The 150th Anniversary of the Second Affiliated Hospital Zhejiang University School of Medicine

UNIVERSAL BENEVOLENCE

In the buzzling center of Hangzhou, where the 2016 G20 Summit was held, stands a tall red archway and a bowing statue. The archway is engraved with four bold Chinese characters on the top, 济人寿世, meaning "spreading benevolence and saving people." Next to it is a statue of a physician and a patient bowing to each other with equal modesty and respect, symbolizing the humanity in medical services. These landmarks help you find the Second Affiliated Hospital Zhejiang University School of Medicine (SAHZU), a 150-year-old renowned hospital.

Originally known as Hangzhou Guangji Hospital (meaning "spreading benevolence around the world" or "universal benevolence"), SAHZU was founded in 1869 by the British Church Missionary Society and was considered the best hospital in the Far East. As the cradle of western medicine in Zhejiang, SAHZU educated a large number of medical talents, and several health care institutions can trace their roots to SAHZU. Those doctors and institutions have become the bedrock of clinical medicine in Zhejiang. And the hospital itself has been a beacon of the medical science: in 1989, it was recognized by the Ministry of Health as one of the first 3A hospitals in China; in 2013, it became one of the first Joint Commission International–accredited academic medical centers in the world.

Over the past 150 years, SAHZU has built several disease-specific research institutes and a fully integrated research platform from basic research, translational research to clinical trials. Via the Guangji Innovation Club, SAHZU is establishing efficient collaborations among hospitals, academic institutions, government, industry, and venture capitals.

The hospital has two campuses with a total of 3,200 beds and 5,509 employees, including 2,433 physicians and researchers in 50 clinical departments, many of which are national clinical departments or disciplines approved by the National Health Commission. SAHZU has become the role model for Chinese hospitals in the field of transcatheter valve intervention, the micro-incision cataract surgery, colorectal cancer, and severe burns. With over 5 million outpatients, 170,000 inpatients, and 140,000 surgeries, SAHZU is one of the most efficient general public hospitals in China. And it attracts numerous foreign physicians with training programs accredited by the ACGME (the Accreditation Council for Graduate Medical Education in the United States).

The hospital name has changed with the passage of time, but the Guangji spirit of providing quality health care has not. Today, the hospital's core values remain the same as they did back then: the needs of patients and customers come first.

HEART CENTER
HEART RECONSTRUCTION EXPERT

Cardiovascular disease is the leading cause of death in the world. As early as the 1980s, the Heart Center at SAHZU began to explore the application of tea polyphenols in the prevention and treatment of coronary heart disease. In recent years, the center has strived to provide patients the best customized services in maintaining good health through innovation, intervention, and heart transplantation, placing SAHZU the sixth among cardiology centers in the nation. Since the turn of the century, the center has put forward a holistic solution for heart function reconstruction, targeting the congestive heart failure caused by valvular heart disease or myocardial infarction. Recognized for its contribution, the center is the only co-chair institution in Asia of CSI (congenital and structural interventions).

The heart valve team at the center first mapped valvular heart disease by examining 140,000 patients, discovering a new mutation in *ADAMTS5* that causes bicuspid aortic valve-associated aortic stenosis. Based on further research in epidemiology, genetics, and pathogenesis, the team then developed the Hangzhou Solution, a comprehensive solution of transcatheter aortic valve replacement that specifically accommodates Chinese heart valvular disease patients. This systematic approach allows a cardiologist to choose valve size according to patients' supravalvular annulus structure. With a 4.0% one-year mortality, a 9.3% severe conduction abnormality, and 4.9% moderate and severe paravalvular regurgitation, the Hangzhou Solution significantly improves patient quality of life. The team went on to develop the first Chinese-designed retrievable and navigable artificial heart valve, the VenusA-Plus, which has been successfully implanted in patients at over 50 medical centers in South America, Europe, and Asia. NEJM Catalyst published an article about this unique collaboration model between the government, a university, a hospital, and a company.

In addition, SAHZU cardiovascular scientists conducted one of the world's first controlled clinical studies of mesenchymal stem cell treatment for myocardial infarction, showing improved efficacy for some patients without side effects. They also proposed that hypoxic preconditioning could enhance the secretion of stem cell's paracrine to promote heart function reconstruction. Furthermore, the investigators carried out the biggest sample size study of mesenchymal stem-cell and human pluripotent stem-cell treatment for myocardial infarction in non-human primates, assessing the safety and efficacy of the treatment. The results were published in *Circulation Research*, an American Heart Association journal, with the honor of the 2016 Best Manuscript Award. Some results were also included in the European Society of Cardiology consensus statement.

