surgery; and with more than 400 cases of pediatric ECMO performed in total, ZCH leads the country in annual cases for years, and achieves the world best in success rate.

Third, for five consecutive years, ZCH has been among top-three children's hospitals according to Science and Technology Evaluation Metrics for Chinese Hospitals and Medical Schools. Its journal, World Journal of Pediatrics, boasts an impact factor of 6.1, placing it the sixth (Q1) among pediatric journals worldwide and earning recognition as one of "China's academic journals with the greatest international influence".

Fourth, it has introduced nearly a hundred professionals of various disciplines and specialties. Prof. MA Daqing, a Member of the Academy of Europe, is the first international top talent to work full-time at ZCH. Prof. SHU Qiang, a senior expert of Zhejiang Province, serves as the Director of the Dual Centers. Additionally, ZCH also launches a sustainable training program for pediatricians that includes pre-graduation education, post-graduation training, and international exchange.

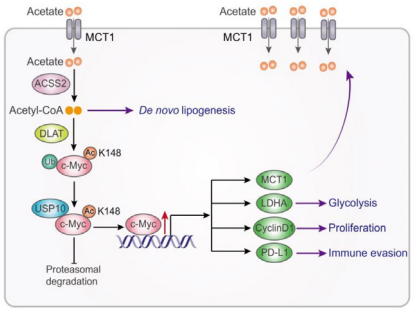
Fifth, as the chair institution, it sets up a provincial system of birth defects prevention and control, which integrates the screening of genetic metabolic diseases, congenital heart disease, and hearing impairment. With a coverage rate of 100%, this system effectively reduces the neonatal mortality rate. In addition, ZCH establishes a transport system for pediatric critical cases across seven provinces in Eastern China, with a 100% success rate in patient transfers.

Sixth, in the latest national performance monitoring and assessment of tertiary public hospitals, ZCH ranks the second among all children's hospitals. It also passes the national level-6 assessment for electronic medical record and receives the gold medal in the National Contest of Improving Medical Services. As a leader among intelligent children's hospitals, ZCH aims to set a national benchmark for pediatric medical and healthcare services.

In the medium and long term, the Dual Centers will focus on national strategies and critical needs for children's health. ZCH aims to become a top-tier research-intensive hospital by enhancing its system of scientific innovation and medical services with collaboration, efficiency, and quality. ZCH looks forward to making progress in clinical research in children's health and development, achieving breakthroughs in both comprehensive critical care and major disease prevention and control technologies, enhancing its capacity for scientific innovation, improving its quality of medical services, upgrading its healthcare model, and tapping into digitalization.

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

Tumor Cells "Feast on Acetate" to Enhance Immune Evasion



Acetic acid, also known as acetate, is an essential component of short-chain fatty acids. The concentration of acetate in the blood circulation fluctuates significantly, ranging from approximately 50 μM to 800 μM. Acetate levels in the human body are determined by the diet (for instance, vinegar, dairy products, processed meats and bread, alcohol and indigestible carbohydrates), as well as the breakdown of dietary fiber by the intestinal microbiota and acetylated metabolites within the body.

Tumors utilize acetate for acetyl-CoA production in an acetyl-CoA synthetase 1/2 (ACSS1/2)-dependent manner, which is instrumental in ATP synthesis, lipogenesis and histone acetylation. However, whether the acetate metabolism in tumor cells influences the acetylation status of non-histone proteins and plays a role in the tumor microenvironment remains unclear.

On May 3rd, 2024, the team of Professor LU Zhimin from the Institute of Translational Medicine, the First Affiliated Hospital of Zhejiang University, and the National Center for Basic Science, Zhejiang University, in collaboration with the team of HE Jie from the National Cancer Center, Chinese Academy of Medical Sciences Cancer Hospital, and the National Center for Basic Science, published an article online entitled "Acetate reprograms tumor metabolism and promotes PD-L1 expression and immune evasion by upregulating c-Myc" in ***Nature Metabolism***, which demonstrates that tumor cells have a preference for "sour taste", leading to inhibition of $CD8^+$ T cell infiltration and enhanced tumor immune evasion.

To measure the concentration of short-chain fatty acids in human non-small cell lung cancer (NSCLC) tissues, the authors performed mass spectrometry analyses and found that acetate was the most abundant short-chain fatty acid. Correspondingly, ^{18}F-acetate PET imaging revealed that acetate is rapidly consumed by tumor cells. Next, isotope labelling and metabolic flux mass spectrometry further confirmed that monocarboxylate transporter 1 (MCT1), which is highly expressed in epithelial tumor cells, is responsible for the increased acetate uptake and ACSS2-mediated acetyl-CoA production and promotes lipogenesis. In addition, c-Myc was identified as a protein with considerable acetate-enhanced acetylation. Of note, they found that dihydrolipoamide S-acetyltransferase (DLAT), a known metabolic enzyme, performs a non-metabolic function in c-Myc acetylation at Lys148, which recruits ubiquitin-specific peptidase 10 (USP10) for deubiquitination and stabilization of c-Myc, and subsequently activating the transcription of immune checkpoint protein PD-L1, glycolytic enzyme LDHA, MCT1, and cell cycle protein CyclinD1. Both the mouse orthotopic model of lung cancer and the subcutaneous tumorigenesis experiments showed that acetate supplementation in the drinking water inhibits $CD8^+$ T cell infiltration and promotes tumor growth, whereas disruption of acetate uptake or its metabolic pathway in tumor cells inhibits immune evasion. The authors found that combined treatment with a USP10 inhibitor and an anti-PD-1 antibody in lung tumors in mice notably promoted $CD8^+$ T cell infiltration and anti-tumor immunity in the tumor microenvironment. Immunohistochemical (IHC) staining of human NSCLC specimens showed that the level of c-Myc Lys148 acetylation was positively correlated with the MCT1 expression levels and the reduction of $CD8^+$ T cell infiltration. Consistently, c-Myc Lys148 acetylation, MCT1 and USP10 expression levels were inversely associated with the prognosis of non-small cell lung cancer patients.

This study reveals the important mechanism by which MCT1-dependent acetate uptake reprogrammes NSCLC cell metabolism and plays a role in tumor immune evasion by upregulating c-Myc acetylation and stabilization, underscoring the potential of controlling acetate metabolism to curb tumor growth and improve the response to immune checkpoint blockade therapy.

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

Promising 'All-in-One' Treatment for Aggressive Blood Cancers

Combining CAR-T cell therapy and stem cell transplantation could help patients with difficult-to-treat blood cancers.

A new 'all-in-one' treatment that integrates CAR-T cell therapy with more established stem cell transplantation therapy might improve treatment outcomes for patients with blood cancers, according to a study led by researchers at Zhejiang University in China.

The treatment exploits the way CAR-T cell therapy kills cancer cells and also depletes the donor T cells that cause severe adverse effects, so that fewer toxic drugs are required for a successful stem cell transplant. The study was published in the ***New England Journal of Medicine***.

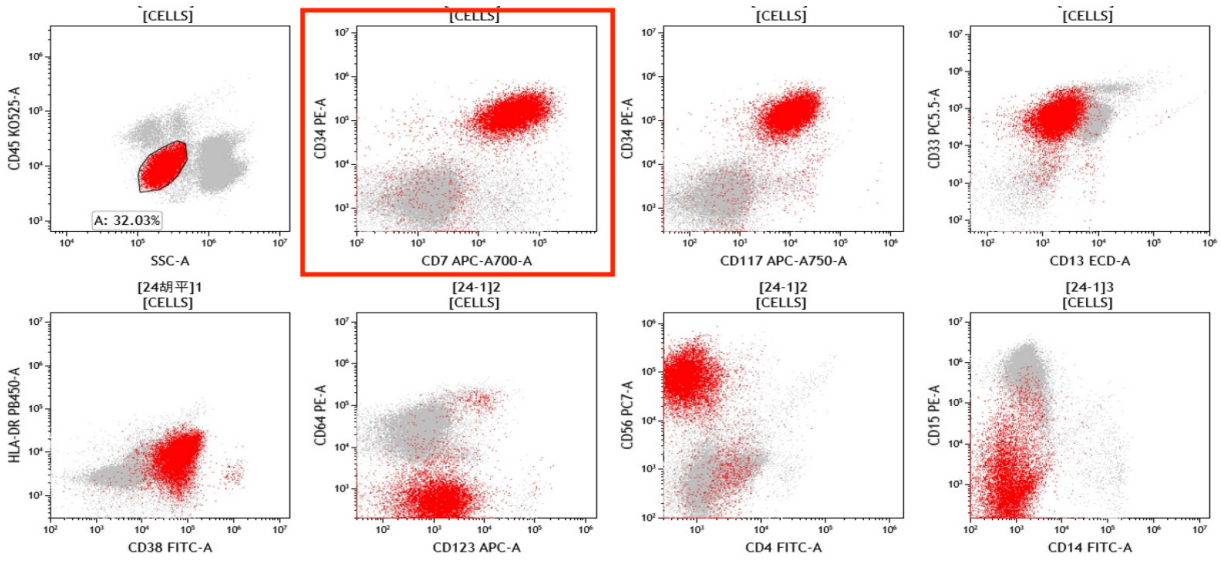
"This approach might be particularly beneficial for patients with relapsed or refractory haematological cancers who are not eligible for conventional stem cell transplantation," says HUANG He, director of the Bone Marrow Transplantation Center at the First Affiliated Hospital, Zhejiang University School of Medicine.

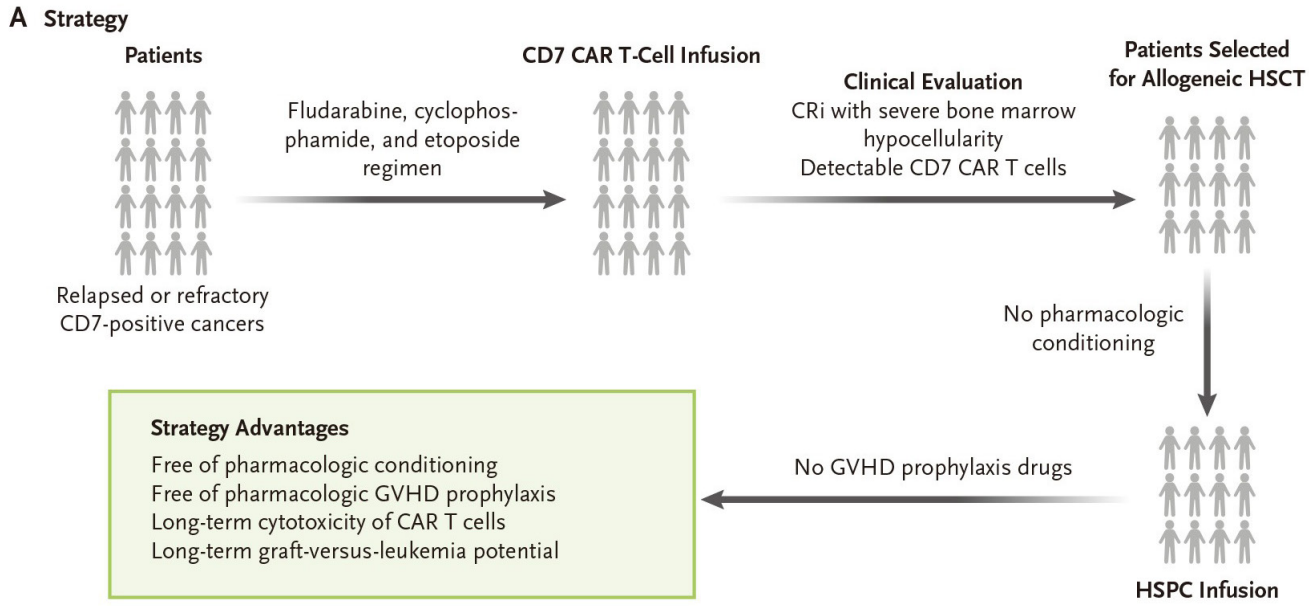
Seek and destroy

In the trial, 17 patients with relapsed or treatment-resistant CD7-positive leukaemia or lymphoma, aggressive blood cancers, characterised by CD7 antigens on the cancer cells – first received CAR-T cell therapy. This is a new type of immunotherapy where T cells from patients or donors are genetically modified to recognize a specific antigen – in this case CD7 – and then infused back into the patient, where they seek out and destroy cancer cells.

Ten patients were then proceeded to the next stage in which they received a haematopoietic stem cell transplantation (HSCT) from a donor – in this case, a close family member whose tissue type is half-matched to the patient. The new stem cells move to the bone marrow and produce healthy blood cells to replace the ones with cancer.

Among the 10 selected patients, the CAR-T cell therapy had completely destroyed the cancer cells, which can be detected in the patients' blood. In addition, their bone marrow was not fully recovered, but they had no severe graft-versus-host disease (GvHD), in which transplanted cells attack

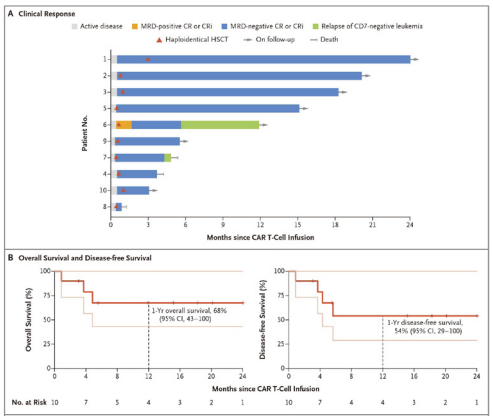


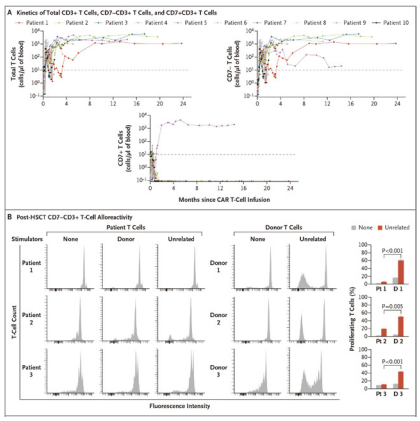


the patient's tissues and cells. These conditions indicated that these patients' bone marrow can allow for stem cell engraftment. Critically, this meant that, unlike with conventional HSCT, the 10 patients didn't have to receive the aggressive chemotherapy — namely myeloablative conditioning — to destroy the bone marrow before HSCT and the immunosuppressive agents to reduce GvHD. Those treatments are so toxic that they prevent many patients from using HSCT to treat their cancer. The approach also allowed the cancer-destroying CAR-T cells to remain in the body after the transplant.

Underlying mechanisms

For the majority of patients, the all-in-one treatment appeared to cause long-term remission, with manageable side-effects – such as very low blood cell counts or moderate symptoms of GvHD. During a median follow-up period of around 15 months, six patients had no detectable disease. Most notably, the research team analysed the recovered T cells after HSCT, and revealed their intrinsic characteristics to reduce the severity of GvHD without immunosuppressive agents. However, two patients experienced a relapse with CD7-negative leukaemia and two died from treatment-related complications. Larger clinical studies are needed to validate the findings, say the researchers. "Further research will probably focus on larger, more homogeneous cohorts to validate these findings and optimize the therapeutic strategy," says HU Yongxian, vice director of the Bone Marrow Transplantation Center. "Additional studies may also explore the mechanisms underlying leukaemia relapse and long-term effects of persisting CAR T-cells."

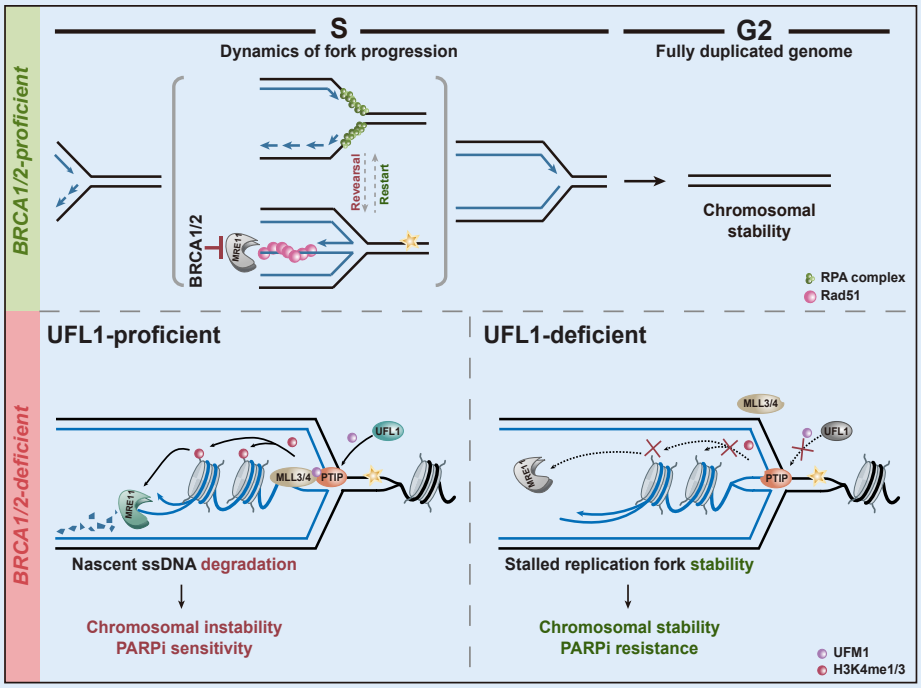




The researchers also need to address the toxicities associated with both treatments, says Hu. "Another major challenge is the relapse of CD7-negative leukaemia. This occurs when the cancer cells lose the CD7 antigen, making them invisible to CD7-targeted CAR-T cells, leading to disease relapse after initial remission."