CANCER CENTER **THE FOUNDER OF COLORECTAL CANCER RESEARCH IN CHINA**

The incidence of colorectal cancer (CRC) is growing fast in China. In the 1970s, the Cancer Center at SAHZU started to explore a Chinese model of CRC prevention and treatment. By setting up two observation sentries at Jiashan and Haining in Zhejiang, the Cancer Center began a large scale epidemiological study of high-risk factors of CRC. Two hundred and sixty thousand people were surveyed; 4,300 of them with rectal polyps were followed up with colonoscopies for the next 20 years. Significant reduction in CRC incidence was observed in the following 3–5 years based on a subsequent cohort study. The researchers provided a creative solution to the early diagnosis and treatment of CRC in general population — asking high-risk patients with nine yes-or-no questions combined with a fecal blood test. The screening is convenient, sensitive, and effective, which is especially useful for countries with a large population. It was designated as a National Public Health Key Standard Technology Program in 2007. By the end of 2018, more than six million people were screened with a 5‰ detection rate of precancerous lesion. Having developed a self-testing kit for fecal occult blood with CE approval from the European Union and sold to India and other countries, the SAHZU researchers are also investigating molecular markers for early CRC diagnosis. In addition, SAHZU scientists identified two CRC-related genes and found that tumor-infiltrating γδT17 cells are the predominant IL-17-producing cells and promote the accumulation and expansion of myeloid-derived suppressor cells in human CRC, suggesting new target for treatment and prevention. The work was published in *Immunity* as a cover article.

The Cancer Center also developed a procedure, called TILA-TACE (targeting-intratumoral-lactic-acidosis transarterial chemoembolization), with a markedly higher efficacy than the conventional TACE in treating hepatocellular carcinoma (HCC). The team further formulated a comprehensive strategy by simultaneously treating the main lesion, the vascular invasion/tumor thrombus, and the intrahepatic spread.

EYE CENTER **THE LIGHT ENABLER**

Cataracts cause vision problems and place heavy burden on patients as well as society. The Eye Center at SAHZU transforms basic research findings into clinical practice and has made many breakthroughs in the surgical and medical treatment of cataracts. The center ranks seventh in the country and is the best eye department in a comprehensive hospital. The director of the Eye Center is the chair of the Chinese Ophthalmological Society and the vice chair of the Asia-Pacific Association of Cataract and Refractive Surgeons.

The center has revolutionized cataract surgeries in China five times and written all six Chinese expert consensus statements on cataract treatment. With the standardized protocols, the "China Model" makes cataract surgery safer and more efficient. Adopted in 73 Chinese hospitals, this model lowered the incidence of endophthalmitis — the most severe complication after cataract surgery — from 0.22-0.42% to 0.033-0.11%, benefiting 1.33 million patients. To help people in remote highland areas, the center launched the Mobile Eye Hospital Project and performed more than 10,000 free cataract surgeries. Additionally, SAHZU ophthalmologists are particularly experienced in the femtosecond laser-assisted cataract surgery and have conducted prospective multicenter studies. The femtosecond laser assistance is also applied to treat multiple subtypes of complex cataract at the center. By using this technique, the rate of corneal endothelial cell loss after hard nuclear cataract surgery decreased from 19.96% to 7.85%, and the postoperative visual acuity recovery time is shortened from 3 months to 1 month. In addition to surgeries, the center also developed a novel assembly-line type of drug screening platform from molecular structures to cell and animal models. Based on the platform, the center has identified five drug candidates with potential therapeutic efficacy for cataract.

BRAIN CENTER **THE MASTER OF BRAIN SCIENCE**

The Brain Center at SAHZU is one of China's first National Clinical Key Departments. Ranking seventh in the country, the center has not only trained most of the leading neurosurgeons in eastern China but also attracts foreign trainees.

In 2011, Niuniu, a two-year-old girl who fell from the 10th floor, was eventually saved after 65 days of treatment by the SAHZU neurosurgery team. The success was considered a "miracle" by Dr. William Oppenheim, a professor of pediatric orthopedics at UCLA, who consulted this case through video conference. Niuniu is now in primary school with no growth difference from her peers.

Pioneering results have also been achieved in brain-computer interface (BCI) research. In 2014, SAHZU was the first in China to perform clinical work using BCI technology: the team attained direct brain control of robotic hands with neural signals from the human brain using an electrocorticography-based system. In August 2019, the team completed the first clinical trial in China of Utah array implantation in the primary motor cortex on a paraplegic patient with upper cervical spinal cord injury, who is now expected to have better movement functions through the brain-controlled external device. Moreover, a bidirectional BCI system for responsive electrical stimulation treatment of refractory epilepsy was developed recently.