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

ZJU Scientists Unveil Mechanism Behind PARP Inhibitor Resistance in BRCA1/2-Deficient Tumors

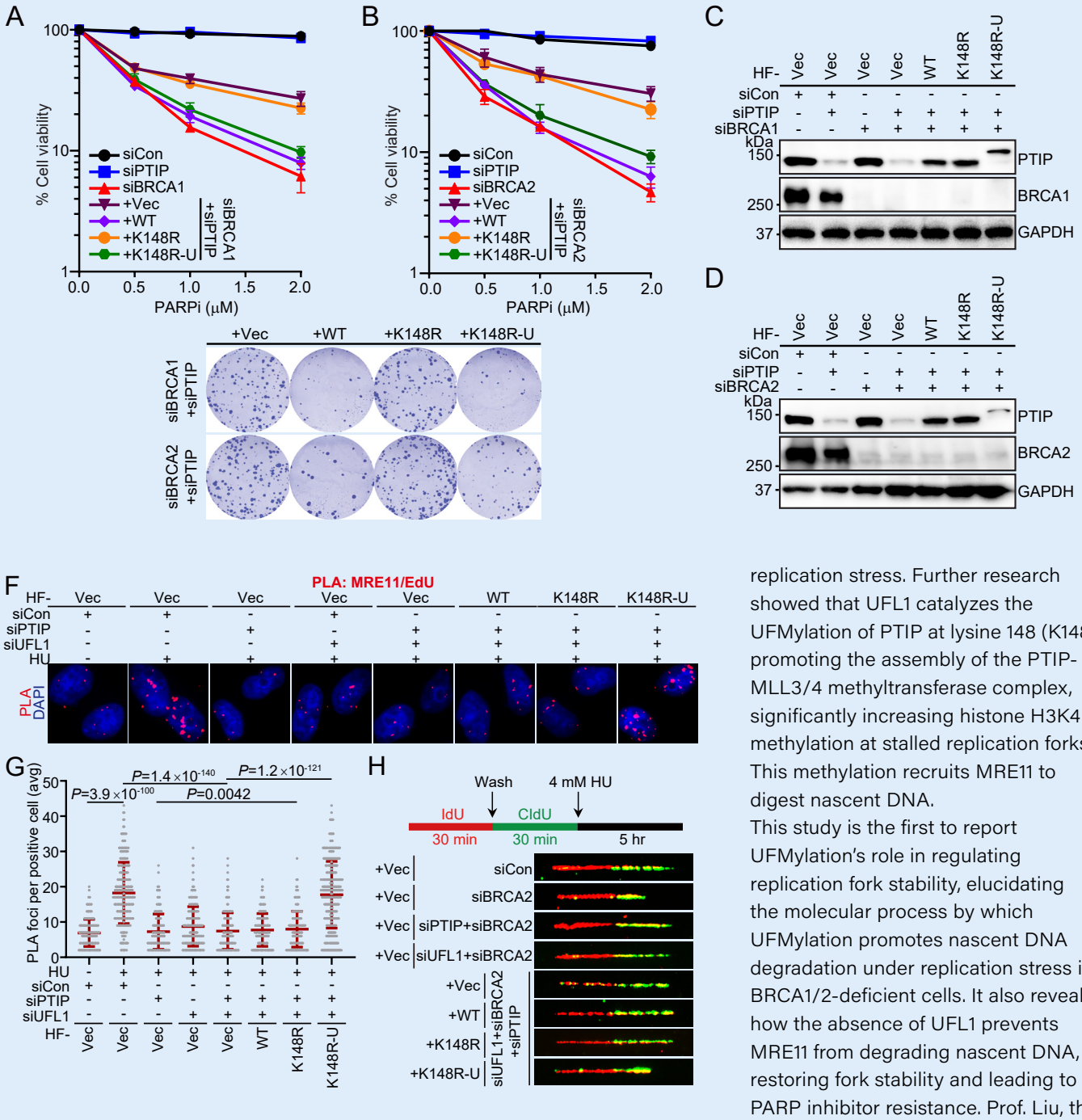


Genomic instability is a hallmark that distinguishes cancer cells from normal cells and is a critical factor driving tumorigenesis. Defects in the DNA damage response (DDR) lead to genomic instability, making DDR-related genes highly promising targets for precision cancer therapy. PARP inhibitors are the first clinically applied DDR inhibitors, exploiting synthetic lethality to effectively target tumor cells with BRCA1/2 (Breast Cancer Susceptibility Genes) deficiencies, which holds significant clinical promise. However, some tumor cells develop resistance to PARP inhibitors by restoring homologous recombination repair or stabilizing replication forks, posing challenges for clinical treatment. The molecular details of how BRCA1/2-deficient tumor cells restore fork stability to gain resistance to PARP inhibitors remain largely unknown.

On April 22, 2024, LIU Ting's team from Zhejiang University School of Medicine published a groundbreaking paper titled 'UFL1 triggers replication fork degradation by MRE11 in BRCA1/2-deficient cells' in ***Nature Chemical Biology***. This discovery highlights a novel molecular mechanism: BRCA1/2-deficient cells can resist PARP inhibitors by disabling the UFMylation pathway to stabilize replication forks.

During replication stress, events such as the decoupling of helicases and polymerases and excision by nucleases expose single-stranded DNA (ssDNA). This ssDNA is subsequently coated by the RPA complex, which is later replaced by recombinase RAD51 to form an ssDNA-RAD51 filament. Translocases such as SMARCAL1, ZRANB3, HLTF, and PICH, along with DNA topoisomerase TOP2A and SUMO E3 ligase ZATT, facilitate a two-step reversal process. The two reversed nascent ssDNAs are then paired to form a four-way Holliday Junction structure, temporarily stabilizing the stalled replication fork. RAD51 plays a crucial role in promoting this reversal process, thereby counteracting the replication fork restart induced by helicase BLM.

Liu's team has long been dedicated to researching DDR-related mechanisms, and recently, they have made a series of discoveries in maintaining replication fork stability. In February 2024, Liu's team published a paper in ***Nature Communications*** detailing how the TFIP11 protein binds to stalled replication forks, competitively inhibiting BLM and promoting RAD51's interaction with the replication fork to facilitate reversal. To ensure replication stability, the stalled replication fork must avoid excessive recruitment of the SLX4 nuclease complex, which could otherwise cut and collapse the fork. In April 2024, Liu's team published another paper in ***The EMBO Journal*** explaining how the ATR kinase,



recruited by the ssDNA-RPA complex, prevents excessive SLX4 recruitment, thereby preventing replication fork collapse.

UFMylation is a ubiquitin-like modification involving a cascade reaction where UFM1 (Ubiquitin-fold modifier 1) is covalently linked to substrate proteins' lysine residues. UFL1 is the only known E3 ligase for UFMylation.

In this study, Liu's team found that knocking down UFL1 in BRCA1/2-deficient cells partially restores genomic stability disrupted by PARP inhibitors, not through homologous recombination repair, but by preventing nascent DNA degradation under replication stress. Further research showed that UFL1 catalyzes the UFMylation of PTIP at lysine 148 (K148), promoting the assembly of the PTIP-MLL3/4 methyltransferase complex, significantly increasing histone H3K4 methylation at stalled replication forks. This methylation recruits MRE11 to digest nascent DNA.

This study is the first to report UFMylation's role in regulating replication fork stability, elucidating the molecular process by which UFMylation promotes nascent DNA degradation under replication stress in BRCA1/2-deficient cells. It also reveals how the absence of UFL1 prevents MRE11 from degrading nascent DNA, restoring fork stability and leading to PARP inhibitor resistance. Prof. Liu, the team leader, believes that this research could potentially provide new insights for the clinical application of PARP inhibitors.

For more information
Contact us: ***liuting518@zju.edu.cn***

UBE2F-CRL5^{ASB11} Axis: A Promising Therapeutic Target for Pancreatic Cancer

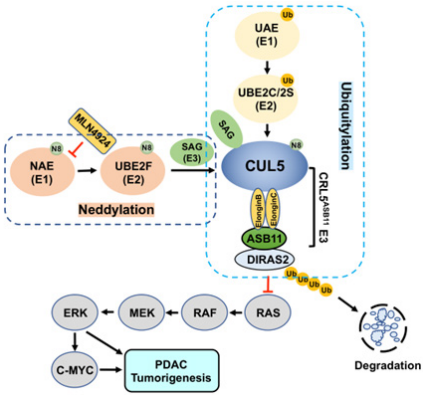
Pancreatic ductal adenocarcinoma (PDAC) is one of the most common malignancies of the digestive tract. Featured by its insidious onset, late diagnosis, aggressive progression, and limited effective therapies, PDAC is one of the deadliest malignancies with extremely poor patient survival rates. While mutational activation of Kras and/or inactivation of p53 were known to be the drivers of PDAC, identification of their collaborative genes during PDAC tumorigenesis should provide new approach for targeted therapy.

Neddylation pathway is over-activated in a variety of human cancers, which is positively correlated with poor survival rates of cancer patients. UBE2F is a neddylation E2 conjugating enzyme that couples with RBX2/SAG E3 ligase to neddylate cullin-5 for activation of Cullin-RING Ligase-5 (CRL5), which promotes ubiquitylation and degradation of a proapoptotic protein, NOXA, for example, to confer apoptosis resistance in lung cancer cells. The role of UBE2F in Kras^{G12D}-induced pancreatic tumorigenesis was previously unknown.

"We found that UBE2F is essential for growth and survival of pancreatic cancer cells and its inactivation significantly inhibits neoplastic progression of pancreatic tumorigenesis induced by Kras^{G12D}. Furthermore, the promotion of pancreatic tumorigenesis by UBE2F depends on its activation of CRL5 ligase for targeted degradation of DIRAS2, a negative regulator of the RAS-MAPK-cMYC signals." said Dr. SUN Yi, a professor at Cancer Institute of the 2nd Affiliated Hospital and Institute of Translational Medicine, Zhejiang University School of Medicine. "We believe that UBE2F is a promising therapeutic target for pancreatic cancer with KRAS mutation". The findings were published in ***Developmental Cell*** on April 3, 2024.

The team found that in the Kras^{G12D}-induced PDAC mouse model, Ube2f deletion significantly suppresses pancreatic tumorigenesis from ADM to mPINs then to PDAC. Specifically, UBE2F activates CRL5 to promote ubiquitylation and degradation of DIRAS2. They further identified ASB11 as a substrate receptor of CRL5, mediating DIRAS2 binding and ubiquitylation. Notably, DIRAS2 acts as a tumor suppressor in pancreatic cancer cells, and suppression of pancreatic tumorigenesis by Ube2f deletion can be largely rescued by simultaneous Diras2 deletion, indicating a causal role of Diras2. Finally, the study revealed that DIRAS2 is down-regulated in PDAC and low levels of DIRAS2 combined with high levels of UBE2F predict poor survival of PDAC patients.

"This study elucidated the oncogenic-promoting role of the UBE2F-CRL5 axis and the tumor suppressive



function of DIRAS2 in pancreatic tumorigenesis. It further validated the UBE2F-CRL5^{ASB11} axis as a compelling therapeutic target for pancreatic cancer. Furthermore, the levels of UBE2F and DIRAS2 may be useful biomarkers for the prognosis of PDAC patients in clinical practice." said Professor SUN Yi.

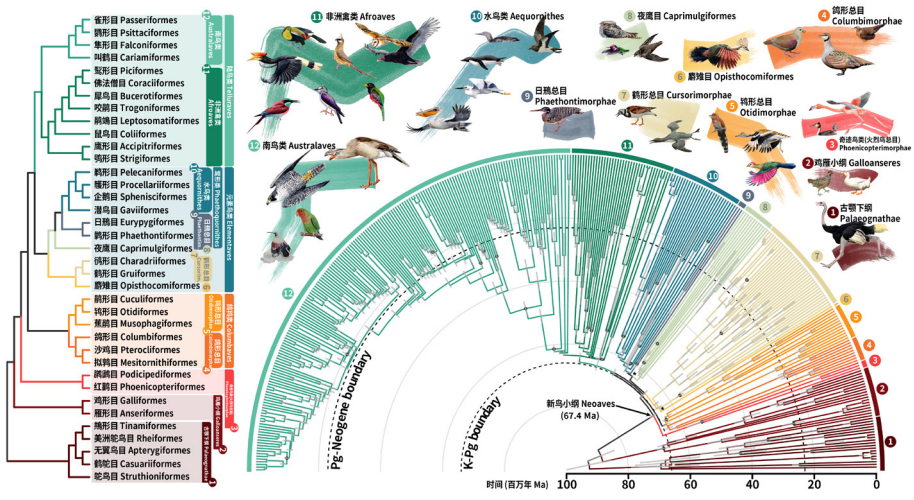
A schematic representation of the mechanistic insight into how the UBE2F-CRL5^{ASB11} axis positively regulates pancreatic tumorigenesis induced by Kras^{G12D}. CRL5^{ASB11}, upon activation by UBE2F, promotes ubiquitylation and degradation of tumor suppressor DIRAS2, leading to activation of the MAPK-c-MYC signals, thus serving as an attractive PDAC target.

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

A New Family Tree Revises Our Understanding of Bird Evolution

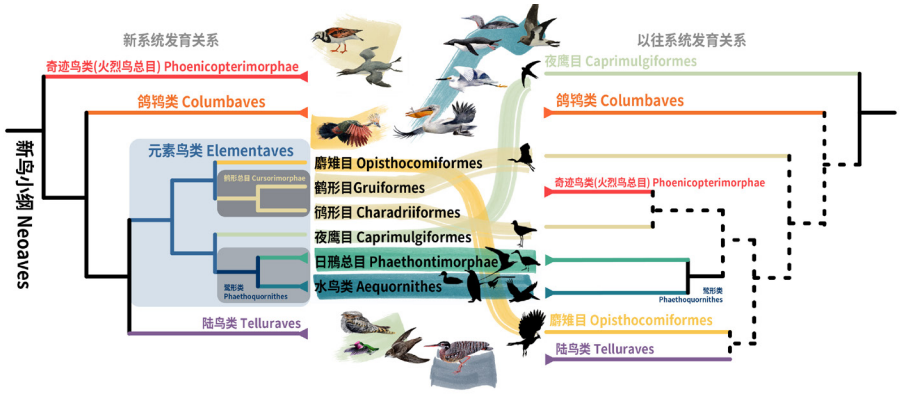
A team of researchers from the Bird 10,000 Genomes (B10K) consortium, initiated by Professor ZHANG Guojie of Centre for Evolutionary & Organismal Biology at Zhejiang University and collaborators, has reported a new bird family tree that promises to reshape our understanding of avian evolution. Published in ***Nature*** on April 1st, 2024, the study entitled "Complexity of avian evolution revealed by family-level genomes" marks a pivotal advancement in the long-contested evolutionary relationships among living birds.

Birds are the only dinosaur lineage that survived until today. About 66 million years ago at the Cretaceous–Paleogene (K–Pg) boundary, a mass extinction event destroyed all non-avian dinosaurs, providing an opportunity for birds to diversify rapidly and occupy a wide range of ecological niches. Neoaves, a diverse group comprising approximately 95% of all bird species today, emerged from this radiation. From the towering condors of the Andes to the diminutive hummingbirds flitting through tropical forests, Neoaves encompass a stunning diversity of forms and functions. Despite considerable efforts to reconstruct avian evolutionary history and the impacts of the K-Pg event using morphological data and molecular data, the precise branching order and relationships among the neoavian lineages remained contentious.



"Previous studies on small datasets from different genomic regions often produced conflicting results with respect to the topology of bird tree", said ZHANG Guojie, senior author of the paper, a chair professor on evolutionary biology in Zhejiang University, and one of the initiators of the B10K project. "In this study, for the first time we employed full genome-scale data to construct the tree for bird species from almost all representative families." This full genomic dataset was produced by the B10K consortium in its second phase that includes 363 bird species covering all major bird lineages.

The new family tree is breaking new ground in the long journey to unravel the mysteries of bird evolution. According to this updated bird family tree, a group containing flamingos and grebes (called Mirandornithes) were among the first neoavian lineages to evolve. The new tree is challenging the organization of Neoaves by classifying this big group into four major clades: Mirandornithes, Columbaves, Elementaves, and Telluraves. Elementaves is a newly proposed grouping comprising ca. 14% of all species of modern birds including disparate groups such as the enigmatic hoatzin, shorebirds, hummingbirds and tropicbirds. Elementaves is named to reflect the group's remarkable diversity in ecological niches, representing



the major elements of earth, air and water. This new family tree resolves some long-standing debates over the relationships among avian species and lays a solid foundation for studying avian evolution and trait development.

By employing full genome data across 363 bird species, this is the largest-ever dataset used for phylogenetic analyses of birds. The team built a new pipeline to extract over 150,000 regions spread out across the genome. "We characterized phylogenetic relationships across the entire genome and identified patterns associated with the genomic context and sequence characteristics", said Josefin Stiller, the leading author of this study and an Assistant Professor in evolutionary biology at the University of Copenhagen, "We found that various parts of the genome, for example individual chromosomes or protein-coding genes, often support vastly different trees. This likely explains why studies that only analyzed certain genomic parts were in conflict".

The study highlights the importance of using high-quality and large datasets to produce a robust phylogenetic tree. The team discovered that for most branches, a consensus on their relationships can be reached when a sufficient amount of data was used. But the phylogenetic positions for some bird groups like owls and hawks remain puzzling even with a full-genome scale of data. "More data does not necessarily produce a better solution", Zhang said. Siavash Mirarab, co-senior author of the study, a professor of electrical and computer engineering at the University of California, San Diego, added that, "The reason for this may be some complex evolutionary history like ancient cross-mating between two lineages, incomplete lineage sorting, long-branch attraction, and biased DNA sequence content, all of which can interfere with the reconstruction of phylogenetic trees." The study reports new insights on which of these factors impact which branches of the tree, providing a more comprehensive and genuine picture of the origin of these avian groups. The study also proposes a more accurate time scale for the diversification of modern birds, suggesting that a rapid radiation occurred at or near the mass extinction at the Cretaceous–Paleogene (K–Pg) boundary and to a lesser degree shortly after the Paleogene–Neogene boundary. The researchers found that these radiations coincided with remarkable genetic and morphological changes among birds, including greater mutation rates, smaller body sizes, and larger brains, and larger effective population sizes. "This illustrates the power of comparative genomics: by comparing genomes of living species, we can uncover traces of events that happened 66 million years ago," Stiller said.

"Our work has changed many traditional views on the evolutionary history of birds. This new family tree will serve as a solid backbone for mapping the evolutionary history of all bird species with important implications for ornithological research and biodiversity studies," Zhang concluded.

More information:

The Bird 10,000 Genomes (B10K) Project is an initiative aiming to map the genomes of all approximately 10,500 existing bird species. This ambitious project seeks to construct an all-encompassing avian tree of life from a whole-genome perspective, decoding the links between genetic variation and trait differences, unraveling the molecular evolution, biogeography, and biodiversity interrelations, assessing the impact of environmental changes and human activities on species evolution and biodiversity, and revealing the population history of the entire avian group.

The B10K was initiated by Professor ZHANG Guojie from Zhejiang University, along with professors M. Thomas P. Gilbert from University of Copenhagen, Erich D. Jarvis from The Rockefeller University, LEI Fumin from Chinese Academy of Sciences, Carsten Rahbek from University of Copenhagen, and Gary R. Graves from the National Museum of Natural History Smithsonian Institution. The B10K consortium brings together hundreds of experts across the globe that study various aspects of avian biology.