Advancements have been made in the diagnosis and treatment of neurological and motor disorders, too. The neurogenetic team completed the first mutation spectrum of Wilson's disease (WD) patients in China after analyzing *ATP7B* gene mutation in the world's largest cohort. They also developed a genetic diagnosis kit with >90% sensitivity for early WD patients and treatment strategy with low-dose zinc alone for presymptomatic WD individuals. In addition, this team identified *PRRT2* as the causative gene of paroxysmal kinesigenic dyskinesia (PKD). Detection of the *PRRT2* mutation has become the gold standard for PKD diagnosis. The researchers further proved that a very small dose of carbamazepine (0.05g/d) can completely control the disease onset after a long-term follow-up. The team also found some genetic mutations can lead to early-onset Parkinson's disease (PD) and demonstrated a significant increase of iron deposition in patient's substantia nigra as one of the pathogenic mechanisms of PD.

While neuroscientists at the center are investigating brain disease mechanisms, the neurologists there are using novel techniques to operate on the brain. Precision localization followed by surgery achieved a long-term seizure remission rate of about 80% for drug-resistant epilepsy. For more than 10 years, the SAHZU stroke team has been using multidimensional, data-driven individualized imaging solutions to identify patients with acute ischemic stroke who can benefit from reperfusion therapy beyond the standard time window. These solutions earned the center the title of Advanced Chinese Stroke Center.

GENERAL SURGERY **THE SCALPEL OF HOPE**

The first Whipple surgery in China was completed at SAHZU. Since the 1990s, the advances in surgical management of complicated and difficult hepatopancreatobiliary diseases continue apace at SAHZU. For example, Peng's binding pancreaticojejunostomy after pancreaticoduodenectomy and Peng's multifunction operative dissector have already been recognized as standards in China.

In recent years, SAHZU has been devoted to organ transplantation and precision surgery. On one occasion, surgeons were able to perform 12 organ transplants (one heart, two lungs, three livers, and six kidneys) in 15 hours. Besides expertise in adult organ transplants, SAHZU excels in pediatric living-donor liver transplant, too. The overall survival rate of organ transplantation and the five-year survival rate of surgeries for hepatobiliary and pancreatic tumors at SAHZU are among the highest in the world. SAHZU surgeons first described the transient small-for-size syndrome and proposed its prevention and treatment. They authored the first expert consensus on perioperative ERAS of liver transplant in the world. Furthermore, the living-donor full-right split liver transplantation in an adult was performed at SAHZU, a first in China. SAHZU is also home to the most influential Chinese endoscopic thyroid surgery training center, a leader of the thyroidectomy via transoral vestibular approach.

TRAUMA MEDICINE
DESTINATION FOR CRITICALLY ILL PATIENTS

SAHZU's Emergency Medicine Center was one of the first of its kind in China and was an original member of the Chinese Association of Emergency Medicine. A nationally renowned trauma center, it has rich expertise in the management of critically injured patients and complex, difficult, and severe cases. In 2019, it was designated the National Trauma Care Center in eastern China. The center is equipped with state-of-the-art facilities, such as world-class one-stop emergency resuscitation units. Its cutting-edge 5G-connected ambulances can improve pre-hospital communications, and they are a crucial part of "prehospital service-trauma unit-ICU-hospitalization-rehabilitation" process. To ensure efficient emergency responses during major public events, SAHZU pioneered a hospital-wide code system in China.

The burn team at SAHZU is another vital part of the trauma center. In 1978, the team performed a miracle by rescuing a severely burned female steelworker with 100% burn area and 74% third-degree burns — a groundbreaking success in China. In 2014, the team worked another miracle: 19 severely burned adult patients, including seven with 60% burn area, were managed within one hour after arrival at the hospital. All 19 patients survived thanks to SAHZU's quick response, well-structured emergency system, and experienced mechanisms.

Additionally, to treat extensive or severe skin injury, SAHZU burn physicians carried out research in developing artificial dermis and co-invented an antimicrobial peptide (ε-polylysine) and catechol-based anti-infection wound dressing.

PULMONARY CENTER
A PURIFYING FORCE

In the late 19th century, SAHZU set up one of the first tuberculosis hospitals in Hangzhou and pioneered modern pulmonary medicine in China. One-and-a-half centuries later, SAHZU pulmonary team members have made groundbreaking achievements in their research of asthma pathogenesis and the diagnosis and treatment of severe refractory or atypical asthma. For example, their research demonstrated for the first time a causative relationship between eosinophil (EOS) and asthma pathogenesis, and the critical role of EOS in regulation and mobilization of bone marrow stem cell. To tackle the challenges in early diagnosis of atypical asthma, the team identified a new asthma subtype named as chest tightness variant asthma and suggested that the same treatment protocol be used for both typical and atypical asthma. For steroid-resistant asthma that is difficult to treat and has a higher mortality rate, the pulmonary team showed in animal models therapeutic effects by Bcl2 inhibitors that can induce apoptosis of both EOS and neutrophils.