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

The Potential of Gut Bacteria to Improve Cancer Therapies

Some gut bacteria can collaborate to promote T-cell action against tumours in mice, raising hopes for treatments.

A new study led by Zhejiang University researchers has identified ways by which some microbes might influence cancer immunotherapy, suggesting a potential microbial-based adjuvant approach to improve the responsiveness of immunotherapy. Their results were published in ***Cell*** in March 2024.

Doctors and scientists have long been puzzled about why some patients respond better than others to treatments. That's especially the case for a new wave of cancer therapies that aim to harness the power of the body's own immune system to fight tumours. The effects of such immunotherapy can vary widely, even between patients with similar cancers.

One possible reason is the impact of bacteria in the gut and other organs. Long considered passive passengers, these microbes are now thought to play a significant role in many physiological processes.

"The gut microbiome can influence the efficacy of immunotherapy, but the specific bacterial components and underlying mechanisms remain elusive," says WANG Liangjing, a professor of internal medicine at the Second Affiliated Hospital at the School of Medicine, Zhejiang University.

His team investigated components of the microbiome, and revealed the beneficial effects of the bacteria Lactobacillus johnsonii and Clostridium sporogenes.

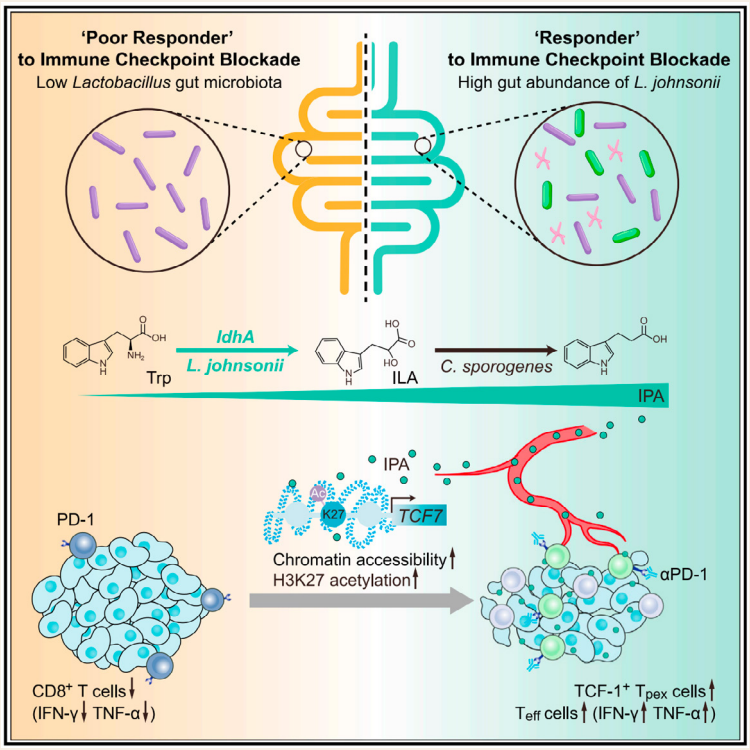
Mouse model

The mouse study looked at how the two bacteria worked together to produce a chemical called indole-3-propionic acid (IPA). This is important because IPA changes the behavior of T-cells, the immune cells that are often targeted in cancer immunotherapy.

Specifically, the IPA was found to boost the so-called 'stemness' of the T-cells, a term used to describe their stem cell-like behavior, including self-renewal and capacity to differentiate into different types of cell. This improved their responsiveness to treatments called immune checkpoint blockade (ICB) therapies in several types of cancer.

The team then looked at whether IPA might also be able to improve the response to ICB therapies in humans. They tested this approach in vitro, using human T-cells in the lab, and found they were better able to target tumours and express helpful proteins when exposed to IPA.

"Collectively, these results demonstrate that modulating the stemness programme of T-cells through microbiota-derived IPA may be a promising approach to reinforce the effectiveness of tumour ICB therapy in clinical settings," Wang says.



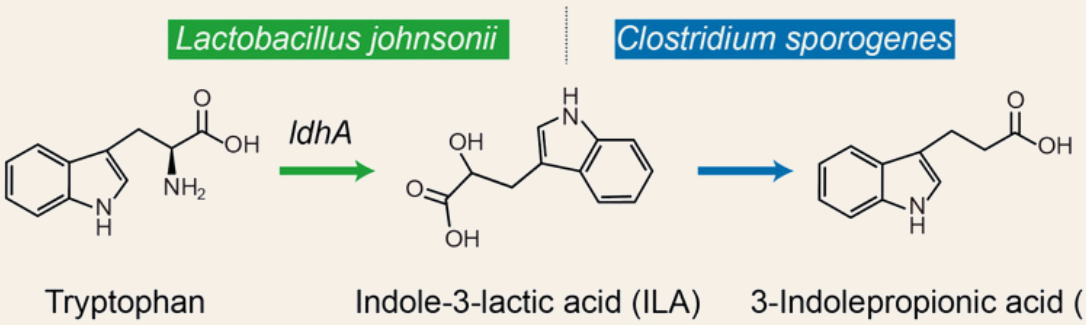
New trials

The research also produced some surprising results. The scientists could not detect IPA in the medium in which they grew the Lactobacillus johnsonii bacteria. That could indicate the microbe needs to collaborate with others to produce the target chemical. Wang and his team are now working to confirm exactly how the IPA enables the useful modification of the T-cells. The team is also carrying out trials to explore how the presence of other bacteria could boost immunotherapy further in several cancers.

As the effects of IPA on immune response are consistent across multiple cancer types, Wang says it could suggest broad "pan-cancer" applications for the approach.

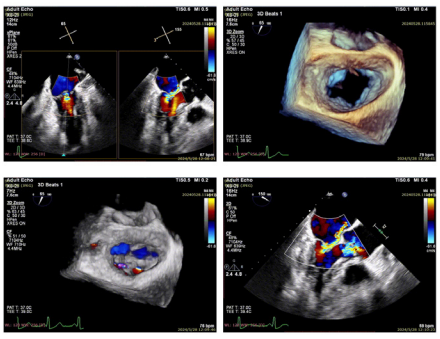
"We're hopeful that gut microbiota and microbial metabolites will shine in the process of adjuvant tumour immunotherapy," Wang adds.

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



Two Procedures Demonstrated at CSI Frankfurt 2024 by SAHZU Cardiologists

Invited by CSI Frankfurt 2024, the top academic event on interventional cardiology in the international community, SAHZU Chairman Prof. WANG Jian'an and his team demonstrated one transcatheter edge to edge mitral repair (TEER) and one Liwen Procedure on the conference. It highlights China's innovation and solution in the field of structural heart disease interventional therapy and the panelists on the conference spoke highly of Prof. Wang and his team's performance.



In the TEER procedure, the patient was diagnosed with mitral valve prolapse, severe mitral regurgitation (MR4+, Carpentier type II) and enlarged left atrium. Considering the preoperative echo assessment result, the team decided to implant the DragonFly ™ MitraClip in the A2/P2 position (puncture site height: 4.0cm).

TEE: Jet width: 1.0cm; A2/P2 leaflet length: 1.89/1.18cm; mitral valve area: 4.22cm^2

During the procedure, under transesophageal ultrasound guidance, the clip was delivered to the left atrium, and after its adjusting the position, direction and path, it entered the left ventricle to capture the valve leaflets, and then the team released the clip after evaluating its position and effect. After release, there was no residual prolapse of the mitral valve, only trace regurgitation observed. The result was ideal, and the procedure was a complete success.

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

Affiliatd Sir Run Run Shaw Hospital Launched the Country's First "Intelligent Physician Assistant" Based on a Large Language Model

At the 2024 China Health Science and Technology Innovation and Discipline Construction Conference & Conference on High-Quality Development of Chinese Modern Hospitals, Sir Run Run Shaw Hospital (SRRSH) affiliated with the Zhejiang University School of Medicine released the "Futuristic Man of SRRSH" powered by the large language model (LLM), which attracted wide attention from all walks of life.

Leveraging artificial intelligence large model and digital human technology, "Futuristic Man of SRRSH" empowers the smart hospital system by focusing on the "trinity" of smart medical care, smart management and smart service, aiming to further improve the public's experience of medical care and injecting new energy for the high-quality development of the hospital.

As one of the important components of "Futuristic Man of SRRSH", the first "Intelligent Physician Assistant" (IPA) based on LLM has been fully implemented in SRRSH. From pre-diagnosis, then real-time voice recording and clinical semantic analysis during the consultation, to post-diagnosis follow-up and re-examination reminders, it creates a more comprehensive and convenient medical service system.

"Scan the QR code and see the doctor in advance," is how patients engage with the IPA. When patients are waiting for consultation, they can scan the barcode on the appointment form with their cell phones to enter the Wechat Mini Program, where the IPA will ask questions by simulating the clinician's thinking and collect information such as chief complaints, accompanying symptoms, history of present illness, past history and family history in multiple rounds of voice or text dialogues. The IPA will automatically generates and transmitted a draft medical record to the doctor workstation in 5 seconds, so that the doctor can understand the patient's medical history before the patient enters the consultation room.

Mr. Wu, a patient, praised the IPA for making waiting time more valuable. "I am often too nervous to articulate my symptoms clearly when facing the doctor, and sometimes I forget some important details. With the IPA, I can speak into my phone, And my voice is converted to text. and if I remember anything else, I can go on to add it, which puts me at ease."

During the consultation, the doctor only need to press the recording button of the IPA to record the communication with the patient, IPA can understand the clinical semantics and transform the voice into structured text, then automatically generate standardized electronic medical records, which greatly improves the efficiency and quality of consultation and allows doctors to focus more on communicating with patients.

According to SRRSH, the IPA applies six major kinds of technology, namely, advanced computational capabilities of the large model base, continuous tuning of the medical large language model, intelligent recognition and transformation of the medical speech engine, active elimination of irrelevant interfering factors, AIGC-formatted medical record text generation, and intelligent image and picture recognition algorithms.

Prof. CAI Xiujun, president of SRRSH, said that under the new era of artificial intelligence, which is promoted by the intersection of the two major strategies of "Healthy China" and "Digital China", the life science and health industry have ushered in a new opportunity for high-quality development and SRRSH has been continuously exploring how to further promote the in-depth fusion of emerging technologies with healthcare, in order to truly benefit the people's livelihood and well-being. In the future, SRRSH will continue to enhance its ability to apply AI technology to improve the overall level of information construction in the hospital, and dedicate itself to providing patients with more accurate, personalized and warmer medical services.

For more information
Contact us: ***srrsh@163.com***

The First SMA Child Diagnosed Through Newborn Genetic Screening in China and Treated Before Onset

A few days ago, Bei Bei's parents took Bei Bei to the Genetics and Metabolism Department of the Children's Hospital of Zhejiang University School of Medicine (ZCH) for a follow-up visit and expressed their heartfelt thanks to the medical team that diagnosed and treated their daughter.

Bei Bei is a baby born in the spring of 2022. The arrival of their daughter filled the young parents with great happiness. After Bei Bei was born, besides routine newborn screening, the young couple voluntarily participated in a newborn screening study for genetic diseases led by ZCH.

To their surprise, the screening results indicated a high likelihood of spinal muscular atrophy (SMA) in Bei Bei.

SMA is an autosomal recessive disorder caused by motor neuron survival gene 1 (SMN1) mutation and can result in muscle weakness and muscular atrophy characterized by neuromuscular disease. SMA patients can show symptoms of hypotonia, significantly slow motor development, and being unable to walk independently. It can even be life-threatening, with a high possibility of disability and fatality.

At first, Bei Bei's parents couldn't believe that their lovely daughter had this rare disease. They immediately took their daughter to the Genetics and Metabolism Department of ZCH for further diagnosis and treatment. Unfortunately, it was confirmed that Bei Bei is a child with SMA after a series of genetic tests. If the patient with SMA is not treated in time, it is likely to progress within 6-18 months, affecting neuromuscular development and potentially causing death.

As a child with a rare disease, Bei Bei is undoubtedly unfortunate, but fortunately, she was diagnosed with the disease very early before the symptoms manifested thanks to the newborn genetic screening.

"We started the neonatal genetic screening program in 2022. Bei Bei was the first child diagnosed with SMA through newborn genetic screening and also the first child with SMA in China to be treated with specific drugs before the disease onset", YANG Xin said.

Thanks to the joint efforts of experts from the Genetics and Metabolism Department and Neurology Department of ZCH and Bei Bei's parents, Bei Bei has been receiving Nosinasan sodium injection treatment since she was less than 2 months old.

The effect of the treatment is beyond imagination. Now she is two years old, she grows up in the same way as other children of the same age. Watching Bei Bei grow so well, Bei Bei's parents feel very lucky and grateful.

Dr. YANG Rulai, director of the Genetics and Metabolism Department of ZCH, introduced the newborn genetic screening program, which refers to the genetic sequencing of heel blood after the birth of the newborn to predict the risk of some monogenic diseases with relatively high incidence. It can be seen as a new application of next-generation sequencing technology in the field of neonatal disease screening.

The current neonatal disease screening system of ZCH, as the tertiary prevention and control system of social health, has played an important role in the prevention and control of birth defects. Relying on the strong clinical research capability of ZCH, the Zhejiang Neonatal Disease Screening Center is responsible for the disease screening and management of newborns in Zhejiang Province.

Professor SHU Qiang, director of Zhejiang Neonatal Disease Screening Center, said, "It is hoped that through the clinical application of neonatal genetic screening, more neonatal diseases will be screened. At the same time, birth defect prevention and treatment will be improved. The successful experience of neonatal genetic metabolic disease screening will be applied to more rare diseases so that children like Bei Bei can be diagnosed and treated early."

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

A Breakthrough! School of Medicine Achieves New Success in the National Teaching Innovation Competition for College Teachers

From July 28th to 31st, the national competition of the Fourth National Teaching Innovation Competition for College Teachers, organized by the China Association of Higher Education under the guidance of the Higher Education Department of the Ministry of Education, was held at the University of Electronic Science and Technology of China in Chengdu, Sichuan. The teachers from the School of Medicine achieved remarkable success once again, the team led by Professor Liang Weiwei from the Second Clinical Medical School won second prize in the New Medicine Associate Professors' Group, and the team led by Professor Wei Xiaoli from the Basic Medical School secured third prize in the Curriculum Ideology and Politics Associate Professors' Group. This marks our school's first national-level award in the Curriculum Ideology and Politics category, which represents a breakthrough.

Under the theme "Promoting Teaching Innovation, Cultivating First-Class Talent," the competition aimed to fulfill the fundamental mission of fostering virtue through education, advance teaching reform and innovation, and guide teachers to focus on education with dedication. It provided a high-quality platform for college teachers across the country to exchange teaching experiences, hone their teaching skills, showcase their teaching styles, and enhance their teaching abilities, thereby promoting innovation in college teaching and the cultivation of first-class talent in the new era.

Throughout the competition journey, I have experienced both the challenges and the joys of innovation. I have fully recognized the importance of respecting students as the main focus, setting clear objectives, and continuously reflecting on the outcomes. The award is not only an acknowledgment of my past efforts but also an inspiration for my future pursuit of teaching innovation.

— LIANG Weiwei, Second Prize Winner of the New Medicine Category

Under the guidance of the Objective-based Education (OBE) teaching philosophy, the team led by Professor Liang Weiwei employed Marzano's taxonomy of educational objectives to establish an evaluation framework for "Entrustable Professional Activities in Clinical Internship." It developed a three-tiered, cyclical, clinical internship model. Through repeated practice, the clinical thinking and practical skills of the clinical interns were significantly improved. Through preparation and participation in the competition, the team members gained in-depth understanding of both the hardships and joys associated with teaching innovation, which represents not only a reform of the traditional teaching methods but also a refinement of teachers' professional competencies. The teachers expressed that the competition provided them with new insights into course development, effective teaching, and understanding student needs. This valuable experience lays a solid foundation for them to achieve further advancements in teaching innovation.

Participating in the competition was not only a valuable learning and growth experience for me but also a motivation for me to continue learning, thinking, and exploring in the field of medical education. Competing alongside many outstanding participants, we encouraged each other, progressed together, and became better versions of ourselves. This award is a summary of the past teaching efforts and a new motivation for future teaching innovations.

— WEI Xiaoli, Third Prize Winner of the Curriculum Ideology and Politics Category

Professor WEI Xiaoli's team has consistently focused on cultivating "compassionate, innovative, and excellent medical talents," with a strong emphasis on student development. They took the pathology laboratory course as a key point for improvement, restructuring the teaching content, integrating various teaching methods and evaluations, and achieving significant breakthroughs in teaching innovation with impressive teaching results. They expressed their gratitude for the teaching innovation competition, stating that the preparation process deepened their reflection on teaching, broadened their perspectives, and provided a precious learning opportunity that encouraged rapid growth, providing more insights and motivation for future teaching efforts.

The National Teaching Innovation Competition for College Teachers is a platform for showcasing advanced teaching concepts and teaching reform achievements, as well as a means of promoting teaching innovation and cultivating first-class talent. The competition adopts a three-tiered system, with events taking place at the school level, provincial level (including autonomous the regions, municipalities, and the Xinjiang Production and Construction Corps), and national level. It aligns closely with the theme of high-quality development in higher education and the needs of higher education reform. The competition covers seven categories: New Engineering, New Agriculture, New Medicine, New Liberal Arts (the “Four New” disciplines), Basic Courses, Curriculum Ideology and Politics, and Industry-Education Integration. During the competition, participating teachers focused on teaching innovation. Guided by the initiative to develop the "Four New" disciplines, they emphasized student growth and integrated teaching outlines with practical experience. By presenting their innovative design ideas, measures, and outcomes, they fully demonstrated the educational commitment and mission of college teachers in the new era.

2024 Graduation Ceremony

・*The Graduation Concert*

・ *Grade 2019, Department of Clinical 1,Group A1, pictured*

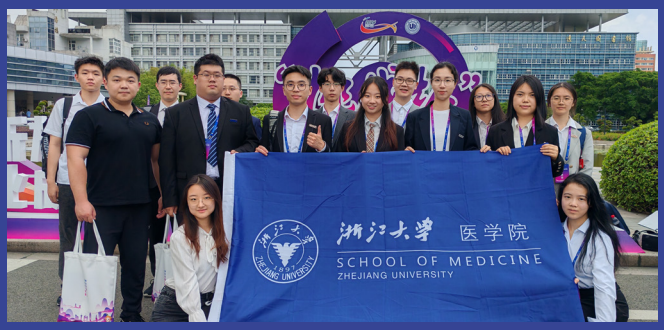
・*Graduation ceremony*

・*Taking photos with junior high school, Senior high school, undergraduate and master students*

・*Graduation Message Wall*

Five Golds and One Silver! Showcasing the Excellence of Student Teams at School of Medicine

The 14th Zhejiang Provincial "Challenge Cup" College Student Entrepreneurship Competition concluded on May 19th. Following a series of intense contests, the entrepreneurial team from the Zhejiang University School of Medicine achieved an outstanding five golds and one silver.