Another focus of SAHZU pulmonologists is airway epithelial injury. Recently, they demonstrated for the first time that DNA replication in damaged epithelial cells could also occur in the mitotic phase, suggesting a new direction in epithelial damage research and targeted tumor therapy. Furthermore, the pulmonologists clarified the key roles of mTOR-autophagy pathway in regulation of airway epithelial injury induced by cigarette smoke, airborne particles, allergens, or endotoxins.

BONE CENTER
THE GUARDIAN OF MOBILITY

SAHZU recorded an amputation and prosthesis surgery under anesthesia by chloroform in the early 1880s. In 1971, a novel transpositional replantation for a patient whose lower limbs were severely injured in a car accident was conducted at SAHZU. Orthopedic surgeons connected the patient's right thigh and left lower leg, and they fitted him with a unilateral prosthesis. The patient is still alive today.

Since the 1970s, the center has advanced the diagnosis and management of bone tumors. The osteosarcoma center at the Bone Center is at the forefront of standardized treatment. It regularly performs limb salvage surgery, hyperthermic isolated limb perfusion, and many other advanced surgeries with novel techniques such as upshifting of the proximal femur.

Based on basic and clinical research, SAHZU orthopedic surgeons and scientists established the Hangzhou strategy of a reconstructive ladder for degenerative spine diseases. The strategy recommends injection of biomimetic materials for early- and mid-stage degeneration to differentiate stem cells into nucleus pulposus cells, promoting biological regeneration. For mid- to late-stage degeneration, they successfully developed a minimal invasive lumbar interbody fusion technique (crenel lumbar interbody fusion). This innovative surgical technique is not only widely adopted in China but also being recommended by doctors in the United States, Germany, Australia, Malaysia, and other countries.

Moreover, the sports medicine doctors at SAHZU provide services to world championship swimmers, keeping them healthy and helping them recover from injuries.

150th ANNIVERSARY
SAHZU

MEDICAL IMAGING CENTER
PROFESSIONAL FACILITIES

Radiology Medicine

SAHZU radiologists have been offering their services since 1911, when the most advanced X-ray machine was used at the hospital. Recently, SAHZU radiologists have made remarkable accomplishments in diagnosis of PD by a multimodal MRI-based computer-assisted approach. A clinical-genetic-imaging database with 500 PD patients and 300 healthy controls has been established, and radiologists at SAHZU have started to use machine learning to explore early biomarkers, which can help doctors identify PD patients and distinguish different subtypes.

Ultrasound Medicine

Ranked among the top 10 in China, SAHZU is held in high esteem by peers in ultrasound medicine, especially in ultrasonic cavitation-based precision diagnosis and treatment. The team designed a more efficient therapeutic ultrasonic transducer with sub-wavelength periodic structure and proposed an entropy-based real-time algorithm for ultrasonic cavitation. It also developed an ultrasound transmitting system that can precisely control the power ultrasonic cavitation. The system has been tested successfully on animal models for targeted gene delivery and β cell regeneration. It can also be used to control peripheral glucose in a type 2 diabetes cynomolgus monkey model and to suppress tumor growth by blocking the intratumoral vessels in a rabbit orthotopic liver tumor model.

Nuclear Medicine Imaging

The nuclear medicine imaging at SAHZU is focused on precision diagnosis and treatment of major diseases, including pediatric epilepsy and cognitive dysfunction using PET molecular imaging. They have built up a functional metabolite database of pediatric epilepsy based on brain PET/CT imaging, improving the detection rate of epileptogenic foci to 79% versus an international average of 15–39%. The PET-MRI is also used at SAHZU to integrate functional and structural information with the detection rate increased by 60%. To assess the cognitive dysfunction caused by antiepileptic drugs, the nuclear medicine team developed a PET molecular biomarker imaging system based on the dopamine D2 receptors in the caudate nucleus and the 5-HT2A receptors in the cortex. Moreover, the team developed the first modular microfluidic system for the synthesis of PET molecular imaging probes .

SAHZU is currently planning a world class medical center in south Hangzhou. The new campus covering 333,000 m2 (82 acres) is designed to provide quality services, enhance multidiscipline cooperation, foster clinical innovation, and train medical talents, as well as develop centers of excellence. One-hundred-and-fifty-year-old SAHZU looks forward to walking hand-in-hand with its global colleagues for the future of human health.

RECRUITMENT INFORMATION

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