GOLD AWARD TEAMS

Project Overview

Bone tissue, the second most commonly transplanted tissue after blood, faces an increasing demand due to the increasing aging population. There is an urgent market need for bone materials that are both cost-effective and high-performance. Bone Miracle Technologies addresses this need by innovatively using autologous collagen tissue as the material source. Through the ultra-fast biomimetic mineralization technology known as BoneEngine, the first biomimetic mineralized bone scaffold derived from non-bone autologous tissue—BoneStand—has been successfully synthesized. This series of innovations not only promises to reduce the cost of synthetic bone grafts significantly but also provides a superior treatment option for patients with bone defects.

Project Overview

Jianying Technology is a global pioneer in the development of cancer nanotechnology. Their flagship product, Nano-TCA, is a targeted imaging agent, designed to address the challenges related to early cancer detection. By directly binding to cancer cells, Nano-TCA offers imaging sensitivity that is five times greater than that offered by the conventional contrast agents, thus revolutionizing the field of cancer imaging. Additionally, the team has pioneered the use of self-assembly technology to create nanoprobes that can specifically target various cancer markers, enabling the precise navigation and identification of cancerous tissues. These advancements have significantly improved the sensitivity of clinical imaging, reducing the detectable size of tumors from 1cm to less than 0.5cm and achieving earlier cancer detection by an average of 93.06 days. As a result, Jianying Technology has earned a reputation for being "China's eyes" for early cancer detection.

Project Overview

Addressing the global challenge related to the early diagnosis and treatment of liver tumors, this team developed a cutting-edge AI system that is capable of segmenting multiphase liver lesions. The system facilitates the precise, fully-automated segmentation of medical images, with a lesion localization accuracy of 86.4% and a diagnostic accuracy of 89.9%, placing it at the forefront of the field. The team has secured a strong intellectual property position, with 11 patents.

Project Overview

As an emerging cancer immunotherapy, CAR-T cell therapy has shown promising results regarding the treatment of refractory/recurrent B-cell malignancies in the hematologic system. The project team utilized T cells derived from healthy individuals to design a universal CAR-T product, targeting CD19 and CD22, improving efficacy, reducing adverse reactions, lowering the production costs, and enabling mass production. This product offers a safer, more effective, accessible CAR-T cell therapy for patients, on demand.

Project Overview

FlyDrug is an integrated intelligent platform for new drug discovery, that combines AI technology with the entire drug discovery process, including target identification, drug screening, molecular generation, and property prediction. Developed from the cross-disciplinary innovation of "AI + Pharmacy" at Zhejiang University, this platform closely integrates AI with new drug development. It has created a pioneering intelligent cloud platform for drug discovery, setting industry-leading standards in various technical metrics and representing a significant milestone in the field.

SILVER AWARD TEAM

Project Overview

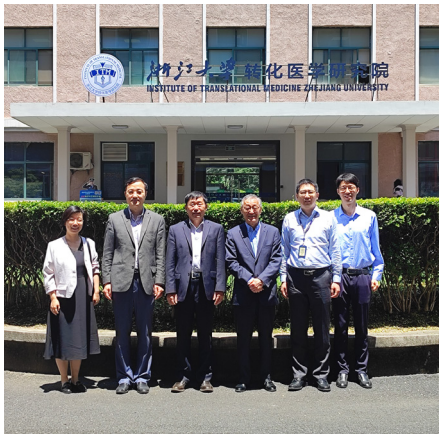
MicroBone is a team that is committed to developing orthopedic research instruments and setting the industry standards. This team, mainly composed of undergraduate students, has tackled existing challenges in the field by developing a groundbreaking series of instruments for precise bone defect modeling. By initiating standardized modeling techniques, MicroBone aims to unify the measurement standards in orthopedic research and establish a standardized system across the industry.

World-Class Universities Visit Zhejiang University School of Medicine for an Academic Exchange

On April 30th, a delegation from Loma Linda University Health, headed by President Richard Hart, visited Zhejiang University School of Medicine (ZUSM). Vice President LI Xiaoming welcomed the guests, and the two parties discussed ways to enhance medical education collaborations. Specifically, they explored opportunities for clinical rotations and residency training. Both institutions expressed a keen interest in establishing a formal partnership with each other.

Loma Linda University Health, an academic medical center based in Los Angeles, was founded in 1905. Loma Linda played a pivotal role in managing the Sir Run Run Shaw Hospital, affiliated with Zhejiang University School of Medicine, during its early years (1994-1999). Following the successful completion of their first five-year collaboration, the two institutions signed a long-term agreement to continue to foster international collaborations at Sir Run Run Shaw Hospital. This partnership was instrumental in helping the hospital to become the first medical institution in China to achieve international medical accreditation.

From May 12th-14th, Professor Dennis Kunimoto, Vice Dean of Faculty Affairs at the University of Alberta's Faculty of Medicine & Dentistry, and Professor LI Xinmin, a Fellow of the Canadian Academy of Health Sciences and Vice Dean, visited ZUSM. Both professors participated in the School of Medicine's "Apricot Grove" Academic Forum, delivering keynote speeches on the role of artificial intelligence in advancing medical education. They also engaged in discussions with various departments at ZUSM, including the School of Nursing, the Affiliated Mental Health Center, and the Institute of Translational Medicine, to explore areas for potential future collaboration.



Professor Marcale del Carmen, President of Massachusetts General Hospital, Harvard Medical School, visited Zhejiang University from May 20th to 25th.

She was warmly welcomed by REN Shaobo, Chairman of the University Council, and Vice President LI Xiaoming, among others. During her visit, Professor del Carmen visited Zhejiang University's School of Medicine, the 1st and 2nd Affiliated Hospitals, the International School of Medicine, Zhejiang University-University of Edinburgh Institute, and the Institute of Translation Medicine. She engaged in in-depth discussions with the leaders of these institutions in order to explore potential collaborations. Professor del Carmen also delivered two keynote addresses. She spoke at the "School of Medicine's 'Apricot Grove' Academic Forum" and also the "Master Teachers and Physicians Lecture Series," sharing her insights with both the faculty and students.

Advancing Global Reproductive Health, Building a Healthier Future Together

——The 2024 International Reproductive Genetics Conference Concludes Successfully

The 2024 International Society of Reproductive Genetics Conference was successfully held in Hangzhou, Zhejiang Province, from May 31st to June 2nd. REN Shaobo, Chairman of the University Council; LU Wenliang, Vice President of the Chinese Association of Integrative Medicine; SHI Dongcai, Deputy Director of the Department of Science and Technology of Zhejiang Province; CHAI Kequn, President of the Zhejiang Association of Integrative Medicine; and HUANG Hefeng, Academician of the Chinese Academy of Sciences, Dean of Zhejiang University School of Medicine, and Chair of the Conference, attended the opening ceremony and delivered speeches. The opening ceremony was presided over by ZHANG Dan, Executive Chair of the Conference and Vice Dean of Zhejiang University School of Medicine.

HUANG Hefeng, on behalf of the Organizing Committee, expressed her sincere gratitude and warm welcome to all of the leaders, experts, and colleagues in attendance. She highlighted the significant potential of emerging technologies in reproductive genetics to revolutionize patient care through personalized precision medicine. Exciting breakthroughs have been achieved in the theoretical research on the genetic mechanisms of developmental diseases, paving the way to conquering reproductive genetic diseases. She hoped that the conference would serve as a platform for exchanging cutting-edge knowledge and technologies related to reproductive genetics, disseminating new findings, fostering collaborations, and integrating the best of both Chinese and Western medicine. By doing so, she envisioned jointly shaping the future of reproductive medicine and driving innovation in the field, ultimately contributing to improved human health.

Among the attendees at the opening ceremony of the conference were notable figures such as Professor Catherine Racowsky, former President of the American Society for Reproductive Medicine; Professor Ben Mol from Monash University, Australia; Professors Stephen J. Lye and Stephen G. Matthews from the University of Toronto, Canada; Professor Stuart A. Scott from Stanford University, USA; Academician Dennis Lo, Vice Dean of the Faculty of Medicine at the Chinese University of Hong Kong; Academician Peter CK Leung from the University of British Columbia; and Academicians YANG Huanming, QIAO Jie, JI Weizhi, LI Jinsong, GAO Shaorong, and XIE Xiaoliang, along with Professor YANG Zhihong, co-founder and secretary-general of the International Society of Reproductive Genetics. These were joined by other well-known experts and scholars from both domestic and international institutions.

The 2024 International Conference on Reproductive Genetics is organized by the International Society for Reproductive Genetics, the Chinese

Association of Integrative Medicine, and the Zhejiang Association of Integrative Medicine. Co-hosted by the School of Medicine at Zhejiang University, its affiliated Department of Obstetrics and Gynecology, and the Obstetrics and Gynecology Hospital affiliated with Fudan University, the conference features an array of sessions including an Academicians' Forum, an Interdisciplinary Forum, a Forum on Fertility Preservation and Safety in Assisted Reproduction, a Young Investigator Forum, a Forum on Precision Diagnosis and the Prevention of Genetic Disorders, a Forum on Clinical and Basic Research in Reproductive Disorders, and a Forum on Integrated Chinese-Western Reproductive Medicine. These forums will showcase the latest research advances, technological innovations, and future directions in the fields of reproductive genetics and medicine, providing a high-level platform where experts may exchange ideas and advance their knowledge.

SAHZU Eye Center Signs MoU with Singapore National Eye Centre

Chief Executive Officer of Singapore National Eye Centre (SNEC) Prof. AUNG Tin visited SAHZU Eye Center on May 15. During the visit, SAHZU, SAHZU Eye Center and SNEC together signed a Memorandum of Understanding (MoU) to jointly promote collaboration in research innovation and faculty training in ophthalmology, with an ultimate goal to make adequate contribution to the global ophthalmology community.

Chairman of SAHZU and Academician of Chinese Academy of Sciences Prof. WANG Jian'an expressed his warm welcome to Prof. AUNG and congratulated on the signing of MoU with SNEC. He said that SAHZU has been always seeking for opportunities to collaborate with international medical institutions. He expects that the two sides can work together to bridge Chinese and Singaporean ophthalmologists and achieve win-win outcomes.

Prof. AUNG Tin briefly introduced SNEC in the ceremony. SNEC is a young and energetic eye institution that is developing robustly. He hopes that both SAHZU Eye Center and SNEC could give full play to their advantages and further strengthen exchanges and cooperation.

With an aim to provide world-class eye treatment and services, SAHZU Eye Center is actively engaging itself with international medical community under its Chair Prof. YAO Ke's leadership. Prof. YAO hopes that this precious linkage between SAHZU Eye Center and SNEC could finally bring mutual benefits to patients in China and Singapore.

After the signing ceremony, Prof. AUNG Tin toured in the SAHZU Eye Center and interacted with the subspecialty of glaucoma.

Chen Yizhang: Seventy Years of Tireless Dedication to Medicine, Research, and Education: Scaling New Heights

CHEN Yizhang was born in September 1927 and was among the very first people to graduate from the School of Medicine, Zhejiang University, in 1952. He is an academician of the Chinese Academy of Sciences, a retired professor from Naval Medical University, and a former dean of the School of Medicine, Zhejiang University. His primary research focused on the central nervous system's physiology, and he has received numerous awards, including the Military Science and Technology Progress Award and the National Natural Science Award. Between the ages of 82 and 87 years, he authored a 700,000-word scientific monograph titled *Synapses*, which has been acclaimed as "the first domestic academic work to provide a comprehensive review of synapse research from the forefront of contemporary scientific development."

From Engineering to Medicine: A Journey of Unwavering Dedication

In 1946, CHEN Yizhang became a student at the Department of Mechanical Engineering in the School of Engineering, Zhejiang University. Later, influenced by his family, he switched to studying medicine. Reflecting on this decision, Chen commented, "In 1938, my grandfather died of cholera in the countryside within a day, as there were no doctors in the town. My father also believed that becoming a doctor would also offer me a better income." Since the transfer period had already passed, Chen first took some medical courses before officially transferring to the School of Medicine in his third year. From then on, he dedicated his life to the field of medicine and public health.

After his graduation in 1951, CHEN Yizhang moved to Shanghai, where he spent the subsequent 70 years. His career evolved from being a trainee to a teaching assistant, lecturer, associate professor, professor, and eventually the director of the Institute of Neuroscience. In 1995, he was elected an academician of the Chinese Academy of Sciences. In 1953, Chen Yizhang began his scientific research. During the 1960s, he discovered that a single electrical stimulation event could cause long-term potentiation of the dendritic potentials in the cerebral cortex of young rabbits. During the 1980s, he was the first to propose, in an international context, the hypothesis of non-genomic mechanisms or membrane receptor hypotheses for the action of glucocorticoids on neurons, which significantly expanded his research on rapid, non-genomic actions to encompass other aspects of neuronal functioning. His research attracted high praise from the international academic community and is referenced in renowned international endocrinology textbooks. As Chen noted, "This paper has influenced several decades of research." The famous Dutch neurophysiologist Professor de Kloet remarked, "This research has made a tremendous contribution to our understanding of the central nervous system." Throughout his life, CHEN Yizhang has been tirelessly dedicated to teaching and research. He edited six monographs, including ***Electrophysiology of the Nervous*** System and ***Molecular Neurobiology***. Two of his papers have been cited nearly a

hundred times internationally, marking them as significant contributions to the field.

Chain Letters Sent Across the Country

After graduating in 1951, CHEN Yizhang and his classmates dispersed to various cities across China—Beijing, Shenyang, Changchun, Changsha, Nanjing, and Shanghai—to contribute to national development. In 1993, as a representative of the first wave of graduates from the School of Medicine, Zhejiang University, CHEN Yizhang initiated a "chain letter" activity. This involved one person writing to another, and these letters were circulated among the group until they arrived back with the initiator. Chen described the process as follows: "We had a sequence and continuity, with 14 to 15 participants. The letters started with me, went to two of my former classmates in Wenzhou, then to Hangzhou, then to Chengdu, Chongqing, Beijing, and Tianjin, before returning to me." After each cycle, Chen would take out the letters and preserve them carefully before adding new ones.

Eventually, he donated the entire set of these "chain letters" to the School of Medicine. By 2014, these letters had passed through dozens of cycles and, over the 21-year period, their content had gradually changed. "Over time, fewer people wrote, and the conversations were mostly about how to prevent and treat geriatric diseases and avoid falls." As time passed, the original participants of the "chain letters" passed away, but the heartwarming story of the "chain letters" and the enduring friendships that were fostered among the classmates occupy an important place in the history of the School of Medicine, Zhejiang University.

Creating Research Peaks with a Spirit of "Seeking Truth and Pursuing Innovation"

Under Chen Yizhang's deanship from 1999 to 2003, the School of Medicine at Zhejiang University achieved remarkable scientific milestones. Reflecting on his experience, he stated, "Firstly, I worked hard." Every month, he would take the train to Hangzhou and stay there for a week. During his first year's annual summary, he commented, "Our School of Medicine published too few papers last year." During his tenure as dean, Chen Yizhang devoted himself to public service, vigorously promoting talent development and advancing teaching and research at the School of Medicine. Through his efforts, the School of Medicine cultivated a group of high-caliber talents. After experiencing rapid development in the new century, "Now, the papers from the School of Medicine and its affiliated hospitals are overwhelming in number," Chen Yizhang stated with satisfaction.

"Regarding 'Seeking Truth, Pursuing Innovation,' in my life, I have identified two seminal innovations in my career the long-term potentiation of dendritic potentials and the non-genomic mechanism of glucocorticoids on neurons. I added a third, which I believe is the pericellular modulation of neuronal excitability, and am very satisfied with that, even after turning 90 years-old." CHEN Yizhang concluded.

Mastering Solid Skills and Techniques

Emphasizing clinical teaching and cultivating solid skills has always been a fine tradition at the School of Medicine, Zhejiang University. The old campus of the School of Medicine was located on Qingchun Road in Hangzhou, where the School of Science, School of Engineering, and Law School were also situated. At that time, students took classes in the University Road area, while the clinical teaching was conducted at Tianjiayuan Zhejiang University Hospital, now known as the First Affiliated Hospital, Zhejiang University School of Medicine. CHEN Yizhang recalled, "Our clinical teaching was very solid, thanks to the efforts of Mr. WANG Jiwu, who attracted excellent faculty to teach us." Mr. WANG Jiwu, CHEN Yizhang's mentor and the dean of the School of Medicine at that time, attracted well-known professors from the academic community in Shanghai to Hangzhou to teach the students. Distinguished scholars, such as Professor ZHANG Yuanchang from Huashan Hospital (neurology) and Professor XIA Zhenyi from Shanghai Medical College (psychiatry), all left their mark on the teaching platform of Zhejiang University School of Medicine.

In 2000, Professor XU Renbao and Academician CHEN Yizhang established the "XU Renbao – CHEN Yizhang Scholarship," which supports undergraduates from financially disadvantaged backgrounds who demonstrate both academic excellence and a good character, thus providing strong support for talent cultivation at the School of Medicine. "A little assistance can significantly improve the living conditions of students from poorer families," CHEN Yizhang commented. "Professor XU Renbao and I agreed to create the XU Renbao – CHEN Yizhang Scholarship to help these students." With solid technical skills and capable medical professionals, the nation's healthcare system can remain firmly in Chinese hands, a point that CHEN Yizhang strongly emphasized, when he commented, " 'It's crucial for our healthcare system to promote solid medical expertise to ensure that our students are thoroughly trained, so it remains firmly in the hands of the Chinese people."

Having spent over 70 years dedicated to medicine, teaching, and research, setting standards, serving as an example, scaling new heights, and tirelessly working, academician CHEN Yizhang has truly lived these principles.

"Dream Show" for Children with Cancer

"I want to be a doctor," "I want to be a firefighter," "I want to be a star"... On April 15th, on the eve of World Cancer Day, a special "Dream Show" was held at the Children's Hospital of Zhejiang University School of Medicine. The ten young participants, all battling solid tumors, took to the stage, in uniforms representing their dream professions. With confidence, they proudly showcased their most beautiful and handsome selves.

浙江大学 医学院
SCHOOL OF MEDICINE
ZHEJIANG UNIVERSITY

ZJU MEDICINE
SHOWCASING THE BEST OF ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

Seeking Truth and Innovation with
Benevolence and Humane Proficiency

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